# Chapter 2

# Exposure Measurement and Prevalence

## 2.1 Introduction

This chapter provides background information on the prevalence and measurement of exposure to ETS, and emphasizes investigation and monitoring methods used in epidemiological evaluations of health effects. Section 2.2 briefly reviews the physical and chemical properties of ETS, and identifies some of the important biologically active constituents present in ETS. Section 2.3 discusses various techniques that have been used to measure ETS concentrations in indoor environments. Determination of ETS contamination is a challenge as ETS is a complex mixture of over 4,000 compounds and it is neither feasible nor practical to characterize every individual constituent of ETS. Given the complex nature of ETS, markers and tracers of ETS are measured to assess ETS exposures. The role and limitations of some ETS markers, such as nicotine, particulate matter in air, and polycyclic aromatic hydrocarbons, are discussed in this section. Section 2.4 addresses the use of biomarkers to measure ETS exposure. In addition to ETS concentration in air, the level of biomarker measured is also dependent on an individual's uptake, distribution, metabolism, and excretion of the chemical of interest. This section describes the use and limitations of some of the biomarkers, such as nicotine and cotinine in physiological fluids, in determining ETS exposure.

One problem with ETS markers and biomarkers is that most of them are only capable of estimating ETS exposure over a relatively short period of time, from a few hours to several weeks; whereas, many health effects of ETS are believed to be associated with long-term exposures that are measured in months if not years. In order to address this difficulty, most epidemiological studies cited in this report used questionnaires or interviews to determine the status of the subjects regarding long-term exposure to ETS. Some studies also used measurements of ETS markers and biomarkers as supplemental information. And just like any epidemiological study that relies on questionnaire or interviews for exposure information, these studies are subjected to the problem of misclassification. Section 2.5 of this chapter describes some of the difficulties associated with classifying subjects into exposure categories based on the smoking status of other household members. As of today, no perfect method for quantifying ETS exposure has been found. Yet as demonstrated by many studies cited in the other chapters of the report, epidemiologists are able to use the information obtained from questionnaires or interviews in classifying the subjects into categorical groups of ETS exposure (*e.g.*, none, low, medium or high). The categorical exposure information is then used to evaluate health risks associated with ETS exposure. However, one drawback of this approach is that it decreases the sensitivity or power of a study, *i.e.*, it will not show a positive association when ETS exposure and a health effect is only moderately related to ETS exposure.

Though many ETS monitoring methods (*e.g.*, nicotine and respirable suspended particulates in air, cotinine in body fluids) are discussed in this chapter, risk assessment of ETS exposure is seldom performed based on monitoring results. Some of the reasons include short sampling duration in most studies; large uncertainty in extrapolating the ETS levels measured at a specific

location to the general population; and large uncertainty in estimating the frequency and duration of ETS exposure of the general population. Consistent with the approach used by the National Research Council (NRC, 1986), U.S. EPA (1992), DiFranza (1996), and Wells (1994), this report uses prevalence assessment for the estimation of health risks that are associated with past or recent ETS exposure. Epidemiologists often use prevalence assessment, which makes use of semi-quantitative exposure information such as job classification or duration of exposure, for the estimation of health risks associated with occupational and environmental hazards.

Section 2.6 discusses the prevalence of ETS exposures and factors affecting prevalence, especially in California. In support of the assessment of reproductive and developmental effects presented in the chapters addressing these effects, information on both measurement and prevalence of ETS exposures of the developing child (*in utero*, and during infancy and childhood) is described when available.

## 2.2 Properties of ETS and Its Constituents

### 2.2.1 Physical and Chemical Properties[1] of ETS

ETS is a complex mixture of chemicals generated during the burning of tobacco products. The principal contributor to ETS is "sidestream smoke," the material emitted from the smoldering tobacco product between puffs. Other components of ETS include exhaled mainstream smoke, mainstream smoke emitted at the mouthpiece during puff drawing, and compounds diffused through the wrapper. "Mainstream smoke" is the complex mixture that exits from the mouthpiece of a burning cigarette when a puff is inhaled by the smoker.

When a cigarette is smoked, approximately one-half or more of the smoke generated (by weight) is sidestream smoke emitted from the smoldering cigarette. The chemical composition of mainstream smoke has been more extensively characterized than that of sidestream smoke, but they are produced by the same fundamental processes, such that many chemical constituents are present in both. Over 4,000 individual constituents have been identified in mainstream smoke, and approximately 400 compounds have been measured quantitatively in both mainstream and sidestream smoke.

The large number of constituents results from the chemical composition of tobacco and the variety of chemical and physical processes that occur as a cigarette is smoked. The majority of the compounds present in mainstream smoke are formed during combustion, in a pyrolysis-distillation zone just behind the heat-generating combustion zone (Baker, 1981). Estimates have been made that the total number of constituents in mainstream smoke actually may be 10 to 20 times the number identified to date; that is, mainstream smoke may comprise over 100,000 constituents. However, these unidentified components comprise less than 5% of the mass of mainstream smoke and would be present only at very low concentrations (Guerin *et al.*, 1992).

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[1] The U.S. EPA (1992) report is the primary source of information presented in this section; unless a specific reference is provided, the information in this section has been taken from that report.

Although many constituents present in mainstream and sidestream smoke are the same, there are important differences in the rates they are emitted into the air, due to physical and chemical differences in the burning conditions present during their generation. As discussed in the *Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders* (U.S. EPA, 1992: pages 3-2 to 3-10), some constituents have a higher rate of release into sidestream than mainstream smoke; while for others, the reverse is true. Once emitted into the air, sidestream smoke may undergo various physical and chemical changes. Dilution, chemical reactions, deposition and other removal processes may decrease the concentration of the airborne constituents of ETS, alter the size distribution of suspended particles, and chemically modify some of the more reactive constituents of ETS.

The delivery of selected agents in the mainstream smoke of nonfilter cigarettes and the ratios of the relative distribution of these agents in sidestream to mainstream smoke are given in U.S. EPA (1992: Table 3-1). As discussed by U.S. EPA (1992: pages 3-4 to 3-6), sidestream to mainstream ratios are highly variable and can be misleading, as a number of factors affecting cigarette design (*e.g.*, presence of a filter and filter ventilation) and smoking patterns (*e.g.*, puff volume) have a substantial impact on the emissions of mainstream smoke. In contrast, sidestream smoke emissions show relatively little variability as a function of most of these same factors. A study of the influence of puff volume and filter ventilation on sidestream and mainstream deliveries illustrates this point (Browne *et al.*, 1980). The mainstream delivery of particulate matter and carbon monoxide increases with puff volume, but decreases with increasing filter ventilation. Because the sidestream delivery of these constituents remains relatively constant, the corresponding sidestream to mainstream ratios will decrease or increase as a function of the specific condition and constituent examined (Table 2.1).

Data on sidestream emission rates from filtered and commercial cigarettes for many compounds of public health interest are tabulated in U.S. EPA (1992: Table 3-2). While the data are limited, they suggest that sidestream deliveries are relatively constant across a number of products, with differences ranging two to three-fold when measured under standard smoking conditions. These results are consistent with the finding that sidestream deliveries are primarily related to the weight of the tobacco and paper consumed during smoldering, rather than to cigarette design (Guerin *et al.*, 1992).

### 2.2.2 Biologically Active Constituents of ETS

A number of chemicals known or suspected to contribute to adverse health effects are present in tobacco smoke (mainstream and sidestream smoke), including eye and respiratory irritants, systemic toxicants, mutagens, carcinogens, and reproductive toxicants. It is outside the scope of this review to assess exposure to each of the numerous individual constituents of ETS or their specific contribution to the health effects associated with ETS. This section provides a brief discussion of some of the more toxicologically significant compounds identified in tobacco smoke.

#### 2.2.2.1 Toxicants with Acute Effects

Irritants and toxicants with other acute health effects identified in ETS include ammonia, acrolein, carbon monoxide, formaldehyde, hydrogen cyanide, nicotine, nitrogen oxides, phenol and sulfur dioxide. Ammonia, formaldehyde and sulfur dioxide are respiratory irritants and may exacerbate the condition of people with breathing difficulties. Several components, including acrolein, crotonaldehyde, formaldehyde, and hydrogen cyanide, affect mucociliary function and at a sufficiently high concentration can inhibit clearance of smoke particles from the lung (Battista, 1976). Nicotine, which is the principal alkaloid in tobacco, is a major contributor to the addictive properties of tobacco. Nicotine has diverse pharmacologic and toxicological actions, ranging from acute poisoning to chronic effects, some of which may be responsible for some of the adverse health effects associated with smoking.

#### 2.2.2.2 Toxicants with Carcinogenic Effects

Over 50 compounds have been identified in tobacco smoke which are recognized as known or probable human carcinogens. These compounds, which may occur naturally in tobacco or which are formed during combustion, reside mainly in the particulate phase (IARC, 1986). Most of the major classes of carcinogens, including both organic and inorganic constituents, are represented. Table 2.2 lists those compounds detected in tobacco smoke for which there is evidence of animal or human carcinogenicity, as evaluated by the U.S. EPA or the IARC. Also in Table 2.2 are compounds listed as carcinogens under California's Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65) (California Code of Regulations, Title 22, Section 12000), and a number of tobacco smoke constituents that have been identified as Toxic Air Contaminants by the California Air Resources Board (ARB, 1993). Tobacco smoke itself is listed as a carcinogen under Proposition 65.

Conditions in the burning cone of a cigarette are favorable for the formation of polycyclic aromatic hydrocarbons (PAHs). Over 35 PAHs have been identified in tobacco smoke (IARC, 1986), several of which are carcinogenic (*e.g.*, benz[a]anthracene, benzo[a]pyrene, and dibenz[a,h]anthracene). *N*-Nitrosamines are formed during the curing (drying) of the tobacco leaf, and in large part, during combustion while smoking. *N*-Nitrosamines identified in tobacco smoke include volatile (*e.g.*, *N*-nitrosodimethylamine), nonvolatile (*e.g.*, *N*-nitrosodiethanolamine), and tobacco-specific compounds (*e.g.*, *N*-nitrosonornicotine), formed by *N*-nitrosation of nicotine and other pyridine alkaloids. Most of the identified nitrosamines are carcinogens in experimental animals and some (*e.g.*, *N*-nitrosodimethylamine) are present in sidestream smoke in amounts 10 to 200 times greater than in mainstream smoke (U.S. DHHS, 1986; Lofroth, 1989). By weight, the tobacco-specific nitrosamines are the most prominent of the suspected carcinogens identified thus far (IARC, 1986). In addition, the inhalation of nitrogen oxides and amines in tobacco smoke may contribute to the endogenous formation of carcinogenic *N*-nitrosamines (Hoffmann and Brunneman, 1983; Ladd *et al.*, 1984). Other well-established organic carcinogens identified in tobacco smoke are aromatic amines (*e.g.*, 4-aminobiphenyl, 2-naphthylamine and *o*-toluidine), benzene, hydrazine, and vinyl chloride.

Like other plant tissues, tobacco contains minerals and other inorganic constituents derived from soil, fertilizers, agricultural sprays, and polluted rainfall. Upon combustion, most metals remain in the ash; however, some are vaporized or carried in fragments of ash and thus are also found in

tobacco smoke. Several of these metals, including arsenic, cadmium, and chromium, are known to be carcinogenic to humans following inhalation.

Tobacco contains a number of naturally occurring radionuclides, of which the most important is the alpha-emitter polonium-210 (Cohen *et al.,* 1980). Polonium-210 and lead-210 in tobacco originate from phosphate fertilizers (Tso, 1966) and/or from airborne particles containing lead-210 that are trapped by the trichomes of tobacco leaves (Martell, 1974). Although not a direct source of radon, ETS in indoor environments is associated with an increase in the airborne concentrations of radon decay products, presumably because newly formed decay products are more likely to attach to smoke particles than to other surfaces in a room (Bergman *et al.,* 1986). All radioactive chemicals can cause cancer in humans and animals.

Though not all mutagens are carcinogens, mutagenicity tests have shown to be useful in identifying chemicals that can alter the integrity of genetic materials and may have carcinogenic potentials. Several studies have shown that the semivolatile and particle-bound organic fractions of sidestream smoke are mutagenic in bacterial systems (Löfroth *et al.,* 1983; Ong *et al.,* 1984; Lofroth and Lazaridis, 1986; Ling *et al.,* 1987; Claxton *et al.,* 1989). The results from a variety of short-term tests for genetic endpoints on mainstream smoke and tobacco smoke condensate have been reviewed by DeMarini (1983), Obe *et al.,* (1984), and IARC (1986). In addition, many of the individual constituents of ETS are positive in one or more short-term tests for genetic activity (Claxton *et al.,* 1989).

#### 2.2.2.3 Toxicants with Effects on Development and Reproduction

Several compounds listed as developmental or reproductive toxicants under California's Proposition 65 have been detected in tobacco smoke (Table 2.2). ETS constituents identified as developmental toxicants under Proposition 65 are carbon disulfide, carbon monoxide, lead, nicotine, cadmium and toluene. Lead and carbon disulfide have also been identified as agents causing male and female reproductive toxicity. Additional ETS constituents investigated as possible mediators of the developmental or reproductive toxicity of tobacco smoke include PAHs, which have been found to cause developmental and reproductive effects in experimental animals. Exposure to tobacco smoke due to active smoking has been listed as a developmental toxicant as well as a female and male reproductive toxicant under Proposition 65 (listed as "tobacco smoke (primary)"); however, ETS has not been listed.

## 2.3 Exposure Measurement: ETS Concentrations in Indoor Environments

### 2.3.1 Introduction to Exposure Measurement

This section summarizes a number of different techniques used by researchers for estimating the degree of ETS exposure of their subjects. In order to investigate the health effects of ETS exposure, epidemiologists characterize the exposure level of their subjects to determine the extent to which exposure is correlated with an adverse health effect. Given the extreme spatial and temporal variation of ETS concentration in indoor and outdoor environments, it is not feasible, technically and economically, to accurately determine the long-term ETS exposure history of an individual. Yet often times it is the long-term exposure to ETS that is of interest in examining health effects, such as developmental effects and cancers. Epidemiologists

circumvent this difficulty by using questionnaires or interviews to determine the status of the subjects with respect to long-term exposure to ETS and then classifying the subjects into categorical groups of ETS exposure (*e.g.*, none, low, medium, or high). In this way, they make the best use of the semi-quanitative exposure information available without compromising the validity of the study results. One drawback of this approach is that it decreases the sensitivity or power of the study, *i.e.*, a study will not show a positive association when ETS exposure and an adverse health effect are only moderately related. Some of the indirect and direct methods used by researchers in the study of ETS exposure are discussed in the following sections.

Indirect methods for assessing exposure include measurements of indoor air concentrations of ETS constituents (discussed in this section) and population surveys and questionnaires used to assess the characteristics, patterns and extent of exposure (Section 2.5). Direct methods for assessing ETS exposure include the use of personal monitors (discussed in this section and in Section 2.4) and measurement of biomarkers of exposure. Personal monitors measure concentrations of ETS constituents at or near the breathing zone and can be worn by individuals to assess exposures occurring in a specific location or accumulated throughout the day, thus providing an integrated measure of short-term exposure. They are often used in conjunction with other methods to compare or validate assessment of exposure. Measurement of biomarkers, ETS constituents or their metabolites in physiological fluids (such as urine, serum, and saliva), is the most direct assessment of ETS exposure available (Section 2.4). Biomarkers are often used to study exposure prevalence and evaluate the degree of misclassification in epidemiologic studies.

Modelling exposure on the basis of measured or modeled air concentrations and the time an individual spends in a specific environment is another indirect method for assessing ETS exposure. Recently, some researchers have developed and successfully applied models for predicting airborne ETS constituent concentrations (Ott *et al.*, 1992). For example, using an estimated cigarette source strength, air exchange rate and volume of the room, Klepeis *et al.* (1996) were able to predict minute-by-minute indoor time series and time-averaged respirable suspended particle concentrations from ETS. However, airborne ETS constituent concentrations derived from this type of model are location- and situation-specific, and cannot be easily applied to the general population. Such air models are not discussed further in this document.

### 2.3.2 Indoor Air Measurements of ETS

Given the complex chemical composition of ETS[2], air concentrations are typically assessed by measuring individual ETS constituents, referred to as tracers, markers, or proxy compounds. Nicotine and respirable suspended particulates (RSP)[3] are the most widely used markers for the

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[2] The information presented refers primarily to ETS derived from cigarettes because few data are available for cigars and pipes.

[3] The term respirable suspended particulates (RSP) has been inconsistently applied in the literature. Typically, it is used to refer to PM2.5 or PM10, *i.e.*, particles for which the mean aerodynamic diameter is 2.5 or 10 microns, respectively. Particles associated with ETS are typically smaller than 1 micron, and are included in both PM2.5 and PM10.

presence and concentration of ETS in indoor environments. Recently, some researchers have used 3-ethenylpyridine, solanesol, and ultraviolet particulate matter as markers of ETS and suggested that they may be better correlated with other constituents of ETS than nicotine and RSP (Hodgson *et al*., 1996; Jenkins *et al*., 1996).

Airborne nicotine is specific to tobacco combustion and is emitted in large quantities in ETS. Although not specific to tobacco combustion, large quantities of RSP are emitted during cigarette smoking, resulting in measurable increases over background levels even under conditions of high ventilation and low smoking rates. There are other common combustion-related sources of indoor RSP, such aswood-burning fireplaces, gas stoves, and kerosene space heaters, but the levels of RSP produced by these sources are much lower than that produced by tobacco smoke. Other ETS constituents have been measured in field studies assessing the contribution of smoking to indoor air quality. Typically, these constituents are not unique to ETS, but studies indicate that concentrations of some constituents are higher in environments where smoking takes place as compared to those where it does not.

While fixed location measurements of air concentrations of ETS constituents indicate the presence of ETS and allow an estimation of the contribution of ETS to indoor air contaminant levels, such measurements do not constitute a direct measure of an individual's total ETS exposure. During the course of a single day, an individual spends varying amounts of time in a number of different environments; for that individual, the total exposure is the sum of the concentration at each location multiplied by the time spent at that location. Further, for different individuals exposed to the same concentration levels of ETS constituents in the same room, the actual dose will vary as a function of a number of factors, including gender, age, specific activity level, and breathing rate at the time of exposure.

The data presented in the following sections on individual ETS constituents have been summarized from a large number of studies of different microenvironments, primarily within the United States. The measured concentrations of individual constituents in homes and other indoor environments show marked spatial and temporal variation as a result of the complex interaction of factors related to the introduction, removal, and dispersion of ETS constituents. These factors include the rate of tobacco consumption, room size, the location at which smoking occurs, the placement of air monitors, the ventilation or infiltration rate, air mixing, and removal of contaminants by air filters or deposition. With few exceptions, studies were not designed to determine representative ETS concentrations within a particular environment or area of the country. However, it is expected that the ranges reported are typical of similar environments within California. Measurements from the few studies specific to California are reported separately.

### 2.3.3 Indoor Air Concentrations of Nicotine

Over 25 separate studies have measured concentrations of nicotine in well over 100 different indoor microenvironments. The results of these studies are summarized in U.S. EPA (1992: Section 3.3.1 and Figures 3-4 and 3-7). An extensive compilation of measured nicotine concentrations in various indoor environments is also given in Guerin *et al.* (1992). Because airborne nicotine is generally specific to the combustion of tobacco, any detectable

concentrations can be attributed to ETS (the few exceptions include areas such as work environments in which tobacco is processed). Both chamber studies (Baker and Proctor, 1990; Eatough *et al.,* 1990; Nelson *et al.,* 1992) and indoor air measurements (Lofroth, 1993) suggest that nicotine disappears from air faster than other ETS constituents, and hence, its use as a marker may underestimate the relative concentrations of other constituents.

Measurements taken in a wide variety of indoor environments in the U.S. indicate that most average concentrations of nicotine range about 100-fold, from 0.3 to 30 $\mu g/m^3$. The average concentration in residences with one or more smokers typically ranges from 2 to 10 $\mu g/m^3$, with high values of up to approximately 14 $\mu g/m^3$. Measured concentrations are typically higher in the winter than in summer months. In data collected from the mid 1970s through 1991, concentrations of nicotine in the workplace were similar to those measured in residences, with the range of average concentrations showing considerable overlap for the two locations. However, the maximum values for workplaces were considerably higher than in residences. In a recent paper, Hammond (1995) showed that ETS exposures in workplaces that allow smoking are comparable with, and often greater than, ETS exposures in smokers' homes. The highest nicotine concentrations in indoor environments were measured in bars and in the smoking sections of airplanes, with levels reaching as high as 50 to 75 $\mu g/m^3$ (U.S. EPA, 1992) (note: for several years, smoking has been prohibited on domestic flights of commercial airplanes). In a comprehensive survey of indoor measurements, the maximum nicotine concentrations were 30 $\mu g/m^3$ or less in over 50% of the studies examined, and less than 100 $\mu g/m^3$ in 90% of the studies (Guerin *et al.,* 1992). The highest reported level in the survey was 1010 $\mu g/m^3$, measured in a passenger car with the ventilation system shut off. In selected studies using controlled and field conditions, the concentrations of nicotine were found to increase as a function of the number of smokers present and the number of cigarettes consumed (U.S. EPA, 1992: Section 3.3.1.2 and pages 3-32 to 3-33).

Results of four studies (three in the U.S.) using personal monitors to assess exposure of nonsmokers to nicotine are presented in U.S. EPA (1992: page 3-37). The average personal exposures associated with the specific microenvironments in the U.S. for which measurements were taken ranged from 4.7 to 20.4 $\mu g/m^3$. In comparing the levels determined from stationary and personal samples, Guerin *et al.* (1992) reported that in one study, concentrations determined by the stationary sampler were higher than those from the personal monitor. In a second study, the reverse was found to be true. In a more recent study (Jenkins *et al*., 1996), breathing zone air samples were taken of approximately 100 nonsmoking individuals in each of 16 metropolitan areas of the U.S. The mean 24-hour time weighted average nicotine concentration for those who were exposed to ETS at work and away from work (3.27 $\mu g/m^3$) was higher than those who were only exposed to ETS away from work (1.41 $\mu g/m^3$) or those who were only exposed at work (0.69 $\mu g/m^3$). The mean nicotine concentration measured by personal monitoring for those who were not exposed to ETS was 0.05 $\mu g/m^3$.

Nicotine measurements in California residences were included in a large-scale field study of particle exposure in Riverside in 1990, in which 178 nonsmokers over the age of 10 wore personal particle monitors for two consecutive 12-hour periods (Ozkaynak *et al.,* 1994). Particle

samples were taken concurrently in indoor and outdoor air. Due to budget constraints, only a portion of the samples from nonsmoking homes were analyzed for nicotine, while all samples from smoking homes were analyzed. Approximately 30% of all personal and indoor samples analyzed were above the detection limit (about 0.05 $\mu g/m^3$), with 76% of the personal samples from individuals reporting one or more minutes of exposure to ETS above the limit of detection. For those samples exceeding the detection limit, the mean personal 12-hour nicotine concentration for individuals reporting exposure to ETS was 0.96 $\mu g/m^3$, and 0.11 $\mu g/m^3$ for individuals with no reported exposure. The mean indoor concentration of nicotine in homes in which at least one cigarette was smoked (1.07 $\mu g/m^3$) was significantly higher than in homes with no reported smoking (0.10 $\mu g/m^3$).

### 2.3.4 Indoor Air Concentrations of Particulate Matter

A large number of studies have measured concentrations of ETS-associated RSP in indoor microenvironments. These studies are summarized in U.S. EPA (1992: Figures 3-5, 3-8, and 3-10). An extensive compilation of RSP measurements is also given in Guerin *et al.* (1992). In contrast to nicotine, RSP is not specific to ETS and thus RSP measurements in environments where smoking occurs must be compared to concentrations in comparable environments where smoking does not occur. Similar to nicotine, measured concentrations of ETS-associated RSP range about 100-fold, from 5 to 500 $\mu g/m^3$, over a wide variety of indoor environments. In residences with one or more smokers, average daily or weekly concentrations of ETS-associated RSP are increased about 20 to 100 $\mu g/m^3$ over concentrations in similar nonsmoking environments. Somewhat lower levels are reported in the workplace (offices), with average concentrations ranging from approximately 2 to 60 $\mu g/m^3$ over concentrations in similar nonsmoking environments. Both the maximum reported concentration (1,370 $\mu g/m^3$) measured in any environment and the highest range of average concentrations (approximately 35 to 986 $\mu g/m^3$) were for restaurants (U.S. EPA, 1992: Figure 3-8).

Studies comparing RSP concentrations in similar locations in which smoking does and does not take place consistently show higher RSP concentrations in environments where smoking occurs. Typically, the differences range from less than 10% to approximately three-fold higher, although larger differences have been reported (Guerin *et al.*, 1992). Under selected and controlled field conditions, the concentration of ETS-associated RSP has been found to increase with increased smoking (U.S. EPA, 1992: page 3-34).

Recently, Ott *et al*. (1996) measured RSP in a large sports tavern in Northern California on 26 dates between 1992 and 1994 during which smoking was allowed, and subsequently made additional measurements during the year after smoking was prohibited. Though the degree of active smoking in the tavern was characterized as low by the authors, they reported that the average RSP concentration indoors was 56.8 $\mu g/m^3$ above the outdoor concentration. After smoking was prohibited, another set of 26 follow-up visits (matched by time of day, day of the week, and season to the earlier smoking visits), yielded an average RSP concentration that was 77% of the average concentration during the smoking period. No decrease in tavern attendance was evident after smoking was prohibited.

Results of five studies using personal monitors to assess exposure of nonsmokers to RSP are presented in U.S. EPA (1992: page 3-38). Only three studies reported exposures integrated over several different environments, with exposure to ETS-associated RSP resulting in increased concentrations of 18 to 64 $\mu g/m^3$. Those individuals reporting exposure to ETS had substantially increased exposure to RSP as compared to individuals reporting no ETS exposure. In a more recent study, Jenkins *et al.* (1996) took breathing zone air samples of approximately 100 nonsmoking individuals in each of 16 metropolitan areas of the U.S. The mean 24-hour time weighted average RSP concentration for those who were exposed to ETS at work and away from work (47 $\mu g/m^3$) was higher than for those who were only exposed to ETS away from work (33 $\mu g/m^{3)}$ or those who were only exposed at work (28.7 $\mu g/m^3$). The mean RSP concentration measured by personal monitoring of those who were not exposed to ETS was 18.1 $\mu g/m^3$.

Data specific to California are available from one field study conducted in 178 randomly-selected homes in the city of Riverside (Pellizzari *et al.*, 1992). Indoor air concentrations of particles 10 micrometers or less aerodynamic diameter (PM10) were significantly higher in homes in which smoking occurred (n= 28 homes for daytime measurement, 30 for nighttime), as compared to the homes without smoking (n= 139 homes for daytime measurement, 131 for nighttime) (samples from a few homes were lost due to pump or power failure, or quality control concerns). Mean PM10 levels in the homes with smoking were elevated (125.6 $\mu g/m^3$ for the 12-hour daytime measurement, 92.9 $\mu g/m^3$ nighttime) above those in homes without smoking (87.8 $\mu g/m^3$ daytime, 54.6 $\mu g/m^3$ nighttime) by a consistent amount (approximately 38 $\mu g/m^3$ ) (Pellizzari *et al.*, 1992). Average personal exposures to PM10 were significantly higher for those persons (n = 29) reporting exposure to ETS during the nighttime period as compared to persons (n = 139) reporting no ETS exposure during the nightime (104.2 versus 71.4 $\mu g/m^3$). However, no significant difference in average personal exposures to PM10 was found for the daytime period (n= 61 ETS-exposed, 110 unexposed; 155.2 $\mu g/m^3$ versus 146.8 $\mu g/m^3$).

### 2.3.5 Indoor Air Concentrations of Other ETS Constituents

Numerous field studies have been conducted to assess the contribution of smoking to indoor air pollution. Data for select constituents of public health concern, including *N*-nitrosamines, benzene, benzo[a]pyrene and total PAHs, carbon monoxide, formaldehyde, and toluene are presented in U.S. EPA (1992: Table 3-3 and Figure 3-3), as are references to the literature (U.S. EPA, 1992: Section 3.3.1). An extensive compilation of data from measurements of a variety of ETS-derived constituents is also given in Guerin *et al.* (1992).

Because sources other than ETS exist for many of these constituents, it has been difficult for studies to consistently demonstrate elevated concentrations in smoking environments. For example, formaldehyde, which is present in a number of consumer products and building materials, is emitted from these sources at rates usually exceeding those from smoldering cigarettes. Carbon monoxide (CO) is also released from other sources, including gas stoves and heaters, and may be found indoors from air exchange with outdoor air contaminanted by vehicle exhaust; thus, it is often difficult to ascertain the contribution to indoor CO levels due to cigarette smoke (Guerin *et al.*, 1992). However, for many constituents, concentrations in environments where smoking occurs are elevated above levels in comparable environments where smoking

does not occur, particularly for those environments in which heavy smoking occurs. Concentrations of ETS-associated constituents measured in different indoor environments are highly variable, depending on factors such as extent of smoking, air exchange rates, and room size.

2.3.5.1 Polycyclic Aromatic Hydrocarbons

Concentrations of a variety of toxic air pollutants have been measured in California homes. Indoor concentrations of 13 PAHs measured in the homes in the Riverside field study (Pellizzari *et al.,* 1992) described in Section 2.3.4 were reported by Sheldon *et al.* (1992b) The concentrations of most of the PAHs analyzed were significantly higher (approximately 1.5- to 2-times higher) in homes in which smoking occurred, as compared to the concentrations in homes without smoking (number of samples in homes with smoking/ homes without: daytime, 17/93; nighttime, 21/85). Included in the analyses were five PAHs (benzo[a]anthracene, benzo[a]pyrene, benzo[k]fluoranthene, chrysene, and indeno[1,2,3-cd]pyrene) which are listed as carcinogens under Proposition 65 and detected in ETS. As an example of the magnitude of the concentrations measured, the average 12-hour daytime indoor concentration of benzo[a]pyrene was 0.51 ng/m$^3$ in homes in which smoking occurred and 0.20 ng/m$^3$ in homes without smoking (Sheldon *et al.,* 1992b).

A second field study in California (Sheldon *et al.,* 1993) examined the relationship between indoor concentrations of 14 PAHs and different combustion sources (tobacco smoking, fireplaces, woodstoves, and gas heaters); measurements were taken in 280 homes in Placerville and Roseville. Indoor PAH concentrations in the 64 homes in which tobacco smoking occurred were significantly higher (approximately 1.5 to 4 times higher) than in the 39 homes with no specified indoor combustion source. Of the indoor combustion sources examined, tobacco smoking appeared to have the strongest effect on indoor levels of PAHs. As an example of the magnitude of the measured concentrations, the average 24-hour concentrations of benzo[a]pyrene associated with indoor combustion sources were as follows: tobacco smoking, 2.2 ng/m$^3$; woodstove use, 1.2 ng/m$^3$; fireplace use, 1.0 ng/m$^3$; gas heat use, 0.41 ng/m$^3$; and no specified indoor combustion source, 0.83 ng/m$^3$ (Sheldon *et al.,* 1993).

2.3.5.2 Other Organic Compounds

Other toxic air pollutants (30 volatile and semivolatile organic compounds) were measured in a study of 128 homes in the city of Woodland. Indoor samples were collected in all homes and personal monitoring samples for volatile organic compounds were collected for 93 individuals. About 61% of the homes were non-smoking homes, and smoking occurred in about 39% of the homes during the monitoring period. Homes (n=15) in which heavy smoking (>20 cigarettes smoked/ 24-hour period) occurred had elevated concentrations of benzene, para-dichlorobenzene[4], tetrachloroethylene, trichlorethylene[4], and xylene (ortho and meta/para) as compared to homes with no smoking. Personal monitoring air concentration samples of benzene and para-dichlorobenzene were also higher for persons in homes with “any smoking” and those with "heavy smoking" compared to homes with no smoking. However, for both the indoor and personal air measurements, these differences were not statistically significant at the p = 0.05 level, as determined using pairwise t-tests (Sheldon *et al.,* 1992a). Hodgson *et al*. (1996), using

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[4] Although measured at elevated concentrations in homes with heavy smoking, para-dichlorobenzene and trichloroethylene are not expected to be associated with ETS (Guerin *et al.,* 1992)

3-ethenylpyridine as a tracer, investigated the contribution of ETS to the measured volatile organic compounds concentrations in several environments in California where smoking was allowed. In their report, ETS was estimated to contribute 57-84% of the formaldehyde concentrations, 43-69% of the 2-butanone concentrations, 37-58% of the benzene concentrations, and 20-70% of the styrene concentrations. The fractional contributions of ETS to the concentrations of acetone, toluene, ethylbenzene, xylene isomers, and d-limonene were all less than 50% (Hodgson *et al*., 1996).

## 2.4 Exposure Measurement: Biological Markers

This section addresses use of biomarkers to measure ETS exposure, with a focus on nicotine and cotinine. Topics covered include: measured concentrations in physiological fluids of adults; comparisons of levels in smokers, ETS-exposed nonsmokers, and unexposed nonsmokers; and concentrations in physiological fluids of infants and children, and in breast milk and amniotic fluid. The use of levels of exhaled carbon monoxide and blood levels of carboxyhemoglobin, as well as thiocyanate levels in blood, urine and saliva as biomarkers of ETS exposure are also addressed. Measurement of DNA and protein adducts, and other approaches to assessing tobacco smoke exposure, are discussed briefly. Other sections of this chapter summarize studies of exposure prevalence as determined by the presence of nicotine or cotinine in body fluids (Section 2.6) and studies using biomarkers to ascertain smoking status and estimate the degree of misclassification in epidemiological studies (Section 2.5).

### 2.4.1 Introduction to Biological Markers of ETS Exposure

Exposure to ETS can be assessed directly by the analysis of physiological fluids (urine, saliva, and serum) for tobacco smoke constituents or their metabolites, referred to as “biomarkers.” Nicotine, cotinine, thiocyanate, carboxyhemoglobin, hydroxyproline, *N*-nitrosoproline, aromatic amines, and certain protein or DNA adducts have been used as indicators of exposure to tobacco smoke. These biomarkers do not indicate the presence of disease, however, or of an individual's susceptibility to disease due to exposure to tobacco smoke. The appropriateness of a given biomarker depends on the nature of the study and the type of exposure being assessed (*e.g.*, recent or long-term). Ideally, the biomarker should be specific to tobacco smoke, although few markers fully meet this criteria.

The relationship between a biomarker and exposure is complex, and varies as a function of both environmental and physiological factors. As previously discussed (Section 2.3), the degree of exposure is a function of the time an individual spends in each setting and the air concentration of tobacco-related constituents in that environment. Factors affecting air concentrations include smoking intensity, room size, and room ventilation. For a given air concentration, several factors will affect an individual’s intake, such as gender, age, weight, and activity level (and corresponding inhalation rate) at the time of exposure. In addition, individual differences in uptake, distribution, and metabolism will affect the biomarker concentration in physiological fluids. Although the presence of a biomarker indicates that tobacco smoke exposure has occurred, the level of biomarker measured may not be directly related to the intake level of the tobacco smoke constituent(s) potentially implicated in the effect of interest (*e.g.*, using cotinine as a biomarker of ETS exposure in a study of cancer incidence).

**Exposure Measurement and Prevalence**

## 2.4.2 Biomarkers: Nicotine and Cotinine

### 2.4.2.1 Nicotine and Cotinine: General methodological issues

Nicotine and cotinine, a major metabolite of nicotine, are the most widely used biomarkers of ETS exposure. In general, the presence of nicotine or its metabolites in physiological fluids can be attributed to exposure to tobacco smoke. The few exceptions include occupational exposure to tobacco leaves (Gehlback *et al.*, 1975) and nicotine products, use of smokeless tobacco products, chewing of nicotine gum, and use of nicotine patches or other aids for smoking cessation. Low levels of nicotine have been found in tea and in edible solanaceous plants including eggplant, green pepper, and tomato (Castro and Monji, 1986; Sheen,1988; Davis *et al.*, 1991; Domino *et al.*, 1993a,b). While some authors have claimed that dietary intake of nicotine may be of practical importance in the use of nicotine and cotinine as biomarkers of ETS exposure (Domino *et al.*, 1993a,b), others dispute this assertion (Henningfield, 1993; Jarvis, 1994; Repace, 1994; Benowitz, 1996; Pirkle *et al*., 1996). In general, the levels of nicotine and its metabolites in physiological fluids resulting from the ingestion of foods has not been found to significantly impact the levels resulting from exposure to nicotine from tobacco sources.

As biomarkers of exposure, nicotine and/or cotinine are typically measured in blood, saliva, or urine. For studies requiring a quantitative assessment of exposure, blood has been recommended as the fluid of choice, although saliva and urine are also considered acceptable (Watts *et al.*, 1990). Cotinine levels in saliva and plasma tend to be similar, whereas the ratio of urinary to plasma levels is generally a factor of 5 to 6 (Repace and Lowrey, 1993; Benowitz, 1996).

Urinary cotinine excretion is variable across and within individuals, depending on renal function, urinary flow rate, and urinary pH (Benowitz, 1983). Urinary results may be expressed as nanograms of cotinine per milligram of creatinine in order to correct, in part, for differences in dilution effects. Because the amount of endogenous creatinine produced is a function of muscle mass, and hence, age and sex, interindividual excretion rates of creatinine are also variable. In particular, cotinine:creatinine ratios may not be appropriate for comparisons between males and females. In addition, low levels of creatinine in infants relative to adults may result in cotinine to creatinine ratios for infants that fall into the range reported for active smokers (Watts *et al.*, 1990). In general, it is preferable to collect urine over 24 hours, although is impracticable for most studies.

The average half-life of cotinine in different body fluids (plasma, saliva and urine)is about the same, approximately 15 to 19 hours (Jarvis *et al*., 1988; Benowitz *et al*., 1994), making it a good indicator of the integrated ETS exposure over the previous two to three days. The half-life is typically longer in infants and children, averaging approximately 65 hours in neonates, 60 hours in infants under 18 months, and 40 hours in children over 18 months (U.S. EPA, 1992: page 3-41). Nicotine, with its shorter half-life of approximately two hours, is a good indicator of exposures occurring within the previous few hours.

An interlaboratory study of data from 11 laboratories in six countries was conducted to compare analytical results for nicotine and cotinine in serum and urine (Biber *et al.*, 1987). The results of the study indicate that both gas chromatography (GC) and radioimmunoassay (RIA) techniques

reliably quantitate nicotine and cotinine in urine and serum samples and that both techniques are capable of discriminating between smokers and nonsmokers. However, interlaboratory variability was high. While the coefficient of variation for spiked samples was low (9-13%), the coefficient of variation for samples from smokers was fairly large, ranging from 18% to 45% for serum and from 21% to 59% for urine. In addition, cotinine levels reported for urine, as determined by RIA, were about 60% higher than the levels determined by GC. Besides cotinine, some less specific immunoassays can also react with other metabolites of nicotine. Cotinine levels reported for nonsmokers were extremely variable, and a number of laboratories could not detect cotinine in serum from exposed nonsmokers. Because of these various factors, caution should be used in making quantitative comparisons across studies. However, limitations in the design of this study have been noted (Watts *et al.*, 1990); additional studies are required to assess the comparability of these two assay methods and the results from different laboratories, as well as the performance of other methods (*e.g.*, high pressure liquid chromatography (HPLC)).

#### 2.4.2.2 Nicotine and Cotinine: Measured Concentrations in Physiological Fluids of Adults

A large number of studies are available which report concentrations of cotinine in physiological fluids of smokers and nonsmokers. The levels of ETS encountered by exposed nonsmokers during their daily activities are sufficiently high that nicotine and cotinine are detected in their urine, blood, and saliva. The physiological concentrations of cotinine detected in saliva and plasma of nonsmokers typically range from 0.5 ng/ml to 10 or 15 ng/ml (Guerin *et al.*, 1992; U.S. EPA, 1992), and urinary concentrations range to 50 or more ng/mL. For example, Cummings *et al.* (1990) reported that a population of 663 self-reported nonsmokers attending a cancer-screening clinic in New York had a mean urinary cotinine concentration of 8.84 ng/ml (range: 0 to 85 ng/ml) (in the Cummings *et al.* study, a cutoff level of 90 ng/ml was used to distinguish between smokers and nonsmokers). In a population-based study of Hispanics in New Mexico, mean salivary concentrations of cotinine in various age groups ranged from 0 (not detected) to 6.0 ng/ml (Coultas *et al.*, 1987). The studies by Coultas *et al.* (1987) and Cummings *et al.* (1990) are described in Section 2.6.3. However, it is important to realize that some of the differences in cotinine levels reported here could be explained by the different analytical methods used. For example, cross-reactivity of cotinine immunoassays with trans-hydroxycotinine and/or cotinine glucuronide is probably an important contributor to the often significantly higher levels of urinary cotinine measured by this method compared to those measured by GC. Thus, in comparing cotinine levels reported in various studies, it is important to consider the analytical method employed and what the analytes are that were being measured.

Studies of individuals exposed in locations of exceptionally high concentrations of ETS provide some indication of the maximum concentrations of nicotine and cotinine reported in nonsmokers. Jarvis *et al.* (1992) reported a median salivary cotinine concentration of 7.95 ng/ml in 42 nonsmoking bar staff in England, with a maximum concentration of 31.3 ng/ml. In a study of individuals exposed on commercial airline flights, the highest average urinary cotinine concentrations among those who were measured was approximately 30 ng/mg creatinine (Mattson *et al.*, 1989).

In one of the few controlled studies in which both ambient air and biomarker concentrations were measured, uptake of nicotine and cotinine was determined in 10 nonsmoking volunteers. The

subjects were exposed for 80 minutes in a 16 $m^3$ bare room into which sidestream smoke (generated by the machine smoking of 2 to 4 cigarettes) was continuously injected. (The mainstream smoke was released outside the room.) The ventilation rate was six air exchanges per hour, reported to correspond to the average ventilation conditions in offices in the U.S. Concentrations of measured ETS constituents attained stable levels within approximately 10 to 15 minutes, at which time the air concentration of nicotine from the continuous smoking of four cigarettes was 280 $\mu g/m^3$. The levels of nicotine and cotinine in urine, saliva, and serum for individuals exposed to the continuous smoking of four cigarettes are shown in Table 2.3. The average concentrations of nicotine in saliva increased significantly, reaching a maximum concentration of 880 ng/ml after 60 minutes of exposure. Following cessation of exposure, nicotine concentrations decreased rapidly, reaching pre-exposure levels in two to three hours. Cotinine concentrations continued to increase throughout the duration of the experiment, reaching concentrations of 3.4 ng/ml and 55 ng/mg creatinine in serum and urine, respectively, six hours and twenty minutes after exposure began (Hoffman *et al.,* 1984).

Limited information on cotinine concentrations in California subjects is available from a large multinational study which included a center located in Los Angeles (Riboli *et al.,* 1990). Study subjects were 100 nonsmoking women with the following marital and employment status: 13% married to a smoker and employed; 39% married to a smoker and unemployed; 16% not married to a smoker and employed; and 32% not married to a smoker and unemployed. The mean urinary cotinine:creatinine concentration was approximately 8.5 ng/mg for the entire population, and 10.5 ng/mg for those with detectable urinary concentrations. The differences in cotinine levels were found to be large and statistically significant between the 13 centers, and the concentrations at the Los Angeles center was one of the three highest of the centers in the study.

#### 2.4.2.3 Nicotine and Cotinine: Comparison of Levels in Smokers, and ETS-exposed and Unexposed Nonsmokers

Studies comparing ETS-exposed and unexposed nonsmokers and active smokers (Matsukura *et al.,* 1979; Wilcox *et al.,* 1979; Williams *et al.,* 1979; Haley *et al.,* 1983; Hill *et al.,* 1983; Jarvis and Russell, 1984; Wall *et al.,* 1988) have consistently found that measurement of cotinine in the urine, saliva, or serum can distinguish active smokers from unexposed and ETS-exposed nonsmokers. Findings have been less consistent with regard to the use of such assays to distinguish between self-reported unexposed and ETS-exposed nonsmokers. As discussed by Wall *et al.* (1988), potential reasons for this include intersubject variability in nicotine metabolism (Benowitz *et al.,* 1982); time of day of sample collection (Jarvis and Russell, 1984); misreporting of smoking status (Jarvis and Russell, 1984; Jarvis *et al.,* 1987); misreporting of non-smoking status; adjustment of cigarette consumption for nicotine content (Benowitz *et al.,* 1983); and over- or underreporting of ETS exposure. Another reason is that in the past some of the methods used for cotinine analysis were simply not sensitive enough to detect the very low concentration of cotinine in saliva or serum resulting from ETS exposure.

The levels of nicotine, cotinine and other ETS biomarkers measured in a study by Jarvis and Russell (1984) are shown in Table 2.4. Study subjects were 100 outpatients, mostly elderly, attending cardiology and vascular clinics at a London hospital. Individuals reported their degree of exposure to ETS over the three-day period preceding sample collection. In general,

concentrations of nicotine and cotinine in ETS-exposed nonsmokers were higher than those in nonsmokers reporting no exposure to ETS. The levels of cotinine in all fluids were significantly higher in smokers than in ETS-exposed and unexposed nonsmokers, with cotinine levels in ETS-exposed nonsmokers approximately 1% of the levels found in active smokers. In this study, concentrations of plasma nicotine were not related to reported exposure.

Recently, an increasing number of epidemiological studies have used biomarkers in assessing tobacco smoke exposure. Biomarkers can be used to categorize individuals as exposed or unexposed, identify deceivers (individuals misreporting their smoking status), or estimate relative degree of exposure. In a comparison of tests to distinguish smokers from nonsmokers, Jarvis *et al.* (1987) analyzed questionnaire responses and biochemical measures of exposure to cigarette smoke in 211 hospital outpatients. The optimal cutoff levels for distinguishing smokers and nonsmokers in plasma, saliva, and urine, as reported in that study, are shown in Table 2.5. Examples of typical cutoff levels for distinguishing smokers from nonsmokers reported in studies using cotinine as the marker of exposure are shown in Table 2.6. (The use of biomarkers to ascertain smoking status and estimate the degree of misclassification in epidemiological studies is discussed in Section 2.5.)

For all body fluids, the concentration distributions for smokers and exposed nonsmokers have been found to overlap; cotinine concentrations in the occasional smoker are similar to those of the heavily exposed nonsmoker. This is shown in Figure 2.1, in which the distributions of plasma cotinine concentrations for self-reported smokers and nonsmokers are shown to overlap. The distribution of values for self-reported nonsmokers is bimodal, suggesting some denial of active smoking (*i.e.*, deceivers) among the study subjects. For nicotine and other biomarkers of ETS exposure, the concentration distributions similarly overlap and are bimodal, presumably reflecting a certain degree of misreporting by the active smoker (Jarvis *et al.*, 1987).

#### 2.4.2.4 Nicotine and Cotinine: Concentrations in Physiological Fluids of Infants and Children

ETS exposure of infants and children has been examined in a number of studies in which nicotine and cotinine were used as biomarkers of exposure. Infants can be exposed prenatally to tobacco smoke constituents if the mother smokes or if the mother is exposed to ETS during pregnancy. Postnatal ETS exposure may occur directly, via inhalation, and indirectly, from ingestion of breast milk.

Henderson *et al.* (1989) examined the relationship between levels of nicotine in home air and the urinary cotinine concentrations in 27 children, 11 months to 5 years of age, attending a day care center at which they were not exposed to ETS. Fifteen children resided in homes with smokers and 12 did not. The average concentration of air nicotine in the homes of children who did and did not live with smokers was 3.74 $\mu g/m^3$ and 0.34 $\mu g/m^3$, respectively. Urinary cotinine concentrations were greater than 30ng/mg creatinine in 12 of the 15 children who lived with smokers, whereas concentrations were consistently less than 30 ng/mg creatinine in the 12 children without home exposure to ETS; three of the exposed children had urinary cotinine concentrations consistently in the upper range of values observed in unexposed children. The

average home air nicotine concentrations were related to the average log urinary cotinine to creatinine concentration ($r = 0.68$, $p = 0.006$).

Greenberg *et al.* (1984) measured the concentrations of nicotine and cotinine in the urine and saliva of 32 ETS-exposed and 19 unexposed infants less than 10 months of age visiting a primary care clinic in North Carolina. An infant was categorized as exposed if the caregiver reported at least two exposure episodes during the previous 24 hours and unexposed if no exposure had occurred during the previous week. Breast-fed infants were excluded from this study in order to examine inhalation exposure only. The concentrations of both nicotine and cotinine were significantly higher in the saliva and urine of the exposed group as compared to the unexposed group, with the best indicator of exposure reported to be the ratio of urinary cotinine to creatinine. The median ratio in the exposed group was 350 ng/mg as compared to 4 ng/mg in the unexposed group ($p<0.0001$). The mother's self-reported smoking behavior (number of cigarettes smoked during the previous 24 hours) was related to infant urinary concentration ($r = 0.67$, $p = 0.0001$). In a later study from the same group (Greenberg *et al.* (1989), described in Section 2.6.3), cotinine was detected in 60% of the 433 infants examined; the median concentration was 121 ng/mg creatinine (range: 6 to 2,273 ng/mg).

In a large population-based study of infants receiving routine well-child care in private physicians' offices in the greater Portland, Maine area, Chilmonczyk *et al.* (1990) collected urine samples from 518 infants, six to eight weeks of age, and obtained information on household smoking habits (this study is also discussed in Section 2.6.3). In the 305 households where no smoking was reported, 8% of the urinary cotinine values were equal to or greater than 10 ng/ml (the concentration of 10 ng/ml is defined by the authors on the basis of data in this study as a cutoff indicating significant ETS absorption). Median urinary cotinine concentrations in infants were 1.6 ng/ml in the 305 nonsmoking households, 8.9 ng/ml in the 96 households where a member other than the mother smoked, 28 ng/ml in the 43 households where only the mother smoked, and 43 ng/ml in the 74 households where both the mother and another household member smoked. In households where the mother smoked, breast feeding was associated with significantly higher infant urinary cotinine levels. These higher levels were seen both in the presence of other smokers in the household (median urinary cotinine: 213 ng/ml with breast feeding and 39 ng/ml without breast feeding) and in the absence of other smokers in the household (median urinary cotinine: 87 and 25 ng/ml, respectively.)

Several other studies have examined the relative contribution of inhalation versus ingestion of mother's milk to an infant's intake of nicotine and cotinine (Luck and Nau, 1985; Woodward *et al.*, 1986; Labrecque *et al.*, 1989; Schulte-Hobein *et al.*, 1992). In general, breast-fed infants whose mothers smoke were reported to have median urinary cotinine to creatinine ratios 2- to 10-fold higher than bottle-fed infants exposed only through inhalation, with the urinary cotinine levels in the infant related to the number of cigarettes smoked by the mother. Concentrations of urinary cotinine in breast-fed and bottle-fed babies as a function of the number of cigarettes smoked by the mother are shown in Figure 2.2.

2.4.2.5 Nicotine and Cotinine: Concentrations in Breast Milk and Amniotic Fluid

The observation that ingestion of breast milk is a significant contributor to infant exposure to ETS constituents (discussed above) is consistent with the findings of numerous studies in which nicotine and cotinine have been measured in milk of mothers who smoke (Ferguson *et al.,* 1976; Hardee *et al.,* 1983; Luck and Nau, 1984; Woodward *et al.,* 1986; Luck and Nau, 1987; Labrecque *et al.,* 1989; Schulte-Hobein *et al.,* 1992) and in milk of mothers exposed to ETS (Hardee *et al.,* 1983; Schulte-Hobein *et al.,* 1992). Results from these studies are summarized in Table 2.7. For smokers, mean nicotine concentrations in breast milk ranged from 5.16 to 91 ng/ml (range: 0.9 to 512 ng/ml) and mean cotinine concentrations, from 5.6 to 439 ng/ml (range: not detected to 738 ng/ml). The concentrations of nicotine measured in the breast milk of nonsmokers exposed to ETS were much lower than those reported for smokers. Nicotine and cotinine were often not detected in the milk of nonsmoking women; for samples in which these compounds were detected, nicotine concentrations ranged from 1 to 7 ng/ml (Hardee *et al.,* 1983) and cotinine concentrations from 2 to 277 ng/ml (Hardee *et al.,* 1983; Schulte-Hobein *et al.,* 1992).

The transfer of nicotine from blood into breast milk is very rapid, with milk concentrations approximately three times higher than in serum (Luck and Nau, 1984; Dahlstrom *et al.,* 1990). The half-life of nicotine in milk is approximately the same as that in blood (Luck and Nau, 1987). For cotinine, the reported milk/serum ratio ranges from 0.78 to 1 (Luck and Nau, 1984; Dahlstrom *et al.,* 1990). In general, the concentration of cotinine in milk has been found to increase with increasing nicotine consumption (Woodward *et al.,* 1986; Labrecque *et al.,* 1989; Schulte-Hobein *et al.,* 1992).

The exposure of a nursed infant to nicotine depends on the daily intake of breast milk as well as the smoking pattern of the mother, including the number of cigarettes she consumes daily, the extent she inhales, her smoking frequency prior to nursing, and the time interval between nursing and the last cigarette smoked (Luck and Nau, 1987). Because of the relatively short half-life of nicotine, diurnal milk concentrations are highly variable; 5- to 10-fold increases in the concentration of nicotine were observed in milk samples collected during the day, as compared to samples collected in the early morning after night time smoking abstinence (Luck and Nau, 1987; Dahlstrom *et al.,* 1990). Because of the longer half-life of cotinine, its concentrations in milk are relatively constant.

No information was available on the levels of other ETS constituents in breast milk, although it is possible that other compounds would also be transferred to breast milk. Their relative concentrations in milk would depend on a number of factors, including their concentrations in mainstream (or sidestream) smoke, biological half-life, and lipid solubility.

Cotinine has also been detected in the amniotic fluid of ETS-exposed pregnant women and in the urine of their neonates (Jordanov, 1990). Mean concentrations of cotinine in amniotic fluid collected at parturition were 15 umol/l in unexposed nonsmokers (women not living with a smoker), 25 umol/l in exposed nonsmokers (smoker resided in household), and 111 umol/l in active smokers. Cotinine was also detected in the urine, collected on the first day of life, of their

neonates. Neonates of nonsmokers exposed to ETS had significantly higher concentrations of urinary cotinine than neonates of unexposed nonsmokers ($p<0.01$).

### 2.4.3 Biomarkers: Carbon Monoxide and Carboxyhemoglobin

Carbon monoxide, both in exhaled alveolar air and as carboxyhemoglobin in blood, originates from endogenous processes as well as from environmental sources. In addition to cigarette smoke, common environmental sources include vehicle exhaust, gas stoves and furnaces, and kerosene space heaters. Although carbon monoxide and carboxyhemoglobin have been used to distinguish smokers from nonsmokers (Ohlin *et al.,* 1976; Sillett *et al.,* 1978; Jarvis *et al.,* 1983 and 1987), they are generally not good indicators of ETS exposure because of their lack of sensitivity and specificity. In nonsmokers exposed to environments heavily polluted with ETS, elevated levels of exhaled carbon monoxide and carboxyhemoglobin in blood have been detected when measured within 30 minutes following cessation of exposure. However, several studies of more typical exposure situations did not find significant differences in the carboxyhemoglobin levels in subjects reporting no, low, or high levels of ETS exposure (Jarvis *et al.,* 1983; Jarvis and Russell, 1984) (see Table 2.4).

### 2.4.4 Biomarkers: Thiocyanate

Present in the vapor phase of tobacco smoke, hydrogen cyanide is metabolized in the liver, yielding thiocyanate ($SCN^-$). Thiocyanate levels in blood, urine, and saliva have been used to distinguish smokers from nonsmokers, or in combination with assays for nicotine or cotinine, to distinguish smokers from individuals using smokeless tobacco or other nicotine-containing products (Haley *et al.,* 1983; Hauth *et al.,* 1984; U.S. DHHS, 1986; Jarvis *et al.,* 1987). Sources of thiocyanate are also present in the diet, particularly cruciferous vegetables (Haley *et al.,* 1983); thus, levels of thiocyanate in body fluids are not specific to exposure to tobacco smoke. In studies examining the use of thiocyanate as a biomarker of ETS exposure, it was not possible to distinguish between ETS-exposed and unexposed nonsmokers (Hauth *et al.,* 1984; Jarvis and Russell, 1984) (see Table 2.4). For this reason, thiocyanate is not very useful as a biomarker of ETS and has not been widely used for monitoring ETS exposure.

### 2.4.5 Biomarkers: Protein and DNA Adducts

Protein and DNA adducts represent both markers of exposure and measures of a biochemical effect. One of the more common protein adducts measured is the hemoglobin adduct of 4-aminobiphenyl. Tobacco smoke is the primary source of environmental 4-aminobiphenyl. Because of the relatively long half-life of these adducts, their levels reflect exposures occurring over the previous four months. Levels of 4-aminobiphenyl in ETS-exposed nonsmokers compared to those of active smokers present an interesting contrast to cotinine levels measured in these two groups. The levels of 4-aminobiphenyl adducts in nonsmokers are approximately 10% to 20% of the levels measured in smokers. Although this finding appears to be inconsistent with the results for urinary cotinine, for which levels in ETS-exposed nonsmokers are about 1% of those in smokers, the results may be explained by the available information on the relative levels of emission of nicotine and 4-aminobiphenyl into mainstream and sidestream smoke (see U.S. EPA, 1992: Table 3-1). Approximately twice as much nicotine is emitted in sidestream as in

mainstream smoke, whereas about 31 times as much 4-aminobiphenyl is emitted in sidestream as in mainstream smoke, and as a result, the smoker/nonsmoker ratio for 4-aminobiphenyl is about 15 times higher than that for cotinine.

Another group of protein adducts which have been measured are the albumin adducts of polycyclic aromatic hydrocarbons (PAHs). Multiple PAHs are present in tobacco smoke. Crawford *et al*. (1994) analyzed PAH-albumin levels in peripheral blood of 87 mothers and their preschool children (2-5 years of age) (discussed in more detail in Chapter 7, *Carcinogenic Effects*, Section 7.1.2.1). They found PAH-albumin levels were significantly higher in the children whose mothers smoked than in the children of non-smoking mothers ($P<0.05$). Among the non-smoking mothers, regression of PAH-albumin against total ETS exposure also showed a significant association with cotinine ($r^2=0.25$; $P=0.04$).

DNA adducts of tobacco smoke constituents can also be measured. The distribution of DNA adducts of benzo[*a*]pyrene diol epoxide, the ultimate carcinogenic metabolite of benzo[*a*]pyrene, a PAH present in tobacco smoke, has been analyzed by Denissenko *et al*. (1996) in the *P53* tumor suppressor gene. These authors reported that exposure of human bronchial epithelial cells to benzo[*a*]pyrene diol epoxide resulted in strong and selective DNA adduct formation within the *P53* gene at mutational hotspots identified in non-radon associated human lung cancer tissues obtained from smokers. This mapping of DNA adduct formation to mutational hotspots provides a direct etiological link between a specific tobacco smoke carcinogen and human cancer.

## 2.4.6 Biomarkers: Other Approaches

Testing for other compounds in body fluids and for the mutagenicity of those fluids has been conducted to identify other approaches to assessing tobacco smoke exposure which are potentially more relevant to health endpoints of concern (*e.g.*, cancer). In a recent study by Hecht *et al.* (1993), five male nonsmokers were exposed to sidestream cigarette smoke generated by machine smoking for 180 minutes on each of two days, six months apart. The air concentrations of nicotine to which the men were exposed were reported to be comparable to levels found in a heavily smoke-filled bar. The mean concentrations of 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronide were significantly higher after exposure than at baseline (33.9 versus 8.4 ng per 24-hour urine sample). The compound NNAL and its glucuronide are metabolites of 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone (NNK), a potent lung carcinogen in rodents (IARC, 1985). NNAL is also a lung carcinogen in rodents (Castonguay *et al.*, 1983; Rivenson *et al.*, 1988). NNK is formed by the oxidation and nitrosation of nicotine during the curing (drying) and smoking of tobacco (IARC, 1985).

Body fluids from active smokers and ETS-exposed nonsmokers have been assayed for genotoxic activity in a number of studies, primarily using the Ames *Salmonella* test. While the mutagenicity of the urine of cigarette smokers has been confirmed in a number of studies (IARC, 1986), the results using the urine from ETS-exposed nonsmokers have been less conclusive. Bos *et al.* (1983) reported that mutagenic activity of the urine of nonsmokers was significantly higher ($p<0.02$) in samples collected following exposure to ETS than in samples collected prior to exposure, when tested in the *Salmonella* assay. In other studies, however, no increases or insignificant increases in mutagenic activity were reported (Sorsa *et al.*, 1985; Husgafvel-

Pursiainen *et al.*, 1987; Mohtashamipur *et al.*, 1987; Scherer *et al*, 1987). Limitations of some of these studies include small numbers of subjects tested and lack of consideration of dietary factors, which have been shown to influence urinary mutagenicity (Sasson *et al.*, 1985).

## 2.5 Exposure Measurement: Use of Questionnaires

Epidemiologic studies typically evaluate exposure to ETS using questionnaires in which the subject reports his or her own exposure history and smoking status. In studies using questionnaires alone to assess ETS exposure, misclassification of true exposure status can result from a number of factors, including: limited questions (*e.g.*, spousal smoking status only); possible deception in reporting spousal smoking status; or inadequate recall of exposure (*e.g.*, parental smoking status; lack of awareness of contemporary exposure). Many studies cited in this report recognized the possibility of misclassification bias and took appropriate steps to minimize its impact or adjusted the analysis to account for this source of error. This section summarizes the results of a number of studies that have examined the reliability and validity of information collected using questionnaires regarding ETS exposure and smoking status.

### 2.5.1 Reliability of Questionnaire Responses on ETS Exposure

#### 2.5.1.1 Reliability: Test-retest of the Same Subject

Studies employing a "test-retest" design have been used to assess the reliability of information obtained in questionnaires on past exposures to ETS. Coultas *et al.* (1989) interviewed a sample of 149 adult nonsmokers on two occasions, six months apart, with regard to whether their parents had smoked during their childhood. Concordance was 94% for mothers' smoking, 93% for fathers' smoking, and 85.9% for maternal smoking during pregnancy. However, information provided by the subjects on the amounts smoked (*i.e.*, number of cigarettes or hours of smoking per day) was found to be less reliable.

In a study of similar design, Pron *et al.* (1988) interviewed 117 subjects (controls in a case-control study of lung cancer) on two occasions separated by an average of six months. Agreement of responses with regard to the subjects' residential exposure (*i.e.*, if the subject ever resided in the same household as a regular smoker) was generally good (kappa = 0.66 for all subjects combined). Smoking by spouses was reported with high reliability (kappa = 0.89 for both husband and wife). Response agreement for exposure at work (kappa = 0.46 for both sexes) was lower than for residential exposure. Similar to the findings of the preceding study by Coultas *et al.* (1989), quantitative measures of exposure (*i.e.*, number of cigarettes smoked and duration of exposure) were less reliably reported.

#### 2.5.1.2 Reliability: Self Versus Surrogate Respondents

A number of studies have examined the quality of information provided by surrogate respondents. Use of surrogate respondents occurs frequently in studies of ETS exposure. Studies examining the effects of exposure to spousal or household smoking often ask subjects to report on the smoking habits of members of their households. In retrospective studies of adult health risks from exposures occurring early in life, subjects who are now adults are questioned concerning parental smoking habits.

The quality of parental smoking histories was evaluated in a North Carolina study of cancer risk from childhood exposure to ETS (Sandler and Shore, 1986). A total of 1,036 subjects (cases and controls, aged 15 to 59 years) were asked about parental smoking habits during the subject's childhood and prior to the subject's birth. Parents or siblings of 70% of the study subjects were also interviewed to obtain the same information. Interviews were conducted with 355 mothers, 33 fathers, and 261 siblings. Concordance of subjects and their mothers was greater than 93% on questions concerning mothers' smoking and 85% regarding fathers' smoking. The study found that the responses were less accurate for information provided about dates or the number of cigarettes smoked. When extent of smoking was categorized as none, less than 1 pack, 1 pack, or greater than 1 pack, agreement between mothers and subjects was 82% with respect to mothers' smoking.

Similar findings were reported by McLaughlin *et al.* (1987) in a study of the reliability of surrogate information. The responses of children about smoking by their deceased parents agreed closely with information given 10 years previously by the parents themselves, with the level of agreement ranging from 80 to 96%.

Of the study populations examining the quality of information on smoking habits provided by surrogate respondents, most consisted of husband-wife pairs, although other family members were included in some studies (Rogot and Reid., 1975; Kolonel *et al.*, 1977; Pershagen, 1984; Lerchen and Samet 1986; McLaughlin *et al.*, 1987). Information was obtained directly from interviews with both members of the pair or from an interview with one individual and the medical history of the other. These studies consistently found good agreement in responses concerning spousal smoking status, ranging from 90% to 100%. However, similar to the findings of studies on parental histories, quantitative information on the number of years or cigarettes smoked was less accurate.

In summary, the results of these studies indicate that information on childhood exposure to ETS provided by individuals who are now adults is of good quality, particularly with regard to qualitative information. Similarly, qualitative information on spousal smoking is of good quality. However, in both cases, quantitative information on the number of years of smoking, dates of smoking, or number of cigarettes smoked per day is sometimes less reliably provided.

## 2.5.2 Validity of Questionnaire Responses on ETS Exposure

### 2.5.2.1 Validity of ETS Exposure Status Based on Spousal / Household Smoking

A number of the early epidemiologic studies classified an individual's exposure to ETS solely on the basis of spousal smoking. Information presented in Sections 2.6.2 and 2.6.3 indicates that in California and nationwide, locations outside the home are also important sources of ETS exposure. The validity of ETS exposure status based on spousal or household smoking has been examined in a number of studies (Friedman *et al.*, 1983; Coultas *et al.*, 1987; Coghlin *et al.*, 1989; Cummings *et al.*, 1990). Methods used to validate exposure status include: gathering information on the extent to which nonsmokers report exposure outside the home; comparison of ETS biomarker levels of those with smoking and nonsmoking spouses; and comparison of indoor air levels of nicotine in houses with members who do and do not smoke. Results from these

studies indicate that misclassification may occur when smoking by a spouse or other household member is the basis for determining ETS exposure.

In a study by Friedman *et al.* (1983), married couples were asked about their smoking habits and weekly exposure to ETS. Over 90% of nonsmokers married to nonsmokers reported no weekly exposure to ETS in the home; however, 40% of the nonsmoking females and 49% of the nonsmoking males reported ETS exposures outside the home. Conversely, substantial percentages of nonsmokers married to smokers (47% of women, 39% of men) reported no weekly exposure to ETS in the home. These studies indicate that classifying an individual's exposure to ETS on the basis of spousal smoking habits may result in misclassification.

Biomarker studies have shown that a proportion of subjects reporting no exposure to ETS have measurable biomarker concentrations, indicating that the subject either forgot or was not aware of his ETS exposure. In a study of 663 nonsmokers attending a cancer-screening clinic, Cummings *et al.* (1990) reported that 84% of subjects not living with a smoker had detectable urinary cotinine levels. In an unpublished analysis of only those subjects who were currently employed nonsmokers in this study, 76% of those reporting no exposure to ETS at home reported exposure at work (Cummings, 1994). Coultas *et al.* (1987) reported that in 727 households, approximately 35% of adults and children not living with a smoker had detectable levels of salivary cotinine. (These studies are described in Section 2.6.3).

Comparison of reported exposures and questionnaire responses has also been examined using results from air monitoring of nicotine. Coghlin *et al.* (1989) questioned 37 nonsmokers with nonsmoking spouses and 15 nonsmokers with smoking spouses about their weekly exposure to ETS at home, work, in public places, and in vehicles. Personal nicotine monitors were worn by study participants to obtain measurements of actual exposure. Of the nonsmokers with nonsmoking spouses, 22% had personal nicotine levels similar to those measured for smokers, while 13% of nonsmokers with smoking spouses had low nicotine levels. In addition, 88% of nonsmoking women with nonsmoking spouses reported work-related exposure and 80% reported social exposure.

In a study by Leaderer and Hammond (1991), measurable concentrations of nicotine were detected in 13% of residences reporting no smoking in the home, while nicotine was not detected in 28% of the households with occupants who smoked. For the latter, smoking could have occurred in rooms other than the primary activity room in which samples were taken.

In summary, studies have consistently shown that subjects are misclassified with regard to their ETS exposure status when the sole basis for classification is the smoking status of other household members. The overall impact of misclassification would be an underestimation of the health impacts of ETS exposure.

#### 2.5.2.2 Validity of Self-Reported ETS Exposure: Biomarker Concentrations

Biomarkers have been used to examine the quantitative relationships between the degree of ETS exposure self-reported on questionnaires and concentrations of nicotine in ambient air (Coultas *et al.*, 1989; Haley *et al.*, 1989a; Cummings *et al.*, 1990; Riboli *et al.* 1990). Depending on the

study design and endpoints examined, the reported correlations among the various exposure indices ranged from moderate to high. Because of the many limitations of these studies, inconsistencies among studies is not unexpected. Significant differences in uptake, distribution, metabolism, and excretion of nicotine are found among individuals (Benowitz *et al.*, 1982), and thus cotinine levels in biological fluids vary among individuals exposed under identical conditions. In those studies in which urinary cotinine is used as the measure of exposure, cotinine concentrations are often assessed from a single urine sample, which may not adequately represent the exposure period in question. For studies in which ambient air concentrations of nicotine serve as the exposure measure, it has been shown that air concentrations vary within the same room; intake will depend on the location of the individual relative to the smoker, the exposure duration, and the physical characteristics of the exposed individuals (*e.g.*, activity level and corresponding breathing rate).

### 2.5.3 Reliability and Validity of Self-Reported Smoking Status

In a test-retest study of the reliability of subjects' report of their own smoking habits, Lee (1987) found that responses from 93% of 166 subjects regarding current or past smoking status were consistent with responses to the same questions asked five years earlier.

A number of studies have used biomarkers to validate self-reported smoking status (Coultas *et al.*, 1989; Haley *et al.*, 1989a; Cummings *et al.*, 1990; Riboli *et al.* 1990; Perez-Stable *et al.*, 1992). Self-reported nonsmokers who appear to be smokers on the basis of biochemical measurements are generally considered "deceivers" of their true smoking status. In a summary of 11 studies in which questionnaire responses regarding smoking status were compared with cotinine or nicotine measurements (Perez-Stable *et al.*, 1992), the estimated misclassification rates (self-reported nonsmokers with elevated cotinine or nicotine levels indicative of active smoking) ranged from zero in a small study to nearly 10% in a sample of nonsmokers from a clinical setting. These studies are summarized in Table 2.6. Misclassification of an individual who is a smoker as a nonsmoker may increase the apparent relative risk of smoking-related diseases in nonsmokers. However, Perez-Stable *et al.* (1992) suggest that most smokers misclassified as nonsmokers are very light smokers or occasional smokers who binge.

## 2.6 Exposure Prevalence and Determinants

### 2.6.1 Introduction

Because the various health endpoints reviewed in other chapters of the overall ETS assessment may be the result of either acute or chronic exposures, both present and past patterns of exposure are of interest and information on both is included here. Studies of the prevalence of ETS exposure and its demographic and social determinants summarized below (Sections 2.6.2 and 2.6.3) should be considered representative only of the general time periods covered by the study. Smoking prevalence, smoking behaviors, and other factors contributing to exposure to ETS have continued to change as smoking customs have changed in the U.S., with a number of important changes occurring within the past few years. Thus, it is expected that the number of individuals exposed to ETS and the patterns of exposure have also changed over time (see Section 2.6.4).

For California, information is available from population-based surveys in which self-reported exposure to ETS was assessed (Friedman *et al.,* 1983; Phillips *et al.,* 1991; Wiley *et al.,* 1991a, 1991b; Burns and Pierce, 1992; Jenkins *et al.,* 1992; Pierce *et al.,* 1994). With one exception (Friedman *et al.,* 1983), these studies relied solely on self-reported exposure and did not validate questionnaire responses using biomarker data. A certain amount of misreporting occurs in studies relying on self-reported exposure; several studies have been conducted to evaluate the relationship among self-reported exposure and other exposure indices (*e.g.,* ambient air concentrations of ETS constituents and cotinine levels in biological fluids) and these are discussed in Section 2.5.

For areas outside of California, information on exposure prevalence is available from a variety of studies, using either self-reported exposure or the presence of biological markers as the measure of exposure (Coultas *et al.,* 1987; Greenberg *et al.,* 1989; Chilmonczyk *et al.,* 1990; Cummings *et al.,* 1990; Overpeck and Moss, 1991; CDC, 1993b; Pirkle *et al.,* 1996). In general, only limited comparisons can be made between the findings on exposure prevalence for California and those available for other areas, primarily because of important differences in study objectives and study design. However, indirect indicators of ETS exposure suggest that the prevalence of ETS exposure in California is less than that of the rest of the U.S. population. A discussion of these indicators and other factors in California expected to affect trends in exposure prevalence are discussed in Section 2.6.4. The studies presented in the following sections are summarized in Tables 2.8 and 2.9.

Taken as a whole, the various studies discussed below indicate that, within California and the United States, exposure to ETS was widespread during the time period of the studies (1979 through 1992). Analyses of ETS exposure within California indicated that the workplace, home, and other indoor locations contributed significantly to the exposure of adults; for children, the home was the most important single location contributing to ETS exposure. In all studies using both self-reporting and a biological marker (cotinine level) as measures of exposure, prevalence was higher when determined using the biological marker.

## 2.6.2 Prevalence of ETS Exposure in California

*Friedman et al. (1983)*

In one early study, the prevalence and extent of weekly exposure to ETS was assessed from questionnaire responses of 37,881 nonsmokers and exsmokers receiving multiphasic health checkups in 1979 and 1980 (Friedman *et al.,* 1983). The population consisted of members of the Kaiser-Permanente Medical Care Program in Oakland and San Francisco. Altogether, 63.3% of the respondents reported some exposure to ETS, with 28.8% reporting exposure durations of between 1 and 9 hours per week, 18.6% reporting exposure durations of between 10 and 39 hours per week, and 15.9% reporting exposure durations of 40 or more hours per week. The reported locations of exposure were the home (23.8%), other small areas (40.4%, defined in the study as "such as airplane, office, or car, etc.") or a large indoor area (46.5%, defined in the study as "such as restaurant, hotel lobby, lecture hall, etc.").

Exposure was strongly related to age, with 78.2% of those in their twenties reporting exposure, decreasing to 13.9% of those aged 80 and over. Serum thiocyanate and expired-air concentrations of carbon monoxide were determined for 267 persons who completed the questionnaire. The correlations between self-reported ETS exposure and the biomarkers were all positive, but small. While the correlations of thiocyanate levels with non-home small area, large area, and total exposure were at, or close to, the $p < 0.05$ level of statistical significance, for CO, no correlation approached statistical significance. These findings are not surprising given that sources of thiocyanate and carbon monoxide in addition to tobacco smoke are present in the environment. More recent studies indicate that, in general, they are not suitable as markers of ETS exposure (see Sections 2.4.2 and 2.4.3).

*Wiley et al. (1991a, b), Phillips et al. (1991), and Jenkins et al. (1992)*

In the late 1980s, the California Air Resources Board (ARB) funded a statewide survey to obtain information on activity patterns of Californians and on their use of and proximity to air pollutant sources, including ETS (Wiley *et al.*, 1991a; Jenkins *et al.*, 1992). The study consisted of telephone interviews with 1,579 English-speaking adults and 183 adolescents (12 to 17 years of age) who were members of households with telephones in California. The interviews were conducted over four seasons, from October 1987 through September 1988. The participants completed a verbal recall diary of their activities and locations of the previous day, and for each activity and location, were asked whether anyone smoking a cigarette was present.

In a second study of similar design (*i.e.*, telephone interviews with English-speaking individuals) conducted from April 1989 through February 1990, information was obtained on the activity patterns of 1,200 children (Phillips *et al.*, 1991; Wiley *et al.*, 1991b). In this study, children from 9 to 11 years old were interviewed directly. For children 6 to 8 years of age, the interview was conducted with a parent or guardian who was encouraged to consult with the child, and for younger children, the interview was conducted with the adult household member having spent the most time with the child on the diary day. Because exposure to ETS was not the primary focus of either the adult or childhood study, the ETS responses had not been fully analyzed. At the request of the Office of Environmental Health Hazard Assessment, additional unpublished analyses of the responses on ETS exposures were conducted by the ARB for inclusion in this report (Jenkins, 1992; Jenkins, 1994, personal communication; Lum, 1994a and b, personal communication).

Figures 2.3 and 2.4 show the percent of nonsmokers in California reporting exposure to ETS and the average daily duration as determined in this study. Of adult nonsmokers, 43% reported exposure to ETS, as did 64% of nonsmoking adolescents (Jenkins *et al.*, 1992). For smokers and nonsmokers combined, approximately 61% of adults and 70% of adolescents (age 12 through 17) reported exposure to ETS at some time during the day (at the time of the survey, 22.5% of the population reported active smoking on a given day). The groups with the lowest percent reporting exposure were children and infants and preschoolers, ranging from 35% to 45%, as a function of age and sex. About 38% of children under age 12, statewide, were exposed to ETS at some time during a typical day. Among those infants and preschoolers who were exposed to ETS, the average duration of their exposure was as long as that of adults (about four

hours); children aged 6-11 years who were exposed had an average exposure duration of three hours (Lum, 1994a,b, personal communication).

A separate analysis of the survey data was conducted to determine the relative proportion of the population's ETS exposure duration (measured in person-minutes) occurring in different locations (Lum, 1994a,b, personal communication). The various locations identified in the study were grouped into three or four mutually exclusive categories for each population subgroup and the mean duration of reported exposure to ETS while in those locations was determined. For adults, the categories were home, work, other indoor, and outdoor; for adolescents and children, home, school, other indoor, and outdoor; and for infants and preschoolers, home, other indoor, and outdoor. The relative person-minutes of reported exposure at each location (*i.e.*, the product of the number of individuals reporting ETS exposure and the average reported exposure duration, divided by the total number of person-minutes of reported ETS exposure at all locations) was then calculated to provide a crude index of the relative importance of each exposure location.

Although the concentration of ETS at each location is also an important parameter in estimating exposure, measurements of ETS concentrations were not obtained in this study, which focused primarily on time-activity patterns. In other studies (see Section 2.3.3), home and workplace concentrations of nicotine (as an indicator of ETS) fall within the same general range. Thus, this location/duration index provides a rough estimate of the relative extent of the population's exposure at these locations. However, ETS concentrations at locations grouped as other indoor (*e.g.*, bars, restaurants, banks, or hospitals) are highly variable, and little information is available on concentrations in outdoor environments (*e.g.*, at parks or bus stops). Overall, the index provides an indication of the locations at which exposure occurs, but not of the relative dose incurred at each location.

The results of the analysis are shown in Figure 2.5. For male adult nonsmokers, the highest exposure index was estimated for the workplace (46%), with the index at other locations (*i.e.*, the home, other indoor, and outdoor) ranging from 15% to 23%. For female nonsmokers, the highest indexes were for the workplace (35%) and other indoor locations (31%), followed by the home (20%), and outdoor locations (13%). Somewhat different patterns were found for adult smokers reporting exposures to ETS from someone else's smoking. For male smokers, the exposure index was similar at all locations, ranging from 21% to 29%. For female smokers, the highest index was for the home (53%), ranging from 12% to 22% at other locations. Different patterns were observed for adolescents and children. For adolescents, the exposure index was approximately the same for home and other indoor locations (41% to 42%), followed by outdoor locations (13%) and school (4.5%). (It should be noted that the values for adolescents are based on a small sample size of 183.) Not unexpectedly, for children (6 to 11 years old) and infants and preschoolers (0 to 5 years old) the highest exposure index (54% and 62%, respectively) was for the home.

Workplace exposures to ETS were also examined (Jenkins, 1994, personal communication). Approximately 40% of nonsmokers working outside the home reported exposure to ETS in the workplace. While fewer nonsmoking working females (30%) reported exposure than nonsmoking working males (47%), their average exposure duration at work was somewhat

longer (females, 5.8 hours; males, 5.2 hours). The proportion of the total daily reported exposure duration occurring in the workplace for these nonsmoking workers was 51% for males, and 38% for females.

*Burns and Pierce (1992), Borland et al. (1992)*

Limited information on exposure to ETS is also available from a survey on tobacco use in California, conducted between June 1990 and July 1991 (Burns and Pierce, 1992). Using a stratified random-digit dialing technique, the head of household in 32,135 homes was surveyed briefly (in either English or Spanish) to enumerate household members and determine the smoking status of each household member. From this information, all adult household members who were reported as having smoked within the past five years were scheduled for an in-depth interview, as were 28% of nonsmokers. The prevalence of active smoking, as reported in this study, was 22.2%, with males (25.5%) smoking more than females (19.1%). Information was obtained on household ETS exposure of children up to 18 years of age. The study found that 32.2% of children under 5 years of age live in homes with one or more smokers. Similar values were reported for children 6 to 11 years old (32.2%) and 12 to 17 years old (36.5%).

Using data collected in the California tobacco-use survey (Burns and Pierce, 1992) described above, Borland *et al.* (1992) examined the extent of exposure of nonsmoking workers to ETS according to type of work-site smoking policy, work area, workplace size, and demographic characteristics. The analysis reported by Borland *et al.* is for weighted population estimates and differs slightly from that in the original report of Burns and Pierce (1992). The sample consisted of 7,301 nonsmokers from the larger study who reported that they worked primarily indoors. Workplace ETS exposure of these individuals was assessed by asking the question, "During the past two weeks has anyone smoked in the area in which you work?" Additional questions were not asked to define the frequency and extent of exposure. Overall, 31.3% of the nonsmoking workers reported workplace ETS exposure at least once in the preceding two weeks. Examined as a function of work-site smoking policy, workplace exposure of nonsmokers was 9.3% for those working in a smoke-free worksite, 23.2% for those working where there was a work-area smoking restriction, 46.7% for those working where the smoking policy did not include the work area, and 51.4% for those working where there was no work-site smoking policy. The study also found that a greater percentage of male workers reported exposure than did female workers (35.8% versus 22.9%); that more workers under 25 reported exposure than did older workers (41.9% versus 26.4%); and that the number of workers reporting exposure decreased with increasing level of education, from 43.1% of those with less than 12 years of education to 18.6 % of those with a college education.

*California Department of Health Services (1995 and 1996) and Pierce et al. (1994; 1996, personal communication)*

The California Department of Health Services (CDHS) conducts annual telephone surveys of a representative sample of Californians - the California Adult Tobacco Survey (CATS). The 1995 survey interviewed over 4000 adults about their smoking behavior. According to 1995 data from the California Adult Tobacco Survey and an additional survey (Behavioral Risk Factors Survey), CDHS estimated that 16.7% of the adult population in California smokes.

**Exposure Measurement and Prevalence**

Survey results from 1994 and 1995 indicate increasing percentages of non-smoking and smoking California adults reporting that smoking is prohibited at their work sites (1994: 84% (non-smokers) and 75% (smokers); 1995: 89% (non-smokers) and 78% (smokers)). Similarly, the percentages of non-smoking and smoking adults in California reporting that smoking is prohibited in public areas of their work has also increased (1994: 74% (non-smokers) and 63% (smokers); 1995: 82% (non-smokers) and 85% (smokers)). The percentages of adults reporting a complete ban of smoking in their own homes has also increased (1994: 64% (non-smokers) and 24% (smokers); 1995: 80% (non-smokers) and 34% (smokers)).

The California Adult Tobacco Surveys in 1990, 1992 and 1993 were conducted for CDHS by Pierce *et al*. (1994) at the University of California, San Diego, who sampled relatively large numbers of Californians: 8,224 to 30,716 adults (18 years and older) and 1,789 to 5040 teenagers (12-17 years of age) (CDHS, 1996). From the results of those surveys, prevalence of active smoking and ETS exposure for various subpopulations can be estimated. For example, of the 2,047 women interviewed in 1992 who were pregnant over the previous five years, 15.1% smoked prior to pregnancy and of these, 37.5% quit during the pregnancy; thus, a prevalence estimate of 9.4% for California women smoking throughout pregnancy can be obtained. Regarding ETS exposure of women of child-bearing age, Pierce *et al.* (1996, personal communication) estimated that in 1993 of the 6,513.891 women aged 18-44 in California, 634,028 were non-smokers exposed to ETS at home, 564,411 were non-smokers exposed indoors through their work, and 46,083 were exposed at both work and home. From this, the proportion of nonsmoking women in California of child-bearing age who are ETS-exposed is estimated to be 22.1%. Regarding childhood exposures, the 1993 survey suggests 19.6% of those age 17 and under, and 17.7% of those under age 5 may be exposed to ETS in their homes (Pierce *et al*., 1994).

### 2.6.3 Prevalence of ETS Exposure in the United States

Historically, the main focus of large population-based studies of tobacco smoke exposure has been on active smoking, with little or no information obtained on exposure to ETS. More recently, several studies in the U.S. have addressed various aspects of ETS exposure, including exposure prevalence in various population subgroups. The measures of exposure used in these studies include both questionnaire responses and measured levels of biological markers (primarily cotinine). As previously noted, self-reporting can result in some degree of misclassification. The use of biomarkers can also result in some misclassification, however, in that it is not always possible to distinguish between a nonsmoker heavily exposed to ETS and a very light smoker; another concern is that, in some studies, the timing of sample collection relative to exposure may not have been appropriate. In addition, most biomarkers reflect exposures occurring within the past few days, whereas the exposure period of interest for many studies extends over a time period of many years. These factors are discussed in Section 2.4.1. For those studies summarized below in which prevalence was assessed using biomarkers, the biomarker levels detected in biological fluids are mentioned. The use of biomarkers as an exposure measure is discussed in detail in Section 2.4.

#### 2.6.3.1 General Population Studies

*Centers for Disease Control (CDC, 1993b; Pirkle et al., 1996)*

As part of the Third National Health and Nutrition Examination Survey (NHANES III), the National Centers for Environmental Health and the National Center for Health Statistics of the Centers for Disease Control (CDC) measured serum levels of cotinine to assess exposure to tobacco of persons in the United States aged 4 years and older. The study was conducted from 1988 through 1994; preliminary information was available in 1993 (CDC, 1993b), and final results of the 1988 to 1991 survey were recently published (Pirkle *et al.*, 1996). In the 1988 to 1991 survey, 14,269 persons aged 4 years and older were interviewed, of those 12,678 were examined, and of those examined, 10,642 had serum cotinine measurements taken. Reported data on ETS exposure in the home were available for 3185 children aged 2 months to 3 years, 3011 aged 4 to 11 years, and 878 aged 12 to 16 years. Serum cotinine levels were available on 737 adolescents and 7740 adults with complete information on tobacco use and ETS exposure.

Of US children 11 years and younger, 43% lived in homes of at least one smoker, as did 37% of adult non-tobacco users. Serum cotinine levels, however, indicated more widespread exposure to nicotine, with 87.9% of non-tobacco users with detectable levels of serum cotinine. Both the number of smokers in the home and the hours exposed at work were significantly and independently associated with increased serum cotinine levels ($p < 0.001$, multiple regression t test). Identified groups with higher exposure to ETS were children, non-Hispanic blacks, and males. Dietary variables showed no consistent association with serum cotinine levels, with dietary contributions, if any, appearing to be extremely small.

*Cummings et al. (1990)*

Cummings *et al.* (1990) assessed the prevalence of ETS exposure of 663 nonsmokers and exsmokers who attended the Roswell Park Memorial Institute cancer screening clinic in Buffalo, NY in 1986. Both self-reported exposure and measured urinary cotinine were used as measures of exposure. An interviewer questioned subjects about their exposure over the four-day period preceding the interview and a single urine sample was collected on the day of the interview. A total of 76% of the subjects reported some exposure to ETS during the four days preceding the interview. The average number of exposures over the four-day period was 3.3 (range: 0 to 21), and for those exposed, the average daily reported exposure was two hours (range: <1 to 13.25 hours/day). The reported exposure locations were work (28%), home (27%), restaurants (16%), private social gatherings (11%), car or airplane (10%), and public buildings (8%). Cotinine was detected in the urine of 91% of samples (detection limit not given), suggesting that individuals are not always able to recall exposures or are not aware that exposure has occurred. It is also possible that for some subjects, cotinine was detected as a result of exposures that occurred preceding the four days reported in the interview. The measured cotinine levels for self-reported nonsmokers ranged from 0 to 85 ng/ml (average, 8.84 ng/ml), with 92% of the values less than 20 ng/ml.

In a recent additional (unpublished) analysis of this study, Cummings (1994) examined ETS exposure at work among currently employed nonsmoking subjects (n=339) who did and did not report exposure to tobacco smoke in the home. Of currently employed nonsmokers, substantial percentages (81% and 76%, respectively) reported ETS exposure at work, both among those who

were exposed at home (n=122) and those who were not (n=217). Overall, exposure to ETS at home was not predictive of being exposed to ETS at work. Mean urinary cotinine values for employed nonsmoking subjects in the study were analyzed by self-reported exposure to tobacco smoke at work and at home. Subjects exposed both at work and at home had mean urinary cotinine (12.8 ng/ml) very similar to those exposed at home but not at work (11.0 ng/ml), with those exposed at work and not at home showing lower mean cotinine (7.5 ng/ml). As noted by the author, many of the subjects took time off work to attend the clinic where the study was conducted, and thus a stronger influence of home exposure on mean urinary cotinine is not surprising. Subjects reporting no exposure at work or at home had a mean urinary cotinine level (8.7 ng/ml) which is indicative of exposure to ETS.

*Coultas et al. (1987)*

Coultas *et al.* (1987) conducted a population-based household survey of respiratory disease in 2,029 Hispanic children and adults in New Mexico, in which salivary cotinine was measured for 1,360 nonsmokers and ex-smokers. Nonsmoking status was ascertained on the basis of self-reported smoking status and a salivary cotinine concentration of less than 20 ng/ml; the reported detection limit in this study was 0.78 ng/ml saliva. Exposure prevalences, estimated using data presented in the report, were: 39% for adults (18 years and older), 48% for adolescents (13-17 years), 45% for children (6-12 years), and 54% for infants and preschoolers (5 years of age and under). The mean salivary concentrations in the various age groups ranged from 0 (not detected) to 6.0 ng/ml.

The prevalence of a detectable level of cotinine was about 35% for those living in a nonsmoking household and increased with the number of cigarettes smoked by household members. In a multiple logistic regression model, the major determinants of a detectable level of cotinine in children were mother's smoking (odds ratio (OR) = 3.2), father's smoking (OR = 2.1), and the smoking of other household members (OR = 4.0; the other household smokers were primarily grandparents (41%), siblings (26%), or aunts and uncles (15%)). Among adults, the effects of spouse's smoking were smaller, with ORs of 1.3 and 1.4 for husband's and wife's smoking, respectively.

2.6.3.2 Studies of infants and children

Infants and young children are particularly susceptible to the adverse effects of ETS (See chapters on *Developmental and Reproductive Effects of Exposure to ETS*, and *Respiratory Health Effects of Exposure to ETS*). A number of studies have examined exposures of this population group (Greenberg *et al.*, 1989; Chilmonczyk *et al.*, 1990; Overpeck and Moss, 1991).

*Overpeck and Moss* (1991)

In 1988 the National Center for Health Statistics collected information on household exposure to ETS for a sample of 5,356 children five years of age and under (Overpeck and Moss, 1991). The information was obtained as part of the National Health Interview Survey, a continuous cross-sectional survey representing the household population of the United States (the authors report that the sample is representative of 86% of U.S. children of this age group). Overall, the survey found that about one-half of all U.S. children five years of age and under are exposed to tobacco

smoke constituents due to prenatal maternal smoking and/or are exposed to ETS from household members after birth. Of the total sample, 28% had both prenatal and postnatal exposure, 21% were exposed only after birth, with 1.2% exposed prenatally only.

Forty-two percent of the children were currently living in a household with a smoker. Of these children, a disproportionately high number were from homes comprising the lower income and educational categories. Children in families at the lowest income level category were almost twice as likely to live in a home with a current smoker (58%) compared to children in families at the highest income level (30%). More than twice as many children whose mothers had not completed high school (61%) were currently exposed to household smoke as compared to children whose mother had completed one year or more of college (28%).

*Greenberg et al. (1989)*

In a study of infant exposure to ETS, Greenberg *et al.* (1989) obtained detailed information on household smoking habits from mothers of 433 infants from a representative population of healthy neonates in central North Carolina during 1986 and 1987; infant urine samples were also collected. Approximately 55% (239) of the study infants lived in a household with at least one smoker. As determined from the questionnaire responses, 42% of the infants were exposed to ETS during the week preceding data collection, where exposure was defined as the production of smoke in the same room or vehicle as the infant. As in other studies, prevalence was higher when the metric of exposure was cotinine. Of the 433 infants, cotinine was detected in 60% of the urine samples. Measured concentrations ranged from 6 to 2,273 ng/mg creatinine, with a median concentration of 121 ng/mg creatinine. (see Section 2.4.2.1 for a discussion of cotinine to creatinine ratios).

*Chilmonczyk et al. (1990)*

In a large population-based study of infants receiving routine well-child care in private physicians' offices in the greater Portland, Maine area, Chilmonczyk *et al.* (1990) collected urine samples from 518 infants, 6- to 8-weeks of age, and obtained information on household smoking habits. Forty-one percent of the study population lived in households in which at least one household member smoked. Of the total sample, 80% had detectable urinary cotinine concentrations (concentrations less than 1 μg/L were reported as not detected), with concentrations greater than 2 μg/L in 64% of the samples. In the 305 households where no smoking was reported, 8% of the infants' urinary cotinine values were equal to or greater than 10 μg/L (on the basis of data in the study, the authors defined the concentration of 10 μg/L as a reasonable estimate of significant ETS absorption). Corresponding rates of urinary cotinine $\geq$10 μg/L were 44% in infants living in the 96 households where a member other than the mother smoked, 91% for those in the 43 households where only the mother smoked, and 96% for those in the 74 households where both the mother and another household member smoked.

## 2.6.4 Factors Influencing Exposure to ETS

Because data are not available to quantify trends in ETS exposure in California, this section examines trends in the prevalence of smoking, the results of legislative efforts to limit smoking, and other factors contributing to ETS exposure of the nonsmoker. Indirect evidence (*e.g.*,

smoking prevalence trends) suggest that exposure to ETS in California is declining and that ETS exposure prevalence in California may be lower than elsewhere in the U.S.

#### 2.6.4.1 Smoking Prevalence Trends: California versus U.S.

Data from 1965 to 1985 show that there has been a continual decline in smoking prevalence among U.S. adults, with an annual rate of decline of 0.5% over that time period and a 1.1% annual decrease between 1987 and 1990 (U.S. DHHS, 1989; CDC, 1992). In a 1991 survey of a representative sample of the U.S. civilian population (18 years and older), 49.8% of the population were ever-smokers and 25.7% were current smokers (CDC, 1993a). Comparative data for the U.S. and California indicate that both smoking prevalence and cigarette consumption are lower in California than in the rest of the U.S., and that the annual rate of decline in California has been somewhat more rapid over the last decade (Figures 2.6 and 2.7; Burns and Pierce, 1992; Pierce *et al*., 1994; CDHS, 1996). Limited information is available to determine whether there have been corresponding decreases in ETS exposures of nonsmokers, either nationwide or in California. Although smoking prevalence is clearly related to ETS exposures, other factors associated with smoking behavior that contribute to exposure of nonsmokers (*e.g.*, location of smoking) must also be considered.

#### 2.6.4.2 Smoking Prevalence Trends in Subpopulations

Although overall trends in smoking prevalence and other factors suggest that ETS exposure is decreasing, this may not be true for all population subgroups and/or the rate of decline may differ among different groups. Patterns of cigarette smoking in the U.S. have shifted over the years among sex, race, educational, and socioeconomic groups (Fiore *et al.*, 1989; Pierce *et al.*, 1989; U.S. DHHS, 1989; Overpeck and Moss, 1991), with differential impacts on ETS exposure of the nonsmoker. As one example, although the overall prevalence rates of smoking have declined among men and women during the last decade, smoking has decreased at a slower rate among women. In 1991, it was reported that the onset of smoking for females is occurring at younger ages and until recently, smoking initiation was increasing for the least educated females. As a result, the differential risk of ETS exposure of infants and children may have changed because of the smoking patterns among women with higher than average birth rates and those who spend more time with the developing child (Overpeck and Moss, 1991).

Teenagers are another important example of a population subgroup with smoking prevalence trends that differ from overall trends. Smoking prevalence among 16- to 18-year-olds declined fairly steadily from 1975 through 1981, and again from 1984 through 1988. After 1988, this trend was reversed and smoking prevalence among California adolescents began to increase; however, data for 1992 and 1993 indicate that the rising trend may not be continuing (Pierce *et al.*, 1994). This trend is significant because the teen years are the time when most people who become smokers start smoking. The age of smoking initiation in the U.S. has been declining and now peaks among 16- to 18-year-olds (Pierce *et al.*, 1994).

Hammond *et al.* (1995) measured occupational exposures to ETS in 25 diverse settings in Massachusetts, including offices and production areas, to evaluate the effectiveness of smoking restrictions in the workplace. Average weekly concentrations of nicotine, measured by 15 to 25 passive samplers in each worksite, were used to indicate ETS exposure. The researchers found that worksite smoking policies had a major effect on the ETS exposure, with median nicotine concentrations lowered by a factor of 6 by smoking restrictions and by a factor of 30 by smoking

bans in open offices at worksites. Non-office worksites were similarly affected, with restrictions lowering exposure by a factor of 3 and bans by a factor of 10.

2.6.4.3 Factors Affecting ETS Exposure in California: Proposition 99 Efforts

Within the last several years, there has been a major public health effort in California to reduce smoking prevalence and ETS exposure of the nonsmoker. These efforts are due, in part, to the Tobacco Tax and Health Protection Act (Proposition 99) passed in 1988 by voters in California. The measure raised the tax on cigarettes by 25 cents per pack, providing funding for a statewide health education program to reduce tobacco use. Funds from this measure have also supported the collection of data on smoking behavior; telephone surveys of California households have been conducted using both cross-sectional and longitudinal designs. These California Tobacco Surveys (CTS) as analyzed by Pierce *et al.* (1994) were the main sources used to estimate the prevalence trends described below.

Analyses of CTS data to evaluate the effectiveness of programs implemented as a result of the passage of Proposition 99 suggest that these programs have been effective in reducing smoking prevalence (Burns and Pierce, 1992; Pierce *et al.,* 1994). Among adults, smoking prevalence in California for the year before the tax increase (*i.e.*, 1987) was 26.8%; the 1990 estimate was 22.2%, a 17% decline in three years (Burns and Pierce, 1992); the 1995 estimate is 16.7% (CDHS, 1996) (Figure 2.6). More recent information indicates that the prevalence of smoking among adults 20 years and older has dropped even further, to an estimated 19.1% in 1993, while for adolescents 16 to 18 years old, prevalence is estimated to be 7.75% (based on 1990 data) (Pierce *et al.,* 1994). If the decline in smoking prevalence observed in California between 1988 and 1993 continues through the 1990s, smoking prevalence among Californian adults will be 10.2% by the year 1999. This rate of decline in smoking prevalence will not achieve the California Department of Health Services (CDHS) Tobacco Control Program's legislatively set goal of a 75% reduction in smoking prevalence (to 6.5%) by the year 1999 (Pierce *et al.,* 1994). Although the decline in smoking may fall short of the set goal, the program has been successful in reducing smoking prevalence among adults; the 1993 prevalence level was 16% lower than it would have been had the 1984 through 1988 pre-program trend continued.

A decline in per capita consumption of cigarettes in California has also been observed from 1980 through 1993 (Figure 2.7). Similar to the observations with respect to smoking prevalence, a sharp acceleration in the rate of decline in tobacco consumption was observed at the time of the Proposition 99 tax increase. As shown in Figure 2.7, the rate of change of per capita consumption appears to have leveled off following an initial rapid decline (Burns and Pierce, 1992). More recent information on cigarette consumption indicates that per capita consumption in 1992 was 5.34 packs per month, 13.82% lower than the 6.23 packs per month predicted if consumption trends before the passage of Proposition 99 had continued through 1992 (Glasscock *et al.,* 1992-93). Per capita cigarette consumption dropped even lower in 1993 to 4.84 packs per month (Pierce *et al.,* 1994). These declines have been attributed to the 1988 tax increase and subsequent tobacco education efforts.

Children have been a priority of the CDHS Tobacco Control Program's efforts to reduce ETS exposure and its associated health costs. The home is the primary location of exposure of young

children and efforts have been made to reduce exposure at this location. Data available for the last two years suggest that exposure of children is decreasing: in 1992, 75.5% of children 18 years of age and younger lived in a smokefree household; in 1993, this proportion had increased significantly to 80.4% ($p<0.05$) (Pierce *et al.,* 1994).

2.6.4.4 Factors Affecting ETS Exposure in California: Smoking Laws and Ordinances

As indicated in Section 2.6.2, the workplace represents an important ETS exposure location in California. Over the last several years, an increasing number of workplaces have adopted policies restricting smoking, and studies have shown that reported nonsmoker exposure to ETS decreases with increasing degree of worksite restriction on smoking (Borland *et al.,* 1992; Pierce *et al.,* 1994). More specifically, it is estimated that the percentage of indoor workers with smokefree workplaces (*i.e.*, smoking is prohibited in all areas) nearly doubled in California from 1990 to 1993, from 35% to 65%; in 1993, the proportion of workers covered by at least a work area ban on smoking (*i.e.*, smoking is prohibited in the work area) was 87.3% (Pierce *et al.,* 1994). Recent legislation (discussed below) can be expected to further lower these numbers. Thus, the relative importance of the workplace as an exposure location is expected to decline in California as more workplace restrictions are imposed through the enactment of new laws or implementation of smoking policies by the private sector.

Data available for California and the United States suggest that workplace exposure in California is less than in the country as a whole, although the different time periods for which the data are available and the rapid change in workplace smoking policies limit the conclusions that can be made. Approximately 36% of workers (smokers and nonsmokers) in California worked in a smokefree worksite (data for 1990), as compared to only 3% of workers in the U.S. population as a whole (data for 1986). Further, 71.3% of indoor workers in California reported some type of work-site smoking policy in 1990, compared with only 45% nationally in 1986 (Pierce and Hatziandreu, 1986).

In California, smoking in state-owned buildings and leased space, state prisons and hospitals, and state-owned passenger vehicles was banned in 1993 by Executive Order (W-42-93), with full compliance required by December 31, 1993 (Gov. Code, Section 19994.30). Restrictions on smoking in a wide range of workplaces in California went into effect on January 1, 1995, as the result of legislation (AB13 - Friedman) passed in 1994 and signed by Governor Pete Wilson. This addition to the California Labor Code (Section 6404.5) provides that “no employer shall knowingly or intentionally permit, and no person shall engage in, the smoking of tobacco products in an enclosed space at a place of employment.” All restaurants are included under the statute. Private residences are not included under the statute, except for those which are licensed as family day care homes, during the hours of operation and in those areas where children are present. The law specifies other “places of employment” which are not covered, including (for example): portions of hotels (designated lobby areas and guest rooms, and meeting rooms); bars and taverns; cabs of trucks; warehouses; and certain places of employment where fewer than five persons work. This workplace smoking prohibition could have substantial impact on ETS exposures in California.

In addition to limitations on smoking in the workplace, an increasing number of cities and counties in California have placed various types of restrictions on smoking. These include restrictions on smoking in city- and county-owned facilities, restaurants, workplaces, and other public locations; also included are restrictions on the sale or promotion of tobacco products, typically by restricting the location of vending machines, advertising, or sampling activities. As of July 1994, 77 cities and 16 counties in California have local ordinances which require all workplaces and all restaurants to be 100% smokefree (Americans for Nonsmokers' Rights, 1994). An additional 72 California cities have ordinances requiring 100% smokefree workplaces, and 91 have ordinances requiring 100% smokefree restaurants (California Smokefree Cities, 1994).

Smoking has also been prohibited in all day care centers and in private residences licensed as family day care homes during hours of operation (AB 615, 1993). A similar law, called the Pro-Children Act of 1994, was passed on the national level which prohibits smoking in any health care, day care, or early development services facility, and in facilities providing kindergarten, elementary or secondary education or library services to children (HR 1804, Section 1041, 1994).

#### 2.6.4.5 Other Factors Affecting ETS Exposure in California

Finally, other less quantifiable changes in smoking behavior may also be contributing to changing patterns of ETS exposure of the nonsmoker. For example, increased awareness of the potential health effects of ETS exposure and increased willingness of nonsmokers to object to smoking in their presence may result in changes in smoking behavior; for example, smokers may refrain from smoking in the presence of children, or may confine smoking to outdoor areas, even at home. Recent data indicate that half of all Californians surveyed voluntarily made their homes smokefree by 1993, and 20% had some household smoking restrictions, where smoking was permitted only in certain rooms or at certain times. The number of smokers reporting a smokefree home increased from 18.8% of those surveyed in 1992 to 27.1% of those surveyed in 1993 (Pierce *et al.*, 1994). Smokers who had young children living in the home were more likely than smokers living without children to report a smokefree home.

## 2.7 Chapter Summary and Conclusions

ETS can be a major source of indoor air contaminants in environments where smoking occurs. Composed of both sidestream and mainstream smoke, ETS contains over 50 compounds identified as carcinogens and five identified as developmental and reproductive toxicants (under Proposition 65). Although changes in cigarette design (*e.g.*, filters) have had substantial impact on the composition of mainstream smoke, these changes have had little impact on the composition of sidestream smoke, the principal contributor to ETS.

In many indoor environments that have been monitored, ETS has been detected, and studies consistently show that concentrations of a number of toxic and carcinogenic constitutents (*e.g.*, PAHs, nitrosamines) are elevated in environments where smoking is allowed as compared to those where it is not. Levels of ETS encountered by exposed nonsmokers, including infants and children, during their daily activities are sufficiently high that ETS constituents have been detected in their urine, blood, and saliva.

Although the presence of cotinine (and other biomarkers) in the fluids of nonsmokers provides evidence of the degree of exposure to ETS, the ratio of cotinine levels in ETS-exposed nonsmokers to those in smokers may not be indicative of the exposure ratio for other ETS constituents. The ratio of sidestream to mainstream emissions is not constant for all constituents, and indoor air measurements suggest that different constituents are removed from air at differing rates. In addition, differences exist in the uptake and metabolism of individual constituents.

Although nicotine and cotinine are typically used as markers of exposure to ETS, a limited number of studies have examined other biomarkers more directly related to a biological effect. For example, hemoglobin adducts of 4-aminobiphenyl (a human carcinogen) have been used as biomarkers of exposure in some epidemiologic studies. More work is needed to expand the use of biomarkers such as hemoglobin adducts of 4-aminobiphenyl which have relevance to the health effects under study.

Questionnaires, widely used in assessing ETS exposure, provide accurate qualitative information on self-reported exposure to spousal, parental or other household smoking, although quantitative information is less reliable. Because of the importance of the workplace and other indoor locations for adult exposures, misclassification may occur when exposure status is based solely on exposure at home. In addition, biomarker studies have shown that a proportion of subjects reporting no exposure to ETS (at work or at home) have measurable biomarker concentrations, indicating that the subject either forgot or was not aware of his exposure. Thus, biomarker measurements may be useful in validating the questionnaire-based exposure status of ETS-exposed subjects.

Californians spend a major portion of their time indoors, where most exposure to ETS occurs. Estimates from surveys conducted in the late 1980s indicated that 43% of the nonsmoking adult population was exposed to ETS on any given day. In these surveys, ETS exposure was reported for approximately 40% of all children under the age of 12, and for approximately 64% of nonsmoking adolescents. The most significant location of exposure for adult nonsmokers was the workplace, although other locations (home, other indoor, and outdoors) were also important. For infants and children, the home was the most significant exposure location. Thus, at the time of these surveys, a significant proportion of the California population was exposed to ETS.

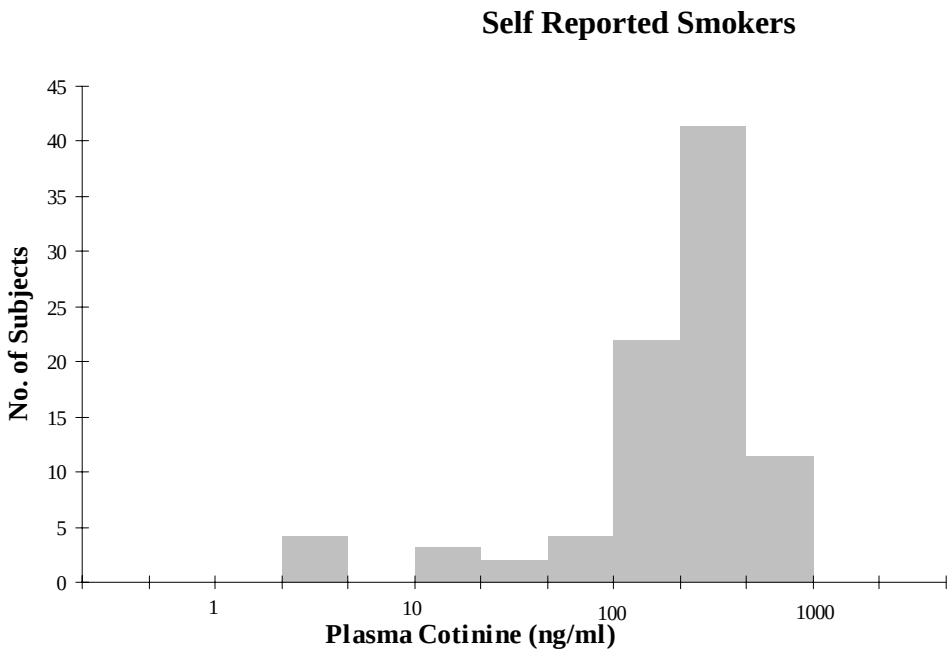
Overall trends in smoking prevalence and other factors, including an increasing number of restrictions on smoking in the workplace and public locations, suggest that exposure to ETS is decreasing in California. These decreases can be attributed, in part, to programs implemented under California's Proposition 99, passed in 1988; further decreases are expected due to the passage of AB 13, effective in January 1995, which restricts smoking in most workplaces. Lower rates of smoking and per capita consumption of cigarettes in California as compared to the entire U.S. suggest that exposure to ETS is lower in California than nationwide. However, certain subpopulations (*e.g.*, low income women, teenagers) may be experiencing different smoking trends, which may affect ETS exposure rates of others (*e.g.*, infants). Because the teen years are the time when most people who become smokers start smoking, continued surveillance of this subpopulation is needed to identify public health efforts which will further reduce ETS exposures in California.

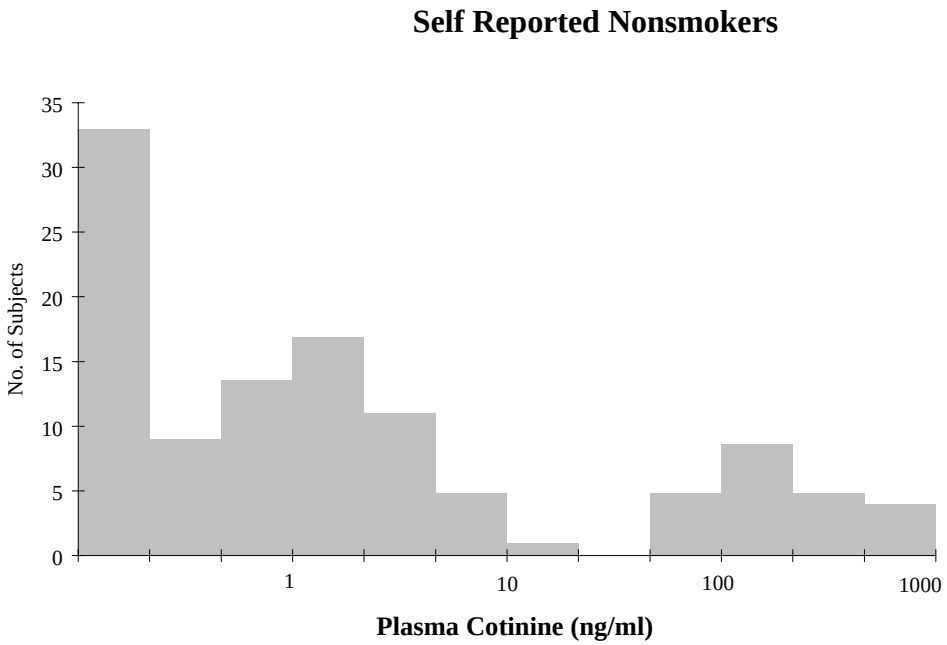
**Exposure Measurement and Prevalence**

Despite the decreasing prevalence of ETS exposure of California nonsmokers due to increasing restrictions on smoking in the workplace and public locations, exposure of young Californians, especially infants and young children, is of continuing public health concern. The timing and routes of infants' exposure to tobacco smoke constituents are unique, in that they can be exposed prenatally if the mother smokes or is exposed to ETS during pregnancy; postnatal exposure may occur directly through inhalation and indirectly, from ingestion of breast milk. Studies of nursing infants indicate that mother's milk contributes significantly to urinary cotinine levels in nursing infants. It is possible that other ETS contituents are also present in breast milk and ingested by the infant. Persons exposed as infants to potentially large doses (relative to their small bodyweight) of the carcinogenic constituents in ETS may face a relatively higher risk due to this early exposure. Those exposed *in utero* and in early life to the developmental toxicants found in ETS may be at higher risk for a number of negative health outcomes. With the home as the most significant ETS exposure location for these age groups, educational efforts for women who are pregnant (or plan to become pregnant) and their partners about reducing their children's ETS exposure are warranted.

The potential adverse health effects resulting from these exposures are addressed in the other chapters of this assessment.

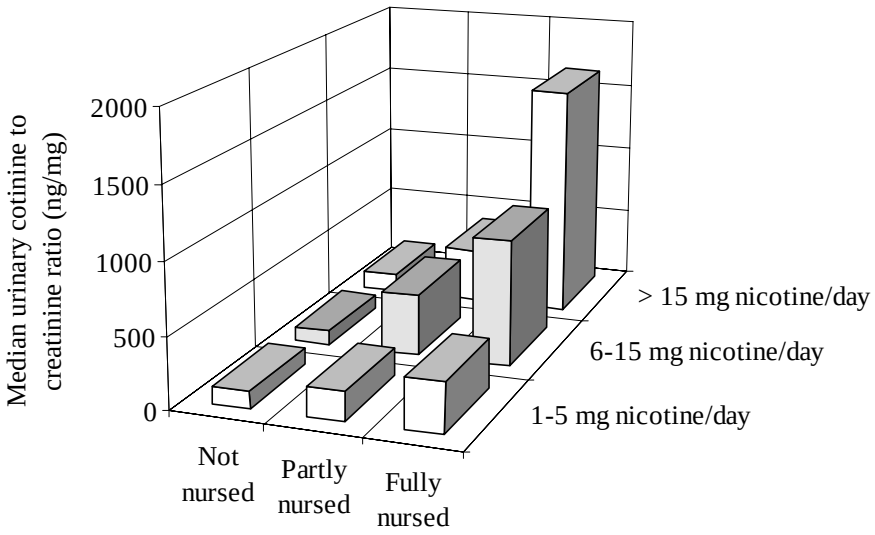
**FIGURE 2.1**
**PLASMA CONTININE CONCENTRATIONS**
**IN SELF-REPORTED SMOKERS AND NONSMOKERS**



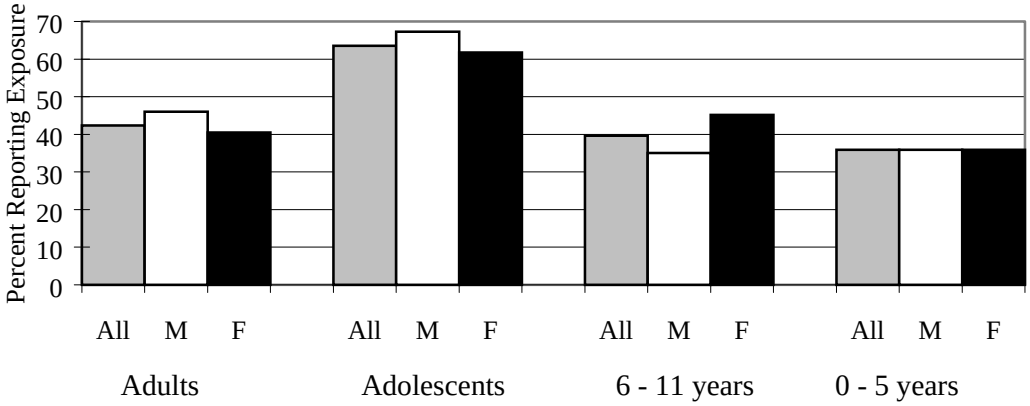

From Jarvis *et al*., 1987, with permission

**FIGURE 2.2**
**URINARY COTININE OF BREAST-FED INFANTS IN RELATION TO MATERNAL CIGARETTE SMOKING**




Source: Schulte-Hobein *et al.*, 1992

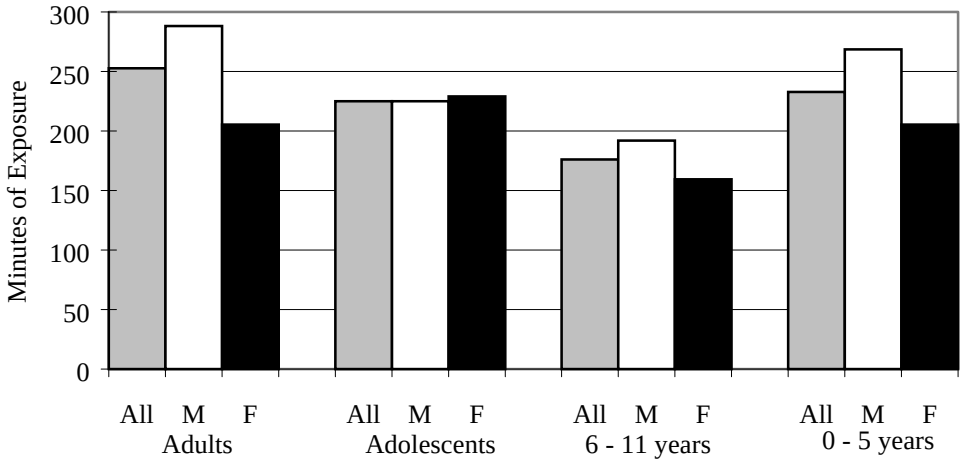
**FIGURE 2.3**
**PERCENT OF NONSMOKERS IN CALIFORNIA**
**REPORTING ETS EXPOSURE***




*Smoking status of 6 - 11 year olds not determined in the study. Data from 1989-1990.

Source: Jenkins *et al*., 1992; Lum, 1994b

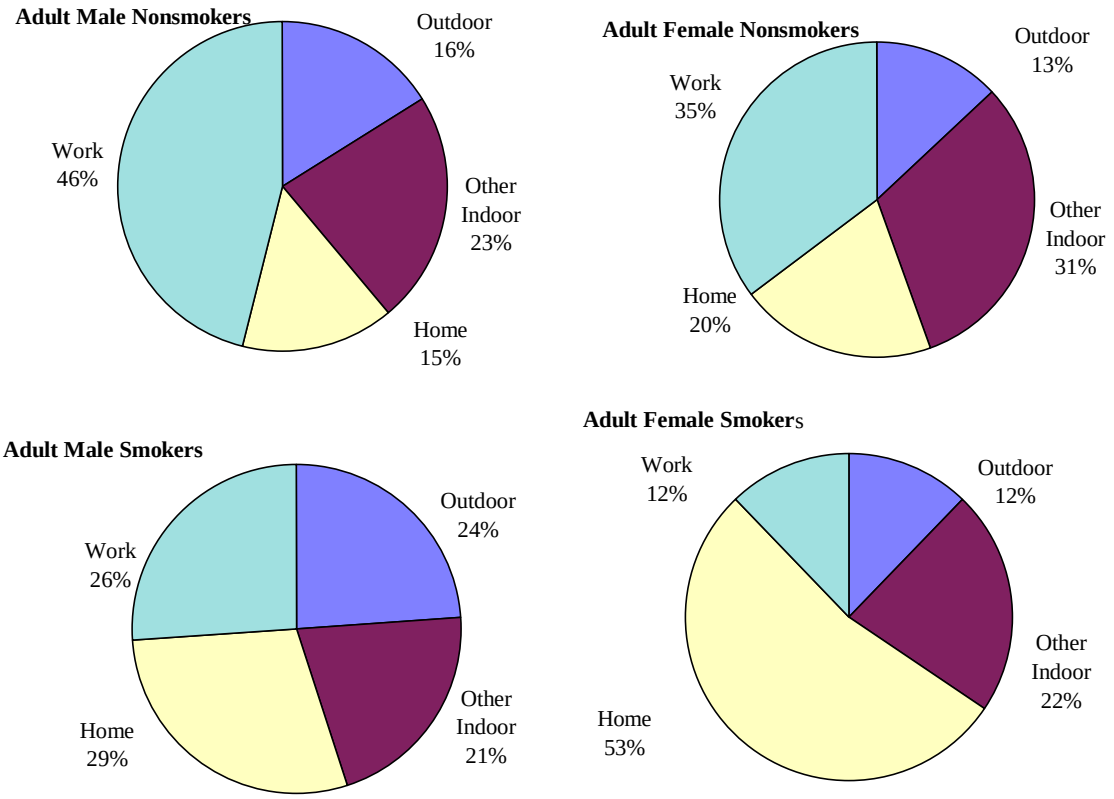
**FIGURE 2.4**
**REPORTED AVERAGE DAILY ETS EXPOSURE DURATION***
**IN CALIFORNIA**




*Exposure duration is the average value for individuals reporting ETS exposure. For adults, values are for nonsmokers only. For adolescents, values are for both smokers and nonsmokers. The smoking status of 6 - 11 year olds was not determined. Data from 1989-1990.

Source: Lum, 1994a,b

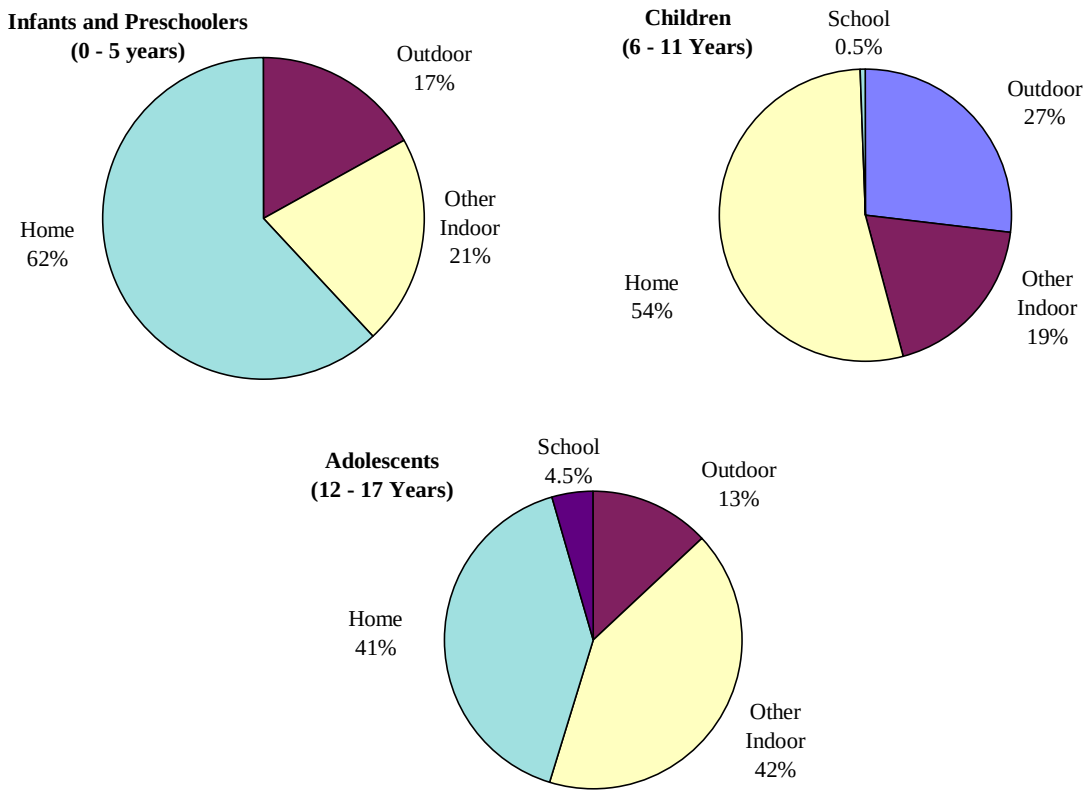
**FIGURE 2.5**
**RELATIVE PERSON-MINUTES OF ETS EXPOSURE***
**IN DIFFERENT ENVIRONMENTS**




*Percentages may not add to 100 due to rounding errors. Data from 1989-1990.

Source: Lum, 1994a,b

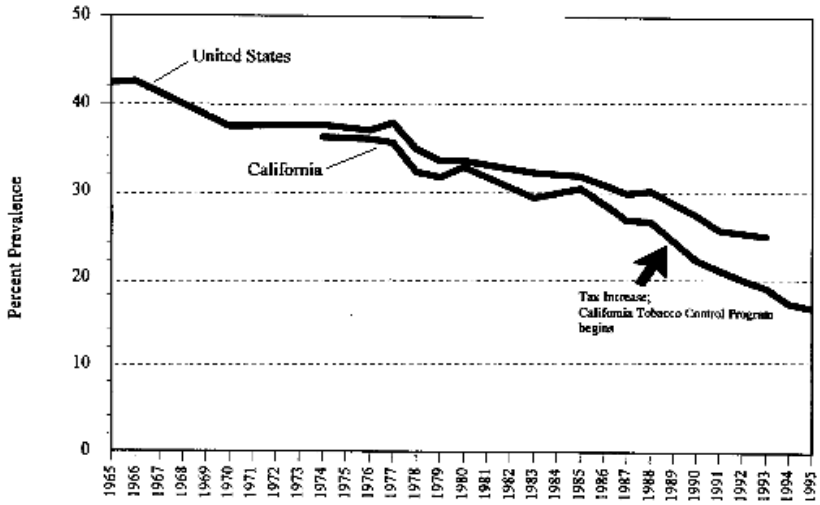
**FIGURE 2.5 (continued)**
**RELATIVE PERSON-MINUTES OF ETS EXPOSURE***
**IN DIFFERENT ENVIRONMENTS**




*Percentages may not add to 100 due to rounding errors. Data from 1989-1990.

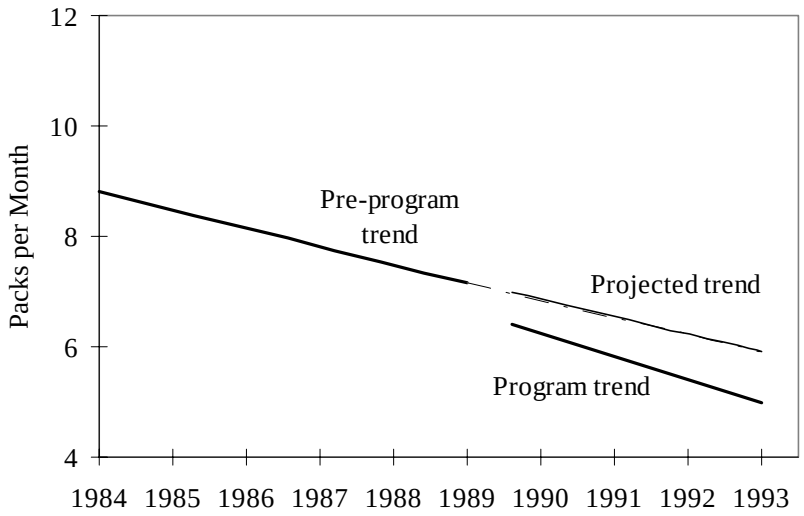
Source: Lum, 1994a,b

**FIGURE 2.6**
**ADULT SMOKING PREVALENCE**
**CALIFORNIA AND THE UNITED STATES 1965-1995**




Source: California Department of Health Services, 1996

**FIGURE 2.7**
**LINEAR TREND IN PER CAPITA CONSUMPTION OF CIGARETTES IN CALIFORNIA BEFORE AND AFTER PROPOSITION 99 AND TAXATION PROGRAM**




Source: Pierce *et al.*, 1994

**TABLE 2.1**

**INFLUENCE OF PUFF VOLUME AND FILTER VENTILATION ON DELIVERIES OF PARTICULATE MATTER AND CARBON MONOXIDE IN MAINSTREAM AND SIDESTREAM SMOKE**

| | | Milligrams per Cigarette and SS/MS Ratio | | | | | |
|---|---|---|---|---|---|---|---|
| | Number | | Particulate Matter | | Carbon Monoxide | | |
| **Variable**[a] | **of Puffs** | **MS** | **SS** | **SS/MS** | **MS** | **SS** | **SS/MS** |
| Puff Volume | | | | | | | |
| None, free burn | 0 | -- | 23 | -- | -- | 58 | -- |
| 17.5 cc | 9.6 | 29 | 23 | 0.8 | 9 | 63 | 7 |
| 35 cc | 8.7 | 46 | 20 | 0.4 | 19 | 50 | 2.6 |
| 50 cc | 7.4 | 55 | 21 | 0.4 | 20 | 56 | 2.8 |
| Filter Ventilation[b] | | | | | | | |
| 0% | 8.7 | 46 | 20 | 0.4 | 19 | 50 | 2.6 |
| 33% | 8.8 | 32 | 21 | 0.6 | 13 | 49 | 3.8 |
| 48% | 9.8 | 21 | 21 | 1.0 | 7 | 58 | 8.3 |
| 83% | 10.6 | 12 | 21 | 1.8 | 2 | 56 | 2.8 |

Browne *et al*. (1980)

[a] USA blend cigarette, FTC smoking conditions unless otherwise noted.
[b] Percent of mainstream puff air entering through periphery of filter.

**TABLE 2.2**
**CHEMICAL CONSTITUENTS OF TOBACCO SMOKE THAT HAVE BEEN CLASSIFIED OR IDENTIFIED AS TO THEIR CARCINOGENICITY, REPRODUCTIVE TOXICITY OR OTHER HEALTH HAZARD**

| COMPOUND | IARC CLASSIFICATION[a] | U.S. EPA CLASSIFICATION[b] | CAL/EPA PROP 65[c]//TAC[d] |
|---|---|---|---|
| ***Organic Compounds*** | | | |
| Acetaldehyde | 2B | B2 | yes//yes |
| Acetamide | 2B | | yes//yes |
| Acrolein | 3 | C | --- //yes |
| Acrylonitrile | 2A | B1 | yes//yes |
| 4-Aminobiphenyl | 1 | | yes//yes |
| Aniline | 3 | B2 | yes//yes |
| o-Anisidine | 2B | | yes//yes |
| Benz[a]anthracene | 2A | B2 | yes//yes |
| Benzene | 1 | A | yes//yes |
| Benzo[b]fluoranthene | 2B | B2 | yes//yes |
| Benzo[j]fluoranthene | 2B | | yes//yes |
| Benzo[k]fluoranthene | 2B | B2 | yes//yes |
| Benzo[a]pyrene | 2A | B2 | yes//yes |
| 1,3-Butadiene | | B2 | yes//yes |
| Captan | 3 | | yes//yes |
| Carbon disulfide[e] | | | yes//yes |
| Carbon monoxide[e] | | | yes//--- |
| Chrysene | 3 | B2 | yes//yes |
| DDT | 2B | | yes//--- |
| Dibenz[a,h]acridine | 2B | | yes//yes |
| Dibenz[a,j]acridine | 2B | | yes//yes |
| Dibenz[a,h]anthracene | 2A | B2 | yes//yes |

Sources: ARB (1993); IARC (1985, 1986, 1987, 1992); California Code of Regulations (1994); U.S. EPA (1994)

[a] International Agency for Research on Cancer (IARC) Classification: 1, carcinogenic to humans; 2A, probably carcinogenic to humans; 2B, possibly carcinogenic to humans; 3, not classifiable as to its carcinogenicity to humans.

[b] U.S. EPA Classification: A, human carcinogen; B1, probable human carcinogen (primarily on the basis of epidemiological data); B2, probable human carcinogen (primarily on the basis of animal data); C, possible human carcinogen.

[c] Chemicals listed under Proposition 65 are known to the State to cause cancer or reproductive toxicity (California Health and Safety Code Section 25249.5 *et seq*.).

[d] Substances identified as Toxic Air Contaminants by the Air Resources Board (ARB), pursuant to the provisions of AB 1807 and AB 2728 (includes all Hazardous Air Pollutants listed in the Federal Clean Air Act Amendments of 1990).

[e] Reproductive toxicant

**TABLE 2.2 (continued)**
**CHEMICAL CONSTITUENTS OF TOBACCO SMOKE THAT HAVE BEEN CLASSIFIED OR IDENTIFIED AS TO THEIR CARCINOGENICITY, REPRODUCTIVE TOXICITY OR OTHER HEALTH HAZARD**

| COMPOUND | IARC CLASSIFICATION[a] | U.S. EPA CLASSIFICATION[b] | CAL/EPA PROP 65[c]/TAC[d] |
|---|---|---|---|
| ***Organic Compounds*** | | | |
| 7H-Dibenzo[c,g]carbazole | 2B | | yes//yes |
| Dibenzo[a,e]pyrene | 2B | | yes//yes |
| Dibenzo[a,h]pyrene | 2B | | yes//yes |
| Dibenzo[a,i]pyrene | 2B | | yes//yes |
| Dibenzo[a,l]pyrene | 2B | | yes//yes |
| 1,1-Dimethylhydrazine | 2B | | yes//yes |
| 1-Naphthylamine | 3 | | yes//--- |
| 2-Naphthylamine | 1 | | yes//--- |
| Nicotine[e] | | | yes//--- |
| 2-Nitropropane | 2B | | yes//yes |
| N-Nitrosodi-n-butylamine | 2B | B2 | yes//--- |
| N-Nitrosodiethanolamine | 2B | B2 | yes//--- |
| N-Nitrosodiethylamine | 2A | B2 | yes//--- |
| N-Nitroso-n-methylethylamine | 2B | B2 | yes//--- |
| N'-Nitrosonornicotine | 2B | | yes//--- |
| N-Nitrosopiperidine | 2B | | yes//--- |
| N-Nitrosopyrrolidine | 2B | | ---//yes |
| Styrene | 2B | | ---//yes |
| Toluene[e] | | | yes//yes |
| 2-Toluidine | 2B | | yes//yes |
| Urethane | 2B | | yes//--- |
| Vinyl chloride | 1 | | yes//yes |

Sources: ARB (1993); IARC (1985, 1986, 1987, 1992); California Code of Regulations (1994); U.S. EPA (1994)

[a] International Agency for Research on Cancer (IARC) Classification: 1, carcinogenic to humans; 2A, probably carcinogenic to humans; 2B, possibly carcinogenic to humans; 3, not classifiable as to its carcinogenicity to humans.

[b] U.S. EPA Classification: A, human carcinogen; B1, probable human carcinogen (primarily on the basis of epidemiological data); B2, probable human carcinogen (primarily on the basis of animal data); C, possible human carcinogen.

[c] Chemicals listed under Proposition 65 are known to the State to cause cancer or reproductive toxicity (California Health and Safety Code Section 25249.5 *et seq*.).

[d] Substances identified as Toxic Air Contaminants by the Air Resources Board (ARB), pursuant to the provisions of AB 1807 and AB 2728 (includes all Hazardous Air Pollutants listed in the Federal Clean Air Act Amendments of 1990).

[e] Reproductive toxicant

**TABLE 2.2 (continued)**
**CHEMICAL CONSTITUENTS OF TOBACCO SMOKE THAT HAVE BEEN CLASSIFIED OR IDENTIFIED AS TO THEIR CARCINOGENICITY, REPRODUCTIVE TOXICITY OR OTHER HEALTH HAZARD**

| COMPOUND | IARC CLASSIFICATION[a] | U.S. EPA CLASSIFICATION[b] | CAL/EPA PROP 65[c]/TAC[d] |
|---|---|---|---|
| ***Inorganic compounds*** | | | |
| Arsenic | 1 | A | yes//yes |
| Cadmium | 2A | B1 | yes//yes |
| Chromium V1 | 1 | A | yes//yes |
| Lead[e] | 2B | B2 | yes//yes |
| Nickel | 1 | A | yes//yes |

Sources: ARB (1993); IARC (1985, 1986, 1987, 1992); California Code of Regulations (1994); U.S. EPA (1994)

[a] International Agency for Research on Cancer (IARC) Classification: 1, carcinogenic to humans; 2A, probably carcinogenic to humans; 2B, possibly carcinogenic to humans; 3, not classifiable as to its carcinogenicity to humans.

[b] U.S. EPA Classification: A, human carcinogen; B1, probable human carcinogen (primarily on the basis of epidemiological data); B2, probable human carcinogen (primarily on the basis of animal data); C, possible human carcinogen.

[c] Chemicals listed under Proposition 65 are known to the State to cause cancer or reproductive toxicity (California Health and Safety Code Section 25249.5 *et seq*.).

[d] Substances identified as Toxic Air Contaminants by the Air Resources Board (ARB), pursuant to the provisions of AB 1807 and AB 2728 (includes all Hazardous Air Pollutants listed in the Federal Clean Air Act Amendments of 1990).

[e] Reproductive toxicant

**TABLE 2.3**

**MEAN CONCENTRATIONS OF NICOTINE AND COTININE IN THE SALIVA, PLASMA, AND URINE OF ETS - EXPOSED VOLUNTEERS[a]**

| | Saliva (ng/ml) | | Plasma (ng/ml) | | Urine (ng/mg creatinine) | |
|---|---|---|---|---|---|---|
| **Time** | **Nicotine** | **Cotinine** | **Nicotine** | **Cotinine** | **Nicotine** | **Cotinine** |
| Minutes of exposure | | | | | | |
| 0 (baseline) | 3 | 1.0 | 0.2 | 0.9 | 17 | 14 |
| 40 | 830 | 1.1 | 0.3 | 0.9 | --[b] | --- |
| 60 | 880 | 2.1 | 0.3 | 1.2 | -- | -- |
| 80 | 730 | 1.4 | 0.5 | 1.3 | 84 | 28 |
| Minutes post exposure | | | | | | |
| 30 | 148 | 1.7 | 0.4 | 1.8 | -- | -- |
| 150 | 17 | 3.1 | 0.7 | 2.9 | 100 | 46 |
| 240 | 3 | 2.0 | 1.1 | 3.3 | -- | -- |
| 300 | 7 | 3.5 | 0.6 | 3.4 | 48 | 55 |

Source: Hoffman *et al.* (1984)

[a] Individuals were exposed to ETS generated from continuous smoking of 4 cigarettes by machine. The air concentration of nicotine stabilized at approximately 280 ug/m$^3$ within 10 to 15 minutes.

[b] Samples not taken for this exposure interval.

**TABLE 2.4**
**COMPARISON OF BIOMARKERS IN**
**UNEXPOSED AND ETS-EXPOSED NONSMOKERS, AND ACTIVE SMOKERS[a]**

| Biochemical parameter | Unexposed Nonsmokers n = 46 Mean value | % of active smokers' value | ETS-Exposed Nonsmokers n = 54 Mean value | % of active smokers' value | Active smokers (n = 94) Mean value |
|---|---|---|---|---|---|
| CO in expired air (ppm [mg/m$^3$]) | 5.7 [6.5] | 27 | 5.5 [6.3] | 26 | 20.8 [24] |
| | | | | | |
| COHb (%) | 0.9 | 23 | 0.8 | 21 | 3.9 |
| | | | | | |
| Nicotine (ng/ml) | | | | | |
| in plasma | 1.0 | 7 | 0.8 | 5.4 | 14.8 |
| in saliva | 3.8 | 0.6 | 5.6 | 0.8 | 672.5 |
| in urine | 3.9 | 0.2 | 12.1* | 0.7 | 1749.9 |
| | | | | | |
| Cotinine (ng/ml) | | | | | |
| in plasma | 0.8 | 0.3 | 2.0* | 0.7 | 275.2 |
| in saliva | 0.7 | 0.2 | 2.5** | 0.8 | 309.9 |
| in urine | 1.6 | 0.1 | 7.7** | 0.6 | 1391.0 |
| | | | | | |
| Thiocyanate (µmol/l) | | | | | |
| in saliva | 48 | 39 | 53 | 43 | 123 |
| in plasma | 1270 | 52 | 1327 | 54 | 2450 |
| in urine | 73 | 47 | 77 | 50 | 155 |

[a] From IARC (1986) using data from Jarvis and Russell (1984).
* indicates $p<0.01$ between exposed and unexposed nonsmokers
** indicates $p<0.001$ between exposed and unexposed nonsmokers

**TABLE 2.5**

**CUT-OFF, SENSITIVITY AND SPECIFICITY OF BIOMARKERS FOR DISCRIMINATING TRUE SMOKING STATUS[a]**

| Biomarkers | Cut-off Value | % Smokers Detected | % Nonsmokers Detected | 95% CI for % Accuracy |
|---|---|---|---|---|
| Carbon Monoxide | | | | |
| ECO (ppm) | 8.0 | 90 | 89 | 86.2-91.7 |
| COHb (%) | 1.6 | 86 | 92 | 83.0-89.2 |
| Nicotine (ng/ml) | | | | |
| Plasma | 2.3 | 88 | 99 | 89.4-93.8 |
| Saliva | 21.8 | 90 | 99 | 91.6-95.2 |
| Urine | 58.6 | 89 | 97 | 93.3-96.3 |
| Cotinine (ng/ml) | | | | |
| Plasma | 13.7 | 96 | 100 | 98.3-99.1 |
| Saliva | 14.2 | 96 | 99 | 98.5-99.3 |
| Urine | 49.7 | 97 | 99 | 98.4-99.2 |
| Thiocyanate | | | | |
| Plasma (μmol/l) | 78.0 | 84 | 91 | 81.1-87.9 |
| Saliva (mmol/l) | 1.64 | 81 | 71 | 66.0-76.0 |
| Urine (μmol/l) | 118.0 | 59 | 89 | 67.0-77.0 |

Jarvis *et al*. (1987), with permission

[a] True smokers were those who reported smoking cigarettes, pipes, or cigars (n = 90) and 21 “deceivers.” Non-smokers were the self-reported non-smokers minus the deceivers (n = 100).

[b] Accuracy defined as overall % correct classification, and estimated for a population with equal proportions of smokers and nonsmokers.

**TABLE 2.6**

**STUDIES OF COTININE MEASUREMENTS IN SELF-REPORTED NONSMOKERS AND CRITERIA USED TO DISTINGUISH SMOKERS FROM NONSMOKERS**

| | | | Self-Reported Nonsmokers | | |
|---|---|---|---|---|---|
| **Study** | **Marker** | **Assay[a]** | **Sample Size** | **Percent Misclassified[b]** | **Criteria (ng/ml)** |
| Wald *et al.* (1986) | Urinary cotinine | RIA | 221 | 0.9 | --[c] |
| Cummings *et al.* (1990) | Urinary cotinine | HPLC | 669 | 0.9 | 90 |
| Pojer *et al.* (1984) | Plasma cotinine | GC | 181 | 3.3 | 42 |
| Jarvis and Russell (1984) | Plasma cotinine | GC | 215 | 9.8 | 20 |
| Lee (1987) | Saliva cotinine | GC | 808 | 2.5 | 30 |
| Pierce *et al.* (1987) | Saliva cotinine | GC | 622 | 7.4 | 25 |
| Coultas *et al.* (1988) | Saliva cotinine | RIA | 683 | 6.0 | 20 |
| Haddow *et al.* (1988) | Serum cotinine | RIA | 1,508 | 1.9 | 10 |
| Riboli *et al.* (1990) | Urinary cotinine | RIA | 1,369 | 3.4 | 50[d] |
| Wagenknecht *et al.* (1991) | Serum cotinine | RIA | 3,445 | 4.2 | 14 |
| Perez-Stable *et al.* (1992) | Serum cotinine | GC | 189 | 6.3 | 14 |

Modified from Perez-Stable *et al.* (1992)

[a] Abbreviations: GC, gas chromatography; RIA, radioimmunoassay; HPLC, high pressure liquid chromatography

[b] percentage of self-reported nonsmokers with cotinine levels above criteria listed

[c] >10% smokers' median

[d] ng/mg creatinine

**TABLE 2.7**
**CONCENTRATIONS OF NICOTINE AND COTININE IN MOTHERS' MILK**

| Study | Constituent | Concentration (ng/ml) Mean (SD) | Range | Study population | Comments |
|---|---|---|---|---|---|
| **Smokers** | | | | | |
| Ferguson *et al.* (1976) | Nicotine | 91 | 20-512 | 28 samples from 9 women were collected. Most subjects smoked 0.5-1.5 packs/day. | Concentrations of nicotine varied greatly in samples from the same donor taken at different times of the day. |
| Hardee *et al*. (1983) | Nicotine<br>Cotinine | --<br>-- | 20-150<br>50-300 | Samples from 3 women | |
| Luck and Nau (1984) | Nicotine<br>Cotinine | --<br>-- | 2-62<br>12-222 | 44 samples from 23 women were collected. The number of cigarettes smoked per day ranged from 5-40. The time between the last cigarette smoked and the collection of samples ranged from 0.25 to 4.0 hours. | |
| Woodward *et al*. (1986) | Nicotine<br>Cotinine | 8.3 ( ± 13.0)<br>84.4 (± 93.3) | --<br>-- | Samples from 20 women smoking 1-20 cigarettes 48 hours prior to sample collection. | |
| | Nicotine<br>Cotinine | 32.6 (± 26.6)<br>234 (± 110.8) | --<br>-- | Samples from 7 women smoking ≥21 cigarettes 48 hours prior to sample collection. | |

**TABLE 2.7 (continued)**
**CONCENTRATIONS OF NICOTINE AND COTININE IN MOTHERS' MILK**

| Study | Constituent | Concentration (ng/ml) Mean (SD) | Range | Study population | Comments |
|---|---|---|---|---|---|
| Luck and Nau (1987) | Nicotine | 8.3 (± 16) | -- | Samples from all nursing periods within 24 hours. Samples from 10 women smoking 1-10 cigarettes/day. | Determinants of milk nicotine levels were the number of cigarettes consumed during the period immediately prior to nursing and the time interval between the last cigarette smoked and nursing. |
| | Cotinine | 76 (± 33) | -- | | |
| | Nicotine | 28 (± 21) | -- | Samples from 11 women smoking 11-20 cigarettes/day. | |
| | Cotinine | 125 (± 60) | -- | | |
| | Nicotine | 48 (± 25) | -- | Samples from 13 women smoking 21-40 cigarettes/day. | |
| | Cotinine | 230 (± 62) | -- | | |
| Labrecque *et al*. (1989) | Cotinine | 195 (± 122) | 28-256 | Samples from 33 mothers smoking on average 9.8 cigarettes in the previous 24 hours. | Cotinine levels were significantly related to the number of cigarettes smoked by the mother in the previous 24 hours (r=0.69, p=0.0002). |
| Schulte-Hobein *et al*. (1992) | Cotinine | 264 | 0-738 | Samples from 69 mothers who smoked more than 5 cigarettes per day during pregnancy and continued smoking after childbirth. Samples (total = 238) were collected at monthly intervals for 1 year. | Cotinine concentrations were dependent on nicotine consumption as reported by mothers (r=0.56, p <0.0001) |

**TABLE 2.7 (continued)**
**CONCENTRATIONS OF NICOTINE AND COTININE IN MOTHERS' MILK**

| Study | Constituent | Concentration (ng/ml) Mean (SD) | Range | Study population | Comments |
|---|---|---|---|---|---|
| Dahlstrom *et al*. (1990) | Nicotine | 5.16 | 0.9-17.3 | Samples from 22 mothers abstaining from cigarettes for 12 hours | |
| | Cotinine | 112 | 18-388 | | |
| | Nicotine | 55 | 10-140 | Samples from 21 mothers 30 minutes after smoking at least 1 cigarette | |
| | Cotinine | 136 | 31-467 | | |
| Schwartz-Bickenbach *et al*. (1987) | Cotinine | 91-322[a] | 41-580 | Samples from 6 mothers smoking < 20 cigarettes/day. | |
| | Cotinine | 305-439[a] | 0-635 | Samples from 15 mothers smoking >20 cigarettes/day. | |
| **Nonsmokers** | | | | | |
| Hardee *et al.* (1983) | Nicotine | -- | 1-7 | Samples from 10 nonsmoking women. | Detected in 3 women reporting workplace exposure to ETS |
| | Cotinine | -- | | | |
| Schulte-Hobein *et al*. (1992) | Cotinine | 0 | 0-277 | Samples from 69 nonsmoking women. | Detected in 7 women who lived with partners who smoked. |

[a] Range of median concentrations measured 1 week to 6 months post partum.

**TABLE 2.8**
**STUDIES WITH INFORMATION ON ETS EXPOSURE PREVALENCE IN CALIFORNIA AND THE U.S.: ADULTS AND ADOLESCENTS**

| Study | Year/ Location | Description | Measure of Exposure | Exposure Prevalence (age) | Comments |
|---|---|---|---|---|---|
| **California** | | | | | |
| Friedman *et al.* (1983) | 1979-1980<br>Oakland and San Francisco, California | 37,881 nonsmoking adults from the Kaiser-Permanente Medical Care Program. | Self-report | 63.3% (≥18yrs) | Exposed individuals defined as those reporting an average exposure to ETS of one or more hours per week. |
| Wiley *et al.* (1991a)<br>Jenkins *et al.* (1992) | 1987-1988 California (statewide) | 1,579 English-speaking adult members of house holds with telephones. | Self-report interview) | 43% (≥18 yrs)<br>64% (12-17 yrs) | Activity-pattern study. Exposed individuals defined as those reporting exposure to ETS on the day preceding the interview. Prevalence given for nonsmokers. |
| Burns and Pierce (1992) | 1990-1991 California (statewide) | Telephone interviews with 32,135 English- and Spanish-speaking households | Interview | 36.5% (12-17 yrs) | Exposed individuals defined as those living in a household with at least one smoker. |

**TABLE 2.8 (continued)**
**STUDIES WITH INFORMATION ON ETS EXPOSURE PREVALENCE IN CALIFORNIA AND THE U.S.: ADULTS AND ADOLESCENTS**

| Study | Year/ Location | Description | Measure of Exposure | Exposure Prevalence (age) | Comments |
|---|---|---|---|---|---|
| **Other U.S. areas** | | | | | |
| Coultas *et al.* (1987) | 1984-1985 Albuquerque, New Mexico | 698 nonsmoking adults from 727 randomly selected Hispanic households. | Salivary cotinine | 39% (≥18 yrs)<br>48% (13-17 yrs) | Exposed individuals defined as those with salivary cotinine concentrations ranging from 0.78 - 20 ng/ml. |
| Cummings *et al.* (1990) | 1986 Buffalo, New York | 663 nonsmoking adults attending a cancer-screening clinic | Self-report (interview) | 76% (≥18 yrs) | Exposed individuals defined as those reporting any exposure to ETS during the 4-day period preceding the interview. |
| | | | Urinary cotinine | 91% (>18 yrs) | Exposed individuals defined as those with detectable concentrations of cotinine (detection limit not given). |

**TABLE 2.8 (continued)**
**STUDIES WITH INFORMATION ON ETS EXPOSURE PREVALENCE IN CALIFORNIA AND THE U.S.: ADULTS AND ADOLESCENTS**

| Study | Year/ Location | Description | Measure of Exposure | Exposure Prevalence (age) | Comments |
|---|---|---|---|---|---|
| Centers for Disease Control (1993b) | 1988-1992 United States | 800 nonsmoking individuals, ages 4-91 years, from 81 U.S. counties. | Serum cotinine | 100% (----)[a] | Exposed individuals defined as those with detectable concentrations of cotinine. Interpretation of the study results limited by the preliminary nature of the report and the sensitive method for analyzing for cotinine (see text). |

[a] Exposure prevalence reported for entire study population

**TABLE 2.9**
**STUDIES WITH INFORMATION ON ETS EXPOSURE PREVALENCE IN CALIFORNIA AND THE U.S.: INFANTS AND CHILDREN**

| Study | Year/ Location | Description | Measure of Exposure | Exposure Prevalence (age) | Comments |
|---|---|---|---|---|---|
| **California** | | | | | |
| Phillips *et al.* (1991) Wiley *et al.* (1991b) | 1989-1990 California (statewide) | 1,200 children (0 to 11 years old) from households with telephones and an English-speaking adult | Surrogate Report | 40% (6-11yrs) 36% (0-5 yrs) | Exposed individuals defined as those reporting exposure to ETS on the day preceding the interview. |
| Burns and Pierce (1992) | 1990-1991 Telephone interviews California (statewide) | Surrogate with 32,135 English- or Spanish-speaking households | 32.2%(6-11 yrs) Report | Exposed individuals 32.2% (0-5 yrs) | defined as those living in a household with one or more smokers. |
| **Other U.S. areas** | | | | | |
| Coultas *et al.* (1987) | 1984-1985 New Mexico | Hispanic children participating in a population-based survey of respiratory disease | Salivary cotinine | 45% (6-12 yrs) 54% (0-5 yrs) | Exposed individuals defined as those with salivary cotinine concentrations ranging from 0.78 to 20 ng/ml. |
| Greenberg *et al.* (1989) | 1986-1987 Central North Carolina | 433 healthy infants | Surrogate Report | 42% (8-51 days) | Exposed individuals defined as those exposed to ETS during the preceding week. |
| | | | Surrogate Report | 55% (8-51 days) | Exposed individuals defined as those living in a household with one or more smokers. |

**TABLE 2.9 (continued)**
**STUDIES WITH INFORMATION ON ETS EXPOSURE PREVALENCE IN CALIFORNIA AND THE U.S.: INFANTS AND CHILDREN**

| Study | Year/ Location | Description | Measure of Exposure | Exposure Prevalence (age) | Comments |
|---|---|---|---|---|---|
| Greenberg *et al.* (1989) (continued) | 1986-1987 Central North Carolina | 433 healthy infants | Urinary cotinine | 60% (8-51 days) | Exposed individuals defined as those with detectable concentrations of urinary cotinine. |
| Chilmonczyk *et al.* (1990) | 1988 Portland, Maine | 518 infants | Surrogate Report | 41% (6-8 wks) | Exposed individuals defined as those living in a household with one or more smokers. |
| | | | Urinary cotinine | 80% (6-8 wks) | Exposed individuals defined as those with detectable concentrations of urinary cotinine. |
| Overpeck and Moss (1991) | 1988 United States | 5,356 children from a cross-sectional survey of household populations | Surrogate Report | 48.8% (0-5 yrs) | Exposed individuals defined as those living in a household in which one member smoked regularly at any time since the child's birth. |
| | | | Surrogate Report | 42% (0-5 yrs) | Exposed individuals defined as those currently living in a household with one or more smokers. |

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