



INDOOR AIR

POLLUTION

A Health Perspective

by JONATHAN W. SAMUELS

and

JOHN D. SPENCER, Ph.D., M.S.

© 1991 The Johns Hopkins University Press
All rights reserved
Printed in the United States of America

The Johns Hopkins University Press
701 West 40th Street
Baltimore, Maryland 21211-2190
The Johns Hopkins Press Ltd., London

The paper used in this book meets the minimum requirements of American National Standards for Information Sciences—Permanence of Paper for Printed Library Materials, ANSI Z39.48-1984.



Library of Congress Cataloging-in-Publication Data

Indoor air pollution : a health perspective / edited by Jonathan M. Samet and John D. Spengler.

p. cm. — (The Johns Hopkins series in environmental toxicology)

Includes bibliographical references and index.

ISBN 0-8018-4124-0. — ISBN 0-8018-4125-9 (pbk.)

1. Indoor air pollution—Health aspects. I. Samet, Jonathan M.

II. Spengler, John D. III. Series.

RA577.5.I54 1991

613'.5—dc20

90-49482

CIP

CONTENTS

CONTRIBUTORS

PREFACE

ACKNOWLEDGMENTS

1. A Perspective on Indoor and Outdoor Air Pollution,
John D. Spengler and Jonathan M. Samet

I. SOURCES, CONCENTRATIONS, AND EXPOSURE

2. Sources and Concentrations of Indoor Air Pollution,
John D. Spengler
3. Building Dynamics and Indoor Air Quality, David T. Harjle
4. Assessment of Indoor Air Quality, John F. McCarthy, David W.
Bearg, and John D. Spengler
5. Personal Exposure to Indoor Air Pollution, P. Barry Ryan
and William E. Lambert

II. HEALTH EFFECTS

6. Environmental Tobacco Smoke, Jonathan M. Samet, William S.
Cain, and Brian P. Leaderer
7. Nitrogen Dioxide, Jonathan M. Samet
8. Carbon Monoxide, David B. Coults and William E. Lambert
9. Wood Smoke, Marian C. Marbury
10. Formaldehyde, Marian C. Marbury and Robert A. Krieger
11. Volatile Organic Compounds, Lance A. Wallace
12. Indoor Air Pollution and Infectious Diseases, Harriet A. Burge
and James C. Feeley

vii
ix
xi

1

33

68

82

109

131

170

187

209

223

253

273

v

13. Biological Agents and Allergic Diseases, David N. Weissman and Mark R. Schnuyler 285
14. Building-related Illnesses, Marian C. Marbury and James E. Woods, Jr. 306
15. Radon, Jonathan M. Samet 323

III. CONTROL AND LEGAL ASPECTS

16. Control Strategies, Jerry F. Ludwig and William Turner 351
17. Legal Aspects of Indoor Air Pollution, Laurence S. Kirsch 379

INDEX 399

CONTRIBUTORS

DAVID W. BEARG, M.S., president, Life Energy Associates, Concord, Mass.
HARRIET A. BURGE, Ph.D., associate research scientist, Division of Internal Medicine, Department of Allergy, University of Michigan

WILLIAM S. CAIN, Ph.D., fellow, John B. Pierce Foundation Laboratory; and professor of epidemiology and psychology, Yale University School of Medicine

DAVID B. COULTAS, M.D., assistant professor of medicine, University of New Mexico Medical Center and New Mexico Tumor Registry

JAMES C. FEELEY, Ph.D., president, Pathogen Control Associates, Tucker, Ga.

DAVID T. HARRJE, M.S., research engineer, Center for Energy and Environmental Studies, School of Engineering and Applied Science, Princeton University

LAURENCE S. KIRSCH, M.S., J.D., associate, Cadwalader, Wickersham and Taft, Washington, D.C.

ROBERT A. KRIEGER, Ph.D., director of environmental toxicology, Delta Environmental Consultants, St. Paul, Minn.

WILLIAM E. LAMBERT, Ph.D., research assistant professor, Department of Family, Community, and Emergency Medicine, University of New Mexico Medical Center and New Mexico Tumor Registry

BRIAN P. LEADERER, Ph.D., M.P.H., associate fellow, John B. Pierce Foundation Laboratory; and associate professor of epidemiology and environmental health, Yale University

JERRY F. LUDWIG, Ph.D., senior scientist, Environmental Health and Engineering, Inc., Newton, Mass.; and research associate, Physical Science and Engineering Program, Department of Environmental Science and Physiology, Harvard School of Public Health

MARIAN C. MARBURY, Sc.D., environmental epidemiologist, Minnesota Department of Health

JOHN F. MCCARTHY, Sc.D., president, Environmental Health and Engineering, Inc., Newton, Mass.

P. BARRY RYAN, M.D., Ph.D., assistant professor, Department of Environmental Science and Physiology, Harvard School of Public Health

MARK R. SCHUYLER, M.D., chief, Medical Service, Veterans Administration Medical Center, Albuquerque; and professor and vice chairman, Department of Medicine, University of New Mexico School of Medicine

WILLIAM TURNER, M.S., manager, Building Air Quality Assessment Group, Hariman Associates, Auburn, Me.

LANCE A. WALLACE, Ph.D., environmental scientist, U.S. Environmental Protection Agency, Warrenton, Va.

DAVID N. WEISSMAN, M.D., Veterans Administration Medical Center, Albuquerque; and assistant professor of medicine, University of New Mexico School of Medicine

JAMES E. WOODS, Jr., Ph.D., William E. Jamerson professor of building construction, College of Architecture and Urban Studies, Virginia Polytechnic Institute and State University

PREFACE

This book provides a comprehensive review of the rapidly enlarging evidence on indoor air quality and health. The audience for this material continues to grow as the dimensions of the indoor air quality problem become more and more apparent. The issues surrounding indoor air quality are diverse, and the large numbers of specialists involved in the research include epidemiologists, risk assessors, experts in air monitoring, microbiologists, engineers, and psychologists. As the hazards posed by indoor air pollution have been recognized, the evidence on adverse health effects has become increasingly relevant for physicians and other health care providers. The dominant contributions of indoor sources to the total personal exposures for some pollutants have given the subject importance for local, state, and federal regulators. Adverse effects of indoor air pollution have also been the subject of litigation.

The impact of indoor air quality problems on property values and sales has been well demonstrated in the case of radon; it is likely that documentation of adequate indoor air quality for radon and other pollutants may eventually be required at the time of sale of all properties. Such a requirement will bring builders, real estate salespersons, and homeowners into the audience for information on indoor air quality. During the last two decades, outbreaks of illness related to work environments other than industrial settings have been reported with increasing frequency. These outbreaks, often referred to as the "sick-building syndrome" or "tight-building syndrome," have added the building operator and the employer to the list of those who should be concerned about indoor air quality.

A single volume cannot address the needs of so diverse an audience. The intent of this book is to provide a review for the health-oriented readership, and for policymakers, engineers, and lawyers. Unfortunately, the book will not serve the

relatively small group of researchers who are directly involved with indoor air quality problems.

The structure of this book reflects the complexity of the problem of indoor air quality. The book begins with a perspective on outdoor and indoor air quality. Subsequent chapters address the sources of indoor air pollution, the levels of pollution in homes, the assessment of indoor air quality, and the operating characteristics of buildings. The major topic of the book is the health effects of indoor pollutants that are specifically considered include carbon monoxide, formaldehyde, other volatile organic compounds, environmental tobacco smoke, nitrogen dioxide, radon, and wood smoke. The effects of biologic agents are considered separately and include infectious agents and those agents that cause disease through immunologic mechanisms. Building-related illnesses are also considered in a separate chapter. The topical problem of indoor asbestos is covered in Chapter 2, but the health risks do not receive separate treatment. The occupational hazards of asbestos have been amply described, and direct evidence on the health risks of indoor asbestos is unavailable. The remaining chapters of the book address such other important dimensions of indoor air quality as the control of pollution and its legal aspects. Policy on indoor air is considered in the introductory chapter.

ACKNOWLEDGMENTS

This book originated with an invitation from Reuben M. Chermiack, editor of the *American Review of Respiratory Disease*, to prepare a "state-of-art" review on indoor air pollution. We accepted and quickly discovered that the task was far larger than we had anticipated. Nevertheless, with our colleague Marian Marbury, we completed the review, which was published in December 1987 and January 1988. Discussions with Zoltan Annau led to an invitation to expand the review into a book for the Johns Hopkins Series in Environmental Toxicology.

During the preparation of this book, we both had support from numerous funding agencies, the availability of which facilitated our work. John D. Spengler derived support from the National Institute of Environmental Health Sciences, the Environmental Protection Agency, the Electric Power Research Institute, the Department of National Health and Welfare Canada, and the Gas Research Institute. Jonathan M. Samet was funded by the Department of Energy, the Health Effects Institute, and the National Heart, Lung, and Blood Institute. Portions of Chapters 2, 6, 7, 9, 10, and 15, in an earlier form, originally appeared in the *American Review of Respiratory Disease* and are reprinted with permission from ARRD 1987, Volume 136, and ARRD 1988, Volume 137. Portions of Chapter 6, in an earlier form, originally appeared in the *Annals of Sports Medicine* 4 (1988). Portions of Chapter 15, in an earlier form, originally appeared in the *Journal of the National Cancer Institute* 81 (1989). Chapter 17 is being published simultaneously in *Indoor Air Pollution: The Complete Resource Guide*, by the Bureau of National Affairs, Inc.

The contributions of many people were needed to complete this book. The authors worked hard in preparing their chapters and in revising them after review. Rebecca Mosher worked tirelessly in entering the material and preparing illustrations. Dorothy Warner also worked on the volume. Lee Fernando kept everyone organized. Rita Elliott edited the volume. Her diligence in assuring that the volume was readable and that the material was correct deserves special thanks. Wendy Harris remained supportive throughout preparation of the manuscript.

ENVIRONMENTAL TOBACCO SMOKE

Jonathan M. Samet, M. D., M.S., William S. Cain, Ph.D.,
Brian P. Leaderer, Ph.D., M.P.H.

Extensive toxicologic, experimental, and epidemiologic data, largely collected since the 1950s, have established that active cigarette smoking is the major preventable cause of morbidity and mortality in the United States (U.S. Department of Health, Education, and Welfare [DHEW] 1979; U.S. Department of Health and Human Services [DHHS] 1989). More recently, involuntary exposure to tobacco smoke has been investigated as a risk factor for disease and also found to be a cause of preventable morbidity and mortality in nonsmokers. The 1986 report of the surgeon general on smoking and health (U.S. DHHS 1986) and a report by the National Research Council (NRC 1986a), also published in 1986, comprehensively reviewed the data on involuntary exposure to tobacco smoke; both reports concluded that involuntary smoking was a cause of disease in nonsmokers.

This chapter will summarize the converging evidence on the health effects of involuntary exposure to tobacco smoke. To date, research on involuntary smoking has focused on respiratory effects although recent investigations have examined associations with diverse conditions including nonrespiratory cancers, ischemic heart disease, age at menopause, sudden infant death syndrome, and birth weight (Table 6.1).

EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE

CHARACTERISTICS OF ENVIRONMENTAL TOBACCO SMOKE

Nonsmokers inhale environmental tobacco smoke (ETS), the combination of the sidestream smoke that is released from the cigarette's burning end with the mainstream smoke exhaled by the active smoker (First 1985). The inhalation of ETS is generally referred to as *passive smoking* or *involuntary smoking*. The exposures of involuntary and active smoking differ quantitatively and, to some

Table 6.1 Established and Potential Health Effects of Involuntary Exposure to Tobacco Smoke

Established
Increased lower respiratory infections in children
Increased respiratory symptoms in children
Reduced lung growth in children
Increased lung cancer risk in nonsmokers
Irritation of the eyes, nose, throat, and lower respiratory tract
Potential
Increased respiratory symptoms in adults
Reduced lung function in adults
Increased risk for asthma
Exacerbation of asthma
Increased risk for cardiovascular disease
Increased risk for nonrespiratory cancers
Earlier age at menopause
Increased risk for sudden infant death
Reduced birth weight

extent, qualitatively (NRC 1981, 1986a; Sterling and Kobayashi 1982; U.S. DHHS 1984, 1986). Because of the lower temperature in the burning cone of the smoldering cigarette, most partial pyrolysis products are enriched in sidestream as compared with mainstream smoke. Consequently, sidestream smoke has higher concentrations of some toxic and carcinogenic substances than mainstream smoke does; however, dilution by room air markedly reduces the concentrations inhaled by the involuntary smoker in comparison with those inhaled by the active smoker. Nevertheless, involuntary smoking is accompanied by exposure to many of the toxic agents generated by tobacco combustion (NRC 1981, 1986a; Sterling and Kobayashi 1982; U.S. DHHS 1984, 1986).

ENVIRONMENTAL TOBACCO SMOKE CONCENTRATIONS

Tobacco smoke is a complex mixture of gases and particles which contains myriad chemical species (U.S. DHEW 1979; U.S. DHHS 1984). Not surprisingly, tobacco smoking in indoor environments increases levels of respirable particles, nicotine, polycyclic aromatic hydrocarbons, carbon monoxide (CO), acrolein, nitrogen dioxide (NO₂), and many other substances (Table 6.2). The extent of the increase in concentration varies with the number of smokers, the intensity of smoking, the ventilation rate of the indoor space, and the use of air cleaning devices. Several components of cigarette smoke have been measured in indoor environments as markers of the contribution of tobacco combustion to indoor air pollution. Particles have been measured most often because both sidestream and mainstream smoke contain high concentrations of particles in the respirable size range (NRC 1986a; U.S. DHHS 1986). Particles are a nonspecific marker of tobacco smoke contamination, however, because numerous sources other than

Table 6.2 Selected Studies of Tobacco Smoke Component Concentrations in Various Environments

Referenced	Location	Component	Mean Concentration
Badre et al. (1978)	Room, 18 smokers	Acrolein	0.19 mg/m ³
Badre et al. (1978)	Room, 18 smokers	Benzene	0.11 mg/m ³
Wallace (1987)	New Jersey homes, smokers	Benzene	16 µg/m ³ , overnight
	New Jersey homes, nonsmokers	Benzene	8.4 µg/m ³ , overnight
Chappell and Parker (1977)	Office	CO	2.5 ppm, 2- to 3-min samples
Chappell and Parker (1977)	Nightclub	CO	13.0 ppm, 2- to 3-min samples
Hinds and First (1975)	Restaurant	Nicotine	5.2 µg/m ³ , 2.5-h samples
Hinds and First (1975)	Train	Nicotine	6.3 µg/m ³ , 2.5-h samples
Muramatsu et al. (1984)	Cafeteria	Nicotine	26.4 µg/m ³
Weber and Fischer (1980)	Office	NO ₂	24 ppb
Repace and Lowrey (1980)	Cocktail party	Particles	351 µg/m ³ , 15-min sample
	Bowling alley	Particles	202 µg/m ³ , 20-min sample
	Bar	Particles	334 µg/m ³ , 26-min sample
Spangler et al. (1981)	Residence, ≥2 smokers	Particles	70 µg/m ³ , 24-h sample
	Residence, 1 smoker	Particles	37 µg/m ³ , 24-h sample
Henderson et al. (1989)	Residence, cigarette smoking	Nicotine	3.4 µg/m ³ , 14-h sample
	Residence, no cigarette smoking	Nicotine	0.3 µg/m ³ , 14-h sample

tobacco combustion add particles to indoor air. Studies of levels of ETS components have been conducted largely in public buildings; fewer studies have been conducted in the home and office environments (NRC 1986a; U.S. DHHS 1986).

The contribution of various environments to personal exposure to tobacco smoke varies with the time-activity pattern, the distribution of time spent in different locations. Time-activity patterns may heavily weight exposures in particular environments for certain groups of individuals. For example, exposure in the home predominates for infants who do not attend day-care (Harlos et al. 1987). For adults residing with nonsmokers, the workplace may be the principal location at which exposure takes place.

The contribution of smoking in the home to indoor air pollution has been demonstrated by studies using personal monitoring and monitoring of homes for respirable particles. Spengler et al. (1981) monitored homes in six U.S. cities for respirable particle concentrations over several years and found that a smoker of one pack of cigarettes daily contributed about 20 µg/m³ to twenty-four-hour indoor particle concentrations. In homes with two or more heavy smokers, this study showed that the old twenty-four-hour national ambient air quality standard of 260 µg/m³ for total suspended particulates could be exceeded. Because cigarettes are not smoked uniformly over the day, higher peak concentrations must occur

when cigarettes are actually smoked. Spengler et al. (1985) measured the personal exposures to respirable particles sustained by nonsmoking adults in two rural Tennessee communities. The mean twenty-four-hour exposures were substantially higher for those exposed to smoke at home, $64 \mu\text{g}/\text{m}^3$ for those exposed versus $36 \mu\text{g}/\text{m}^3$ for those not exposed.

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

The total exposure assessment methodology (TEAM) study, conducted by the U.S. Environmental Protection Agency, provided extensive data on concentrations of twenty volatile organic compounds in a sample of homes in several communities (Wallace 1987). Indoor monitoring showed increased concentrations of benzene, xylenes, ethylbenzene, and styrene in homes with smokers compared with homes without smokers.

More extensive information is available on levels of environmental tobacco smoke in public buildings of various types (Table 6.2). Monitoring in locations where smoking may be intense, such as bars and restaurants, has generally shown elevations of particles and other markers of smoke pollution where smoking is taking place (NRC 1986a; U.S. DHHS 1986). For example, Repace and Lowrey (1980) used a piezobalance to sample aerosols in restaurants, bars, and other locations. In the places sampled, respirable particulate levels ranged up to $700 \mu\text{g}/\text{m}^3$, and the levels varied with the intensity of smoking. Similar data have been reported for the office environment, although the information is more limited (NRC 1986a; U.S. DHHS 1986).

Transportation environments may also be affected by cigarette smoking. Contamination of air in trains, buses, automobiles, airplanes, and submarines has been documented (NRC 1986a; U.S. DHHS 1986). A recent NRC report (NRC 1986b) on air quality in airliners summarized studies of tobacco smoke pollutants in commercial aircraft. In one study, during a single flight, the NO_2 concentration varied with the number of passengers with a lighted cigarette. In another study, respirable particles in the smoking section were measured at concentrations fivefold or greater than in the nonsmoking section. Peaks as high as $1,000 \mu\text{g}/\text{m}^3$ were measured in the smoking section. Mattson and colleagues (1989) used personal exposure monitors to assess nicotine exposures of passengers and flight attendants. All persons were exposed to nicotine, even if seated in the nonsmoking portion of the cabin. Exposures were much greater in the smoking than in the nonsmoking section and were also greater on aircraft with recirculated air.

134 J. M. Samet, W. S. Cain, and B. P. Leaderer

Biologic markers of tobacco smoke exposure can be used to describe the prevalence and the dosimetry of involuntary smoking and to validate questionnaire-based measures of exposure. In both active and involuntary smokers, the detection of smoke components or their metabolites in body fluids or alveolar air provides evidence of exposure to tobacco smoke, and levels of these markers can be used to gauge the intensity of exposure. The risks of involuntary smoking have also been estimated by comparing levels of biologic markers in active and involuntary smokers.

At present, the most sensitive and specific markers for tobacco smoke exposure are nicotine and its major metabolite, cotinine (Jarvis and Russell 1984; NRC 1986a; U.S. DHHS 1988). Neither nicotine nor cotinine is present in body fluids in the absence of exposure to tobacco smoke. Because the circulating half-life of nicotine is generally shorter than two hours (Rosenberg et al. 1980), nicotine concentrations in body fluids reflect more recent exposures. In contrast, cotinine has a half-life in the blood or plasma of active smokers which ranges from less than ten hours to about forty hours (Kyjerematen et al. 1982; Benowitz et al. 1983; U.S. DHHS 1988); hence, cotinine levels provide information about more chronic exposure to tobacco smoke in both active and involuntary smokers. Whether cotinine has the same half-life in plasma, saliva, and urine is presently controversial, as is the choice of the optimal body fluid for measuring cotinine for research purposes (Jarvis et al. 1988; Wall et al. 1988; Coultas and Samet 1990; Haley, Spekovic, and Hoffmann 1989). Thiocyanate concentration in body fluids, concentration of CO in expired air, and carboxyhemoglobin level distinguish active smokers from nonsmokers but are not as sensitive and specific as cotinine for assessing involuntary exposure to tobacco smoke (Hoffman et al. 1984a, 1984b; Jarvis and Russell 1984).

Cotinine levels have been measured in adult nonsmokers and in children (Table 6.3). In the studies of adult nonsmokers, exposures at home, in the workplace, and in other settings determined cotinine concentrations in urine and saliva. The cotinine levels in involuntary smokers ranged from less than 1 percent to about 8 percent of cotinine levels measured in active smokers. Smoking by parents was the predominant determinant of the cotinine levels in their children. For example, Greenberg et al. (1984) found significantly higher concentrations of cotinine in the urine and saliva of infants exposed to cigarette smoke in their homes in comparison with unexposed controls. Urinary cotinine levels in the infants increased with the number of cigarettes smoked during the previous twenty-four hours by the mother. In a study of schoolchildren in England, salivary cotinine levels rose with the number of smoking parents in the home (Jarvis et al. 1985).

The results of studies on biologic markers have important implications for research on involuntary smoking and add to the biologic plausibility of associations between involuntary smoking and disease documented in epidemiologic studies. The data on marker levels provide ample evidence that involuntary exposure leads to absorption, circulation, and excretion of tobacco smoke components.

Table 6.3 Selected Studies of Cotinine Levels in Nonsmokers

Population	Findings
100 adult patients attending clinics in London (Jarvis et al. 1984)	Cotinine levels parallel self-reported exposure. In non-smoking, mean = 1.5 ng/ml in saliva; in active smokers, mean = 309.9 ng/ml.
151 adult males attending a clinic in London and 70 subjects from Oxford (Wald et al. 1984; Wald and Ritchie 1984)	Urinary cotinine level increased with reported duration of smoke exposure. In nonexposed nonsmokers, median level = 2.0 ng/ml; exposed nonsmokers, median = 6.0 ng/ml; active cigarette smokers, median = 1,645 ng/ml. Smoking by wife increased cotinine concentrations threefold in nonsmoking men.
51 infants attending clinics in North Carolina (Greenberg et al. 1984)	In nonexposed, median urinary level = 4 ng/mg creatinine; exposed, median = 351 ng/mg creatinine. Salivary cotinine levels higher in exposed.
472 nonsmoking adults in Japan (Masuoka et al. 1984)	Exposure at home and at work independently increased urinary cotinine level. In nonsmokers, median = 680 ng/mg creatinine; active smokers, median = 8,570 ng/mg creatinine.
569 schoolchildren, age 11-16 years, in Bristol, England (Jarvis et al. 1985)	Salivary cotinine level increased with the number of smoking parents. If neither parent smoked, median = 0.20 ng/ml; if both smoked, median = 2.70 ng/ml.
38 children, age 3-15 months, attending a child center in North Carolina (Pattishall et al. 1985)	Serum cotinine level increased with the number of smokers in the home. In children without household exposure, mean = 1.0 ng/ml; exposed, mean = 4.1 ng/ml.
839 children and adults in a population sample in New Mexico (Coultas et al. 1987)	Salivary cotinine level increased with the number of smokers in the home. If no smokers in the home, median level was zero. If one or more smokers, median was greater than zero and increased with the number of smokers.
260 adult municipal workers in Dallas, Texas (Haley et al. 1989)	Urinary cotinine level about 2.5 times greater for persons living with smokers. Somewhat greater levels for those exposed at work.

nents. The studies of biologic markers also confirm the high prevalence of involuntary smoking, as ascertained by questionnaire (Coultas et al. 1987). The observed correlations between reported exposures and levels of markers suggest that questionnaire methods for assessing recent exposure have some validity.

Comparisons of levels of biologic markers in smokers and nonsmokers have been made in order to estimate the relative intensities of active and involuntary smoking. However, proportionality cannot be assumed between the ratio of the levels of markers in passive and active smokers and the relative doses of other tobacco smoke components. Nonetheless, several investigators have attempted to characterize involuntary smoking in terms of active smoking. For example, Folliart and colleagues (Folliart, Benowitz, and Becker 1983) measured urinary excretion of nicotine in flight attendants during an eight-hour flight and estimated that the

136 J. M. Samet, W. S. Cain, and B. P. Leaderer

average exposure was 0.12-0.25 mg of nicotine. Kussell, Yocum, and Vias (1987) compared nicotine levels in nonsmokers exposed to tobacco smoke with levels achieved following infusion of known doses of nicotine. On the basis of this comparison the investigators estimated that the average rate of nicotine absorption was 0.23 mg/h in a smoky tavern, 0.36 mg/h in an unventilated smoke-filled room, and 0.014 mg/h from average daily exposure. In active smokers the first cigarette of the day resulted in absorption of 1.4 mg of nicotine.

HEALTH EFFECTS OF INVOLUNTARY SMOKING

LOWER RESPIRATORY TRACT ILLNESSES IN CHILDHOOD

Epidemiologic investigations have linked involuntary smoking in children to increased occurrence of lower respiratory tract illness during infancy and childhood; presumably these illnesses are infectious in etiology and do not represent a direct response of the lung to toxic components of ETS. Investigations conducted throughout the world have demonstrated an increased risk of lower respiratory tract illness in infants with smoking parents (Table 6.4). These studies indicate a significantly increased frequency of bronchitis and pneumonia during the first year of life of children with smoking parents. Although the health outcome measures varied somewhat among the studies, the relative risks associated with involuntary smoking were similar, and dose-response relationships with the extent of parental smoking were demonstrable. Although most of the studies have shown that maternal smoking rather than paternal smoking underlies the increased risk, a recent study from China shows that paternal smoking alone can increase the incidence of lower respiratory illness (Yue Chen, Wanxian, and Shunzhang 1986). In these studies (Table 6.4), an effect of passive smoking has not been readily identified after the first year of life. The strength of the effect of passive smoking during the first year of life may reflect higher exposures consequent to the time-activity patterns of young infants, which place them in close proximity to cigarettes smoked by their mothers.

For school-age children, parental smoking also increases the occurrence of chest illnesses. For example, in a survey of 4,071 Pennsylvania children ages five to fourteen years, the proportion of children having a chest illness of three days or more during the past year rose from 8.8 to 11.8 to 13.6 percent with none, one, and two smoking parents, respectively (Schenker, Samet, and Speizer 1983). The findings in other large surveys have been similar (Ware et al. 1984; Somerville, Rona, and Chinn 1988).

RESPIRATORY SYMPTOMS AND ILLNESSES IN CHILDREN

Data from numerous surveys demonstrate a greater frequency of the most common respiratory symptoms, cough, phlegm, and wheeze in the children of smokers (U.S. DHHS 1986). In these studies the subjects have generally been schoolchildren, and the effects of parental smoking have been examined. Thus, the less

Table 6.4 Early Childhood Respiratory Illnesses and Involuntary Smoking

Study Population	Study Design	Effect of Involuntary Smoking	Comments
10,672 births in Israel, 1967-68 (Harlap and Davies 1974)	Antenatal maternal smoking history, monitoring of admissions during first year of life	Significant increase in hospitalization for pneumonia and bronchitis; $RR^* = 1.4$	Dose-response relationship present; maternal smoking only
2,205 births in England, 1963-65 (Leeder et al. 1976)	Prospective cohort with annual questionnaire	Significant increase in bronchitis or pneumonia in first year of life; $RR = 1.7$ if one parent smoked, $RR = 2.6$ if both smoked	Sex of smoking parent not examined
12,068 births in Finland, 1966 (Rantakallio 1978)	Prospective cohort with follow-up of hospitalizations, physician visits, and mortality	Significant increase of hospitalization for respiratory diseases during first 5 years, $RR = 1.7$	Effect largest during first year; maternal smoking only and measured during pregnancy
1,265 births in New Zealand, 1977 (Fergusson and Horwood 1985)	Prospective cohort with diaries, physician, and hospital record review	No effect of paternal smoking; effect of maternal smoking equivocal in second year, absent in third	
1,565 infants in Scotland, 1980 (Ogston, Florey, and Walker 1985, 1987)	Prospective cohort with record review and interview at one year of age	Significant increase in report of a respiratory illness during the first year of life; $RR = 1.54$ if either parent smoked	Incidence lowest for group with mother alone smoking
130 children with RS virus infection in infancy, England (Pullan and Hey 1982)	Case-control with 111 controls, performed 10 years after index illness	Significant effect of maternal smoking at time of illness; $RR = 3.2$	Effect of paternal smoking also present
29 children hospitalized with respiratory syncytial virus infection before age 2 years, and 58 controls, New York (Hall et al. 1984)	Case-control study with controls hospitalized for non-respiratory condition	Significant effect of smoking in the household; odds ratio = 4.8	Smoking by specific parents not considered

*RR = relative risk. Calculated from published data if not provided by the authors.

prominent effects of passive smoking, in comparison with the studies of lower respiratory illness in infants, may reflect lower exposures to ETS by older children who spend less time with their parents.

Recent results from several large studies provide convincing evidence that involuntary exposure to tobacco smoke increases the occurrence of cough and phlegm in the children of smokers although earlier data from smaller studies had been ambiguous (Table 6.5). In a study of ten thousand schoolchildren in six U.S. communities, smoking by parents increased the frequency of persistent cough in their children by about 30 percent (Ware et al. 1984). The effect of parental smoking derived primarily from smoking by the mother. Charlton (1984) conducted a survey on cigarette smoking which included 15,709 English children, ages eight to nineteen years. In the nonsmoking children, the prevalence of frequent cough was significantly higher if either the father or the mother smoked. In another large study in the United Kingdom, parental smoking was associated with day or night cough in children aged five to eleven years (Somerville, Rona, and Chinn 1988).

For the symptom of chronic wheeze, the preponderance of the evidence also indicates an excess associated with involuntary smoking (Table 6.5). In a survey of 650 schoolchildren in Boston, persistent wheezing was the most frequent symptom (Weiss et al. 1980); the prevalence of persistent wheezing increased significantly as the number of smoking parents increased. In the large study of children in six U.S. communities, the prevalence of persistent wheezing during the previous year was significantly increased if the mother smoked (Ware et al. 1984). In English children aged five to eleven years, parental smoking was associated with a

Table 6.5 Prevalence of Respiratory Symptoms in Selected Investigations of Children, by Number of Smoking Parents

Subjects	Respiratory Symptoms			Prevalence (per 100) by Number of Smoking Parents	
				0	1 2
2,426 children, aged 6-14, England (Colley 1974)	Chronic cough			15.6	17.2 22.2
3,105 nonsmoking children, aged 12-13, England (Bland et al. 1978)	Cough during the day or at night			16.4	19.0 23.5
650 children, aged 5-9, Massachusetts (Weiss et al. 1980)	Chronic cough and phlegm			1.7	2.7 3.4
4,071 children, aged 5-14, Pennsylvania (Schenker, Samet, and Speizer 1983)	Persistent wheeze			1.8	6.8 11.8
	Chronic cough			6.3	7.0 8.3
	Chronic phlegm			4.1	4.8 4.0
	Persistent wheeze			7.2	7.7 5.4
8,528 children, aged 5-9, six U.S. cities (Ware et al. 1984)	Chronic cough			7.7	8.4 10.6
1,733 nonsmoking children, aged 8-10, England (Charlton 1984)	Persistent wheeze			9.9	11.0 13.1
	Frequent cough (boys)			35	42 48
	Frequent cough (girls)			32	40 52

Source: abstracted from U.S. DHHS (1986, Table 4, pp. 360-62) and from Charlton (1984).

more frequent report of persistent wheezing (Somerville, Rona, and Chinn 1988). The odds ratio for exposure to twenty cigarettes per day at home was 1.6 (95 percent confidence interval 1.2-2.2) compared with no exposure. McConnochie and Roghmann (1986) assessed predictors of wheeze in a retrospective study of children who had mild bronchiolitis in infancy and of control children. At a mean age of 8.3 years, current exposure to tobacco smoke increased the risk of wheezing (relative risk = 1.9). Parental smoking predicted the occurrence of wheezing at age five years in a study of children at risk for atopy (Cogswell, Mitchell and Alexander 1987). Passive smoking has not been significantly associated with wheezing in all studies, however (Leeder et al. 1976; Schenker, Samet, and Speizer 1983; Tashkin et al. 1984).

Although involuntary exposure to tobacco smoke is associated with the symptom of wheeze, evidence for association of involuntary smoking with childhood asthma is conflicting. Exposure to ETS might cause asthma as a long-term consequence of the increased occurrence of lower respiratory infection in early childhood or through other mechanisms (Samet, Tager, and Speizer 1983; Tager 1988). Gortmaker et al. (1982) collected data from two U.S. population samples. The relative risk for asthma associated with maternal smoking was 1.5 in a midwestern urbanized county and 1.8 in a more rural eastern county. In a longitudinal study of children in Tecumseh, Michigan, parental smoking increased the prevalence of asthma at the first examination and was associated with a doubling of the risk for developing asthma during a fifteen-year follow-up period (Burchfiel 1984). A case-control study in the United Kingdom also showed increased risk for asthma in association with exposure to ETS at home (Kershaw 1987). In contrast, in a longitudinal study in New Zealand, parental smoking habits were not found to affect the incidence of asthma during the first six years of life (Horwood, Ferguson, and Shannon 1985). In another longitudinal study of more than two thousand children in Harrow, England, parental smoking was not a significant predictor of the development of asthma during a five-year follow-up period (Leeder et al. 1976). Some cross-sectional studies have also not demonstrated a relationship between parental smoking and asthma (Schenker, Samet, and Speizer 1983; Tashkin et al. 1984; Somerville, Rona, and Chinn 1988). The inconsistencies among these investigations cannot be readily explained.

Although involuntary exposure to tobacco smoke has not been established as a cause of asthma, recent evidence indicates that involuntary smoking worsens the status of those with asthma. Murray and Morrison (1986) evaluated ninety-four asthmatic children of ages seven to seventeen years. Level of lung function, symptom frequency, and responsiveness to inhaled histamine were adversely affected by maternal smoking. In a study of twenty-one asthmatics, ages six to twenty-one years, O'Connor and colleagues (1987) also found that maternal smoking increased the level of airways responsiveness. Male nine-year-old Italian schoolchildren had greater bronchial responsiveness if their parents smoked; the association with smoking was strongest for children with asthma (Martinez et al. 1988). The increased level of airways responsiveness associated with maternal

smoking would be expected to increase the clinical severity of asthma. In this regard, exposure to smoking in the home has been shown to increase the number of emergency room visits made by asthmatic children (Evans et al. 1987).

Recent studies have also shown that children exposed to cigarette smoke in their homes are at increased risk for middle ear disease. Both acute otitis media (Pukander et al. 1985) and persistent middle ear effusions (Kraemer et al. 1983; Black 1985; Iversen et al. 1985; Strachan, Jarvis, and Feyerabend 1989) have been associated with involuntary smoking.

LUNG FUNCTION IN CHILDREN

On the basis of the primarily cross-sectional data available at the time, the 1984 report of the surgeon general (U.S. DHHS 1984) concluded that the children of smoking parents in comparison with those of nonsmokers had small reductions of lung function, but the long-term consequences of these changes were regarded as unknown. In the two years between the 1984 and the 1986 reports, sufficient longitudinal evidence accumulated to support the conclusion in the 1986 report (U.S. DHHS 1986) that involuntary smoking reduces the rate of lung function growth during childhood. New cross-sectional studies have continued to confirm the evidence reviewed in the 1984 report of the surgeon general (Burchfiel 1984; Tashkin et al. 1984; Tsimoyianis et al. 1987), although not all studies have shown adverse effects of involuntary smoking on the lung function of children (Hoscin and Corey 1984; Lebowitz, Knudson, and Burrows 1984).

The effects of involuntary smoking on lung growth have been demonstrated in three separate longitudinal studies. Based on cross-sectional data from children in East Boston, Massachusetts, Tager and co-workers (1979) reported in 1979 that the level of FEF_{25-75} , a spirometric flow rate sensitive to subtle effects on airways and parenchymal function, declined with increasing number of smoking parents in the household. In 1983, this investigative group reported the results obtained on follow-up of these children over a seven-year period (Tager et al. 1983). Using a multivariate technique, the investigators showed that both maternal smoking and active smoking by the child reduced the growth rate of the one-second forced expiratory volume (FEV_1). Lifelong exposure of a child to a smoking mother was estimated to reduce growth of the FEV_1 by 10.7, 9.5, and 7.0 percent after one, two, and five years of follow-up, respectively.

Recent longitudinal data from the study in six U.S. cities also showed reduced growth of the FEV_1 in children whose mothers smoked cigarettes (Berkey et al. 1986). The growth rate of the FEV_1 from ages six through ten years was calculated for 7,834 white children. From ages six through ten years, the findings of a statistical analysis were that FEV_1 growth rate is reduced by 0.17 percent per pack of cigarettes smoked daily by the mother. This effect was somewhat smaller than that reported by Tager et al. (1983), although if extrapolated to age twenty years, a cumulative effect of 2.8 percent is predicted.

Burchfiel and co-workers (Burchfiel 1984; Burchfiel et al. 1986) examined the effects of parental smoking on fifteen-year lung function change in subjects in

the Tecumseh study, who had been enrolled at ages ten through nineteen years. In the female subjects who remained nonsmokers across the follow-up period, parental smoking did not affect lung function change. In nonsmoking males, parental smoking reduced the growth of the FEV₁, forced vital capacity (FVC), and maximum flow rate at 50 percent of FVC (V_{max50}) although the sample size was limited, and the effects were not statistically significant. For the FEV₁ in males, the analysis estimated 7.4 percent and 9.4 percent reductions in fifteen-year growth associated with one or two smoking parents, respectively.

RESPIRATORY SYMPTOMS AND ILLNESSES IN ADULTS

Only a few cross-sectional investigations provide information on the association between respiratory symptoms in nonsmokers and involuntary exposure to tobacco smoke. These studies have only considered exposure to a smoking spouse and have not evaluated sources of exposure outside the home. Consistent evidence of an effect of passive smoking on respiratory symptoms in adults has not been found (Lebowitz and Burrows 1976; Schilling et al. 1977; Comstock et al. 1981; Schenker, Samet and Speizer 1982; Kauffmann et al. 1989).

Neither epidemiologic nor experimental studies have established the role of ETS in exacerbating asthma in adults. The acute responses of asthmatics to ETS have been assessed by exposing persons with asthma to tobacco smoke in a chamber. This experimental approach cannot be readily controlled because of the impossibility of blinding subjects as to exposure to ETS. However, suggestibility does not appear to underlie physiologic responses of asthmatics to ETS (Urch et al. 1988). Of three studies involving exposure of unselected asthmatics to ETS, only one showed a definite adverse effect (Shepherd et al. 1979; Dahms, Bolin, and Slavin 1981; Wiedemann et al. 1986). Stankus et al. (1988) recruited twenty-one asthmatics who reported exacerbation with exposure to ETS. With challenge in an exposure chamber, seven of the subjects experienced a more than 20 percent decline in FEV₁.

LUNG FUNCTION IN ADULTS

With regard to involuntary smoking and lung function in adults, exposure to passive smoking has been associated with reduction of the FEF₂₅₋₇₅ in cross-sectional investigations. White and Froeb (1980) compared spirometric test results in middle-aged nonsmokers with at least twenty years of involuntary smoking in the workplace with the results in an unexposed control group of nonsmokers. The mean FEF₂₅₋₇₅ of the exposed group was significantly reduced, by 15 percent of predicted value in women and by 13 percent in men. This investigation has been intensely criticized with regard to the spirometric test procedures, the determination and classification of exposures, and the handling of former smokers in the analyses.

A subsequently reported investigation in France examined the effect of marriage to a smoker in more than 7,800 adults in seven cities (Kauffmann, Tessier, and Oriol 1983). The study included 849 male and 826 female nonsmokers exposed to

tobacco smoking by their spouses' smoking. At more than age forty years, the FEF₂₅₋₇₅ was reduced in nonsmoking men and women with a spouse who smoked. The investigators interpreted this finding as representing a cumulative adverse effect of marriage to a smoker. In a subsequent report, the original findings in the French women were confirmed, but a parallel analysis in a large population of U.S. women did not show effects of involuntary smoking on lung function (Kauffmann et al. 1989).

The results of an investigation of 163 nonsmoking women in The Netherlands also suggested adverse effects of tobacco smoke exposure in the home on lung function (Brunkreef et al. 1985; Remijn et al. 1985). Cross-sectional analysis of spirometric data collected in 1982 demonstrated adverse effects of tobacco smoke exposure in the home, but in a sample of the women, domestic exposure to tobacco smoke was not associated with longitudinal decline of lung function during the period 1965 to 1982.

Svendsen and co-workers (1987) assessed the effects of spouse smoking on 1,400 nonsmoking male participants in the Multiple Risk Factor Intervention Trial (MRFIT). The subjects were aged thirty-five to fifty-seven years at enrollment and were at high risk for mortality from coronary artery disease. At the baseline visit, the maximum FEV₁ was approximately 100 milliliters lower for the men married to a smoker.

Masi and colleagues (1988) evaluated the lung function of 293 young adults using spirometry and measurement of the diffusing capacity and lung volumes. The results varied with gender. In men, reduction of the maximal mid-expiratory flow rate was associated with maternal smoking and exposure to ETS during childhood. In women, reduction of the diffusing capacity was associated with exposure to ETS at work.

Other studies have not shown chronic effects of involuntary exposure to tobacco smoke in adult nonsmokers. In two cross-sectional studies, marriage to a smoker was not significantly associated with reduction of ventilatory function (Schilling et al. 1977; Comstock et al. 1981). Jones and co-workers (Jones et al. 1983) conducted a case-control study of twenty- to thirty-nine-year-old nonsmoking women in the longitudinal study in Tecumseh. Subjects from the highest and lowest quartiles of the lung function distribution had comparable exposure to smokers in the home. In a study conducted in Germany, the effects of involuntary and active smoking were examined in a population of 1,351 white-collar workers (Kantner, Triebig, and Weltle 1984). Self-reported exposure to ETS at home and at work was not associated with reduction of spirometric measures of lung function.

A conclusion cannot yet be reached on the effects of ETS exposure on lung function in adults. However, further research is warranted because of widespread exposure in workplaces and homes.

LUNG CANCER

In 1981, reports were published from Japan (Hirayama 1981) and from Greece (Trichopoulos et al. 1981) that indicated increased lung cancer risk in nonsmoking

Table 6.6 Cohort and Case-Control Studies of Passive Exposure to Tobacco Smoke and Lung Cancer

Study	Findings	Comments
Prospective cohort study in Japan of 91,540 nonsmoking females, 1966-81 (Hirayama 1981)	Age-occupation-adjusted SMRs, ^a by husband smoking: Nonsmokers = 1.00 Exsmokers = 1.36 Current smokers <20/day = 1.45 >20/day = 1.91 Age-adjusted SMRs, by husband smoking: Nonsmokers = 1.00 Current smokers <20/day = 1.27 >20/day = 1.10 Age-adjusted mortality ratios for domestic exposure: Males = 3.25 Females = 1.00 Odds ratios by husband smoking: Nonsmokers = 1.0 Exsmokers = 1.8 Current smokers <20/day = 2.4 >20/day = 3.4 Crude odds ratio of 0.75 associated with smoking spouse	Trend statistically significant; all histologies All histologies; effect of husband smoking not significant Preliminary, small numbers of cases Trend statistically significant; histologies other than adenocarcinoma and bronchioloalveolar carcinoma All histologies; two reports are inconsistent on the exposure variable Significant increase for >41 pack years; bronchioloalveolar carcinoma excluded All histologies; findings negative for spouse smoking variable as well All histologies Adenocarcinoma and squamous cell carcinoma only All histologies; careful exclusion of smokers from the case group
Prospective cohort study in the U.S. of 176,139 nonsmoking females, 1960-72 (Garfinkel 1981)		
Prospective cohort study in Scotland of 8,128 males and females, 1972-82 (Gillis et al. 1984)		
Case-control study in Greece of 40 nonsmoking female cases, 149 controls, 1978-80 (Trichopoulos et al. 1981; Tri-chopoulos, Kalandi, and Sparros 1983)		
Case-control study in Hong Kong of 84 female cases and 139 controls, 1976-77 (Chan et al. 1979; Chan and Fung 1982)		
Case-control study in the U.S. with 22 female and 8 male nonsmoking cases, 133 female and 180 male controls (Correa et al. 1983)		
Case-control study in the U.S. 25 male and 53 female nonsmoking cases with matched controls, 1971-80 (Kabat and Wynder 1984)		
Case-control study in Hong Kong with 88 nonsmoking female cases, 1981-82 (Koo, Ho, and Saw 1984; Koo, Ho, and Lee 1985)		
Case-control study in the U.S. with 31 nonsmoking and 189 smoking female cases (Wu et al. 1985)		
Case-control study in the U.S. with 134 nonsmoking female cases (Wu et al. 1985)		

(continued)

women married to cigarette smokers. Subsequently, this controversial association has been examined in investigations conducted in the United States, Scotland, Japan, Hong Kong, Sweden, and China. The association of involuntary smoking with lung cancer derives biologic plausibility from the presence of carcinogens in sidestream smoke and the lack of a documented threshold dose for respiratory carcinogenesis in active smokers (U.S. DHHS 1982).

Time trends of lung cancer mortality in nonsmokers have been examined with the rationale that temporally increasing exposure to ETS should be paralleled by increasing mortality rates (Enstrom 1979; Garfinkel 1981). These data provide only indirect evidence on the lung cancer risk associated with involuntary exposure to tobacco smoke. Epidemiologists have tested directly the association between lung cancer and involuntary smoking utilizing conventional designs: the case-control and cohort studies. In a case-control study, the exposures of nonsmoking persons with lung cancer to ETS are compared with those of an appropriate control group. In a cohort study, the occurrence of lung cancer over time in nonsmokers is assessed in relationship to involuntary tobacco smoke exposure. The results of both study designs may be affected by inaccurate assessment of exposure to ETS, by inaccurate information on personal smoking habits that leads to classification of smokers as nonsmokers, and by the misdiagnosis of a cancer of another site as a primary cancer of the lung.

Methodologic investigations suggest that accurate information can be obtained by interview in an epidemiologic study on the smoking habits of a spouse (i.e., never or ever smoker) (Pron et al. 1988; Coultas, Peake, and Samet 1989; Cummings et al. 1989). However, information concerning quantitative aspects of the spouse's smoking is reported with less accuracy. Misclassification of current or former smokers as never smokers may introduce a positive bias because of the concordance of spouse smoking habits (Lee 1988). The extent to which this bias explains the numerous reports of association between spouse smoking and lung cancer is controversial (Wald et al. 1986; Lee 1988).

The evidence from the case-control and the cohort studies does not uniformly indicate increased lung cancer risk in persons exposed to ETS, but most of the studies indicate increased risk in nonsmokers married to smokers (Table 6.6). Hirayama's (1981) early report was based on a prospective cohort study of 91,540 nonsmoking women in Japan. Standardized mortality ratios for lung cancer increased significantly with the amount smoked by the husbands. The findings could not be explained by confounding factors and were unchanged when follow-up of the study group was extended (Hirayama 1984). Based on the same cohort, Hirayama has also reported significantly elevated standardized mortality ratios for lung cancer of 2.1 and 2.3 in nonsmoking men with wives smoking one to nineteen cigarettes and twenty or more cigarettes daily, respectively (Hirayama 1984).

In 1981, Trichopoulos et al. (1981) also reported increased lung cancer risk in nonsmoking women married to cigarette smokers. These investigators conducted a case-control study in Athens, Greece, which included cases with a diagnosis other than adenocarcinoma or bronchioloalveolar carcinoma and controls selected

Table 6.6 (Continued)

Study	Findings	Comments
62 controls (Inoue and Hirayama 1988)		cigarettes smoked by the husband
Case-control study in Tianjin China with 54 nonsmoking female cases and 93 controls (Geng et al. 1987)	Overall odds ratio = 2.2 for marriage to a smoker	All histologies

*Standardized mortality ratio.

at a hospital for orthopedic disorders. The positive findings reported in 1981 were unchanged with expansion of the study population (Trichopoulos, Kalandidi, and Sparrows, 1983).

The results of other subsequently reported case-control studies have also demonstrated statistically significant associations between involuntary smoking and lung cancer (Table 6.6). The findings from the more recent reports greatly strengthen the evidence from the earlier studies. Several of the newer studies included relatively large numbers of nonsmokers (Garfinkel, Auerbach, and Joubert 1985; Akiba, Kato, and Blot 1986; Dalager et al. 1986; Gao et al. 1987; Lam et al. 1987). Furthermore, in most of these studies, involuntary smoking was assessed in greater detail than in the earlier reports so that exposure-response relationships could be examined more fully.

The results of two other investigations have also been interpreted as showing an increased lung cancer risk associated with passive smoking although both have methodologic limitations. In Germany, Knoth, Bohn, and Schmidt (1983) described a series of fifty-nine female lung cancer cases of which thirty-nine were in nonsmokers. Based on census data, these investigators projected that a much greater than expected proportion of these nonsmokers had lived in households with smokers. This report did not include an appropriate comparison series, however. Gillis et al. (1984) described the preliminary results of a cohort study of 16,171 males and females in western Scotland; domestic exposure to tobacco smoke increased the lung cancer risk for nonsmoking men but not for women. The report was based on only sixteen cases of lung cancer in nonsmokers, however.

The results of some investigations indicate lesser or no effects of exposure to ETS (Table 6.6). In these studies, however, confidence limits for the relative risks associated with marriage to a smoker are wide and overlap with the confidence limits in the studies with significant results (NRC 1986a). Two separate case-control studies in Hong Kong, where lung cancer incidence rates in females are particularly high, did not indicate excess risk from passive smoking (Chan et al. 1979; Chan and Fung 1982; Koo, Ho, and Saw 1984; Koo, Ho, and Lee 1985; Koo et al. 1987). In the more recent of the two studies, the questionnaire comprehensively assessed cumulative exposure from home and workplace sources (Koo, Ho, and Saw 1984; Koo, Ho, and Lee 1985; Koo et al. 1987). A subsequent study in

ENVIRONMENTAL TOBACCO SMOKE 147

Table 6.6 (Continued)

Study	Findings	Comments
Case-control study in England with 15 male and 32 female nonsmoking cases, and 30 male and 66 female nonsmoking controls (Lee, Chamberlain, and Alderson 1986)	or more cigarettes daily at home; significant trend with number of cigarettes smoked at home by the husband	Hospital-based study
Case-control study in Japan with 19 male and 94 female nonsmoking cases, and 110 male and 270 female nonsmoking controls (Akiba, Kato, and Blot 1986)	Overall odds ratio for spouse smoking of 1.1	
Case-control study in Louisiana, Texas, and New Jersey with 99 nonsmoking cases and 736 controls (Dalager et al. 1986)	For females, odds ratio of 1.5 if husband smoked; for males, odds ratio of 1.8 if wife smoked	Clinical or radiologic diagnosis for 43%; all histologies
Case-control study in New Mexico with 28 nonsmoking cases and 292 nonsmoking controls (Humble, Samet, and Pathak 1987)	Adjusted odds ratio for marriage to a smoking spouse was 1.5	Nearly 100% histologic confirmation; all histologies
Case-control study in Sweden with 77 nonsmoking cases, two matched control series (Pershagen, Hrubec, and Svensson 1987)	Adjusted odds ratio for marriage to a smoking spouse was 3.2; no effect in active smokers	All histologies other than bronchioloalveolar carcinoma
Case-control study in Colorado with 102 adenocarcinoma cases, 50 males and 52 females, and 131 controls (Brownson et al. 1987)	Odds ratio for marriage to a smoker was 3.3 for squamous and small cell carcinomas	No effect of exposure for other types; study based within a cohort
Case-control study in Hong Kong with 199 never smoking female cases and 335 controls (Lam et al. 1987)	No effect in entire group; in nonsmoking women, odds ratio of 1.7 for exposure ≥ 4 h/day	Passive smoking effect not significant in nonsmoking women but only 19 such cases included
Case-control study in Shanghai with 246 nonsmoking female cases and 375 controls (Gao et al. 1987)	Overall odds ratio = 1.7, significantly increased for marriage to a smoker; odds ratio = 2.1 for adenocarcinoma	All histologies; no evidence for exposure response
Case-control study in Japan with 90 nonsmoking female cases and 163 controls (Shimizu et al. 1983)	Overall odds ratio = 0.9 for ever living with a smoker; risk increased with duration of living with a smoking husband	All histologies, but majority adenocarcinoma; no effect of childhood exposure
Case-control study in Japan with 28 smoking female cases and	Odds ratio for husband's smoking was 1.1; no effect of exposure at work	All histologies; increased risk from other household members' smoking
	Overall odds ratio = 2.3 for marriage to a smoker	Risk increased with the number of

(continued)

Hong Kong did find a significant association of spouse smoking and lung cancer risk (Lam et al. 1987). Lee and co-workers (Lee, Chamberlain, and Alderson 1986) reported a hospital-based case-control study in England. Although the investigators considered that their findings indicated little or no effect of involuntary smoking, the case series was small. Another recent hospital-based case-control study, conducted in Japan, also did not show an association between lung cancer risk and spouse smoking (Shimizu et al. 1988).

The results of the American Cancer Society's prospective cohort study of mortality in 176,139 nonsmoking women have also been construed by many as not showing an association between involuntary smoking and lung cancer (Garfinkel 1981). However, the standardized mortality ratios for the nonsmoking women with husbands who smoked were greater than unity, but not significantly greater. Recent and preliminary results from a nationwide case-control study also did not demonstrate increased lung cancer risk from domestic exposure to tobacco smoke (Kabat and Wynder 1984). In another case-control study that was performed in Los Angeles, Wu et al. (1985) did not find significantly increased risk for adenocarcinoma associated with involuntary smoking in smoking and nonsmoking women. These investigators estimated exposure from parental smoking, spouse smoking, and workplace sources. The relative risk for lung cancer was slightly, but not significantly, increased by exposure from spouse smoking and from smoking by co-workers.

The current extent of the data on involuntary smoking and lung cancer contrasts with the more extensive literature cited in the 1964 surgeon general's report, which characterized active cigarette smoking as a cause of lung cancer (U.S. Public Health Service [PHS] 1964). The variability of the data on involuntary smoking also contrasts with that on active smoking. However, most of the studies on involuntary smoking and lung cancer have small numbers of cases, and confidence intervals for the effect of involuntary smoking in the various studies would overlap. Variation in the results of the studies may also reflect random and nonrandom errors in the classification of exposure to ETS. In fact, assessment of exposure relevant to lung cancer appears more difficult than for other health effects of involuntary smoking. The relevant exposures may begin at birth and occur under a wide variety of circumstances. Thus, some inconsistency among the studies would be anticipated in the face of the relatively small study populations and the difficulties of estimating exposure.

In spite of the variable epidemiologic evidence, ETS has been characterized as a cause of lung cancer. The International Agency for Research on Cancer of the World Health Organization (IARC 1986) has concluded that "passive smoking gives rise to some risk of cancer." In its monograph on tobacco smoking, the agency supported this conclusion on the basis of the characteristics of sidestream and mainstream smoke, the absorption of tobacco smoke materials during involuntary smoking, and the nature of dose-response relationships for carcinogenesis.

The NRC (NRC 1986a) and the U.S. surgeon general (U.S. DHHS 1986) have also concluded that involuntary smoking increases the incidence of lung cancer in

nonsmokers. In reaching this conclusion, the NRC (NRC 1986a) cited the biologic plausibility of the association between exposure to ETS and lung cancer and the supporting epidemiologic evidence. Based on a pooled analysis of the epidemiologic data which adjusted for bias, the report concluded that the best estimate for the excess risk of lung cancer in nonsmokers married to smokers was 25 percent. The 1986 report of the surgeon general (U.S. DHHS 1986) characterized involuntary smoking as a cause of lung cancer in nonsmokers. This conclusion was based on the extensive information already available on the carcinogenicity of active smoking, on the qualitative similarities between ETS and mainstream smoke, and on the epidemiologic data on involuntary smoking.

The extent of the lung cancer hazard associated with involuntary smoking in the United States remains uncertain, however (U.S. DHHS 1986; Weiss 1986). The epidemiologic studies provide varying and imprecise measures of risk, and exposures have not been characterized for large and representative population samples. Risk estimation procedures have been used to describe the lung cancer risk associated with involuntary smoking, but assumptions and simplifications must be made in order to use this method. For example, Repace and Lowrey (1985) calculated that approximately 5,000 lung cancer deaths occur annually in U.S. nonsmokers as a result of involuntary smoking. Wells (1988) attributed 3,000 lung cancer deaths annually in the United States to involuntary smoking.

OTHER CANCERS

Several recent reports have suggested that exposure to ETS may increase the risk of cancer at sites other than the lung. One study found that in children, maternal exposure to environmental tobacco smoke during pregnancy was associated with increased risk of brain tumors (Preston-Martin et al. 1982), and in another study paternal but not maternal smoking increased the risk of childhood rhabdomyosarcoma (Grufferman et al. 1982). Such effects might arise from smoking-induced changes in germ cells of the parents or through transplacental exposure rather than as a direct effect of smoke inhalation (Everson 1980; Grufferman et al. 1983).

In adults, involuntary smoking has been linked to a generally increased risk of malignancy and to excess risk at specific sites. Miller (1984) interviewed surviving relatives of 537 deceased nonsmoking women in western Pennsylvania concerning the smoking habits of their husbands. A significantly increased risk of cancer death (odds ratio = 1.94, $p < .05$) was found in women who were married to smokers and also not employed outside the homes. The large number of potential subjects who were not interviewed and the possibility of information bias detract from this report.

Sandler and colleagues (Sandler, Everson, and Wilcox 1985; Sandler et al. 1985; Sandler, Wilcox, and Everson 1985) conducted a case-control study on the effects of exposures to ETS during childhood and adulthood on the risk of cancer. The 518 cases included cancers of all types other than basal cell cancer of the skin; the controls and the matched controls were between the ages of fifteen and fifty-nine years. For all sites combined, significantly increased risk was found for parental smoking (crude

odds ratio = 1.6) and for marriage to a smoking spouse (crude odds ratio = 1.5); the effects of these two exposures were independent (Sandler, Wilcox, and Everson 1985). Significant associations were also found for some individual sites: for childhood exposure (Sandler et al. 1985), maternal and paternal smoking increased the risk of hematopoietic malignancy, and for adulthood exposure (Sandler, Everson, and Wilcox 1985), spouse's smoking increased the risk for cancers of the female breast, female genital system, and the endocrine system. These findings are primarily hypothesis generating and require replication. In a case-control study, such as reported by Sandler et al. (1985), biased information on exposure to environmental tobacco smoke is of particular concern. Hirayama (1984) has reported significantly increased mortality from nasal sinus cancers and from brain tumors in nonsmoking women married to smokers in the Japanese cohort. In a case-control study of bladder cancer, involuntary smoke exposure at home and at work did not increase risk (Kabat, Dieck, and Wynder 1986). Cervical cancer, which has been linked to active smoking, was associated with duration of involuntary smoking in a case-control study in Utah (Slattery et al. 1989).

These associations of involuntary smoking with cancer at diverse nonrespiratory sites cannot be supported readily with arguments for biologic plausibility. Increased risks at some of the sites, for example, cancer of the nasal sinus and female breast cancer, have not been observed in active smokers (U.S. DHHS 1982). In fact, the IARC has concluded that effects would not be produced in passive smokers which would not be produced to a larger extent in active smokers (IARC 1986).

CARDIOVASCULAR DISEASE

Although extensive data establish active cigarette smoking as a causal risk factor for cardiovascular diseases (U.S. DHHS 1983), few studies have examined involuntary smoking as a risk factor for these diseases. In the cohort of nonsmoking Japanese women, Hirayama (1983) found a small, statistically significant increased risk of death from ischemic heart disease associated with the husband's smoking. Garland et al. (1985) prospectively determined mortality from ischemic heart disease in nonsmoking older women residing in southern California. After adjustment for established risk factors, marriage to a smoking spouse was associated with a relative risk of 2.7 ($p < .10$). Gillis et al. (1984) assessed the baseline prevalence of cardiovascular symptoms and major electrocardiographic abnormalities in a population sample residing in Scotland and then determined cause-specific mortality for up to ten years of follow-up. In a preliminary report, involuntary smoking was not associated with the prevalence of cardiovascular symptoms at baseline or with cardiovascular mortality on follow-up. A case-control study in England did not show increased risk for ischemic heart disease or for stroke in nonsmokers married to smokers (Lee, Chamberlain, and Alderson 1986).

The effect of involuntary smoking was assessed among the nonsmoking male participants in the MRFTT; these men had been selected to be in the upper 10–15 percent of risk for mortality from coronary artery disease, based on a score from

the Framingham study (Svendsen et al. 1987). In comparison with their situation as nonsmokers, never smokers with smoking wives had increased risk for coronary heart disease (relative risk = 2.11, 95 percent confidence interval 0.69–6.46), fatal or nonfatal coronary heart disease event (relative risk = 1.48, 95 percent confidence interval 0.89–2.47), and death from any cause (relative risk = 1.96, 95 percent confidence interval 0.93–4.11). These relative risks changed little when former smokers were included in the analysis or with adjustment for other risk factors for coronary heart disease.

Helsing and colleagues (1988) reported on the heart disease mortality of non-smokers enrolled in a cohort study in Washington County, Maryland. In comparison with persons married to nonsmokers, both men and women married to smokers had a significantly increased risk of dying from heart disease ($RR = 1.3$ for males and 1.2 for females).

The effects of involuntary exposure to tobacco smoke on athletic performance, which largely depends on cardiovascular responses, have also been examined. Such effects derive plausibility from the composition of ETS, which contains agents that might affect level of lung function and oxygen delivery by the cardiovascular system. Irritation of the upper and lower respiratory tracts following acute exposure might also adversely affect performance when exercise requires high minute ventilation.

Of the many toxic agents in ETS, CO and nicotine are candidates to influence performance adversely because of their cardiovascular effects (Schievebein and Richter 1984). CO interferes with oxygen transport by avidly binding to hemoglobin to form carboxyhemoglobin and by shifting the oxyhemoglobin dissociation curve to the left. Nicotine releases epinephrine and norepinephrine and elevates pulse rate, blood pressure, and oxygen demand. Although these effects of CO and nicotine might impair performance, exposures to ETS are generally at concentrations below which physiologic effects would be expected to occur (Schievebein and Richter 1984; U.S. DHHS 1986).

In two studies, healthy nonsmoking subjects were exposed to tobacco smoke and their performance subsequently assessed (Pimm, Silverman, and Shephard 1978; McMurray, Hicks, and Thompson 1985). In both studies, attempts were made to blind the subjects as to whether clean air or smoke-contaminated air was inhaled. Given the unmistakable odor and other characteristics of cigarette smoke, it seems unlikely that these studies were truly blinded, and their findings must be interpreted with this constraint.

Pimm, Silverman, and Shephard (1978) exposed ten males and ten females to levels of cigarette smoke described as characteristic of "levels typically encountered in public buildings." The subjects were exposed in a chamber and subsequently underwent a progressive exercise test. Maximal oxygen uptake was not significantly affected, and a consistent pattern of adverse effects on lung function was not found. The subjects did have symptomatic responses to the exposure.

In the study conducted by McMurray, Hicks, and Thompson (1985), air or cigarette smoke was inhaled by eight female subjects through a mouthpiece, and

submaximal and maximal exercise performance were assessed. The inhalation of cigarette smoke led to a reduction of maximal oxygen uptake and a reduction of time to exhaustion. Effects on the respiratory exchange ratio (R), maximal blood lactate, and ratings of perceived exertion were also found during the maximal testing. Adverse effects of smoke exposure were also suggested by the submaximal testing.

TOTAL MORTALITY

Several cohort studies provide information on involuntary smoking and mortality from all causes. In the Scottish cohort study, total mortality was increased for women living with a smoker but not for men (Gillis et al. 1984). As described previously, total mortality was also increased among nonsmoking participants in MRFTT who lived with smokers (Svendsen et al. 1987). In contrast, mortality was not increased for nonsmoking female subjects in a study in Amsterdam (Van denbroucke et al. 1984). Neither the study in Scotland nor the study in Amsterdam controlled for other factors that influence total mortality. In the cohort study in Washington County, all-cause mortality rates were significantly increased for men ($RR = 1.17$) and for women ($RR = 1.15$) after adjustment for housing quality, schooling, and marital status (Sandler et al. 1989).

ODOR AND IRRITATION

Tobacco smoke contains numerous irritants, including particulate material and gases (U.S. DHHS 1986). Both questionnaire surveys and laboratory studies involving exposure to ETS have shown annoyance and irritation of the eyes and upper and lower airways from involuntary smoking. In several surveys of nonsmokers, complaints about tobacco smoke at work and in public places were common (U.S. DHHS 1986); about 50 percent of respondents complained about tobacco smoke at work, and a majority was disturbed by tobacco smoke in restaurants. The experimental studies show that the rate of eye blinking is increased by ETS, as are complaints of nose and throat irritation (U.S. DHHS 1986). In the study of passive smoking on commercial airline flights reported by Mattson and colleagues (1989), changes in nose and eye symptoms were associated with nicotine exposure. The odor and irritation associated with ETS merit special consideration because a high proportion of nonsmokers are annoyed by exposure to ETS, and control of the concentrations in indoor air poses difficult problems in the management of heating, ventilating, and air-conditioning systems.

EXPERIMENTAL STUDIES

Experimental exposure of volunteer subjects has provided convincing evidence of the irritant effects of exposure to ETS. Studies reviewed in the 1986 report of the surgeon general (U.S. DHHS 1986) documented eye irritation through both objective measurements of blink rates and of stability of the precorneal tear film and subjective reports. Symptoms of nose and throat irritation were also associated

with ETS exposure. More recent experimental studies have provided further data concerning the odor and annoyance associated with ETS exposure.

The usual experimental setting to assess the effects of indoor contaminants on the senses is exposure in a climate-controlled environmental chamber with relatively inert surfaces, for example, aluminum or stainless steel, and variable ventilation. To investigate occupancy odor, human beings occupy the chamber for a given time. Judges of the odor of interest either enter the chamber briefly or place their faces into a box fed with the atmosphere of the chamber and may thus be considered to visit the space. The odor judgment may comprise a mark on an annotated rating scale (e.g., *no odor to overpowering odor*) or the choice of a matching odor intensity, generally using a device called an *olfactometer*, which delivers the vapor of a standard odorant, such as *n*-butyl alcohol (1-butanol), at various concentrations.

Many modern investigations also obtain judgments of acceptability in order to "calibrate" intensity judgments. Acceptability judgments address the question: How many people object to any given level of odor (or irritation)? The answer depends upon individual differences in olfactory sensitivity and upon aesthetic criteria. Whereas we can expect average intensity judgments to remain constant through the decades for any fixed stimulus, we can expect acceptability judgments to shift with prevailing standards.

Figure 6.1 shows the relationship between ventilation rate and occupant satisfaction in a recent study conducted in a climate chamber with from four to twelve occupants (Cain et al. 1983). Visitors made judgments of air circulated through an outside sampling box and were therefore naïve to the conditions of occupancy. The scale refers to the concentration of 1-butanol matched to the occupancy odor present after one hour of occupancy. Both odor level and dissatisfaction decreased with increases in ventilation rate.

The ventilation standard of the American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE) (1989) recommends a maximum of 20 percent dissatisfaction among visitors to a space. By this criterion, the data from the investigation imply the need for 17 cubic feet per minute (cfm) per occupant for (Figure 6.1). The ASHRAE standard suggests 15 cfm or more per occupant for most spaces, for example, 15 cfm for classrooms, libraries, auditoriums, and dormitories; 20 cfm for offices, conference rooms, dining rooms, and lobbies; 25 cfm for discotheques and beauty shops; 30 cfm for bars and casinos; and 60 cfm for smoking lounges. Thus, the ASHRAE standard specifies sufficient air to control odor associated with the occupants of a space.

When cigarettes were smoked in the climate chamber, odor level increased markedly (Figure 6.2). Figure 6.2 shows ETS odor for various conditions of smoking: intermittent (four cigarettes per hour) or continuous (eight and sixteen cigarettes per hour). The intensity of the odor increased with the number of cigarettes smoked and declined with increasing ventilation. As shown in Figure 6.3, the degree of dissatisfaction mirrored the higher odor level. Based on the rule of 20 percent maximum dissatisfaction, the ventilation rate required per cigarette

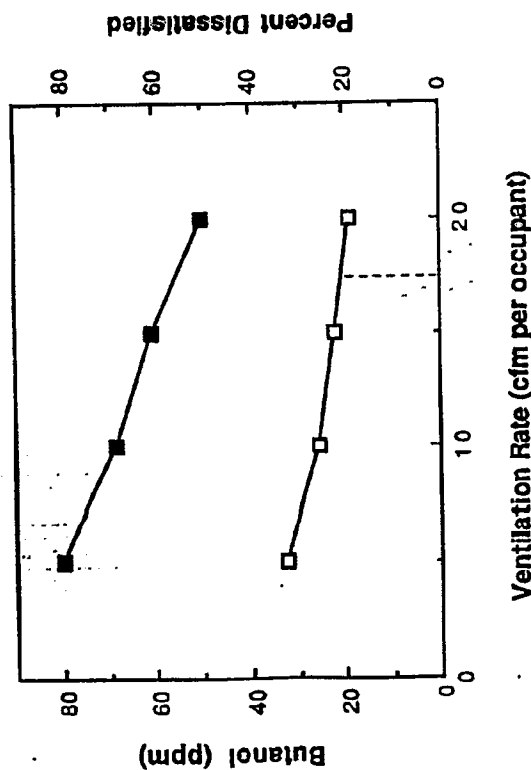


Figure 6.1. Relation between level of occupancy odor (indicated by concentration of 1-butanol matched to the odor [filled squares]) and ventilation rate per occupant when four to twelve persons occupied a climate chamber for an hour. Judgments of odor were made by visitors who sampled the air of the chamber at a remote sampling box. Also shown is the frequency of dissatisfaction expressed by the visitors in response to the question, "Is the air acceptable or unacceptable (unfilled squares)?" The dashed line shows the ventilation rate that led to 20 percent dissatisfaction. Source: Reprinted with permission from *Atmospheric Environment* 17, Cain W. S. et al., Ventilation requirements in buildings—I. Control of occupancy odor and tobacco smoke odor. Copyright 1983, Pergamon Press PLC.

during active smoking exceeded 4,000 ft³. In order to convert ventilation per cigarette into ventilation rate per person for typical conditions of occupancy in a "smoking-permitted" space, we assumed that 10 percent of the occupants would be smoking at any given time. The resulting requirement for ventilation was 53 cfm, more than three times that for nonsmoking occupancy.

The higher ventilation rate for smoking calculated from these data does not appear to represent a special aversion to the odor of cigarettes on the part of the judges. The judges, one-third of whom were smokers and two-thirds of whom were not, seemed to base their dissatisfaction strictly on odor intensity. Degree of dissatisfaction varied with odor intensity in the same way for both occupancy odor and tobacco smoke odor (Figure 6.4); stronger odors yielded greater dissatisfaction regardless of the source of odor.

The adequacy of the ASHRAE standard can be evaluated using these experimental data. The standard recommends 60 cfm per occupant in a smoking lounge, where presumably most or all occupants may be smoking. If 100 percent rather than 10 percent of the occupants smoke simultaneously, then the ventilation rate would need to exceed an unachievable 500 cfm per occupant. If 50 percent smoke

154 J. M. Samet, W. S. Cain, and B. P. Leaderer

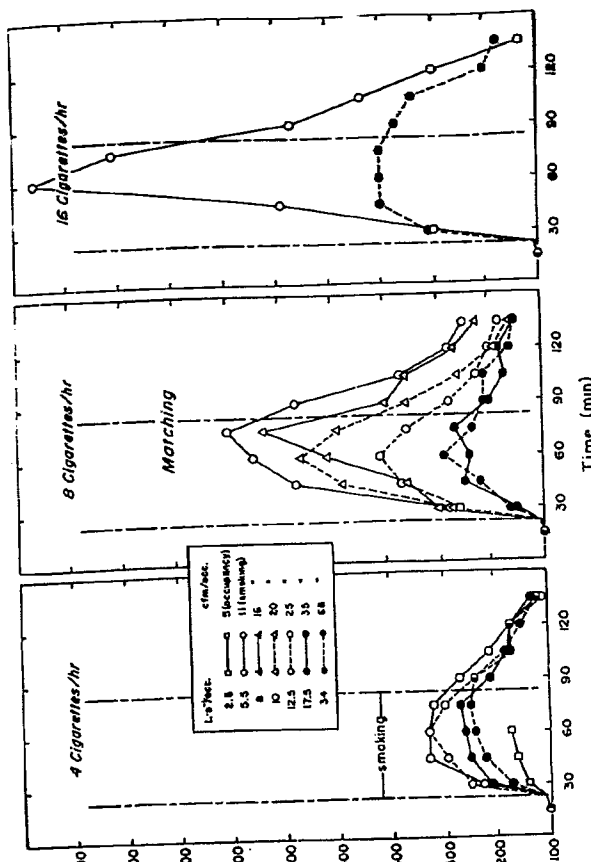


Figure 6.2. Intensity of ETS odor perceived by visitors to the sampling box during and after intermittent (four cigarettes per hour) or continuous (eight to sixteen cigarettes per hour) smoking in the climate chamber. Results are expressed relative to level of butanol matched to odor during presmoking occupancy. The open squares in the left panel show a function for nonsmoking occupancy for comparison. Ventilation rate per occupant under smoking conditions refers to smokers, who were the only occupants in the chamber. Source: Reprinted with permission from *Atmospheric Environment* 17, Cain W. S. et al., Ventilation requirements in buildings—I. Control of occupancy odor and tobacco smoke odor. Copyright 1983, Pergamon Press PLC.

simultaneously, perhaps a more realistic scenario, then the rate would need to exceed a still unachievable 250 cfm per occupant. The maximum achievable rate for typical design occupancy in a mechanically ventilated space will usually equal about 60 cfm per occupant, although a generous allotment of space per person can increase that value.

The smoker, however, seems less concerned about the odor of ETS than the nonsmoker. Smokers as a group seem satisfied with about one-quarter of the ventilation air needed by a group containing a typical proportion of smokers and nonsmokers. Hence, a rate of 60 cfm per occupant in smoking areas may almost meet the customary ASHRAE criterion of a maximum of 20 percent dissatisfaction for a group of smokers. The data from the investigation suggest that under typical conditions of smoking occupancy (10 percent smoking at any given time), nonsmokers would need over 100 cfm per occupant to hold dissatisfaction at only 20 percent. We do not know whether the difference between smokers and nonsmokers reflects olfactory sensitivity to ETS or other criteria.

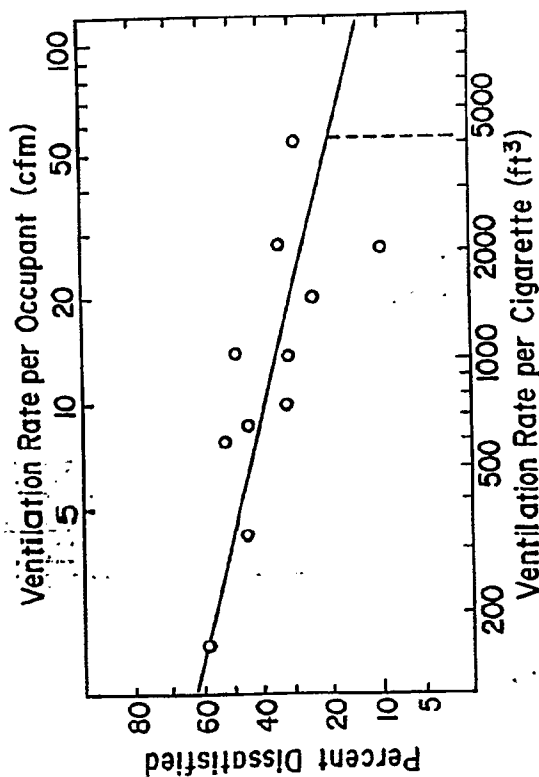


Figure 6.3. Percent dissatisfaction among visitors during the last 15 minutes of smoking in the experiments shown in Figure 6.2. The ventilation rate per cigarette is based on 7.5-minute smoking time per cigarette. The ventilation rate per occupant is adjusted to typical conditions of smoking occupancy in which 10 percent of occupants will be smoking at any given time. Source: Reprinted with permission from *Atmospheric Environment* 17, Cain W. S. et al., Ventilation requirements in buildings—I. Control of occupancy odor and tobacco smoke odor. Copyright 1983, Pergamon Press PLC.

Clausen and co-workers (1986b) found similar differences in tolerance of ETS odor between smokers and nonsmokers. For any given level of odor (expressed as concentration of butanol), nonsmokers expressed much more dissatisfaction than smokers. For both groups, odor intensity and dissatisfaction were associated, but the relationship was steeper for nonsmokers. At the point at which 20 percent of the smokers expressed dissatisfaction, almost half of nonsmokers were dissatisfied with the air quality.

In a laboratory situation in which other sources of combustion can be eliminated, CO can serve as an index of the level of ETS. Clausen related dissatisfaction to concentration of CO in ETS as well as to matched level of butanol; in the experiment, odor intensity and the increment in CO concentration due to smoking were strongly correlated. The concentration at which 20 percent of the nonsmokers expressed dissatisfaction fell about eight times below that at which 20 percent of the smokers expressed dissatisfaction.

As ETS enters the atmosphere, its many chemical constituents react both chemically and physically with each other and with surrounding materials. Nevertheless, the odor of ETS behaves over short time periods as though ETS were a stable contaminant. After the source has been removed, ETS odor decays in a manner

156 J. M. Samet, W. S. Cain, and B. P. Leaderer

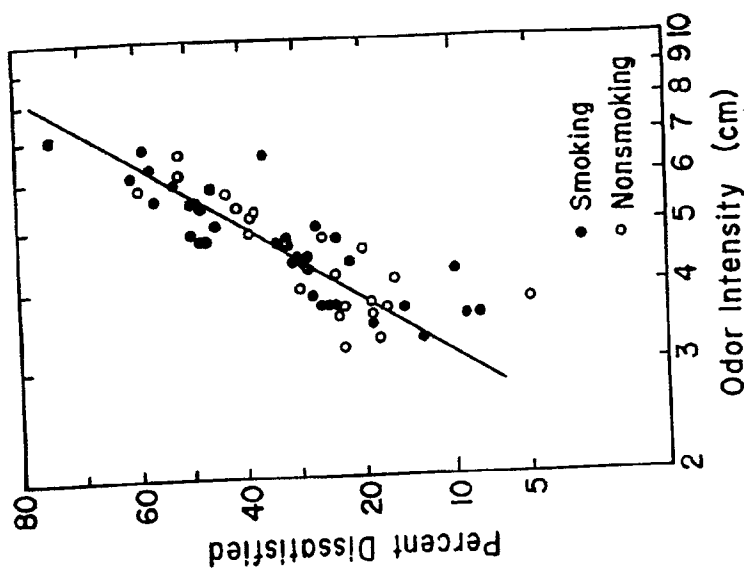


Figure 6.4. Percent dissatisfaction versus odor intensity (graphic rating) during smoking and nonsmoking odors. Source: Reprinted with permission from *Atmospheric Environment* 17, Cain W. S. et al., Ventilation requirements in buildings—I. Control of occupancy odor and tobacco smoke odor. Copyright 1983, Pergamon Press PLC.

entirely predictable from ventilation rate (Clausen et al. 1985). In this respect, it differs from occupancy odor, which has a half-life of 55 minutes, presumably dictated by slow oxidation of chemical constituents into less odorous products (Clausen et al. 1986a).

Standards for ventilation have focused on the reactions of the visitor to a space, rather than those of the occupant, on the assumption that the visitor will be more sensitive to, and hence more critical of, the contaminant than the person who has adapted to it. On the other hand, a focus on the visitor may not adequately address irritation, which is an important time-dependent sensory response of the occupant. Whereas air containing an irritant may initially be only slightly irritating, it may become intolerably so over time.

Figure 6.5 illustrates the time course of eye irritation experienced by occupants

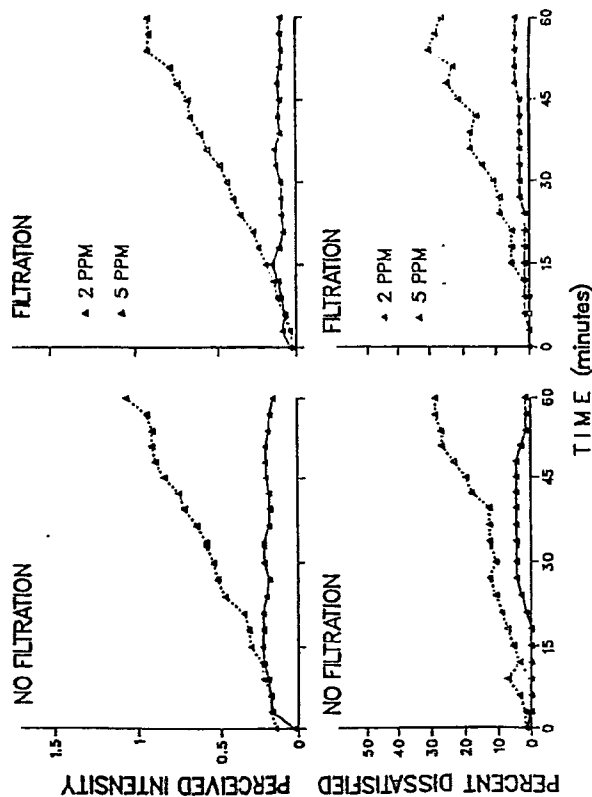


Figure 5.5. Perceived magnitude of eye irritation and degree of dissatisfaction expressed by occupants exposed to ETS for an hour. Concentrations of CO were held constant throughout the exposures and indicate severity of exposure. Filtration refers to elimination of particles via electrostatic precipitation. Filtration had little effect on irritation. Source: Reprinted with permission from *Atmospheric Environment* 21, Cain W. S. et al., Environmental tobacco smoke: Sensory reactions of occupants. Copyright 1987, Pergamon Press PLC.

exposed to ETS at constant concentrations of 2 or 5 ppm of CO, used as an index of ETS concentration (Cain et al. 1987). The lower concentration led to slight, although statistically significant, irritation above the presmoking baseline. The higher concentration led to irritation that increased over time in sensory magnitude and caused an increasing degree of dissatisfaction. Whereas essentially none of the occupants found the irritation objectionable at first, by the end of an hour about 30 percent were irritated. In an extension of this study, Clausen, Mller, and Fanger (1987) found that a level of 20 percent dissatisfaction would occur at a concentration of 3.8 ppm of CO. A comparison with the odor judgments of visitors suggests that only smokers would find such a level tolerable by the "20 percent rule." Clausen, Mller, and Fanger (1987) estimated that the ventilation rate necessary to control irritation of occupants to a dissatisfaction level of 20 percent would equal only one-tenth of that needed to control odor perceived by visitors to the same level of dissatisfaction.

Although Clausen and co-workers did not argue in favor of lowering ventilation to meet only the dissatisfaction of occupants, others have suggested this approach

(Winneke et al. 1984). Cain and co-workers (1987) cautioned against handling irritation and odor in the same fashion. The appropriateness of applying the 20 percent rule to dissatisfaction based on irritation alone, as it is applied to dissatisfaction based on odor alone, has been questioned. Whereas odor may be interpretable narrowly on grounds of comfort, irritation would seem interpretable on grounds of health.

CONTROL

The standards of ASHRAE mandate specific levels of ventilation to provide occupant satisfaction with indoor air quality. The experimental studies reviewed above provide insights concerning the level of ventilation needed to achieve satisfaction for nonsmokers and for smokers in the presence of ETS. In actual indoor environments, when ventilation fails to eliminate the contaminant entirely, the physical interaction of ETS with surfaces may increase the need for ventilation. Because the liquid aerosol of ETS, known in the aggregate as *tar*, adsorbs strongly to walls, fabrics, and so on, it becomes a source of odor as components volatilize to the air. The background odor of the emitted products carries its own demands for ventilation, predictable in part from the typical amount of smoking in a space (Clausen et al. 1986b).

Obviously, ETS can be readily controlled by eliminating smoking from indoor environments or its impact lessened by limiting smoking to specific areas. Air cleaning offers another approach.

Although the odor of ETS can be postulated to come from its vapor phase and the irritation from its particulate phase, recent investigations that have employed electrostatic air cleaning have shown clearly that the gas phase accounts for most of the odor and irritation (Hugod 1984; Weber 1984). Comparison of the right and left sides of Figure 6.5 shows that elimination of the particulate phase had only a trivial effect on the eye irritation caused by ETS at 2 and 5 ppm carbon monoxide (Cain et al. 1987). The findings were similar for judgments of odor and of nose and throat irritation. Clausen, Mller, and Fanger (1987) confirmed these results. In finding that particles played essentially no role in odor, both investigations also confirmed Clausen and colleagues' (1985) earlier experiments with visitors. Particle filtration holds no promise for immediate elimination of the discomfort of exposure to ETS. The major advantage of such air cleaning derives from reduction of haze and collection of tar that would otherwise adsorb elsewhere in the space.

Although both the odor and irritation of ETS come from the vapor phase, the chemical constituents responsible for these two effects may be different. Undoubtedly, the odor comes from a very large number of constituents. The sense of smell responds to almost all airborne organic materials present in sufficient concentration (Cain 1988). For one substance, however, a "sufficient concentration" may fall a millionfold below that of another. Furthermore, individual constituents may combine perceptually in mixtures in complicated, nonlinear ways.

Many single compounds can cause irritation at the concentrations present in ETS, which represents a complex mixture with numerous components capable of

causing odor and irritation. Little is known about the effects upon perception of the combination of ETS irritants although it is known that odor and irritation interact (Cain and Murphy 1980). Irritation can suppress the perception of odor and vice versa (Cain, Sec, and Tosun 1986). Insofar as irritation may have a less complex origin than odor, it may offer easier opportunities for control through filtration. As yet, however, experiments on ETS have told more about what fails to cause irritation than about what causes it (Weber, Jermini, and Grandjean 1976; Weber-Tschopp, Fischer, and Grandjean 1977; Weber-Tschopp et al. 1977; Hugod, Hawkins, and Astrup 1978).

The complexity of ETS more or less assures that almost any means of air cleaning will eliminate part of it even though no simple procedure will eliminate all of it. Through the use of air washing that presumably eliminated some water-soluble constituents of ETS, Clausen, Mäller, and Fanger (1987) achieved some reduction in level of dissatisfaction although not in the perceived intensity of ETS. The results offered little encouragement for using air washing alone but showed that the odor character of ETS can play some role in the degree of acceptance.

A combination of particulate air cleaning and vapor phase cleaning via adsorption on activated carbon or via chemisorption on oxidant-impregnated alumina can likely control both the irritation and odor of ETS to some degree. Unfortunately, standards for assessing the efficacy of vapor phase filtration media have not been developed. The installation of such media occurs more commonly in special environments, for example, libraries and computer facilities, under expert guidance than in spaces designed for general occupancy. In the overwhelming majority of cases, attempts to control ETS rely on ventilation (dilution). As shown by the experimental studies, however, ventilation has limitations.

SUMMARY

The effects of active smoking and the toxicology of cigarette smoking have been examined comprehensively. The periodic reports of the U.S. surgeon general and other summary reports have considered the extensive evidence on active smoking; these reports have provided definitive conclusions concerning the adverse effects of active smoking, which have prompted public policies and scientific research directed at prevention and cessation of smoking.

Although the evidence on involuntary smoking is not as extensive as that on active smoking, health risks of involuntary smoking have been identified. The 1986 report of the U.S. surgeon general (U.S. DHHS 1986) and the 1986 report of the NRC (NRC 1986a) both concluded that involuntary exposure to tobacco smoke increases respiratory infections in children, increases the prevalence of respiratory symptoms in children, reduces the rate of functional growth as the lung matures, and causes lung cancer in nonsmokers. Involuntary smoking may also adversely affect asthmatics, and annoyance and irritation are well documented. These adverse effects of involuntary exposure to tobacco smoke have provided a strong

rationale for policies directed at reducing and eliminating exposure of nonsmokers to ETS (U.S. DHHS 1986). Complete protection of nonsmokers in public locations and the workplace may require the banning of smoking since the 1986 report of the surgeon general (U.S. DHHS 1986) concluded that "the simple separation of smokers and nonsmokers within the same air space may reduce, but does not eliminate, the exposure of nonsmokers to environmental tobacco smoke."

REFERENCES

- Akiba, S.; Kato, H.; and Blot, W. J. 1986. Passive smoking and lung cancer among Japanese women. *Cancer Res.* 46:4804-7.
- American Society of Heating, Refrigerating, and Air-Conditioning Engineers. 1989. ASHRAE Standard 62-1989: *Ventilation for acceptable indoor air quality*. Atlanta, Ga.: ASHRAE.
- Badre, R., et al. 1978. Pollution atmosphérique par la fumée de tabac. *Ann. Pharm. Fr.* 36:443-52.
- Benowitz, N. L., et al. 1983. Cotinine disposition and effects. *Clin. Pharmacol. Ther.* 34:604-11.
- Berkey, C. S., et al. 1986. Indoor air pollution and pulmonary function growth in preadolescent children. *Am. J. Epidemiol.* 123:250-60.
- Black, N. 1985. The aetiology of glue ear: A case-control study. *Int. J. Pediatr. Otorhinolaryngol.* 9:121-33.
- Bland, M., et al. 1978. Effect of children's and parents' smoking on respiratory symptoms. *Arch. Dis. Child.* 53:100-105.
- Brownson, R. C., et al. 1987. Risk factors for adenocarcinoma of the lung. *Am. J. Epidemiol.* 125:25-34.
- Brunekeer, B., et al. 1985. Indoor air pollution and its effect on pulmonary function of adult nonsmoking women, III: Passive smoking and pulmonary function. *Int. J. Epidemiol.* 14:227-30.
- Burchfiel, C. M., III. 1984. Passive smoking, respiratory symptoms, lung function and initiation of smoking in Tecumseh, Michigan. Ph.D. diss., University of Michigan, Ann Arbor.
- Burchfiel, C. M., et al. 1986. Passive smoking in childhood: Respiratory conditions and pulmonary function in Tecumseh, Michigan. *Am. Rev. Respir. Dis.* 133:966-73.
- Cain, W. S. 1988. Olfaction. In *Stevens' handbook of experimental psychology, Vol. 1: Perception and motivation*, rev. ed. Ed. R. C. Atkinson, et al., 409-59. New York: John Wiley & Sons.
- Cain, W. S., and Murphy, C. L. 1980. Interaction between chemoreceptive modalities of odour and irritation. *Nature* 284:255-57.
- Cain, W. S.; Sec, L. C.; and Tosun, T. 1986. Irritation and odor from formaldehyde: Chamber studies. In *IAQ '86: Managing indoor air for health and energy conservation*, 126-37. Atlanta, Ga.: ASHRAE.
- Cain, W. S., et al. 1983. Ventilation requirements in buildings, I: Control of occupancy odor and tobacco smoke odor. *Atmos. Environ.* 17:1183-97.
- Cain, W. S., et al. 1987. Environmental tobacco smoke: Sensory reactions of occupants. *Atmos. Environ.* 21:347-53.

- Chan, W. C., and Fung, S. C. 1982. Lung cancer in nonsmokers in Hong Kong. In *Cancer campaign*, Vol. 6: *Cancer epidemiology*. Ed. E. Grundman, 199-202. Stuttgart: Gustav Fischer Verlag.
- Chan, W. C., et al. 1979. Bronchial cancer in Hong Kong 1976-1977. *Br. J. Cancer* 39:182-92.
- Chappell, S. B., and Parker, R. J. 1977. Smoking and carbon monoxide levels in enclosed public places in New Brunswick. *Can. J. Public Health*, 68:159-61.
- Charlton, A. 1984. Children's coughs related to parental smoking. *Br. Med. J.* 288:1647-49.
- Clausen, G. H. 1986. Tobaksrog: Luftgener og ventilationsbehov. Ph.D. diss., Technical University of Denmark, Copenhagen.
- Clausen, G. H.; Möller, S. B.; and Fanger, P. O. 1987. The impact of air washing on environmental tobacco smoke odor. In *Indoor air '87*, Volume 2. Ed. B. Seifert, et al., 47-51. Berlin: Institute for Water, Soil, and Air Hygiene.
- Clausen, G. H., et al. 1985. The influence of aging, particle filtration and humidity on tobacco smoke odor. In *Clima 2000*, Vol. 4: *Indoor climate*. Ed. P. O. Fanger, 345-49. Copenhagen: VVS Kongres-VVS Messe.
- Clausen, G. H., et al. 1986a. Stability of body odor in enclosed spaces. *Environ. Int.* 12:201-5.
- Clausen, G. H., et al. 1986b. Background odor caused by previous tobacco smoking. In *IAQ '86: Managing indoor air for health and energy conservation*, 119-25. Atlanta: ASHRAE.
- Cogswell, J. J.; Mitchell, E. B.; and Alexander, J. 1987. Parental smoking, breast feeding, and respiratory infection in development of allergic diseases. *Arch. Dis. Child.* 62:338-44.
- Colley, J. R. 1974. Respiratory symptoms in children and parental cigarette smoking and phlegm production. *Br. Med. J.* 2:201-4.
- Comstock, G. W., et al. 1981. Respiratory effects of household exposures to tobacco smoke and gas cooking. *Am. Rev. Respir. Dis.* 124:143-48.
- Correa, P., et al. 1983. Passive smoking and lung cancer. *Lancet* 2:595-97.
- Coultas, D. B., and Samet, J. M. 1990. Comparability of salivary and urinary cotinine determination for assessment of exposure to environmental tobacco smoke. Submitted for publication.
- Coultas, D. B., et al. 1990. Variability of measures of exposure to environmental tobacco smoke in the home. *Am. Rev. Respir. Dis.* 142:602-6.
- Coultas, D. B., et al. 1987. Salivary cotinine levels and involuntary tobacco smoke exposure in children and adults in New Mexico. *Am. Rev. Respir. Dis.* 136:305-9.
- Coultas, D. B., et al. 1988. Variability of measures of exposure to environmental tobacco smoke in the home. Air Pollution Control Association, International specialty conference on combustion processes and the quality of the indoor environment.
- Cummings, K. M., et al. 1989. Measurement of lifetime exposure to passive smoke. *Am. J. Epidemiol.* 130:122-32.
- Dahms, T. E.; Bolin, J. F.; and Slavov, R. G. 1981. Passive smoking: Effect on bronchial asthma. *Chest* 80:530-34.
- Dalager, N. A., et al. 1986. The relation of passive smoking to lung cancer. *Cancer Res.* 46:4808-11.
- Enstrom, J. E. 1979. Rising lung cancer mortality among nonsmokers. *J. Natl. Cancer Inst.* 62:555-60.
- Evans, D., et al. 1987. The impact of passive smoking on emergency room visits of urban children with asthma. *Am. Rev. Respir. Dis.* 135:567-72.
- Evenson, R. B. 1980. Individuals transplacentally exposed to maternal smoking may be at increased cancer risk in adult life. *Lancet* 2:123-27.
- Fergusson, D. M., and Horwood, L. J. 1985. Parental smoking and respiratory illness during early childhood: A six-year longitudinal study. *Pediatr. Pulmonol.* 1:99-106.
- First, M. W. 1985. Constituents of sidestream and mainstream tobacco smoke and markers to quantify exposure to them. In *Indoor air and human health*. Ed. R. B. Gammage and S. V. Kaye, 195-203. Chelsea, Mich.: Lewis Publishers.
- Folliart, D.; Benowitz, N. L.; and Becker, C. E. 1983. Passive absorption of nicotine in flight attendants (letter). *N. Engl. J. Med.* 308:1105.
- Gao, Y. T., et al. 1987. Lung cancer among Chinese women. *Int. J. Cancer* 40:604-9.
- Garfinkel, L. 1981. Time trends in lung cancer mortality among nonsmokers and a note on passive smoking. *J. Natl. Cancer Inst.* 66:1061-66.
- Garfinkel, L.; Auerbach, O.; and Joubert, L. 1985. Involuntary smoking and lung cancer: A case-control study. *J. Natl. Cancer Inst.* 75:463-69.
- Garland, C., et al. 1985. Effects of passive smoking on ischemic heart disease mortality of nonsmokers. *Am. J. Epidemiol.* 121:645-50.
- Geng, G. Y., et al. 1987. On the relationship between smoking and female lung cancer. In *Smoking and health 1987*. Ed. M. Aoki, S. Hisamichi, and S. Tominaga, 483-86. Amsterdam: Excerpta Medica.
- Gillis, C. R., et al. 1984. The effect of environmental tobacco smoke in two urban communities in the west of Scotland. *Eur. J. Respir. Dis.* 65(Suppl. 133):121-26.
- Gortmaker, S. L., et al. 1982. Parental smoking and the risk of childhood asthma. *Am. J. Public Health* 72:574-79.
- Greenberg, R. A., et al. 1984. Measuring the exposure of infants to tobacco smoke: Nicotine and cotinine in urine and saliva. *N. Engl. J. Med.* 310:1075-78.
- Grufferman, S., et al. 1982. Environmental factors in the etiology of rhabdomyosarcoma in childhood. *J. Natl. Cancer Inst.* 68:107-13.
- Grufferman, S., et al. 1983. Parents' cigarette smoking and childhood cancer. *Med. Hypotheses* 12:17-20.
- Haley, N. J.; Sepkovic, D.; and Hoffman, D. 1989. Elimination of cotinine from body fluids: Disposition in smokers and nonsmokers. *Am. J. Public Health* 79:1046-48.
- Haley, N. J., et al. 1989. Biochemical validation of self-reported exposure to environmental tobacco smoke. *Environ. Res.* 49:127-35.
- Hall, C. B., et al. 1984. Long-term prospective study in children after respiratory syncytial virus infection. *J. Pediatr.* 105:358-64.
- Harlap, S., and Davies, A. M. 1974. Infant admissions to hospital and maternal smoking. *Lancet* 1:529-32.
- Harlos, D. P., et al. 1987. Relating indoor NO₂ levels to infant personal exposures. *Atmos. Environ.* 21:369-78.
- Helsing, K. J., et al. 1988. Heart disease mortality in nonsmokers living with smokers. *Am. J. Epidemiol.* 127:915-22.
- Henderson, F. W., et al. 1989. Home air nicotine levels and urinary cotinine excretion in preschool children. *Am. Rev. Respir. Dis.* 140:197-201.
- Hinds, W. C., and First, M. W. 1975. Concentrations of nicotine and tobacco smoke in public places. *N. Engl. J. Med.* 292:844-45.

Hirayama, T. 1981. Nonsmoking wives of heavy smokers have a higher risk of lung cancer: A study from Japan. *Br. Med. J.* 282:183-85.

Hirayama, T. 1983. Passive smoking and lung cancer, nasal sinus cancer, brain tumor and ischemic heart disease. In *Proceedings of the Fifth World Conference on Smoking and Health*, Vol. 1. Ed. W. F. Forbes, R. C. Frecker, and D. Nostbakken, 137-41. Ottawa: Canadian Council on Smoking and Health.

Hirayama, T. 1984. Cancer mortality in nonsmoking women with smoking husbands based on a large-scale cohort study in Japan. *Prev. Med.* 13:680-90.

Hoffman, D., et al. 1984a. Indoor air pollution by tobacco smoke: Model studies on the uptake by nonsmokers. In *Indoor air*, Vol. 2: *Radon, passive smoking, particulates and housing epidemiology*. Ed. B. Berglund, T. Lindvall, and J. Sundell, 313-18. Stockholm: Swedish Council for Building Research.

Hoffman, D., et al. 1984b. Tobacco sidestream smoke: Uptake by nonsmokers. *Prev. Med.* 13:608-17.

Horwood, L. J.; Fergusson, D. M.; and Shannon, F. T. 1985. Social and familial factors in the development of early childhood asthma. *Pediatrics* 75:859-68.

Hosein, R., and Corey, P. 1984. Multivariate analyses of nine indoor factors on FEV₁ of Caucasian children. *Am. Rev. Respir. Dis.* 129(suppl.):140 (abstr.).

Hugod, C. 1984. Indoor air pollution with smoke constituents: An experimental investigation. *Prev. Med.* 13:582-88.

Hugod, C.; Hawkins, L. H.; and Astrup, P. 1978. Exposure of passive smokers to tobacco smoke constituents. *Int. Arch. Occup. Environ. Health* 42:21-29.

Humble, C. G.; Samet, J. M.; and Pathak, D. R. 1987. Marriage to a smoker and lung cancer risk in New Mexico. *Am. J. Public Health* 77:598-602.

Inoue, R., and Hirayama, T. 1988. Passive smoking and lung cancer in women. In *Smoking and health 1987*. Ed. M. Aoki, S. Hisanichi, and S. Tominaga, 283-85. Amsterdam: Excerpta Medica.

International Agency for Research on Cancer. 1986. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans: Tobacco smoking, Vol. 38. Lyon, France: World Health Organization, IARC.

Iversen, M., et al. 1985. Middle ear effusion in children and the indoor environment: An epidemiological study. *Arch. Environ. Health* 40:74-79.

Jarvis, M. J., and Russell, M. A. 1984. Measurement and estimation of smoke dosage to nonsmokers from environmental tobacco smoke. *Eur. J. Respir. Dis.* 65(suppl. 133):68-75.

Jarvis, M. J., et al. 1984. Biochemical markers of smoke absorption and self-reported exposure to passive smoking. *J. Epidemiol. Community Health* 38:335-39.

Jarvis, M. J., et al. 1985. Passive exposure to tobacco smoke: Saliva cotinine concentrations in a representative population sample of nonsmoking school children. *Br. Med. J.* 291:927-29.

Jarvis, M. J., et al. 1988. Elimination of cotinine from body fluids: Implications for noninvasive measurement of tobacco smoke exposure. *Am. J. Public Health* 78:696-98.

Jones, J. R., et al. 1983. Effects of cooking fuels on lung function in nonsmoking women. *Arch. Environ. Health* 38:219-22.

Kabat, G. C., and Wynder, E. L. 1984. Lung cancer in nonsmokers. *Cancer* 53:1214-21.

Kabat, G. C.; Dieck, G. S.; and Wynder, E. L. 1986. Bladder cancer in nonsmokers. *Cancer* 2:362-67.

Kauffman, F.; Tessier, J. S.; and Oriol, P. 1983. Adult passive smoking in the home environment: A risk factor for chronic airflow limitation. *Am. J. Epidemiol.* 117:269-80.

Kauffman, F., et al. 1989. Respiratory symptoms and lung function in relation to passive smoking: A comparative study of American and French women. *Int. J. Epidemiol.* 18:334-44.

Kentner, M.; Triebig, G.; and Weitle, D. 1984. The influence of passive smoking on pulmonary function: A study of 1,351 office workers. *Prev. Med.* 13:656-69.

Kershaw, C. R. 1987. Passive smoking, potential atopy and asthma in the first five years. *J. R. Soc. Med.* 80:683-88.

Knoth, A.; Bohn, H.; and Schmidt, F. 1983. Passivrauch als lung enkrebsursache bei nichtraucherinnen. *Med. Klin.* 2:66-69.

Koo, L. C.; Ho, J. H.; and Lee, N. 1985. An analysis of some risk factors for lung cancer in Hong Kong. *Int. J. Cancer* 35:149-55.

Koo, L. C.; Ho, J. H.; and Saw, D. 1984. Is passive smoking an added risk factor for lung cancer in Chinese women? *J. Exp. Clin. Cancer Res.* 3:277-83.

Koo, L. C., et al. 1987. Measurements of passive smoking and estimates of lung cancer risk among nonsmoking Chinese females. *Int. J. Cancer* 39:162-69.

Kraemer, J. M., et al. 1983. Risk factors for persistent middle-ear effusions: Otitis media, catarrh, cigarette exposure, and atopy. *JAMA* 249:1022-25.

Kyrematen, G. A., et al. 1982. Smoking-induced changes in nicotine disposition: Application of a new HPLC assay for nicotine and its metabolites. *Clin. Pharmacol. Ther.* 32:769-80.

Lam, T. H., et al. 1987. Smoking, passive smoking and histological types in lung cancer in Hong Kong Chinese women. *Br. J. Cancer* 56:673-78.

Lebowitz, M. D., and Burrows, B. 1976. Respiratory symptoms related to smoking habits of family adults. *Chest* 69:48-50.

Lebowitz, M. D.; Knudson, R. J.; and Burrows, B. 1984. Family aggregation of pulmonary function measurements. *Am. Rev. Respir. Dis.* 129:8-11.

Lee, P. N. 1988. *Misclassification of smoking habits and passive smoking*. Heidelberg: Springer-Verlag.

Lee, P. N.; Chamberlain, J.; and Alderson, M. R. 1986. Relationship of passive smoking to risk of lung cancer and other smoking-associated diseases. *Br. J. Cancer* 54:97-105.

Leeder, S. R., et al. 1976. Influence of family factors on the incidence of lower respiratory illness during the first year of life. *Br. J. Prev. Soc. Med.* 30:203-12.

Martinez, F. D., et al. 1988. Parental smoking enhances bronchial responsiveness in nine-year-old children. *Am. Rev. Respir. Dis.* 138:518-23.

Masi, M. A., et al. 1988. Environmental exposure to tobacco smoke and lung function in young adults. *Am. Rev. Respir. Dis.* 138:296-99.

Matsukura, S., et al. 1984. Effects of environmental tobacco smoke on urinary cotinine excretion in nonsmokers: Evidence for passive smoking. *N. Engl. J. Med.* 311:828-32.

Matson, M. E., et al. 1989. Passive smoking on commercial airline flights. *JAMA* 261:867-72.

McConnochie, K. M., and Roghmann, K. J. 1986. Breast feeding and maternal smoking as predictors of wheezing in children age 6 to 10 years. *Pediatr. Pulmonol.* 2:260-68.

McMurray, R. G.; Hicks, L. L.; and Thompson, D. L. 1985. The effects of passive

Rosenberg, J., et al. 1980. Disposition kinetics and effects of intravenous nicotine. *Clin. Pharmacol. Ther.* 28:517-22.

Russell, M. A.; West, R. J.; and Jarvis, M. J. 1985. Intravenous nicotine simulation of passive smoking to estimate dosage to exposed nonsmokers. *Br. J. Addict.* 80:201-6.

Samet, J. M.; Tager, I. B.; and Speizer, F. E. 1983. The relationship between respiratory illness in childhood and chronic air-flow obstruction in adulthood. *Am. Rev. Respir. Dis.* 127:508-23.

Sandler, D. P.; Everson, R. B.; and Wilcox, A. J. 1985. Passive smoking in adulthood and cancer risk. *Am. J. Epidemiol.* 121:37-48.

Sandler, D. P.; Wilcox, A. J.; and Everson, R. B. 1985. Cumulative effects of lifetime passive smoking on cancer risk. *Lancet* 1:312-15.

Sandler, D. P., et al. 1985. Cancer risk in adulthood from early life exposure to parents' smoking. *Am. J. Public Health* 74:487-92.

Sandler, D. P., et al. 1989. Deaths from all causes in non-smokers who lived with smokers. *Am. J. Public Health* 79:163-67.

Schenker, M. B.; Samet, J. M.; and Speizer, F. E. 1982. Effect of cigarette tar content and smoking habits on respiratory symptoms in women. *Am. Rev. Respir. Dis.* 125:684-90.

Schenker, M. B.; Samet, J. M.; and Speizer, F. E. 1983. Risk factors for childhood respiratory disease: The effect of host factors and home environmental exposures. *Am. Rev. Respir. Dis.* 128:1038-43.

Schievebein, H., and Richter, F. 1984. The influence of passive smoking on the cardiovascular system. *Prev. Med.* 13:626-44.

Schilling, R. S., et al. 1977. Lung function, respiratory disease, and smoking in families. *Am. J. Epidemiol.* 106:274-83.

Shephard, R. J., et al. 1979. Effect of cigarette smoke on the eyes and airway. *Int. Arch. Occup. Environ. Health* 135-44.

Shimizu, H., et al. 1988. A case-control study of lung cancer in nonsmoking women. *Tohoku J. Exp. Med.* 154:389-97.

Slatery, M. L., et al. 1989. Cigarette smoking and exposure to passive smoke are risk factors for cervical cancer. *JAMA* 261:1593-98.

Somerville, S. M.; Rona, R. J.; and Chinn, S. 1988. Passive smoking and respiratory conditions in primary school children. *J. Epidemiol. Community Health* 42:105-10.

Spengler, J. D., et al. 1981. Long-term measurements of respirable sulfates and particles inside and outside homes. *Atmos. Environ.* 15:23-30.

Spengler, J. D., et al. 1985. Personal exposures to respirable particulates and implications for air pollution epidemiology. *Environ. Sci. Technol.* 19:700-707.

Stankus, R. P., et al. 1988. Cigarette smoke-sensitive asthma: Challenge studies. *J. Allergy Clin. Immunol.* 82:331-38.

Sterling, T. D., and Kobayashi, D. 1982. Indoor byproduct levels of tobacco smoke: A critical review of the literature. *J. Air Pollut. Control Assoc.* 32:250-59.

Strachan, D. P.; Jarvis, M. J.; and Feyerabend, C. 1989. Passive smoking, salivary cotinine concentrations, and middle ear effusion in 7-year-old children. *Br. Med. J.* 298:1549-52.

Svendsen, K. H., et al. 1987. Effects of passive smoking in the multiple risk factor intervention trial. *Am. J. Epidemiol.* 126:783-95.

Tager, I. B. 1988. Passive smoking-bronchial responsiveness and atopy (editorial). *Am. Rev. Respir. Dis.* 138:507-9.

Tager, I. B., et al. 1979. Effect of parental cigarette smoking on the pulmonary function of children. *Am. J. Epidemiol.* 110:15-26.

inhalation of cigarette smoke on exercise performance. *Eur. J. Appl. Physiol.* 54:196-200.

Miller, G. H. 1984. Cancer, passive smoking and nonemployed and employed wives. *West. J. Med.* 140:632-35.

Muramatsu, M., et al. 1984. Estimation of personal exposure to tobacco smoke with a newly developed nicotine personal monitor. *Environ. Res.* 35:218-27.

Murray, A. B., and Morrison, B. J. 1986. The effect of cigarette smoke from the mother on bronchial responsiveness and severity of symptoms in children with asthma. *J. Allergy Clin. Immunol.* 77:575-81.

National Research Council (committee on indoor pollutants). 1981. *Indoor pollutants*. Washington, D.C.: National Academy Press.

National Research Council (committee on passive smoking). 1986a. *Environmental tobacco smoke: measuring exposures and assessing health effects*. Washington, D.C.: National Academy Press.

National Research Council (committee on airliner cabin air quality). 1986b. *The airliner cabin environment: Air quality and safety*. Washington, D.C.: National Academy Press.

O'Connor, G. T., et al. 1987. The effect of passive smoking on pulmonary function and nonspecific bronchial responsiveness in a population-based sample of children and young adults. *Am. Rev. Respir. Dis.* 135:800-804.

Ogston, S. A.; Florey, C. V.; and Walker, C. H. M. 1985. The Tayside infant morbidity and mortality study: Effect on health of using gas for cooking. *Br. Med. J.* 290:957-60.

Ogston, S. A.; Florey, C. V.; and Walker, C. H. M. 1987. Association of infant alimentary and respiratory illness with parental smoking and other environmental factors. *J. Epidemiol. Community Health* 41:21-25.

Pattishall, E. N., et al. 1985. Serum cotinine as a measure of tobacco smoke exposure in children. *Am. J. Dis. Child.* 139:1101-4.

Pershagen, G.; Hrubec, Z.; and Svensson, C. 1987. Passive smoking and lung cancer in Swedish women. *Am. J. Epidemiol.* 125:17-24.

Pimm, P. E.; Silverman, F.; and Shephard, R. J. 1978. Physiological effects of acute passive exposure to cigarette smoke. *Arch. Environ. Health* 33:201-13.

Preston-Martin, S., et al. 1982. N-Nitroso compounds and childhood brain tumors: A case-control study. *Cancer Res.* 42:5240-45.

Pron, G. E., et al. 1988. The reliability of passive smoking histories reported in a case-control study of lung cancer. *Am. J. Epidemiol.* 127:267-73.

Pukander, J., et al. 1985. Risk factors affecting the occurrence of acute otitis media among 2-3-year-old urban children. *Acta Otolaryngol.* 100:260-65.

Pullan, C. R., and Hey, C. N. 1982. Wheezing, asthma, and pulmonary dysfunction 10 years after infection with respiratory syncytial virus in infancy. *Br. Med. J.* 284:1665-69.

Rantakallio, P. 1978. Relationship of maternal smoking to morbidity and mortality of the child up to the age of five. *Acta Paediatr. Scand.* 67:621-31.

Remijn, B., et al. 1985. Indoor air pollution and its effect on pulmonary function of adult nonsmoking women. I: Exposure estimates for nitrogen dioxide and passive smoking. *Int. J. Epidemiol.* 14:215-20.

Ropace, J. L., and Lowrey, A. H. 1980. Indoor air pollution, tobacco smoke, and public health. *Science* 208:464-72.

Ropace, J. L., and Lowrey, A. H. 1985. A quantitative estimate of nonsmokers' lung cancer risk from passive smoking. *Environ. Int.* 11:3-22.

Tager, I. B., et al. 1983. Longitudinal study of the effects of maternal smoking on pulmonary function in children. *N. Engl. J. Med.* 309:699-703.

Tashkin, D. P., et al. 1984. The UCLA population studies of chronic obstructive respiratory disease. VII: Relationship between parental smoking and children's lung function. *Am. Rev. Respir. Dis.* 129:891-97.

Trichopoulos, D.; Kalandidi, A.; and Sparros, L. 1983. Lung cancer and passive smoking: Conclusion of Greek study (letter). *Lancet* 2:677-78.

Trichopoulos, D., et al. 1981. Lung cancer and passive smoking. *Int. J. Cancer* 27:1-4.

Tsimoyianis, G. V., et al. 1987. Reduction in pulmonary function and increased frequency of cough associated with passive smoking in teenage athletes. *Pediatrics* 80:32-36.

U.S. Department of Health, Education, and Welfare. 1979. *Smoking and health. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHEW Publication no. (PHS) 79-50066.

U.S. Department of Health and Human Services. 1982. *The health consequences of smoking: Cancer. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHHS Publication no. (PHS) 82-50179.

U.S. Department of Health and Human Services. 1983. *The health consequences of smoking: Cardiovascular disease. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHHS Publication no. (PHS) 84-50204.

U.S. Department of Health and Human Services. 1984. *The health consequences of smoking: Chronic obstructive lung disease. A report of the surgeon general*. Washington, D.C.: Government Printing Office. DHHS Publication no. (PHS) 84-50205.

U.S. Department of Health and Human Services. 1986. *The health consequences of involuntary smoking. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHHS, PHS Publication no. (CDC) 87-8398.

U.S. Department of Health and Human Services. 1988. *The health consequences of smoking: Nicotine addiction. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHHS Publication no. (CDC) 88-8406.

U.S. Department of Health and Human Services. 1989. *Reducing the health consequences of smoking: 25 years of progress. A report of the surgeon general*. Washington, D.C.: U.S. Government Printing Office. DHHS Publication no. (CDC) 89-8411.

U.S. Public Health Service. 1964. *Smoking and health. Report of the advisory committee to the surgeon general of the Public Health Service*. Washington, D.C.: U.S. Government Printing Office. PHS Publication no. 1103.

Urch, R. B., et al. 1988. Does suggestibility modify acute reactions to passive cigarette smoke exposure? *Environ. Res.* 47:34-47.

Vandenbroucke, J. P., et al. 1984. Active and passive smoking in married couples: Results of 25-year follow up. *Br. Med. J.* 288:1801-2.

Wald, N., and Ritchie, C. 1984. Validation of studies on lung cancer in nonsmokers married to smokers (letter). *Lancet* 1:1067.

Wald, N. J., et al. 1984. Urinary cotinine as marker of breathing other people's tobacco smoke (letter). *Lancet* 1:230-31.

Wald, N. J., et al. 1986. Does breathing other people's smoke cause lung cancer? *Br. Med. J.* 293:1217-22.

Wall, M. A., et al. 1988. Cotinine in the serum, saliva and urine of nonsmokers, passive smokers, and active smokers. *Am. J. Public Health* 78:699-701.

Wallace, L. A. 1987. *The total exposure assessment methodology (TEAM) study: Summary and analysis*, Vol. 1. Washington, D.C.: Office of Research and Development, U.S.

Environmental Protection Agency. Publication no. EPA/600/6-87/002a.

Ware, J. H., et al. 1984. Passive smoking, gas cooking, and respiratory health of children living in six cities. *Am. Rev. Respir. Dis.* 129:366-74.

Weber, A. 1984. Annoyance and irritation by passive smoking. *Prev. Med.* 13:618-25.

Weber, A., and Fischer, T. 1980. Passive smoking at work. *Int. Arch. Occup. Environ. Health* 47:209-21.

Weber, A.; Jermini, C.; and Grandjean, E. 1976. Irritating effects on man of air pollution due to cigarette smoke. *Am. J. Public Health* 66:672-76.

Weber-Tschopp, A.; Fischer, T.; and Grandjean, E. 1977. Reizwirkungen des Formaldehyds (HCHO) auf den Menschen. (Irritating effects of formaldehyde on men.) *Int. Arch. Occup. Environ. Health* 39:207-18.

Weber-Tschopp, A., et al. 1977. Experimentelle Reizwirkungen von Akrolein auf den Menschen. (Experimentally induced irritating effects of acrolein on men.) *Arch. Occup. Environ. Health* 40:117-30.

Weiss, S. T. 1986. Passive smoking and lung cancer: What is the risk? (editorial). *Am. Rev. Respir. Dis.* 133:1-3.

Weiss, S. T., et al. 1980. Persistent wheeze: Its relation to respiratory illness, cigarette smoking, and level of pulmonary function in a population sample of children. *Am. Rev. Respir. Dis.* 122:697-707.

Wells, A. J. 1988. An estimate of adult mortality in the United States from passive smoking. *Environ. Int.* 14:249-65.

White, J. R., and Froeb, H. F. 1980. Small airways dysfunction in nonsmokers chronically exposed to tobacco smoke. *N. Engl. J. Med.* 302:720-23.

Wiedemann, H. P., et al. 1986. Acute effects of passive smoking on lung function and airway reactivity in asthmatic subjects. *Chest* 89:180-85.

Winneke, G., et al. 1984. Patterns and determinants of reaction to tobacco smoke in an experimental exposure setting. In *Indoor air*. Ed. B. Berglund, T. Lindvall, and J. Sundell. Vol. 2. 351-56. Stockholm: Swedish Council for Building Research.

Wu, A. H., et al. 1985. Smoking and other risk factors for lung cancer in women. *J. Natl. Cancer Inst.* 4:747-51.

Yue Chen, B. M.; Wanxian, L. I.; and Shunzhang, Y. 1986. Influence of passive smoking on admissions for respiratory illness in early childhood. *Br. Med. J.* 293:303-6.

spiratory disease. *Am. Rev. Respir. Dis.*

king, and respiratory health of children
56-74.

nships: A critical review. *J. Air Pollut.*

8

CARBON
MONOXIDE

David B. Coultas, M.D.
William E. Lambert, Ph.D.

Carbon monoxide (CO) is a colorless, odorless gas produced by incomplete combustion of carbonaceous fuels such as wood, gasoline, and natural gas (National Research Council [NRC] 1977). Inhalation of CO, because of its marked affinity for hemoglobin, impairs oxygen transport and often manifests as adverse effects in the cardiovascular system and in the central nervous system. The severity of the health effects increases with the level and duration of exposure to CO.

Exposure to CO may be from outdoor and indoor sources with levels of exposure that vary widely from low concentrations with subtle effects to higher levels and acute poisoning. Although only few data are available on the overall public health impact of CO, it is a public health concern because of its many sources. In the United States, CO is a leading cause of death from poisoning (U.S. Department of Health and Human Services [DHHS] 1987), with an estimated 1,800 accidental deaths annually (U.S. Public Health Service [PHS] 1982). Many of these deaths have been associated with extreme exposures in indoor residential settings caused by faulty or improperly vented combustion appliances. The health effects of low-level exposures to CO are also considered an important public health problem because of the large population at risk.

In this chapter we review exposure to CO as an indoor air pollutant. However, since health data based directly on indoor exposures are limited, we have included information from outdoor exposures or experimental exposures which reflects levels of CO that may be found indoors. The pathophysiology of CO is presented in the first section. This is followed by a description of the sources and levels of exposure to CO. Finally, manifestations of CO intoxication and the health effects of exposures to low levels of CO are reviewed.

PATHOPHYSIOLOGY OF CO EXPOSURE

In its acute toxic action, CO can be conceptualized as an antimetabolite of oxygen. Inhaled CO binds strongly to hemoglobin in the pulmonary capillary bed; the resulting complex is called carboxyhemoglobin (COHb). The rate of absorption of CO is dependent on ventilatory volume, the hemoglobin content of the blood, the rate of diffusion across the alveolar membrane, the mean pulmonary capillary oxygen tension, and COHb levels in the pulmonary capillaries (Coburn, Forster, and Kane 1965). CO binds to hemoglobin with more than two hundred times the affinity of oxygen, thus effectively outcompeting oxygen for available binding sites on the heme groups. The health consequences of this binding are twofold. First, the oxygen-carrying capacity of the blood is directly reduced; and second, CO bound to one heme subunit induces an allosteric change that slows the dissociation of oxygen bound to any of the three other heme sites on the hemoglobin protein (Stryer 1975). Thus, the absolute oxygen-carrying capacity is reduced by displacement, and lower oxygen tensions are required to release oxygen bound to the hemoglobin (Figure 8.1). This leftward shift of the oxyhemoglobin dissociation curve is physiologically significant and explains the hypoxic differential between simple anemia and the equivalent percentage of COHb (Roughton and Darling 1944; Collier 1976).

In addition to the leftward shift of the oxyhemoglobin dissociation curve, several additional mechanisms of toxicity have been postulated. Ultimately, each is based upon competitive binding interactions and includes the binding of CO to heme proteins including myoglobin, cytochrome oxidase, tryptophan deoxygenase, and tryptophan catalase (Coburn 1979). For example, CO bound to myoglobin in the cardiac muscle could impair oxygen delivery to intracellular contractile processes. In the heart, the marked oxygen gradient from coronary blood to myocardial cells and the low tissue and intracellular oxygen tensions may promote significant CO binding even at relatively low blood COHb levels (Wittenberg 1970); however, experimental data are incomplete. The brain and spinal cord, another sensitive organ system, may be affected similarly.

Within the mitochondria, CO bound to cytochrome oxidase can be expected to interfere with electron transport. Flavoprotein prosthetic groups of the cytochrome enzymes contain iron in a porphyrin configuration that resembles hemoglobin. CO bound to cytochrome oxidase, the terminal oxidase in the system, would prevent the phosphorylation of adenosine diphosphate (ADP). Coburn (1979) observed that increased metabolism may reduce intracellular oxygen tensions and thereby promote CO binding although the affinity of CO for cytochrome oxidase is low at typical physiologic oxygen tensions. Although theoretically plausible, the experimental evidence to support this hypothesis remains limited.

It has been postulated that chronic exposure to CO may accelerate atherosclerotic processes by affecting cholesterol uptake in the arterial wall. Results from animal studies and *in vitro* data are conflicting (Astrup, Kjeldsen, and Wanstrup 1970; Theodore, O'Donnell, and Back 1971; Sarma et al. 1975; Armitage, Davies

188 David B. Coultas and William E. Lambert

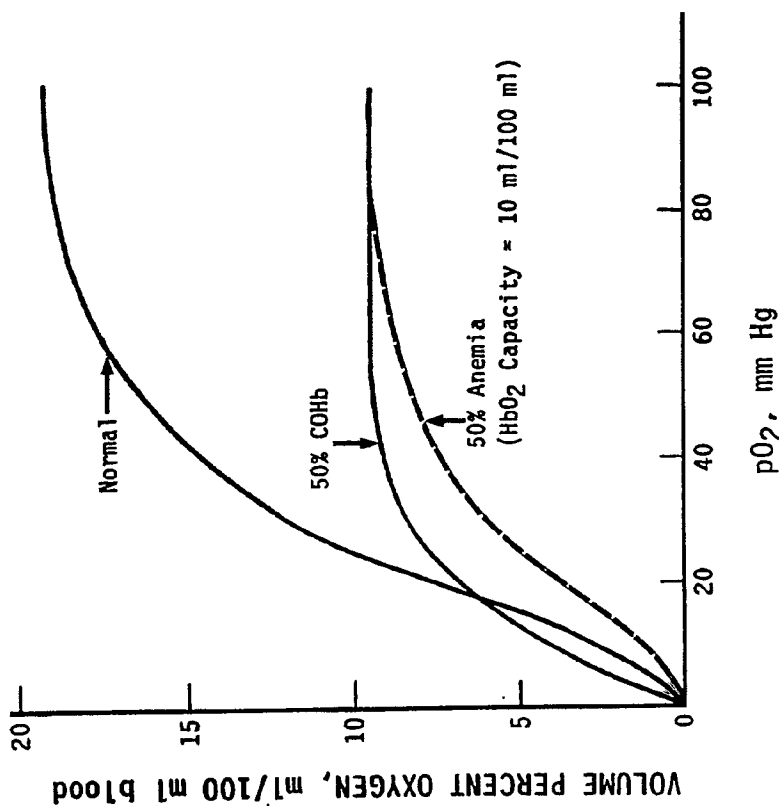


Figure 8.1. Oxyhemoglobin dissociation curves of normal human blood, of blood containing 50 percent COHb, and of blood with a 50 percent normal hemoglobin concentration due to anemia. Source: Reprinted from *Carbon Monoxide*, 1977, with permission from the National Academy of Sciences, Washington, D.C. (NRC, 1977).

and Turner 1976). Confident interpretation of this research is hampered by the high CO exposures and high dietary cholesterol employed in the animal studies and the methodologic difficulties in quantifying morphologic changes in the vessel walls. Limited evidence suggests that CO may accelerate clot lysis time (El-Attr and Sairo 1968) and may increase platelet activity and coagulation (Haft 1979). These alterations in the fibrinolytic system imply that CO could potentially increase risk for thromboembolism in the heart or brain.

CARBON MONOXIDE 189

SOURCES AND LEVELS OF EXPOSURE

There are many opportunities for exposure to CO in indoor environments because of the combustion sources placed or used in these settings. Approximately 47 percent of residences in the United States have gas ranges (U.S. Bureau of the Census 1983), a typically unvented source of combustion emissions. Another important unvented source is the kerosene or gas space heater, used in approximately seven percent of U.S. households (Cooper and Alberti 1984). Vented gas appliances, such as furnaces, water heaters, and clothes dryers, can emit CO into the indoor environment if not properly installed or maintained (Wharton et al. 1989). Similarly, improper use of charcoal cookers, wood-burning stoves or fireplaces, and gasoline engines can inject CO and other pollutants into the indoors. Intensive tobacco smoking in indoor locations may also result in CO buildup. The concentrations resulting from these sources are usually far below those that cause acute poisoning; however, the exposures may still be high enough to affect the blood, heart, and nervous systems adversely. In this section, poisonings and high-level exposure situations are discussed followed by presentation of low-level urban exposures in indoor settings.

ACUTE EXPOSURES AND POISONINGS

Investigations into the cause of poisoning accidents provide a *post facto* measure of the CO exposures experienced by the victims. Caplan et al. (1986) reported indoor residential CO concentrations ranging from 100 to 400 ppm. Invariably, evidence of a malfunctioning combustion appliance or tampering and misuse was discovered. Use of a gas range or oven for space heating may result in elevated indoor CO levels (Sterling, Dirnich, and Kobayashi 1981) and predict symptomatic CO poisoning (Heckerling et al. 1987).

The U.S. Consumer Product Safety Commission (U.S. CPSC) estimates that 7.6 million unvented gas space heaters are in use in the United States, and directly attributes seventy deaths during 1980 to CO exposures resulting from the use of these heating devices in confined spaces (CPSC 1980). Although no measurements of the CO levels in these accidents were reported, it is known that kerosene space heater emissions are capable of increasing indoor CO concentrations to levels exceeding the eight-hour 9 ppm national primary ambient air quality standard (Cooper and Alberti 1984).

The elevated indoor CO concentrations causing poisonings may be expected to occur more often in the cold seasons when heating sources are in use and homes are kept closed to prevent heat loss. Indeed, CO poisonings in Korean residences were strongly correlated with ambient temperature, a surrogate measure of heating (Kim 1985). Many Korean homes are heated by a traditional system of charcoal briquets placed in pails beneath the flooring of the house. Carbon monoxide concentrations have not been reported for Korean homes. In the United States, poisonings associated with space heating are expected to occur more frequently in the winter. However, summertime poisonings associated with exposures in con-

finer spaces can occur. These poisonings can be caused by the use of gas-fueled campstoves, lamps, and lanterns, radiant heaters, and electric generators in or near tents and recreational vehicles (New Mexico Environmental Improvement Agency 1977; Hopkinson, Pearce, and Oliver 1980). Spengler and Cohen (1985) estimated that CO levels as high as 100 ppm could accumulate in tents during gas campstove use.

LOW-LEVEL URBAN EXPOSURES

Substantial data are available on exposures of urban dwellers to CO in the course of their daily activities. The locations generally making the largest contributions to personal exposure are the auto and residence, but industrial buildings and commercial, institutional, and public buildings are frequent contributors. Early attempts at exposure assessment focused largely on vehicular and occupational exposures, but recent advances in instrumentation for exposure monitoring have facilitated monitoring large numbers of urban residents from population-based samples. Using this type of instrumentation, the U.S. Environmental Protection Agency has conducted studies of personal exposure of five hundred residents of Denver, Colorado, and of Washington, D.C. (Table 8.1) (Akland et al. 1985).

Exposures occurring in automobiles and outdoor settings provide an important reference against which indoor exposures may be compared. In fact, personal monitoring studies indicate that in the total daily exposure profile of urban residents, the highest exposures occur during commuting and when near active internal combustion engines (Akland et al. 1985). In-transit exposures average 5 ppm, and residents of Washington, D.C., and Denver were observed to spend an average of two hours per day in an automobile or bus or on a bicycle. Peak

Table 8.1 Range of Mean Concentrations Observed in Major Urban Environments in the Denver, Colorado, and Washington, D.C., CO Exposure Studies

Environmental Setting	Mean CO Concentration (ppm)
Indoor	
Residential	1.2-1.7
Public buildings	
Park garages and automobile service facilities	10.4-18.8
Stores and service establishments	2.5-3.0
Restaurants	2.1-4.2
Outdoor	
Near active roadways	2.6-3.8
Away from roadways, parks	<1.0
In transit	
In vehicle	3.6-8.0
Walking or on bicycle	2.4-4.2

Source: Adapted from Akland et al. (1985), with permission.

exposures of automobile occupants in heavy traffic may attain 50 ppm and average 10–12 ppm (Cortese and Spengler 1976; Flachsbart et al. 1987). Outdoor exposures to CO experienced near roadways and parking areas average 3–4 ppm (Hartwell et al. 1984).

Indoor exposures in residences and public places are generally low (Table 8.1). In the absence of indoor sources, mean indoor CO levels are usually equal to outdoor concentrations. If strong indoor sources are present, however, indoor levels can be severalfold higher than those outside the building. Because CO is an essentially nonreactive gas, removal by ventilation to outside air is the usual route of elimination from the indoor environment. Therefore, in buildings with low ventilation rates, CO may be retained near occupants for extended periods. Residential exposures in Washington, D.C., and Denver during the winter of 1982–83 averaged less than 2 ppm (Hartwell et al. 1984; Johnson 1984; Akland et al. 1985). In Washington, D.C., no significant difference was observed between mean CO levels in residences with an unvented gas stove and in residences with no gas stove when mean levels were integrated over total time spent indoors in the residence (Akland et al. 1985). However, mean personal exposure during cooking activities with a gas stove was higher than those experienced with an electric range and averaged 3 ppm (Hartwell et al. 1984). Similarly, mean hourly CO levels in the kitchens and living rooms of Dutch homes in which unvented gas stoves and infusion water heaters were in use ranged from 1 to 40 ppm, with mean levels of 1–3 ppm (Lebreit 1985); however, anecdotal accounts of exposures experienced during the use of gas stoves for space heating describe indoor concentrations ranging from 25 to 50 ppm (Coburn 1979). In general, cigarette smoking contributes little to indoor CO levels (Sterling, Dimich, and Kobayashi 1982; Lebreit 1985).

Exposures to CO in public buildings averaged 2–4 ppm in the Washington, D.C., and Denver studies (Akland et al. 1985). Highest mean personal exposures were observed in indoor parking garage locations and averaged 10–18 ppm. Average personal exposures in restaurants averaged 2–4 ppm, and stores and shopping malls averaged 2–3 ppm. Higher indoor levels, averaging 12 ppm and exceeding the eight-hour federal standard of 9 ppm, have been measured in a Honolulu shopping mall with an attached garage (Flachsbart and Brown 1985); this result has important implications for employees and shoppers who spend long periods of time in malls of this architectural design. Some office building settings have been associated with chronically high CO levels. Workers in an underground office located on the same level as an enclosed parking garage experienced mean exposures in the range of 12–22 ppm, with peak exposures to 34 ppm (Wallace 1983). Proper use of garage fans and closure of fire doors leading to the parking garage lowered office concentrations to 5 ppm. Thus, indoor CO levels may accumulate if ventilation systems are operated at low flow rates to reduce energy costs.

Indoor exposures to CO, included under the larger classification of urban exposure, may also be evaluated in terms of the resulting COHb levels. As part of the

192 David B. Coultas and William E. Lambert

1976–80 National Health and Nutrition Examination Survey, more than 8,000 blood samples were analyzed for COHb content and classified according to demographic and personal characteristics (Radford and Drizd 1982). Wintertime mean COHb concentration in never smokers aged twelve to seventy-four years living in urban areas was 1.25 percent. More than 4 percent of nonsmoking adults had levels greater than 2.5 percent; however, the source of exposure could not be identified. Children aged three to eleven years, considered to represent a group not exposed from occupational sources and personal tobacco use, had mean COHb levels of 1.01 percent during the winter months; however, their exposures during transportation may be lower than those of adults. Wintertime COHb levels were substantially higher in the three- to eleven-year-old subgroup than in the adult group; 3.3 percent of the children had a COHb level in excess of 2.5 percent. These results, when extrapolated to the nonsmoking adult population, indicate that 3–4 percent of the population may be exposed during the winter to CO levels exceeding the 9 ppm eight-hour and the 35 ppm one-hour standard assigned to keep COHb levels from rising above 1.5 percent.

Only two studies relate specific indoor exposures with COHb levels. In each study, COHb levels were estimated by measuring CO concentrations in samples of end-expired breath. This methodology is reviewed by Lambert, Colome, and Wojciechowski (1988). In Dutch homes, Verhoeff et al. (1983) observed a small but significant increase in breath CO after occupants used infusion water heaters. Wallace (1983) observed increases in breath CO levels of office workers exposed to motor vehicle exhaust.

HEALTH EFFECTS OF EXPOSURE

The health effects of CO have been described through clinical observations of patients with CO intoxication and experimental and epidemiologic investigations of persons exposed to low levels of CO. The health effects of CO vary with the level of COHb (Table 8.2) and range from nonspecific symptoms, headache, dizziness, and fatigue, to death (Winter and Miller 1976). CO poisoning, resulting in death, has been recognized since the nineteenth century (Winter and Miller 1976), but the adverse consequences of exposure to low levels of CO have only recently received attention.

Because of the adverse effects of CO on oxygen delivery to tissues, individuals with a need for high oxygen consumption or who have preexisting disorders of oxygen delivery may be highly sensitive to the effects of CO (Table 8.3). These considerations related to oxygen delivery suggest that the developing fetus (Longo 1977), the growing child (Zimmerman and Truxal 1981), and maximally exercising persons may be particularly susceptible to the effects of hypoxia from CO. Other groups that may be unusually sensitive to the adverse consequences of CO include those with chronic hypoxemia, cardiovascular disease, and hemoglobin abnormalities.

Table 8.2 Health Effects Associated with Different Carboxyhemoglobin Levels

COHb (%)	Symptoms
10	No appreciable effect except shortness of breath on vigorous exertion; possible tightness across the forehead; dilatation of cutaneous blood vessels
20	Shortness of breath on moderate exertion; occasional headache with throbbing in temples
30	Decided headache; irritable; easily fatigued; judgment disturbed; possible dizziness; dimness of vision
40-50	Headache; confusion; collapse; fainting on exertion
60-70	Unconsciousness; intermittent convulsions; respiratory failure; death if exposure is continued for long
80	Rapidly fatal

Source: Winter and Miller (1976), reprinted with the permission of the American Medical Association.

Table 8.3 Conditions That Potentially Increase Susceptibility to Adverse Effects of CO

Fetal development
Children
Chronic hypoxemia
High altitude
Chronic lung disease
Right-to-left shunts
Impaired cardiac output
Cardiomyopathy
Valvular heart disease
Vascular disease
Atherosclerotic heart disease
Cerebrovascular disease
Peripheral vascular disease
Hemoglobin abnormalities
Anemia
Hemoglobinopathy

CO INTOXICATION

Intoxication from CO may be acute or chronic, depending upon concentration and duration of exposure. Generally, clinically apparent problems with acute exposures appear at COHb levels of 10 percent or greater (Table 8.2). However, the severity of symptoms may not correlate well with COHb levels (Sokal and Kralkowska 1985, Kirkpatrick 1987). Furthermore, because of its nonspecific picture, intoxication may be frequently overlooked (Dolan 1985; Barret, Danel, and Faure 1985).

To determine the frequency of misdiagnosis of CO poisoning, Barret, Danel, and Faure (1985) reviewed records from 340 patients with CO poisoning admitted

194 David B. Coultas and William E. Lambert

to a toxicology service in France. Between 1975 and 1977, 50 percent of patients were initially misdiagnosed. The initial diagnoses included food poisoning, neuropsychiatric problems, cardiac disorders, and other intoxications. Food poisoning was the most frequent incorrect diagnosis.

The clinical history and physical examination may suggest the diagnosis of CO intoxication (Table 8.4). However, because the presenting problems of CO poisoning are nonspecific, only a high index of suspicion will result in the correct diagnosis (Hopkinson, Pearce, and Oliver 1980; Heckerling et al. 1987; Kirkpatrick 1987). The history of a potential source of exposure (Heckerling et al. 1987) or the finding of retinal hemorrhages (Kelley and Sophocleous 1978) may provide the first clues to the correct diagnosis. Furthermore, the identification of an index case of CO poisoning should alert the clinician to other potential cases (Wharton et al. 1989).

CO is currently the only air pollutant with a specific and clinically relevant biologic marker, COHb. However, the COHb level may not strongly predict the severity of intoxication, and the duration of exposure may be a better predictor (Sokal and Kralkowska 1985). In a study of thirty-nine patients with CO poisoning, Sokal and Kralkowska (1985) found that the mean duration of exposure was about nine hours among those with clinically severe poisoning, compared with five hours among those with mild to moderate poisoning. There were only slight differences in the COHb levels between the two groups of patients.

CO intoxication, especially with prolonged high levels of COHb, may affect every organ system (Table 8.5). Most complications of CO poisoning are a direct result of tissue hypoxia, and the presence of these complications may provide the first alert to the clinician of possible CO intoxication. For example, an unexplained

Table 8.4 Clinical Findings That Suggest the Possibility of CO Poisoning

History
Exposure to potential source of CO
Nonspecific symptoms (e.g., headache, dizziness, fatigue, nausea, vomiting)
Household members or co-workers with similar symptoms
Unexplained illness/death among household pets
Physical exam
Retinal hemorrhage
Unexplained coma
Unexplained cardiac arrhythmias
Laboratory
COHb $\geq 10\%$ in a nonsmoker
Unexplained lactic acidosis

*May vary depending upon the chronicity and level of exposure and on the time at which the specimen is drawn in relation to the exposure.

Table 8.5 Complications of CO Poisoning

Organ System	Complication
Cardiac	Myocardial ischemia, arrhythmias, angina
Pulmonary	Pulmonary edema, hemorrhage
Muscular	Myonecrosis, compartment syndrome
Renal	Myoglobinuria, acute renal failure
Neurologic	Seizure, encephalopathy, cerebral edema
Ophthalmologic	Retinal hemorrhage, visual defect
Cutaneous	Erythema, listers, bullae
Vestibular/auditory	Vertigo, nystagmus, hearing loss, tinnitus
Hematologic	Thrombotic thrombocytopenic purpura
Fetal	Death, neurologic sequelae

*Source: Adapted from Zimmerman and Truxal (1981), with permission.

lactic acidosis strongly suggests CO poisoning (Sokal and Kralkowska 1985).

Although most patients with CO poisoning recover completely, some develop delayed neurologic complications. These problems, which include headache, memory loss, disorientation, hallucinations, apraxia, and aphasia, appear days to weeks after apparent recovery from an acute exposure (Werner et al. 1985). Among patients who develop these delayed neurologic problems, areas of brain necrosis have been demonstrated by magnetic resonance imaging (Horowitz, Kaplan, and Sarpel 1987).

The immediate therapeutic goal in CO poisoning is reversal of the tissue hypoxia (Winter and Miller 1976). As soon as the diagnosis is considered, 100 percent oxygen should be administered. This will increase the dissolved oxygen in plasma and shorten the half-life of COHb. For severe cases, hyperbaric oxygen treatment may be necessary.

LOW-LEVEL EXPOSURE

The health effects of low levels of CO exposure have been examined with two types of investigations: laboratory studies involving short-term exposure, and population studies. The major health outcomes that have been studied include effects on the fetus, on neurobehavioral mechanisms, and on exercise in normal subjects and in patients with coronary artery disease, peripheral vascular disease, and chronic lung disease. For all of these problems we primarily consider information on indoor exposures but include results based on outdoor exposures if indoor data are limited. Similarly, we review relevant data from animal studies only if human data are unavailable.

Effects on the Fetus Because of the adverse consequences of cigarette smoking on the fetus (U.S. Department of Health, Education, and Welfare [DHEW] 1979), researchers have hypothesized that CO may be the component of cigarette smoke which causes the adverse effects (Longo 1977). Animal experiments have been

conducted in an attempt to isolate from the other components of tobacco smoke the effects of CO on the fetus (Astrup et al. 1972; Garvey and Longo 1978; Singh and Scott 1984).

In animal experiments, the exposures have been designed to simulate active cigarette smoking rather than exposures to lower levels of CO. Most of the experiments have involved exposures to CO levels of 30–500 ppm, resulting in COHb levels of 4–18 percent (Astrup et al. 1972; Garvey and Longo 1978; Singh and Scott 1984). At the lowest level of 30 ppm, Garvey and Longo (1978) exposed pregnant rats from day 3 to day 20 of gestation, resulting in a mean COHb level of 4.8 percent. The animals were killed, and the percentage of successful pregnancies in the exposed group was 69 percent compared with 100 percent in the unexposed. Other investigators have shown lower birth weight and increased fetal and neonatal mortality at higher levels of exposure (Astrup et al. 1972; Singh and Scott 1984).

For humans, few data are available on fetal and neonatal morbidity and mortality from exposure to CO indoors or outdoors. Alderman, Baron, and Savitz (1987) conducted a case-control study of birth weight and maternal exposure to neighborhood CO during the last three months of gestation. The series included 998 low-birth weight infants (2,500 g or less) and 1,872 normal-birth weight infants from Denver. They used ambient CO levels from stationary monitors to categorize the mother's exposure. For the mothers whose CO exposures were considered most accurate, the odds ratio for having a low-birth weight baby was 1.5 (95 percent confidence interval, 0.7–3.5) for an ambient CO level of 3 ppm or greater compared with lower levels. This finding is limited by the lack of personal smoking histories and personal exposure measurements.

Neurobehavioral Effects To determine the effects of low levels of CO on the central nervous system, investigators have assessed effects in normal volunteers (Table 8.6), including effects on visual perception (Halperin et al. 1959; Hosko 1970; Stewart et al. 1970; Horvath, Dahms, and O'Hanlon 1971; Luria and McKay 1979), on auditory perception (Beard and Wertheim 1967; Wright and Shephard 1978), on manual dexterity (Stewart et al. 1970; McFarland 1973), and on vigilance (Benignus et al. 1977). The results from these investigations have been inconsistent (Benignus et al. 1977; Luria and McKay 1979). Potential reasons for the varied findings include small numbers of subjects and different study designs. Despite the inconsistent results, clinically important neurobehavioral effects in normal subjects are not a major concern with COHb levels below 10–20 percent.

Effects on Exercise Performance in Normal Subjects As in the studies of the neurobehavioral effects of CO, researchers have exposed normal volunteers to CO and then tested its influence on exercise performance (Table 8.7). At COHb levels of 5 percent or less, maximal exercise time and maximal oxygen consumption have generally decreased among healthy subjects compared with preexposure exercise

Table 8.6 Selected Experimental Studies of Normal Human Volunteers on the Neurobehavioral Effects of Exposure to Low Levels of CO

Reference	Subjects	Exposure	Measure of Effect	Findings
Halperin et al. (1959)	4 males, 16–25 years of age	100% CO delivered in varying amounts	Discrimination of light intensity	Visual sensitivity was impaired at COHb level of 3.0% and worsened with increasing COHb level
Hosko 1970	14 males, 24–42 years of age	0.25–24 h of <1, 25, 50, 100, 200, 500, and 1,000 ppm CO	EEG and visual evoked response (VER)	Changes from baseline found in VER at COHb levels of 20–22%
Stewart et al. (1970)	18 males, 24–42 years of age	0.5–24 h of <1, 25, 50, 100, 200, 500, and 1,000 ppm CO	Symptoms, VER, visual and auditory tests, tests of reaction time and coordination	Exposure to 100 ppm for 8 h resulted in COHb of 11–13% but no impairment of performance; mild headache noted after 4 h of exposure to 200 ppm CO and 1-h exposure to 500 ppm CO; changes in VER occurred at 20% COHb or above; impairment in manual dexterity only at COHb of 28%
Luria and McKay (1979)	12 nonsmokers, 6 smokers, 19–43 years of age	18 min of 195 ppm CO	Night vision sensitivity, reaction time from visual stimulus, eye movements for letter search, VER	Mean COHb 9% in nonsmokers and COHb level ranged from 10.2 to 13.3% in smokers; no consistent changes in any measures were found
Horvath, Dahms, and O'Hanlon (1971)	10 male nonsmokers, 21–32 years of age	2.25 h of 0, 26, or 111 ppm CO	Tested vigilance by judging light intensities over 1 h	Vigilance impaired at a mean COHb level of 6.6% after breathing 111 ppm CO
Beard and Wertheim (1967)	18 subjects	Varying times at 0, 50, 100, 175, and 250 ppm CO	Discrimination of time intervals with paired tones	The percentage of correct responses decreased with increased exposure; however, COHb levels unavailable
Wright and Shephard (1978)	3 experiments with 2, 7, and 5 subjects, respectively	Experiment 1: 0, 30, 50, and 75 ppm CO Experiment 2: Air or CO exposure combined with surrounding office noise or silent conditions Experiment 3: Air or CO over 10 different days	Discrimination of time interval with paired tones	Experiment 1: the percentage of correct responses decreased with increased exposure and COHb levels of 0.7, 2.0, 3.2, and 4.7% Experiment 2: No consistent effects of CO with the varied exposure conditions Experiment 3: Mean COHb 4.9% but no effect of CO observed
McFarland (1973)	27 subjects, 20–50 years of age	Blinded exposure to air or 700 ppm CO for varying times	Psychomotor tasks, dark adaptation and glare recovery, peripheral vision, depth perception, driving performance	Mean COHb levels were <4, 6, 11, and 17% decrement in peripheral vision with CO exposure, but no effect on other measures
Benignus et al. (1977)	52 males	0, 100, and 200 ppm CO	Vigilance task of reporting when 3 consecutive even or odd digits seen among 667 digits	Mean COHb levels were 0.61, 4.6, 12.6%; no effect of CO on vigilance

Table 8.7 Selected Experimental Studies of Normal Human Volunteers on the Effects of Low Levels of CO on Exercise Performance

Reference	Subjects/Exercise	Exposure	Mean COHb (%)	Findings
Chevalier, Krumholz, and Ross (1966)	10 nonsmokers, mean age 30 years; bicycle ergometer for 5 min with a mean $\dot{V}O_{2\max}$ of 1.8 l/min	2.5–3.5 min of 0.5% CO	3.95 ± 1.87 ^a	Oxygen debt and ratio of oxygen debt to total oxygen uptake increased 12.0 and 14%, respectively, compared with no exposure
Drinkwater et al. (1974)	20 normal males, 10 nonsmokers, and 10 smokers; treadmill exercise to exhaustion	Double-blind: Filtered air 50 ppm CO 0.27 ppm PAN ^b CO + PAN	2.5 ± 0.30	5% decrement in mean total walking time and 1.9% decrement in $\dot{V}O_{2\max}$ for nonsmokers with CO exposure but no decrement among smokers
Aronow and Cassidy (1975)	9 males, 1 female, normal nonsmokers, with mean age 50.7; treadmill exercise to exhaustion	Double-blind, 100 ppm CO for 1 h	3.95 ± 0.49	Mean exercise time decreased 5%
Horvath et al. (1975)	4 healthy males, 24–33 years, 1 pipe smoker; treadmill exercise to exhaustion	Single-blind: Filtered air 75 ppm CO 100 ppm CO delivered by a bolus method or gradual increments on two occasions	3.18–3.35 4.25–4.30	Regardless of delivery mode, $\dot{V}O_{2\max}$ decreased 4.9 and 7.0% at the low and high exposures, respectively
Weiser et al. (1978)	9 male nonsmokers, mean age 24.7 years; treadmill exercise to exhaustion at altitude of 1,610 m	Double-blind: Filtered air CO bolus and rebreathing to achieve 5% COHb	5.09 ± 0.11	With CO exposure, total exercise time decreased 3.8%, total work decreased 10.0%, and $\dot{V}O_{2\max}$ decreased 3.5%
Horvath et al. (1988)	11 males and 12 women nonsmokers; exercised to maximal aerobic capacity at simulated altitudes of 55, 1,524, 2,134, and 3,048 m	Double-blind: 0 ppm CO 50 ppm CO 100 ppm CO 150 ppm CO	Not provided	CO and altitude at ≥2,134 m decreased $\dot{V}O_{2\max}$, but COHb did not result in an additional decline at a given altitude

^aCalculated COHb level from alveolar gas.^bPAN, peroxyacetyl nitrate.

tests. Most exposures have been at sea level, but no additional decrements in exercise performance have been found with CO exposure at higher altitudes (Weiser et al. 1978; Horvath et al. 1988).

Experimental Studies of Effects on Patients with Cardiovascular and Peripheral Vascular Disease Since the early 1970s, numerous investigations studies have been conducted to examine the effects of exposure to low levels of CO on exercise tolerance in patients with vascular disease (Table 8.8). The results of most of these studies have indicated that patients with vascular disease have earlier onset of angina or claudication at COHb levels between about 2 and 5 percent. Although the validity of the investigations conducted by Aronow and his co-workers (1972, 1973, 1974, 1975; Aronow 1981) has been questioned (Budiansky 1983), subsequent investigations have obtained similar results to those reported by Aronow and his co-workers (Table 8.8).

Kleinman and Whittenberger (1989) reported that the exercise tolerance of twenty-four men with reproducible angina was reduced 5.8 percent, and maximal oxygen uptake was decreased 2.2 percent after exposure to 100 ppm for two hours. In a multicenter study (Warren et al. 1989), sixty-three men with reproducible angina and electrocardiographic (ECG) changes indicative of myocardial ischemia were studied at two levels of exposure sufficient to result in COHb levels of 2 and 4 percent. Relative to filtered air, mean time to onset of angina was reduced 4 and 7 percent, respectively. ECG changes preceded angina, and the time to onset of ST segment depression was reduced by 5 and 12 percent, respectively.

Effects on Patients with Chronic Lung Disease The available literature concerning the effects of CO on patients with chronic obstructive lung disease is limited and does not provide definite conclusions (Aronow, Ferlinz, and Glauser 1977; Calverley, Leggett, and Flenley 1981). Calverley, Leggett, and Flenley (1981) studied fifteen patients with severe chronic obstructive pulmonary disease, mean FEV₁ of 0.56 liters, and measured the distances walked during a series of twelve-minute walks after breathing air, 2 liters of oxygen, air, and 0.02 percent CO per minute; and 2 liters of oxygen and 0.02 percent CO per minute. The mean increase in COHb was 9.2 percent, which resulted in a mean decrease of 43 m in the walking distance after breathing air and CO. However, since the CO exposures were always last, the decrease in exercise time may have resulted from fatigue.

Epidemiologic Studies of Effects on Patients with Cardiorespiratory Disease Several investigations have been conducted to examine the relationship between ambient CO levels and cardiorespiratory effects (Cohen, Deane, and Goldsmith 1969; Hexter and Goldsmith 1971; Kuller et al. 1975; Kurt, Mogielnicki, and Chandler 1978; Kurt et al. 1979). The health effects that have been examined have ranged from emergency room visits for dyspnea and nontraumatic chest pain to mortality from myocardial infarction. Most of these studies found an association between outdoor measurements of CO and adverse health outcomes.

Table 8.8 Selected Experimental Studies of the Effects of Low Levels of CO Exposure on Patients with Atherosclerotic Heart Disease

Reference	Subjects/Exposure	Exposure	Mean COHb (%)	Findings
Anderson et al. (1973)	10 males with stable angina, 5 were smokers, mean age 49.9 years, incremental treadmill exercise until onset of angina	Double-blind exposure to room air, 50 or 100 ppm CO for 4 h prior to exercise	50 ppm = 2.9 ± 0.70, 100 ppm = 4.5 ± 0.80	Mean time to onset of angina was reduced 15% with exposure to both concentrations of CO; duration of pain was prolonged with 100 ppm CO; ST segment depression appeared earlier and was deeper with CO exposure; no difference between smokers and non-smokers
Aronow et al. (1972)	10 males with angina, 3 were smokers, mean age 48 years; bicycle ergometer exercise until onset of angina	Driven in an open car on Los Angeles freeway for 90 min during traffic; mean CO level in the car was 53 ± 6 ppm. On a second day subjects breathed compressed air during the drive	5.08 ± 1.19	Mean exercise time was decreased 75 s after exposure to freeway air, and decreased exercise time persisted for 2 h after the exposure compared with base line or while breathing compressed air
Aronow and Isbell (1973)	10 males with angina, non-smokers; bicycle ergometer exercise until onset of angina	Double-blind exposure to air or 50 ppm CO for 2 hours	2.68 ± 0.15	Mean exercise time decreased 37 s with CO exposure compared with air
Aronow et al. (1974)	10 males with intermittent claudication, confirmed angiographically	Double-blind exposure to compressed air or 50 ppm CO for 2 h	2.8 ± 0.19	Mean exercise time decreased 30 s with CO exposure compared with air
Aronow (1981)	15 subjects with stable angina, 14 males, 1 female, nonsmokers; bicycle ergometer exercise until onset of angina	Double-blind exposure to air or 50 ppm CO for 1 h	2.02 ± 0.16	Mean exercise time was decreased 33 s with CO exposure compared with air
Sheps (1985)	30 subjects with ischemic heart disease, non-smokers; type of exercise unknown	Double-blind exposure to air or 100 ppm CO on successive days	4.1 ± 0.10	No effect on time to onset of angina or change in cardiac function with CO exposure
Adams et al. (1987)	30 subjects with ischemic heart disease; type of exercise unknown	Double-blind exposure to air or CO	5.9 ± 0.10	Mean exercise duration decreased 41 s with CO exposure compared with air; angina only occurred with CO exposure; left ventricular ejection fraction with exercise was less after CO exposure
Kleinman and Whittenberger (1989)	24 males with reproducible angina	Double-blind exposure to filtered air or to 100 ppm CO	2.9 ± 0.30	Mean exercise time decreased 5.8% and maximal oxygen uptake decreased 2.2% with CO exposure relative to air
Warren et al. (1989)	63 males, ages 35–75 with stable angina; treadmill exercise until onset of angina	Double-blind exposure to air and two levels of CO to achieve COHb of 2.2 and 4.4%	2.0 ± 0.10 3.9 ± 0.10	4.2 and 7.1% trimmed mean decrease in time to onset of angina at low and high exposures, respectively; 5.1 and 12.1% trimmed mean decreases in time to development of ischemic ST segment changes

However, because the ambient measures of exposure used in these studies may not have been representative of personal exposure to CO (Ott and Flachsbart 1982; Akland et al. 1985), these results must be interpreted carefully. Furthermore, exposure misclassification would tend to bias risk estimates downward, making it more difficult to observe an effect.

In contrast to community studies, occupational settings may provide better estimates of exposure to CO. Increased mortality from arteriosclerotic heart disease has been documented in an occupational environment with exposure to elevated levels of CO in an enclosed space (Stern et al. 1988). Among 5,529 New York City bridge and tunnel officers employed between 1952 and 1981, the overall mortality ratio for arteriosclerotic heart disease was 35 percent higher among tunnel workers compared with bridge workers; the former having the higher exposures to CO. The mortality ratio was highest (1.88) for tunnel workers employed for ten or more years. Differences in smoking habits were not sufficient to explain the differences in mortality.

SUMMARY

Numerous and varied types of observations have documented the adverse health effects of CO. For low levels of CO the effects have largely been studied experimentally with small numbers of subjects. However, these experiments may not provide an accurate description of the free-living environment with variations in exposure, in activity level, and in severity of disease. Nevertheless, the available data demonstrate that levels of COHb greater than 2 percent, which may result from exposure indoors, impair exercise capacity of patients with cardiopulmonary disease and of normal subjects at maximum exercise capacity. Furthermore, CO may exacerbate ischemic symptoms in patients with cardiovascular disease and may contribute to excess mortality. Because nonspecific symptoms result from CO at low or high levels of exposure, a high index of suspicion is necessary to make the diagnosis and to prevent further exposure.

REFERENCES

- Adams, K. F., et al. 1987. Earlier onset of ischemia after exposure to low level carbon monoxide in patients with ischemic heart disease. *J. Am. Coll. Cardiol.* 9:121 (abstr.).
- Akland, G. G., et al. 1985. Measuring human exposure to carbon monoxide in Washington, D.C., and Denver, Colorado, during the winter of 1982-83. *Environ. Sci. Technol.* 19:911-18.
- Alderman, B. W.; Baron, A. E.; and Savitz, D. A. 1987. Maternal exposure to neighborhood carbon monoxide and risk of low infant birth weight. *Public Health Rep.* 102:410-14.
- Anderson, E. W., et al. 1973. Effect of low-level carbon monoxide exposure on onset and duration of angina pectoris: A study in ten patients with ischemic heart disease. *Ann. Intern. Med.* 79:46-50.
- Armitage, A. K.; Davies, R. F.; and Turner, D. M. 1976. The effects of carbon monoxide

204 David B. Coults and William E. Lambert

- on the development of atherosclerosis in the white carneau pigeon. *Atherosclerosis* 23:333-44.
- Aronow, W. S. 1981. Aggravation of angina pectoris by two percent carboxyhemoglobin. *Am. Heart J.* 101:154-57.
- Aronow, W. S., and Cassidy, J. 1975. Effect of carbon monoxide on maximal treadmill exercise: A study in normal persons. *Ann. Intern. Med.* 83:496-99.
- Aronow, W. S., and Isbell, M. W. 1973. Carbon monoxide effect on exercise-induced angina pectoris. *Ann. Intern. Med.* 79:392-99.
- Aronow, W. S.; Ferlinz, J.; and Glauser, F. 1977. Effect of carbon monoxide on exercise performance in chronic obstructive pulmonary disease. *Am. J. Med.* 63:904-8.
- Aronow, W. S.; Stemmer, E. A.; and Isbell, M. W. 1974. Effect of carbon monoxide exposure on intermittent claudication. *Circulation* 69:415-17.
- Aronow, W. S., et al. 1972. Effect of freeway travel on angina pectoris. *Ann. Intern. Med.* 77:669-76.
- Astrup, P.; Kjeldsen, K.; and Wanstrup, J. 1970. Effects of carbon monoxide exposure on the arterial walls. *Ann. N.Y. Acad. Sci.* 174:294-300.
- Astrup, P., et al. 1972. Effect of moderate carbon monoxide exposure on fetal development. *Lancet* 2:1220-22.
- Barret, L.; Danel, V.; and Faure, J. 1985. Carbon monoxide poisoning: A diagnosis frequently overlooked. *Clin. Toxicol.* 23:309-13.
- Beard, R. R., and Wertheim, G. A. 1967. Behavioral impairment associated with small doses of carbon monoxide. *Am. J. Public Health* 57:2012-22.
- Benignus, V. A., et al. 1977. Lack of effects of carbon monoxide on human vigilance. *Percept. Mot. Skills* 45:1007-14.
- Budiansky, S. 1983. Food and drug data fudged. *Nature* 302:560.
- Calverley, P. M. A.; Leggett, R. J. E.; and Flenley, D. C. 1981. Carbon monoxide and exercise tolerance in chronic bronchitis and emphysema. *Br. Med. J.* 283:878-80.
- Caplan, Y. H., et al. 1986. Accidental poisonings involving carbon monoxide, heating systems, and confined spaces. *J. Forensic Sci.* 31:117-21.
- Chevalier, R. B.; Krumholz, R. A.; and Ross, J. C. 1966. Reaction of non-smokers to carbon monoxide inhalation: Cardio-pulmonary responses at rest and during exercise. *JAMA* 198:1061-64.
- Coburn, R. F. 1979. Mechanisms of carbon monoxide toxicity. *Prevent. Med.* 8:310-22.
- Coburn, R. F.; Forster, R. E.; and Kane, P. B. 1965. Considerations of the physiological variables that determine blood carboxyhemoglobin concentration in man. *J. Clin. Invest.* 44:1899-1910.
- Cohen, S. I.; Deane, M.; and Goldsmith, J. R. 1969. Carbon monoxide and survival from myocardial infarction. *Arch. Environ. Health* 19:510-17.
- Collier, C. R. 1976. Oxygen affinity of human blood in the presence of carbon monoxide. *J. Appl. Physiol.* 40:487-90.
- Cooper, K. R., and Alberti, R. R. 1984. Effect of kerosene space heater emissions on indoor air quality and pulmonary function. *Am. Rev. Respir. Dis.* 129:629-31.
- Cortese, A. D., and Spengler, J. D. 1976. Ability of fixed-monitoring stations to represent carbon monoxide exposure. *J. Air Pollut. Control Assoc.* 26:1144-50.
- Dolan, M. C. 1985. Carbon monoxide poisoning. *Can. Med. Assoc. J.* 133:392-99.
- Drinkwater, B. L., et al. 1974. Air pollution, exercise, and heat stress. *Arch. Environ. Health* 28:177-81.

CARBON MONOXIDE 205

El-Attar, O. A., and Sairo, D. M. 1968. Effect of carbon monoxide on the whole fibrinolytic activity. *Industr. Med. Surg.* 37:774-77.

Flachsbart, P. G., and Brown, D. E. 1985. Surveys of personal exposure to vehicle exhaust in Honolulu microenvironments. Honolulu: Department of Urban and Regional Planning.

Flachsbart, P. G., et al. 1987. Carbon monoxide exposures of Washington commuters. *J. Air Pollut. Control Assoc.* 37:135-42.

Garvey, D. J., and Longo, L. D. 1978. Chronic low level maternal carbon monoxide exposure and fetal growth and development. *Biol. Reprod.* 19:8-14.

Haft, J. I. 1979. Role of blood platelets in coronary artery disease. *Am. J. Cardiol.* 43:1197-1206.

Halperin, M. H., et al. 1959. The time course of the effects of carbon monoxide on visual thresholds. *J. Physiol.* 146:583-93.

Hartwell, T. D., et al. 1984. Study of carbon monoxide exposures of residents of Washington, D.C. Paper 84-121.4, presented at the seventy-seventh annual meeting of the Air Pollution Control Association, 24-29 June, San Francisco, Calif.

Hoeckerling, P. S., et al. 1987. Predictors of occult carbon monoxide poisoning in patients with headache and dizziness. *Ann. Intern. Med.* 107:174-76.

Hexter, C. A., and Goldsmith, J. R. 1971. Carbon monoxide: Association of community air pollution with mortality. *Science* 172:265-67.

Hopkinson, J. M.; Pearce, P. J.; and Oliver, J. S. 1980. Carbon monoxide poisoning mimicking gastroenteritis. *Br. Med. J.* 281:214-15.

Horowitz, A. L.; Kaplan, R.; and Sarpel, G. 1987. Carbon monoxide toxicity: MR imaging in the brain. *Radiology* 162:787-88.

Horvath, S. M.; Dahms, T. E.; and O'Hanlon, J. F. 1971. Carbon monoxide and human vigilance. *Arch. Environ. Health* 23:343-47.

Horvath, S. M., et al. 1975. Maximal aerobic capacity at different levels of carboxyhemoglobin. *J. Appl. Physiol.* 38:300-303.

Horvath, S. M., et al. 1988. Maximal aerobic capacity at several ambient concentrations of carbon monoxide at several altitudes. Presented at the fifth Health Effects Institute annual conference, 17-20 April, Colorado Springs, Colo.

Hosko, J. M. 1970. The effect of carbon monoxide on the visual evoked response in man, and the spontaneous electroencephalogram. *Arch. Environ. Health* 21:174-80.

Johnson, T. R. 1984. A study of personal exposure to carbon monoxide in Denver, Colorado. Paper 84-121.3, presented at the seventy-seventh annual meeting of the Air Pollution Control Association, 24-29 June, San Francisco, Calif.

Kelley, J. S., and Sophocleus, G. J. 1978. Retinal hemorrhages in subacute carbon monoxide poisoning: Exposure in homes with blocked furnace flues. *JAMA* 239:1515-17.

Kim, Y. S. 1985. Seasonal variation in carbon monoxide poisoning in urban Korea. *J. Epidemiol. Community Health* 39:79-81.

Kirkpatrick, J. N. 1987. Occult carbon monoxide poisoning. *West. J. Med.* 146:52-56.

Kleinman, M. T., and Whittenberger, J. L. 1989. Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease. Paper 89-54.4, presented at the eighty-second annual meeting of the Air and Waste Management Association, 25-30 June, Anaheim, Calif.

Kuller, L., et al. 1975. Carbon monoxide and heart attacks. *Arch. Environ. Health* 30:477-82.

Kurt, T. L.; Mogielnicki, R. P.; and Chandler, J. E. 1978. Association of the frequency of

206 David B. Coulter and William E. Lambert

acute cardiorespiratory complaints with ambient levels of carbon monoxide. *Chest* 74:10-13.

Kurt, T. L., et al. 1979. Ambient carbon monoxide levels and acute cardiorespiratory complaints: An exploratory study. *Am. J. Public Health* 69:360-63.

Lambert, W. E.; Colome, S. D.; and Wojciechowski, S. L. 1988. Application of end-expired breath sampling to estimate carboxyhemoglobin levels in community air pollution exposure assessments. *Atmos. Environ.* 22:2171-81.

Lebet, E. 1985. *Air pollution in Dutch homes: An exploratory study in environmental epidemiology.* Report R-138. Wageningen Agricultural University, The Netherlands: Department of Environmental and Tropical Health.

Longo, L. D. 1977. The biological effects of carbon monoxide on the pregnant woman, fetus, and newborn infant. *Am. J. Obstet. Gynecol.* 129:69-103.

Luria, S. M., and McKay, C. L. 1979. Effects of low levels of carbon monoxide on visions of smokers and nonsmokers. *Arch. Environ. Health* 34:38-44.

McFarland, R. A. 1973. Low level exposure to carbon monoxide and driving performance. *Arch. Environ. Health* 27:355-59.

National Research Council (committee on medical and biological effects of environmental pollutants). 1977. *Carbon monoxide.* Washington, D.C.: National Academy of Sciences.

New Mexico Environmental Improvement Agency. 1977. *Carbon monoxide hazard reduction in recreational vehicles project: Final report.* Atlanta, Ga.: Centers for Disease Control. Contract no. 200-76-0616.

Ott, W., and Flachsbart, P. 1982. Measurement of carbon monoxide concentrations in indoor and outdoor locations using personal monitors. *Environ. Int.* 6:295-304.

Radford, E. P., and Drizd, T. A. 1982. Blood carbon monoxide levels in persons 3-74 years by age, United States, 1976-80. National Center for Health Statistics: *Advance data from vital and health statistics* no. 76. Hyattsville, Md.: Government Printing Office. DHHS Publication no. (PHS) 82-1250.

Roughton, F. J. W., and Darling, R. C. 1944. The effect of carbon monoxide on the oxyhemoglobin dissociation curve. *Am. J. Physiol.* 141:17-31.

Sarna, S. J. M., et al. 1975. The effect of carbon monoxide on lipid metabolism of human coronary arteries. *Atherosclerosis* 22:193-95.

Sheps, D. S. 1985. Lack of effect of 4% carboxyhemoglobin concentration on cardiac function in patients with ischemic heart disease. *J. Am. Coll. Cardiol.* 5:406 (abstr.).

Singh, J., and Scott, L. H. 1984. Threshold for carbon monoxide induced fetotoxicity. *Teratology* 30:253-57.

Sokal, J. A., and Kralowska, E. 1985. The relationship between exposure duration, carboxyhemoglobin, blood glucose, pyruvate and lactate and the severity of intoxication in 39 cases of acute carbon monoxide poisoning in man. *Arch. Toxicol.* 57:196-99.

Spengler, J. D., and Cohen, M. A. 1985. Emissions from indoor combustion sources. In *Indoor air and human health.* Ed. R. B. Gammage and S. V. Kaye, 261-78. Chelsea, Mich.: Lewis Publishers.

Sterling, T. D.; Dimich, H.; and Kobayashi, D. 1981. Use of gas ranges for cooking and heating in urban dwellings. *J. Air Pollut. Control Assoc.* 32:162-65.

Sterling, T. D.; Dimich, H.; and Kobayashi, D. 1982. Indoor byproduct levels of tobacco smoke: A critical review of the literature. *J. Air Pollut. Control Assoc.* 32:250-57.

Stern, F. B., et al. 1988. Heart disease mortality among bridge and tunnel officers exposed to carbon monoxide. *Am. J. Epidemiol.* 128:1276-88.

- Stewart, R. D., et al. 1970. Experimental human exposure to carbon monoxide. *Arch. Environ. Health* 21:154-64.
- Stryer, L. 1975. *Biochemistry*. San Francisco: W. H. Freeman.
- Theodore, J.; O'Donnell, R. D.; and Back, K. C. 1971. Toxicological evaluation of carbon monoxide in humans and other mammalian species. *J. Occup. Med.* 13:242-55.
- U.S. Bureau of the Census. 1980 *Census of housing, Vol. 1: Characteristics of housing units, Ch. B: Detailed housing characteristics*, Pt. 1: *United States summary*. Washington, D.C.: Government Printing Office. Publication no. HC80-1-B1.
- U.S. Consumer Product Safety Commission. 1980. Commission proposes new CO standard to reduce deaths from unvented gas heaters. Washington, D.C.: News from CPSC, January.
- U.S. Department of Health and Human Services. 1987. *Vital statistics of the United States 1984, Vol. 2: Mortality, part A. National Center for Health Statistics*. Hyattsville, Md.: Government Printing Office. DHHS Publication no. (PHS) 87-1122.
- U.S. Department of Health, Education, and Welfare. 1979. *Smoking and health: A report of the surgeon general*. Washington, D.C.: Government Printing Office. DHEW Publication no. (PHS) 79-50066.
- U.S. Public Health Service. 1982. Carbon monoxide intoxication: A preventable environmental-health hazard. *MMWR* 31:529-31.
- Verhoeff, A. P., et al. 1983. Detecting indoor CO exposure by measuring CO in exhaled breath. *Int. Arch. Occup. Environ. Health* 53:167-73.
- Wallace, L. 1983. Carbon monoxide in air and breath of employees in an underground office. *J. Air Pollut. Control Assoc.* 33:678-82.
- Warren, J., et al. 1989. Acute effects of carbon monoxide exposure on individuals with coronary artery disease. Paper 89-54.3, presented at the eighty-second annual meeting of the Air and Waste Management Association, 25-30 June, Anaheim, Calif.
- Weiser, P. C., et al. 1978. Effects of low-level carbon monoxide exposure on the adaptation of healthy young men to aerobic work at an altitude of 1,610 meters. In *Environmental stress: Individual human adaptations*. Ed. L. J. Follinsbee et al., 101-10. New York: Academic Press.
- Werner, B., et al. 1985. Two cases of acute carbon monoxide with delayed neurological sequelae after a "free" interval. *Clin. Toxicol.* 23:249-65.
- Wharton, M., et al. 1989. Fatal carbon monoxide poisoning at a motel. *JAMA* 261:1177-78.
- Winter, P. M., and Miller, J. N. 1976. Carbon monoxide poisoning. *JAMA* 236:1502-4.
- Wittenberg, J. B. 1970. Myoglobin facilitated oxygen diffusion: Role of myoglobin in oxygen entry into muscle. *Physiol. Rev.* 50:559-636.
- Wright, G. R., and Shephard, R. J. 1978. Carbon monoxide exposure and auditory duration discrimination. *Arch. Environ. Health* 33:226-35.
- Zimmerman, S. S., and Truxal, B. 1981. Carbon monoxide poisoning. *Pediatrics* 68:215-24.

WOOD SMOKE

Marian C. Marbury, Sc.D.

Since the early 1970s, use of wood as a heating fuel has increased substantially. In 1981 approximately 7 percent of homes in the United States used wood as the major or supplementary source of heat, compared with only 1 percent in 1970 (Amundale, Duxbury, and Newman 1983). Increased residential wood use has significantly degraded ambient air quality in several areas of the country, most notably in towns and cities prone to wintertime inversions, such as Vail and Denver, Colorado (Lewis and Einfeld 1985), and Portland, Oregon (Cooper 1980). Research on wood combustion emissions, prompted by the resurgence in wood use, has provided inventories of the pollutants emitted by wood combustion, but data needed for understanding the health consequences of wood burning are still lacking. Few investigations of the effects of wood combustion on indoor air quality have been performed, and data concerning the health effects of domestic exposure to wood smoke remain extremely limited.

Wood is composed primarily of carbon, oxygen, and hydrogen. Under ideal conditions with complete combustion, water and carbon dioxide (CO₂) are the primary end products. Nitrogen oxides and sulfur oxides are also formed; nitrogen oxides are primarily from the combination of atmospheric nitrogen with oxygen during high temperature combustion, and sulfur oxides are from oxidation of sulfur in the wood. Incomplete combustion results in emissions of other pollutants such as particulates, organic compounds including polycyclic organic materials, and carbon monoxide (CO) (Quraishi 1985). Emission rates for these pollutants are highly variable and depend on such factors as burn rate, amount of air available for combustion, size of fuel charge, type and size of wood, and the moisture content of the wood (Quraishi 1985).

DeAngelis and colleagues (1980) sampled flue gases from two airtight cast iron stoves (one baffled and one nonbaffled) and a zero-clearance fireplace and per-