

# The Health Consequences Of Smoking

---

## NICOTINE ADDICTION

---

*a report of the  
Surgeon General*

1988



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Centers for Disease Control  
Center for Health Promotion and Education  
Office on Smoking and Health  
Rockville, Maryland 20857



THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

MAY 3 1988

The Honorable James Wright  
Speaker of the House  
of Representatives  
Washington, D.C. 20515

Dear Mr. Speaker:

I am pleased to transmit to the Congress the 1987 Surgeon General's Report on the health consequences of smoking, as mandated by Section 8(a) of the Public Health Cigarette Smoking Act of 1969. The Act requires the Secretary of Health and Human Services to transmit an annual report to Congress on the health consequences of smoking and such recommendations for legislation as the Secretary may deem appropriate.

This report, entitled The Health Consequences of Smoking: Nicotine Addiction, examines the scientific evidence that cigarettes and other forms of tobacco are addicting. The issue of tobacco addiction has been addressed in previous Surgeon General's Reports and in the medical literature beginning in the early 1900s. Because of the recent expansion of research in this area, a thorough review of this topic is warranted. Despite the significant health risks of tobacco use outlined in previous reports, many smokers have great difficulty in quitting. This report concludes that such difficulty is in large part due to the addicting properties of nicotine, which is present in all forms of tobacco.

The report further concludes that the processes that determine tobacco addiction are similar to those that determine addiction to other drugs such as heroin and cocaine. Through such understanding, health-care providers may be better able to assist tobacco users in quitting.

Private health organizations, health-care providers, community groups, and government agencies should initiate or strengthen programs to inform the public of the addicting nature of tobacco use. A warning label on the addicting nature of tobacco use should be rotated with other health warnings now required on cigarette and smokeless tobacco packages and advertisements. Preventing the initiation of tobacco use must be a priority because of the difficulty in overcoming nicotine addiction once it is firmly established. Because most cases of nicotine addiction begin during childhood and adolescence, school curricula on the prevention of drug use should also include tobacco.

Cigarette smoking, the chief avoidable cause of premature death in this country, is responsible for more than 300,000 premature deaths each year. The disease impact of smoking justifies placing the problem of tobacco use at the top of the public health agenda. The conclusions of this report provide another compelling reason for strengthening our efforts to reduce tobacco use in our society.

Sincerely,

Otis R. Bowen, M.D.  
Secretary

Enclosure



THE SECRETARY OF HEALTH AND HUMAN SERVICES  
WASHINGTON, D.C. 20201

MAY 3 1988

The Honorable George Bush  
President of the Senate  
Washington, D.C. 20515

Dear Mr. President:

I am pleased to transmit to the Congress the 1987 Surgeon General's Report on the health consequences of smoking, as mandated by Section 8(a) of the Public Health Cigarette Smoking Act of 1969. The Act requires the Secretary of health and Human Services to transmit an annual report to Congress on the health consequences of smoking and such recommendations for legislation as the Secretary may deem appropriate.

This report, entitled The Health Consequences of Smoking: Nicotine Addiction, examines the scientific evidence that cigarettes and other forms of tobacco are addicting. The issue of tobacco addiction has been addressed in previous Surgeon General's Reports and in the medical literature beginning in the early 1900s. Because of the recent expansion of research in this area, a thorough review of this topic is warranted. Despite the significant health risks of tobacco use outlined in previous reports, many smokers have great difficulty in quitting. This report concludes that such difficulty is in large part due to the addicting properties of nicotine, which is present in all forms of tobacco.

The report further concludes that the processes that determine tobacco addiction are similar to those that determine addiction to other drugs such as heroin and cocaine. Through such understanding, health-care providers may be better able to assist tobacco users in quitting.

Private health organizations, health-care providers, community groups, and government agencies should initiate or strengthen programs to inform the public of the addicting nature of tobacco use. A warning label on the addicting nature of tobacco use should be rotated with other health warnings now required on cigarette and smokeless tobacco packages and advertisements. Preventing the initiation of tobacco use must be a priority because of the difficulty in overcoming nicotine addiction once it is firmly established. Because most cases of nicotine addiction begin during childhood and adolescence, school curricula on the prevention of drug use should also include tobacco.

Cigarette smoking, the chief avoidable cause of premature death in this country, is responsible for more than 300,000 premature deaths each year. The disease impact of smoking justifies placing the problem of tobacco use at the top of the public health agenda. The conclusions of this report provide another compelling reason for strengthening our efforts to reduce tobacco use in our society.

Sincerely,

Otis R. Bowen, M.D.  
Secretary

Enclosure

## FOREWORD

This 20th Report of the Surgeon General on the health consequences of tobacco use provides an additional important piece of evidence concerning the serious health risks associated with using tobacco.

The subject of this Report, nicotine addiction, was first mentioned in the 1964 Report of the Advisory Committee to the Surgeon General, which referred to tobacco use as “habituating.” In the landmark 1979 Report of the Surgeon General, by which time considerably more research had been conducted, smoking was called “the prototypical substance-abuse dependency.” Scientists in the field of drug addiction now agree that nicotine, the principal pharmacologic agent that is common to all forms of tobacco, is a powerfully addicting drug.

Recognizing tobacco use as an addiction is critical both for treating the tobacco user and for understanding why people continue to use tobacco despite the known health risks. Nicotine is a psychoactive drug with actions that reinforce the use of tobacco. Efforts to reduce tobacco use in our society must address all the major influences that encourage continued use, including social, psychological, and pharmacologic factors.

After carefully examining the available evidence, this Report concludes that:

- Cigarettes and other forms of tobacco are addicting.
- Nicotine is the drug in tobacco that causes addiction.
- The pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

We must recognize both the potential for behavioral and pharmacologic treatment of the addicted tobacco user and the problems of withdrawal. Tobacco use is a disorder which can be remedied through medical attention; therefore, it should be approached by health care providers just as other substance-use disorders are approached: with knowledge, understanding, and persistence. Each health care provider should use every available clinical opportunity to encourage or assist smokers to quit and to help former smokers to maintain abstinence.

To maintain momentum toward a smoke-free society, we also must take steps to prevent young people from beginning to smoke. First, we must insure that every child in every school in this country is educated as to the health risks and the addictive nature of tobacco use. Most jurisdictions require that school curricula include prevention of drug use; therefore, education on the prevention of tobacco use should be included in this effort. Second, warning labels regarding the addictive nature of tobacco use should be required for all tobacco packages and advertisements. Young people in particular may not be aware of the risk of tobacco addiction. Finally, parents and other role models should discourage smoking and other forms of tobacco use among young people. Parents who quit set an example for their children.

Smoking continues to be the chief preventable cause of premature death in this country. Nicotine has addictive properties which help to sustain widespread tobacco use. It is gratifying to see the decline in reported smoking prevalence and cigarette consumption in the United States during the past 25 years. However, we cannot expect to see a sustained decline in rates of smoking-related cancers, cardiovascular disease, and pulmonary disease without sustained public health efforts against tobacco use.

The Public Health Service is committed to preventing tobacco use among youth and to promoting cessation among existing smokers. We hope that this Report will assist the health care community, voluntary health agencies, and our Nation's schools in working with us to reduce tobacco use in our society.

Robert E. Windom, M.D.  
Assistant Secretary for Health

## **PREFACE**

This Report of the Surgeon General is the U.S. Public Health Service's 20th Report on the health consequences of tobacco use and the 7th issued during my tenure as Surgeon General. Eighteen Reports have been released previously as part of the health consequences of smoking series; a report on the health consequences of using smokeless tobacco was released in 1986.

Previous Reports have reviewed the medical and scientific evidence establishing the health effects of cigarette smoking and other forms of tobacco use. Tens of thousands of studies have documented that smoking causes lung cancer, other cancers, chronic obstructive lung disease, heart disease, complications of pregnancy, and several other adverse health effects.

Epidemiologic studies have shown that cigarette smoking is responsible for more than 300,000 deaths each year in the United States. As I stated in the Preface to the 1982 Surgeon General's Report, smoking is the chief avoidable cause of death in our society.

From 1964 through 1979, each Surgeon General's Report addressed the major health effects of smoking. The 1979 Report provided the most comprehensive review of these effects. Following the 1979 Report, each subsequent Report has focused on specific populations (women in 1980, workers in 1985), specific diseases (cancer in 1982, cardiovascular disease in 1983, chronic obstructive lung disease in 1984), and specific topics (low-tar, low-nicotine cigarettes in 1981, involuntary smoking in 1986).

This Report explores in great detail another specific topic: nicotine addiction. Careful examination of the data makes it clear that cigarettes and other forms of tobacco are addicting. An extensive body of research has shown that nicotine is the drug in tobacco that causes addiction. Moreover, the processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

### **Actions of Nicotine**

All tobacco products contain substantial amounts of nicotine. Nicotine is absorbed readily from tobacco smoke in the lungs and from smokeless tobacco in the mouth or nose. Levels of nicotine in

the blood are similar in magnitude in people using different forms of tobacco. Once in the blood stream, nicotine is rapidly distributed throughout the body.

Nicotine is a powerful pharmacologic agent that acts in a variety of ways at different sites in the body. After reaching the blood stream, nicotine enters the brain, interacts with specific receptors in brain tissue, and initiates metabolic and electrical activity in the brain. In addition, nicotine causes skeletal muscle relaxation and has cardiovascular and endocrine (i.e., hormonal) effects.

Human and animal studies have shown that nicotine is the agent in tobacco that leads to addiction. The diversity and strength of its actions on the body are consistent with its role in causing addiction.

### **Tobacco Use as an Addiction**

Standard definitions of drug addiction have been adopted by various organizations including the World Health Organization and the American Psychiatric Association. Although these definitions are not identical, they have in common several criteria for establishing a drug as addicting.

The central element among all forms of drug addiction is that the user's behavior is largely controlled by a psychoactive substance (i.e., a substance that produces transient alterations in mood that are primarily mediated by effects in the brain). There is often compulsive use of the drug despite damage to the individual or to society, and drug-seeking behavior can take precedence over other important priorities. The drug is "reinforcing"--that is, the pharmacologic activity of the drug is sufficiently rewarding to maintain self-administration. "Tolerance" is another aspect of drug addiction whereby a given dose of a drug produces less effect or increasing doses are required to achieve a specified intensity of response. Physical dependence on the drug can also occur, and is characterized by a withdrawal syndrome that usually accompanies drug abstinence. After cessation of drug use, there is a strong tendency to relapse.

This Report demonstrates in detail that tobacco use and nicotine in particular meet all these criteria. The evidence for these findings is derived from animal studies as well as human observations. Leading national and international organizations, including the World Health Organization and the American Psychiatric Association, have recognized chronic tobacco use as a drug addiction.

Some people may have difficulty in accepting the notion that tobacco is addicting because it is a legal product. The word "addiction" is strongly associated with illegal drugs such as cocaine and heroin. However, as this Report shows, the processes that

determine tobacco addiction are similar to those that determine addiction to other drugs, including illegal drugs.

In addition, some smokers may not believe that tobacco is addicting because of a reluctance to admit that one's behavior is largely controlled by a drug. On the other hand, most smokers admit that they would like to quit but have been unable to do so. Smokers who have repeatedly failed in their attempts to quit probably realize that smoking is more than just a simple habit.

Many smokers have quit on their own ("spontaneous remission") and some smokers smoke only occasionally. However, spontaneous remission and occasional use also occur with the illicit drugs of addiction, and in no way disqualify a drug from being classified as addicting. Most narcotics users, for example, never progress beyond occasional use, and of those who do, approximately 30 percent spontaneously remit. Moreover, it seems plausible that spontaneous remitters are largely those who have either learned to deliver effective treatments to themselves or for whom environmental circumstances have fortuitously changed in such a way as to support drug cessation and abstinence.

### **Treatment**

Like other addictions, tobacco use can be effectively treated. A wide variety of behavioral interventions have been used for many years, including aversion procedures (e.g., satiation, rapid smoking), relaxation training, coping skills training, stimulus control, and nicotine fading. In recognition of the important role that nicotine plays in maintaining tobacco use, nicotine replacement therapy is now available. Nicotine polacrilex gum has been shown in controlled trials to relieve withdrawal symptoms. In addition, some (but not all) studies have shown that nicotine gum, as an adjunct to behavioral interventions, increases smoking abstinence rates. In recent years, multicomponent interventions have been applied successfully to the treatment of tobacco addiction.

### **Public Health Strategies**

The conclusion that cigarettes and other forms of tobacco are addicting has important implications for health professionals, educators, and policy-makers. In treating the tobacco user, health professionals must address the tenacious hold that nicotine has on the body. More effective interventions must be developed to counteract both the psychological and pharmacologic addictions that accompany tobacco use. More research is needed to evaluate how best to treat those with the strongest dependence on the drug. Treatment of tobacco addiction should be more widely available and should be



considered at least as favorably by third-party payors as treatment of alcoholism and illicit drug addiction.

The challenge to health professionals is complicated by the array of new nicotine delivery systems that are being developed and introduced in the marketplace. Some of these products are produced by tobacco manufacturers; others may be marketed as devices to aid in smoking cessation. These new products may be more toxic and more addicting than the products currently on the market. New nicotine delivery systems should be evaluated for their toxic and addictive effects; products intended for use in smoking cessation also should be evaluated for efficacy.

Public information campaigns should be developed to increase community awareness of the addictive nature of tobacco use. A health warning on addiction should be rotated with the other warnings now required on cigarette and smokeless tobacco packages and advertisements. Prevention of tobacco use should be included along with prevention of illicit drug use in comprehensive school health education curricula. Many children and adolescents who are experimenting with cigarettes and other forms of tobacco state that they do not intend to use tobacco in later years. They are unaware of, or underestimate, the strength of tobacco addiction. Because this addiction almost always begins during childhood or adolescence, children need to be warned as early as possible, and repeatedly warned through their teenage years, about the dangers of exposing themselves to nicotine.

This Report shows conclusively that cigarettes and other forms of tobacco are addicting in the same sense as are drugs such as heroin and cocaine. Most adults view illegal drugs with scorn and express disapproval (if not outrage) at their sale and use. This Nation has mobilized enormous resources to wage a war on drugs -- illicit drugs. We should also give priority to the one addiction that is killing more than 300,000 Americans each year.

We as citizens, in concert with our elected officials, civic leaders, and public health officers, should establish appropriate public policies for how tobacco products are sold and distributed in our society. With the evidence that tobacco is addicting, is it appropriate for tobacco products to be sold through vending machines, which are easily accessible to children? Is it appropriate for free samples of tobacco products to be sent through the mail or distributed on public property, where verification of age is difficult if not impossible? Should the sale of tobacco be treated less seriously than the sale of alcoholic beverages, for which a specific license is required (and revoked for repeated sales to minors)?

In the face of overwhelming evidence that tobacco is addicting, policy-makers should address these questions without delay. To

achieve our goal of a smoke-free society, we must give this problem the serious attention it deserves.

C. Everett Koop, M.D., Sc.D.  
Surgeon General

## ACKNOWLEDGMENTS

This Report was prepared by the Department of Health and Human Services under the general editorship of the Office on Smoking and Health, Ronald M. Davis, M.D., Director. The Managing Editors were Thomas E. Novotny, M.D., and William R. Lynn, Office on Smoking and Health.

Scientific editors were Neal L. Benowitz, M.D., Professor of Medicine, Chief, Division of Clinical Pharmacology and Experimental Therapeutics, San Francisco General Hospital, University of California, San Francisco, California; Neil E. Grunberg, Ph.D., Department of Medical Psychology, Uniformed Services University of the Health Sciences, Bethesda, Maryland; Jack E. Henningfield, Ph.D., Chief, Biology of Dependence and Abuse Potential Assessment Laboratory, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland; and Harry A. Lando, Ph.D., Professor, Department of Psychology, Iowa State University, Ames, Iowa.

The following individuals prepared draft chapters or portions of the Report.

David B. Abrams, Ph.D., Assistant Professor of Psychiatry and Human Behavior, Brown University Program in Medicine, The Miriam Hospital, Center for Health Promotion, Providence, Rhode Island

Timothy B. Baker, Ph.D., Department of Psychology, University of Wisconsin, Madison, Wisconsin

Neal L. Benowitz, M.D., Professor of Medicine, Chief, Division of Clinical Pharmacology and Experimental Therapeutics, San Francisco General Hospital, University of California, San Francisco, California

Thomas H. Brandon, M.S., Department of Psychology, University of Wisconsin, Madison, Wisconsin

Richard F. Catalano, Ph.D., Research Assistant Professor, Center for Social Welfare Research, School of Social Work, University of Washington, Seattle, Washington

Larry D. Chait, Ph.D., Research Associate (Assistant Professor), Department of Psychiatry, University of Chicago, Chicago, Illinois

Paul B.S. Clarke, Ph.D., Department of Pharmacology and Therapeutics, McGill University, Montreal, Quebec, Canada

Richard R. Clayton, Ph.D., Professor, Department of Sociology,  
University of Kentucky, Lexington, Kentucky

Allan C. Collins, Ph.D., Institute for Behavioral Genetics, School of  
Pharmacy, University of Colorado, Boulder, Colorado

Thomas M. Cooper, D.D.S., Professor, Department of Community  
Dentistry, University of Kentucky, Lexington, Kentucky

Lori A. Crane, M.P.H., Division of Cancer Control, Jonsson Compre-  
hensive Cancer Center, University of California, Los Angeles,  
California

Susan Curry, Ph.D., Center for Health Studies, Group Health  
Cooperative of Puget Sound, Seattle, Washington

D. Layten Davis, Ph.D., Director, Tobacco and Health Research  
Institute, University of Kentucky, Lexington, Kentucky

Ronald M. Davis, M.D., Director, Office on Smoking and Health,  
Center for Health Promotion and Education, Centers for Disease  
Control, Rockville, Maryland

Edward F. Domino, M.D., Professor, Department of Pharmacology,  
University of Michigan, Ann Arbor, Michigan

John L. Egle, Jr., Ph.D., Department of Pharmacology/Toxicology,  
Medical College of Virginia, Virginia Commonwealth University,  
Richmond, Virginia

Joan Ershler, Ph.D., Research Associate, Mt. Sinai Medical Center,  
Milwaukee, Wisconsin

Raymond Fleming, Ph.D., Assistant Professor, University of Wiscon-  
sin-Milwaukee, Mt. Sinai Medical Center, Milwaukee, Wisconsin

Kathleen A. Fletcher, Ph.D., M.P.H., Consultant, The University of  
Texas Health Science Center, Houston, Texas

Paul J. Fudala, Ph.D., Addiction Research Center, National Institute  
on Drug Abuse, Baltimore, Maryland

C. Gary Gairola, Ph.D., University of Kentucky, Tobacco and Health  
Research Institute, Lexington, Kentucky

David Gilbert, Ph.D., Department of Psychology, Southern Illinois  
University, Carbondale, Illinois

Lewayne D. Gilchrist, Ph.D., Research Associate Professor, School of  
Social Work, University of Washington, Seattle, Washington

Donna M. Goldberg, M.A., Annapolis, Maryland

Steven R. Goldberg, Ph.D., Preclinical Pharmacology Research  
Branch, Addiction Research Center, National Institute on Drug  
Abuse, Baltimore, Maryland

John Grabowski, Ph.D., Department of Psychiatry and Behavioral  
Science, The University of Texas Health Science Center, Houston,  
Texas

Neil E. Grunberg, Ph.D., Department of Medical Psychology, Uni-  
formed Services University of the Health Sciences, Bethesda,  
Maryland

Dorothy K. Hatsukami, Ph.D., Department of Psychiatry, University of Minnesota, Minneapolis, Minnesota

J. David Hawkins, Ph.D., Professor, Center for Social Welfare Research, School of Social Work, University of Washington, Seattle, Washington

Jack E. Henningfield, Ph.D., Chief, Biology of Dependence and Abuse Potential Assessment Laboratory, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland.

Ronald I. Herning, Ph.D., Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

Matthew Owen Howard, M.S., M.S.W., Research Assistant, Center for Social Welfare Research, School of Social Work, University of Washington, Seattle, Washington

John R. Hughes, M.D., Departments of Psychiatry, Psychology, and Family Practice, University of Vermont, Burlington, Vermont

Edgar T. Iwamoto, Ph.D., Department of Pharmacology, College of Medicine, University of Kentucky, Lexington, Kentucky

Murray E. Jarvik, M.D., Ph.D., The Neuropsychiatric Institute and Hospital, School of Medicine, University of California, Los Angeles, Veterans' Administration Medical Center, Brentwood Division, Los Angeles, California

Robert C. Klesges, Ph.D., Associate Professor, Center for Applied Psychological Research, Department of Psychology, Memphis State University, Memphis, Tennessee

Lynn T. Kozlowski, Ph.D., Head, Behavioral Research on Tobacco Use, Addiction Research Foundation, Professor of Psychology and of Preventive Medicine and Biostatistics, University of Toronto, Toronto, Ontario, Canada

Howard Leventhal, Ph.D., Professor and Chairman, Department of Psychology, University of Wisconsin, Madison, Wisconsin

Edythe D. London, Ph.D., Chief, Neuropharmacology Laboratory, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

Scott E. Lukas, Ph.D., Assistant Professor of Psychiatry (Pharmacology), Harvard Medical School, Department of Psychiatry, Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, Massachusetts

Alfred C. Marcus, Ph.D., Associate Director, Division of Cancer Control, Jonsson Comprehensive Cancer Center, University of California, Los Angeles, California

Andrew W. Meyers, Ph.D., Professor, Center for Applied Psychological Research, Department of Psychology, Memphis State University, Memphis, Tennessee

Thomas E. Novotny, M.D., Medical Epidemiologist, Office on Smoking and Health, Center for Health Promotion and Education, Centers for Disease Control, Rockville, Maryland

Carol Tracy Orleans, Ph.D., Senior Investigator, Behavioral Medicine and Director of Smoking Cessation Services, Division of Cancer Control, Fox Chase Cancer Center, Philadelphia, Pennsylvania

John P. Pierce, M.Sc., Ph.D., Chief, Epidemiology Branch, Office on Smoking and Health, Center for Health Promotion and Education, Centers for Disease Control, Rockville, Maryland

Ovide F. Pomerleau, Ph.D., Behavioral Medicine Program, University of Michigan, Department of Psychiatry, Ann Arbor, Michigan

Amelie G. Ramirez, M.P.H., Faculty Associate, The University of Texas Health Science Center, Assistant Professor, Baylor College of Medicine, Houston, Texas

Jed E. Rose, Ph.D., Veterans' Administration Medical Center, Wadsworth and Brentwood Divisions, Los Angeles, California

J.A. Rosecrans, Ph.D., Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia

David P.L. Sachs, M.D., Director, Smoking Cessation Research Institute, Palo Alto, California

Mary Anne Salmon, Ph.D., Research Associate, Health Services Research Center, University of North Carolina, Chapel Hill, North Carolina

Nina G. Schneider, Ph.D., Associate Research Psychologist, Department of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine, Research Psychologist, Psychopharmacology Unit, Veterans' Administration Medical Center, Brentwood Division, Los Angeles, California

V.J. Schoenbach, Ph.D., Associate Professor, Department of Epidemiology, Research Associate, Health Services Research Center, University of North Carolina, Chapel Hill, North Carolina

Saul Shiffman, Ph.D., Associate Professor, Department of Psychology, University of Pittsburgh, Pittsburgh, Pennsylvania

Victor J. Strecher, Ph.D., Research Associate, Health Services Research Center, Assistant Professor, Department of Health Education, University of North Carolina, Chapel Hill, North Carolina

David M. Warburton, Professor, Department of Psychology, University of Reading, Whiteknights, Reading, United Kingdom

Elizabeth A. Wells, Ph.D., Post-Doctoral Fellow, Center for Social Welfare Research, University of Washington, Seattle, Washington

Thomas Ashby Wills, Ph.D., Assistant Professor of Psychology, Assistant Professor of Epidemiology and Social Medicine, Department of Epidemiology and Social Medicine, Ferkauf Graduate School of Psychology and Albert Einstein College of Medicine, Bronx, New York

Phillip P. Woodson, Dr.sc.nat., Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

The editors acknowledge with gratitude the following distinguished scientists, physicians, and others who lent their support in the development of this Report by coordinating manuscript preparation, contributing critical reviews of the manuscript, or assisting in other ways.

Leo G. Abood, Ph.D., Department of Pharmacology, University of Rochester Medical Center, Rochester, New York

John S. Baer, Ph.D., Department of Psychology, University of Washington, Seattle, Washington

Timothy B. Baker, Ph.D., Department of Psychology, University of Wisconsin, Madison, Wisconsin

Claudia R. Baquet, M.D., M.P.H., Chief, Special Populations Studies Branch, Division of Cancer Prevention and Control, National Cancer Institute, Bethesda, Maryland

Glen Bennett, M.P.H., Field Studies Advisor, Office of Prevention, Education, and Control, National Heart, Lung, and Blood Institute, Bethesda, Maryland

George E. Bigelow, Ph.D., Associate Professor of Behavioral Biology, Director, Behavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, The Johns Hopkins University School of Medicine, Baltimore, Maryland

Clarice Brown, M.S., Data Analyst, Office of Prevention, Education, and Control, National Heart, Lung, and Blood Institute, Bethesda, Maryland

David M. Burns, M.D., Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine, University of California Medical Center, San Diego, California

Donald R. Cherek, Ph.D., Department of Psychiatry and Behavioral Sciences, Mental Sciences Institute, The University of Texas Health Science Center, Houston, Texas

Paul B.S. Clarke, Ph.D., Department of Pharmacology and Therapeutics, McGill University, Montreal, Quebec, Canada

Ro Nemeth-Coslett, Ph.D., Psychologist, Prevention Research Branch, Division of Clinical Research, National Institute on Drug Abuse, Rockville, Maryland

Thomas J. Crowley, M.D., University of Colorado Health Sciences Center, Denver, Colorado

Joseph W. Cullen, Ph.D., Deputy Director, Division of Cancer Prevention and Control, National Cancer Institute, Bethesda, Maryland

K. Michael Cummings, Ph.D., M.P.H., Research Scientist, Department of Cancer Control and Epidemiology, Roswell Park Memorial Institute, Buffalo, New York

Susan Curry, Ph.D., Center for Health Studies, Group Health Cooperative of Puget Sound, Seattle, Washington

Vincent T. DeVita, Jr., M.D., Director, National Cancer Institute, National Institutes of Health, Bethesda, Maryland

Sir Richard Doll, University of Oxford, Oxford, England

Manning Feinleib, M.D., Dr.P.H., Director, National Center for Health Statistics, Centers for Disease Control, Hyattsville, Maryland

William H. Foege, M.D., Executive Director, The Carter Center of Emory University, Atlanta, Georgia

Richard R. Frecker, M.D., Ph.D., Head, Biomedical Research, Department of Pharmacology, Addiction Research Foundation, Toronto, Ontario, Canada

K.H. Ginzler, Ph.D., Professor, Department of Pharmacology and Interdisciplinary Toxicology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

Russell E. Glasgow, Ph.D., Oregon Research Institute, Eugene, Oregon

Nancy P. Gordon, Sc.D., Behavioral Scientist, Division of Research, Kaiser Permanente Medical Group, Oakland, California

Roland R. Griffiths, The Johns Hopkins University School of Medicine, Baltimore, Maryland

Ellen R. Gritz, Ph.D., Director, Division of Cancer Control, Jonsson Comprehensive Cancer Center, University of California, Los Angeles, California

Sharon M. Hall, Ph.D., Professor, Department of Psychiatry, Center for Social and Behavioral Sciences, University of California, San Francisco, California

Louis S. Harris, Ph.D., Senior Science Advisor, National Institute on Drug Abuse, Alcohol, Drug Abuse, and Mental Health Administration, Rockville, Maryland

Ronald I. Herning, Ph.D., Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

Dietrich Hoffmann, Ph.D., Associate Director, Naylor Dana Institute, Valhalla, New York

Leo Hollister, M.D., Medical Director, Harris County Psychiatry Center, Houston, Texas

Enid Hunkeler, Senior Investigator, Kaiser Permanente Medical Care Program, Oakland, California

Peyton Jacob III, Ph.D., Division of Clinical Pharmacology, San Francisco General Hospital, University of California, San Francisco, California

Jerome Jaffe, M.D., Director, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

Murray E. Jarvik, M.D., Ph.D., The Neuropsychiatric Institute and Hospital, School of Medicine, University of California, Los Angeles



geles, and Veterans' Administration Medical Center West Los Angeles, Brentwood Division, Los Angeles, California

Martin Jarvis, M.Phil., Senior Lecturer, Addiction Research Unit, Institute of Psychiatry, London, England

Chris-Ellen Johanson, Ph.D., Department of Psychiatry, Pritzker School of Medicine, University of Chicago Drug Abuse Research Center, Chicago, Illinois

Reese T. Jones, Ph.D., Department of Psychiatry, University of California School of Medicine, San Francisco, California

Kenneth J. Kellar, Ph.D., Department of Pharmacology, Georgetown University Medical Center, Washington, D.C.

Lynn T. Kozlowski, Ph.D., Head, Behavioral Research on Tobacco Use, Addiction Research Foundation, Toronto, Ontario, Canada

Richard J. Lamb, Ph.D., Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland

Charles L. LeMaistre, M.D., President, University of Texas Systems Cancer Center, Houston, Texas

Claude Lenfant, M.D., Director, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

Howard Leventhal, Ph.D., Professor of Psychology, University of Wisconsin, Madison, Wisconsin

Edward Lichtenstein, Ph.D., Oregon Research Institute, Eugene, Oregon

Donald Ian Macdonald, M.D., Administrator, Alcohol, Drug Abuse, and Mental Health Administration, Rockville, Maryland

G. Alan Marlatt, Ph.D., Professor of Psychology, University of Washington, Seattle, Washington

William R. Martin, M.D., Chairman, Department of Pharmacology, University of Kentucky College of Medicine, Lexington, Kentucky

James O. Mason, M.D., Dr.P.H., Director, Centers for Disease Control, Atlanta, Georgia

J. Michael McGinnis, M.D., Deputy Assistant Secretary (Disease Prevention and Health Promotion), Washington, D.C.

A. Thomas McLellan, Ph.D., Substance Abuse Treatment Research Center, Philadelphia Veterans' Administration Medical Center and The University of Pennsylvania, Philadelphia, Pennsylvania

Nancy K. Mello, Ph.D., Alcohol and Drug Abuse Research Center, McClean Hospital, Belmont, Massachusetts

Gregory J. Morosco, Ph.D., M.P.H., Smoking Education Program Coordinator, National Heart, Lung, and Blood Institute, Bethesda, Maryland

Joseph P. Mulholland, Ph.D., Bureau of Economics, Federal Trade Commission, Washington, D.C.

Herbert W. Nickens, M.D., M.A., Director, Office of Minority Health, Public Health Service, Washington, D.C.

Richard Peto, M.A., M.Sc., Imperial Cancer Research Fund, Cancer Studies Unit, Nuffield Department of Clinical Medicine, Radcliffe Infirmary, University of Oxford, Oxford, England

Roy W. Pickens, Ph.D., Director, Division of Clinical Research, National Institute on Drug Abuse, Rockville, Maryland

John P. Pierce, M.Sc., Ph.D., Chief, Epidemiology Branch, Office on Smoking and Health, Center for Health Promotion and Education, Centers for Disease Control, Rockville, Maryland

John M. Pinney, Executive Director, Institute for the Study of Smoking Behavior and Policy, John F. Kennedy School of Government, Harvard University, Cambridge, Massachusetts

Michael R. Polen, M.A., Research Associate, Division of Research, Kaiser-Permanente Medical Group, Oakland, California

William Pollin, M.D., Former Director, National Institute on Drug Abuse, Bethesda, Maryland

David C. Ramsey, M.P.H., Health Educator, Division of Health Education, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Georgia

Everett R. Rhoades, M.D., Assistant Surgeon General and Director, Indian Health Service, Rockville, Maryland

M.A.H. Russell, F.R.C.P., Addiction Research Unit, Institute of Psychiatry, University of London, London, England

Charles R. Schuster, Ph.D., Director, National Institute on Drug Abuse, Rockville, Maryland

Burt Sharpe, M.D., Hennepin County Medical Center, Department of Medicine, Minneapolis, Minnesota

Donald R. Shopland, Public Health Advisor, Smoking, Tobacco, and Cancer Program, National Cancer Institute, Bethesda, Maryland

Jerome E. Singer, Ph.D., Medical Psychology, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Maxine L. Stitzer, Ph.D., Associate Professor, Behavioral Biology, The Johns Hopkins School of Medicine, Behavioral Pharmacology Research, Francis Scott Key Medical Center, Baltimore, Maryland

David N. Sundwall, M.D., Assistant Surgeon General and Administrator, Health Resources and Services Administration, Rockville, Maryland

Dennis D. Tolsma, M.P.H., Director, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Georgia

Frederick L. Trowbridge, M.D., Director, Division of Nutrition, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Georgia

Frank J. Vocci, Jr., Ph.D., Acting Chief, Drug Abuse Staff, Center for Drug Evaluation and Research, Food and Drug Administration, Washington, DC

Ronald W. Wilson, M.A., National Center for Health Statistics, Centers for Disease Control, Hyattsville, Maryland

Roy A. Wise, Ph.D., Department of Psychology, Concordia University, Montreal, Quebec, Canada  
Faye Wright, Center for Applied Psychological Research, Department of Psychology, Memphis State University, Memphis, Tennessee  
Ernst L. Wynder, M.D., President, American Health Foundation, New York, New York  
James B. Wyngaarden, M.D., Director, National Institutes of Health, Bethesda, Maryland  
Tomoji Yanagita, M.D., Ph.D., Preclinical Research Laboratories, Central Institute for Experimental Animals, Kawasaki, Japan  
Frank E. Young, M.D., Commissioner, Food and Drug Administration, Rockville, Maryland

The editors also acknowledge the contributions of the following staff members and others who assisted in the preparation of this Report.

Margaret Anglin, Secretary, Office on Smoking and Health, Rockville, Maryland  
Charles Appiah, Project Clerk, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
John L. Bagrosky, Associate Director for Program Operations, Office on Smoking and Health, Rockville, Maryland  
Sonia Balakirsky, Secretary, Office on Smoking and Health, Rockville, Maryland  
Carol Bean, Associate Project Director, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Tamara Blair, Production Coordinator, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland  
Catherine E. Burckhardt, Editorial Assistant, Office on Smoking and Health, Rockville, Maryland  
Gayle Christman, Word Processing Specialist, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Carol K. Cummings, Secretary, Office on Smoking and Health, Rockville, Maryland  
Stephanie D. DeVoe, Programmer, Information Systems Department, ATLAS Federal Services, Inc., Rockville, Maryland  
Michael C. Fiore, M.D., M.P.H., Medical Epidemiologist, Office on Smoking and Health, Rockville, Maryland  
David Fry, Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Lynn Funkhauser, Word Processing Specialist, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Mary Gardner, Senior Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia

Amy Garson, M.P.H. student, Office on Smoking and Health, Rockville, Maryland

Arnetta G. Glover, Secretary, Office on Smoking and Health, Rockville, Maryland

William Groskopf, Library Acquisitions Specialist, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland

Evridiki Hatziandreu, M.D., M.P.H., Epidemic Intelligence Service Officer, Office on Smoking and Health, Rockville, Maryland

Susan A. Hawk, Ed.M., M.S., Chief, Technical Information Center, Office on Smoking and Health, Rockville, Maryland

Patricia E. Healy, Technical Information Specialist, Office on Smoking and Health, Rockville, Maryland

Terri L. Henry, Clerk-Typist, Office on Smoking and Health, Rockville, Maryland

Timothy K. Hensley, Technical Publications Writer, Office on Smoking and Health, Rockville, Maryland

Shirley K. Hickman, Data Entry Operator, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland

Robert S. Hutchings, Associate Director for Information and Program Development, Office on Smoking and Health, Rockville, Maryland

Karen Jacob, Senior Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia

Sheila Jones, Word Processing Specialist, Smoking and Health Project, The Circle, Inc., McLean, Virginia

Rick Keir, Senior Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia

Julie Kurz, Graphics Specialist, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland

Diana Lord, Research Assistant, Department of Medical Psychology, Uniformed Services University of the Health Sciences, Bethesda, Maryland

Gerri E. Mast, Secretary, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Georgia

Judy J. Mast, Secretary, Center for Health Promotion and Education, Centers for Disease Control, Atlanta, Georgia

Dixie McGough, Program Manager, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland

Paul G. McGovern, Ph.D., Postdoctoral Research Associate, Smoking Research Group, Department of Psychology, Iowa State University, Ames, Iowa

Dan McLaughlin, Editorial Assistant, Smoking and Health Project, The Circle, Inc., McLean, Virginia

Nancy Miltenberger, Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Cathie O'Donnell, Senior Editor, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Ruth C. Palmer, Secretary, Office on Smoking and Health, Rockville, Maryland  
Russell D. Peek, Library Acquisitions Specialist, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland  
Mary B. Pfeiffer, M.L.S., Librarian, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland  
Margaret E. Pickerel, Public Information and Publications Specialist, Office on Smoking and Health, Rockville, Maryland  
Renate Phillips, Desktop Publishing/Graphic Artist, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Karen Sherman, Production Assistant, Information Management Department, ATLAS Federal Services, Inc., Rockville, Maryland  
Linda R. Spiegelman, Administrative Officer, Office on Smoking and Health, Rockville, Maryland  
Tamara Shipp, Publications Assistant, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Evelyn L. Swarr, Systems Management Projects Supervisor, Information Systems Department, ATLAS Federal Services, Inc., Rockville, Maryland  
Patricia Y. Thomas, Secretary, Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland  
Daniel R. Tisch, Project Director, Smoking and Health Project, The Circle, Inc., McLean, Virginia  
Louise G. Wiseman, Technical Information Specialist, Office on Smoking and Health, Rockville, Maryland

# TABLE OF CONTENTS

---

|   |     |
|---|-----|
| Foreword .....  | i   |
| Preface .....   | iii |
| Acknowledgments .....   | ix  |
| I. Introduction, Overview, Summary, and<br>Conclusions .....                | 1   |
| II. Nicotine: Pharmacokinetics, Metabolism, and Phar-<br>macodynamics ..... | 21  |
| III. Nicotine: Sites and Mechanisms of Actions .....                        | 75  |
| IV. Tobacco Use as Drug Dependence .....                                    | 145 |
| V. Tobacco Use Compared to Other Drug<br>Dependencies .....                 | 241 |
| VI. Effects of Nicotine That May Promote Tobacco<br>Use .....               | 377 |
| VII. Treatment of Tobacco Dependence .....                                  | 459 |
| Appendix A: Trends in Tobacco Use in the United<br>States .....             | 561 |
| Appendix B: Toxicity of Nicotine .....                                      | 589 |
| Index .....   | 619 |