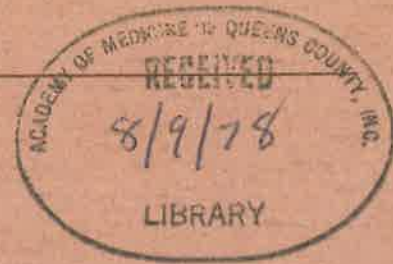




TOBACCO AND HEALTH



Research Studies of
The Relationship of Tobacco and Health



TOBACCO AND HEALTH

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The Relationship of Tobacco and Health



TOBACCO AND HEALTH

Compiled by the
AMA-ERF Committee for
Research on Tobacco and Health

1978
American Medical Association
Education and Research Foundation

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American Medical Association
Education and Research Foundation
535 North Dearborn Street
Chicago, Illinois 60610

Dedication

This book is dedicated to Maurice H. Seevers, M.D., Ph.D., who served as Chairman of the AMA-ERF Committee for Research on Tobacco and Health from the time of its inception in 1964 until his death in May 1977. Doctor Seevers was Professor and Chairman of the Department of Pharmacology at the University of Michigan Medical School from 1942 until his retirement. He distinguished himself as an authority on drug and drug abuse not only at the medical school level but as a consultant to state, federal and foreign governments, private industry, medical publications, the American Medical Association and health organizations around the world.

During his career, he served as a member of the Surgeon General's Committee on Smoking and Health, the President's Committee on Marihuana and Drug Abuse, the White House Conference Drug Abuse Panel on Narcotics and Drug Abuse, the National Research Council's Committee on Problems of Drug Abuse, the AMA Committee on Alcohol and Drug Dependence, the AMA Council on Drugs, and as a consultant on Drug Abuse to Japan, Thailand, Australia and the United States.

The AMA-ERF Committee for Research on Tobacco and Health is pleased to have had the privilege of serving with Doctor Seevers and herewith dedicates this publication to his memory as a physician, scientist, educator, leader and humanitarian.

Richard J. Bing, M. D.
Stuart Bondurant, M. D.
Earl A. Evans, Ph. D.
Robert J. Hasterlick, M. D.
Paul Kotin, M. D.
Marvin Kuschner, M. D.
Paul S. Larson, Ph. D.
Richard D. Remington, Ph. D.
Ira Singer, Ph. D.

Acknowledgement

The AMA-ERF Committee for Research on Tobacco and Health wishes to thank the many individuals both in this country and abroad who participated in the research which resulted in this publication. Special thanks goes to Edward Domino, M.D., Professor of Pharmacology, University of Michigan Medical School, who assisted the Committee in summarizing Section IV, Central and Autonomic Nervous System, following the death of Doctor Seevers. We also wish to thank Dr. John C. Ballin and Dr. Ira Singer who served as scientific secretaries to the Committee, and Mr. Leo E. Brown who provided the final stimulus for the production of this publication.

Special appreciation is due Ms. Barbara Newkirk, Mrs. Susan Remley, and Mrs. Shirley Sullivan of the AMA secretarial staff, and to the personal secretaries of our Committee members. To Mr. Ralph Linnenburger, Director, and to Ms. Irene Parks Foster, Production Editor of the AMA Department of Creative Services, and Mr. Joseph Giacalone, we are indebted for the design and the typography of this publication.

“A Research Study on Tobacco and Health — devoted to the study of human ailments that may be caused or aggravated by smoking, the particular element or elements that may be the causal or aggravating agents and the mechanisms of their action.”*

* AMA House of Delegates Action
December 1963

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Preface

In January of 1964, the American Medical Association Education and Research Foundation (AMA-ERF) entered into a five year agreement with six tobacco companies¹ to conduct a comprehensive program of research on Tobacco and Health. The research was to be devoted to the study of human ailments that may be caused or aggravated by smoking, the particular element or elements that may be the causal or aggravating agents and the mechanisms of their action.

The six participating tobacco companies pledged to contribute a total of ten million dollars to the AMA-ERF to finance this five-year research effort. The AMA-ERF Board of Directors appointed an eminently qualified Scientific Committee² to develop guidelines and suggestions on research policies and procedures, identify significant areas of research and screen applications for research grants.

The agreement was renewed in 1969 for another five years, terminating in December 1973. On July 18, 1972, it was altered to eliminate industry's financial commitment in 1972 and 1973 with no new grant applications being accepted in 1973 although grants funded in 1972 were continued to completion.

Between 1964 and 1975, 844 researchers in 85 United States and 13 foreign research institutions produced 795 publications and reports on the relationships of tobacco and health on (1) Absorption, Distribution, Metabolism, Excretion and Toxicology; (2) Carcinogenesis; (3) Cardiovascular System; (4) Central and Autonomic Nervous System; (5) Gastrointestinal Tract; (6) Reproduction; and (7) Respiratory System.

The content of this publication includes a summary of the research projects conducted in each of the above sections, abstracts of the research projects and the names of the participating researchers and institutions. It is hoped that this information will stimulate additional research in the field of tobacco and health.

The American Medical Association and its Education and Research Foundation wish to express its gratitude to the Tobacco Industry for its financial support; the members of the Scientific Committee, the participating institutions and the 196 researchers without whose dedication and intellect this book would not have been possible.

James H. Sammons, M. D.
Executive Vice President
American Medical Association
Education and Research Foundation

¹ see page x

² see page xi

Contributors

American Brands, Inc.

Brown and Williamson Tobacco Corporation

Liggett Group Inc.

Lorillard, A Division of Loews Theatres, Inc.

Philip Morris Incorporated

R. J. Reynolds Industries, Inc.

AMA-ERF COMMITTEE FOR
RESEARCH ON TOBACCO AND HEALTH
(Appointed June 1964 —

Richard J. Bing, M. D. Professor of Medicine University of Southern California Director of Cardiology and Intramural Medicine Huntington Memorial Hospital	1964-1977	Paul S. Larson, Ph.D. Haag Professor of Pharmacology Chairman Emeritus, Department of Pharmacology Medical College of Virginia	1964-1977
Stuart Bondurant, M. D. President and Dean Albany Medical College of Union University	1970-1977	Charles LeMaistre, M. D. Chancellor University of Texas Southwestern Medical School, Dallas, Texas	1964-1966
Earl A. Evans, Jr., Ph.D. Professor and Chairman Emeritus Department of Biochemistry University of Chicago	1969-1977	Richard D. Remington, Ph.D. Dean, School of Public Health University of Michigan	1969-1977
Robert J. Hasterlik, M. D. La Jolla, California	1966-1977	Maurice H. Seevers, M.D., Ph.D.** CHAIRMAN Professor Emeritus Department of Pharmacology University of Michigan	1964-1977
John B. Hickam, M. D.* Chairman, Department of Internal Medicine University of Indiana	1964-1970	Chester M. Southam, M. D. Chairman, Dept. of Oncology Jefferson Medical College of Thomas Jefferson University	1965-1966
Paul Kotin, M. D. Vice President, Health, Safety and Environment Johns-Manville Greenwood Plaza	1966-1977	AMA Staff Secretaries John C. Ballin, Ph.D. American Medical Association	1964-1965
Marvin Kushner, M. D. Dean, School of Medicine Health Science Center State University of New York at Stony Brook	1969-1977	Ira Singer, Ph.D. American Medical Association	1966-1977

* Deceased February 9, 1970

** Deceased April 29, 1977

**Statement
AMA-ERF Committee for Research
on Tobacco and Health**

On January 31, 1964, the American Medical Association-Education and Research Foundation established the Committee for Research on Tobacco and Health. At its first meeting, the Committee agreed to commit available resources to support projects of high scientific interest undertaken by investigators in university and institutional centers. These studies were to be devoted to human ailments thought to be caused or aggravated by smoking, and to the particular elements that might be the causal or aggravating agents. The Committee planned to allocate its resources primarily to three broad categories of research in which there were important gaps in knowledge of the effects of smoking: 1) cardiovascular, 2) respiratory and 3) central and autonomic nervous systems research, the latter because of its relationship to habituation.

In all of its funding endeavors, the Committee attempted to support innovative research. Although the individual research projects were awarded on the basis of specific targeted investigations inevitably many investigators found interesting and fruitful areas for digression which developed during the course of their research. Agreements between investigators and the American Medical Association-Education and Research Foundation required publication of reports in the open scientific literature.

During the ten year active life of the Committee, the membership varied from five to ten. The Committee met on an average of four times per year to consider applications for new grants and to review the progress of the research being funded. The Committee was active in recruiting scientists to participate in Tobacco and Health research, an area in which they had not been previously scientifically active. As further encouragement, a post-doctorate fellowship program was instituted in order to stimulate young scientists to participate in this research program.

Throughout its life, the Committee maintained liaison with the National Institutes of Health and The Council for Tobacco Research, U.S.A. keeping these organizations apprised of current trends in the Committee's work and to minimize duplication of effort. The Committee is grateful for the free exchange of information and the close liaison which was established with these organizations.

To further stimulate informational exchange, the Committee convened three workshops. These also served as a measure of progress among its grantees. The workshops proved to be highly successful. In addition, a scientific presentation of the work of the Committee's grantees was held in conjunction with the American Medical Association Annual Meeting in San Francisco in 1968. This meeting constituted a report of progress and information to the profession. At that time a statement was issued to indicate that the research completed under the aegis of the project had not altered the conclusions of the 1963 report of the Surgeon General.

The summary statements in this volume draw attention to the research which has been done in each area supported through the funds awarded by this project. The summaries are intended to be neither complete nor comprehensive but to indicate trends and results.

The Committee is proud of and satisfied with the work that has been completed under the sponsorship of the American Medical Association's Project for Research on Tobacco and Health. Important contributions have been made to basic medical science as well as to problems associated with tobacco usage. Valuable information has been obtained relating to distribution, metabolism, excretion and toxicity of nicotine absorbed by the human body via cigarette smoking. In the area of carcinogenesis, the Committee restricted the number of awards because cancer research was being generously financed by the National Institutes of Health and other agencies. Nevertheless, the demonstration of potent co-carcinogens in tobacco tar and the potential value of the measure of inducibility of aryl hydrocarbon hydroxylase as a determinant of susceptibility to lung cancer represent some of the more significant contributions in this area. Emphasis was placed on the impact of cigarette smoking on the physiology of the cardiovascular, respiratory and central autonomic nervous systems. The Committee believes that the bulk of research sponsored by this project supports the contention that cigarette smoking plays an important role in the development of chronic obstructive pulmonary diseases and constitutes a grave danger to individuals with preexisting diseases of the coronary arteries. On the central and autonomic nervous system important findings were made related to effects on behavior and on biochemical mediators elicited by nicotine. Gastrointestinal tract studies include new mechanisms by which nicotine *may* influence production of peptic ulcer. In studies in reproduction important insights were gained into the mechanisms of higher center control of releasing factors for pituitary hormone.

The Committee wishes to express its appreciation to the American Medical Association and the tobacco industry for sponsoring this effort and to the many grantees and institutions who participated in attempting to develop information and find solutions to gaps in knowledge in this complicated area of scientific inquiry.

May 27, 1977

Section I

Absorption, Distribution, Metabolism, Excretion, Toxicology

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Participating Institutions

Following is a list of participating institutions which have received awards from the American Medical Association Education and Research Foundation. Names of some institutions may have changed since the work was done. In some cases, grantees may have moved to other institutions.

United States

Argonne National Laboratory, U.S. Atomic Energy Commission, Argonne, IL
Arthur D. Little, Inc., Cambridge, MA
Albany Medical College of Union University, Albany, NY

Baylor College of Medicine, Houston, TX
Bio-Research Institute, Inc., Cambridge, MA

Children's Hospital Medical Center, Boston, MA
Cedars-Sinai Medical Center, Los Angeles, CA
Columbia University College of Physicians and Surgeons, New York, NY
Cornell University Medical College, New York, NY
Cox Coronary Heart Institute, Kettering, OH
College of Medicine & Dentistry of New Jersey, Newark, NJ

Duke University School of Medicine, Durham, NC

Evanston Hospital, Evanston, IL
Emory University School of Medicine, Atlanta, GA

Food and Drug Research Laboratories, Inc., Maspeth, NY

Georgetown University School of Medicine, Washington, D.C.

Harvard Medical School, Boston, MA
Harvard University, Cambridge, MA
Huntington Memorial Hospital, Pasadena, CA

Illinois Institute of Technology Research Institute, Chicago, IL
Indiana State University, Terre Haute, IN
Indiana University Medical Center, Indianapolis, IN
Indiana University School of Medicine, Indianapolis, IN

Kensington Hospital, Philadelphia, PA
Krannert Institute of Cardiology, Indianapolis, IN

Louisiana State University, Baton Rouge, LA
Louisiana State University Medical Center, New Orleans, LA
Lovelace Foundation for Medical Education and Research, Albuquerque, NM

Michigan State University, East Lansing, MI
Medical College of Virginia, Richmond, VA
Medical University of South Carolina, Charleston, SC
Methodist Hospital of Indiana, Indianapolis, IN

National Academy of Sciences-National Research Council, Washington, D.C.
New England Medical Center Hospitals, Boston, MA
New Jersey Mental Health Research and Development Fund, Inc., Skillman, NJ
New York University Medical Center, New York, NY
Northwestern University Medical School, Evanston, IL
Nuclear Science and Engineering Corporation, Pittsburgh, PA

Oregon Regional Primates Research Center, Portland, OR

Philadelphia General Hospital, Philadelphia, PA
Presbyterian St. Luke's Hospital, Chicago, IL

Roswell Park Memorial Institute, Buffalo, NY
Rutgers-The State University of New Jersey, New Brunswick, NJ

Saint Louis University School of Medicine, St. Louis, MO
Saint Vincent Hospital, Worcester, MA
Southwest Foundation for Research and Education, San Antonio, TX
State University of Iowa, Iowa City, IA
Stout State University, Menominee, WI
State University of New York at Buffalo School of Medicine, Buffalo, NY
Southern Research Institute, Birmingham, AL

Tulane University School of Medicine, New Orleans, LA

University of Alabama School of Medicine, Birmingham, AL
University of California, Berkeley, CA
University of California, Davis, School of Medicine, Davis, CA
University of California, Los Angeles, School of Medicine, Los Angeles, CA
University of California, Irvine, California College of Medicine, Irvine, CA
University of California, San Diego, School of Medicine, San Diego, CA
University of California, San Francisco, School of Medicine, San Francisco, CA
University of Southern California School of Medicine, Los Angeles, CA
University of Chicago, The Pritzker School of Medicine, Chicago, IL
University of Cincinnati College of Medicine, Cincinnati, OH
University of Connecticut School of Medicine, Farmington, CT
University of Connecticut Health Center, Hartford, CT
University of Colorado School of Medicine, Denver, CO
University of Hawaii John A. Burns School of Medicine, Honolulu, HI
University of Illinois College of Medicine, Urbana, IL
University of Kansas School of Pharmacy, Lawrence, KS
University of Kentucky College of Medicine, Lexington, KY
University of Louisville School of Medicine, Louisville, KY

University of Miami School of Medicine, Miami, FL
University of Michigan Medical School, Ann Arbor, MI
University of Minnesota Medical School-Minneapolis, Minneapolis, MN
University of Nebraska College of Medicine, Omaha, NB
University of Oklahoma Medical Center, Oklahoma City, OK
University of Pennsylvania School of Medicine, Philadelphia, PA
University of Pittsburgh, Pittsburgh, PA
University of Tennessee, Knoxville, TN
University of Texas Health Science Center at Houston, Houston, TX
University of Texas, Southwestern Medical School at Dallas, Dallas, TX
University of Vermont College of Medicine, Burlington, VT
University of Virginia School of Medicine, Charlottesville, VA
Utah State University, Logan, UT

Veterans Administration Hospital, Bronx, NY

Washington University School of Medicine, St. Louis, MO
Wayne State University School of Medicine, Detroit, MI

Outside of the United States

Central Institute of Experimental Animals, Kawasaki, Japan
Consiglio Nazionale delle Ricerche, Rome, Italy

Hiroshima University School of Dentistry, Hiroshima, Japan

Istituto di Ricerche Farmacologiche "Mario Negri," Milan, Italy

Karolinska Institute, Stockholm, Sweden

Medical College of St. Bartholomew's Hospital, London, England

Nara Medical College, Nara, Japan

Royal Veterinary College, Stockholm, Sweden

University of Iceland Science Institute, Reykjavik, Iceland
University of Melbourne, Victoria, Australia
University of Montreal Faculty of Medicine, Montreal, Canada
University of Sassari, Sardinia, Italy
University of Toronto, Ontario, Canada