SMOKING *and* HEALTH

REPORT OF THE ADVISORY COMMITTEE TO THE SURGEON GENERAL OF THE PUBLIC HEALTH SERVICE

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Foreword

Since the turn of the century, scientists have become increasingly interested in the effects of tobacco on health. Only within the past few decades, however, has a broad experimental and clinical approach to the subject been manifest; within this period the most extensive and definitive studies have been undertaken since 1950.

Few medical questions have stirred such public interest or created more scientific debate than the tobacco-health controversy. The interrelationships of smoking and health undoubtedly are complex. The subject does not lend itself to easy answers. Nevertheless, it has been increasingly apparent that answers must be found.

As the principal Federal agency concerned broadly with the health of the American people, the Public Health Service has been conscious of its deep responsibility for seeking these answers. As steps in that direction it has seemed necessary to determine, as precisely as possible, the direction of scientific evidence and to act in accordance with that evidence for the benefit of the people of the United States. In 1959, the Public Health Service assessed the then available evidence linking smoking with health and made its findings known to the professions and the public. The Service's review of the evidence and its statement at that time was largely focussed on the relationship of cigarette smoking to lung cancer. Since 1959 much additional data has accumulated on the whole subject.

Accordingly, I appointed a committee, drawn from all the pertinent scientific disciplines, to review and evaluate both this new and older data and, if possible, to reach some definitive conclusions on the relationship between smoking and health in general. The results of the Committee's study and evaluation are contained in this Report.

I pledge that the Public Health Service will undertake a prompt and thorough review of the Report to determine what action may be appropriate and necessary. I am confident that other Federal agencies and nonofficial agencies will do the same.

The Committee's assignment has been most difficult. The subject is complicated and the pressures of time on eminent men busy with many other duties has been great. I am aware of the difficulty in writing an involved technical report requiring evaluations and judgments from many different professional and technical points of view. The completion of the Committee's task has required the exercise of great professional skill and dedication of the highest order. I acknowledge a profound debt of gratitude to the Committee, the many consultants who have given their assistance, and the members of the staff. In doing so, I extend thanks not only for the Service but for the Nation as a whole.

SURGEON GENERAL

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PART I

Introduction, Summaries, and Conclusions

Chapter 1

Introduction

Chapter 1

Realizing that for the convenience of all types of serious readers it would be desirable to simplify language, condense chapters and bring opinions to the forefront, the Committee offers Part I as such a presentation. This Part includes: (a) an introduction comprising, among other items, a chronology especially pertinent to the subject of this study and to the establishment and activities of the Committee, (b) a short account of how the study was conducted, (c) the chief criteria used in making judgments, and (d) a brief overview of the entire Report.

HISTORICAL NOTES AND CHRONOLOGY

In the early part of the 16th century, soon after the introduction of tobacco into Spain and England by explorers returning from the New World, controversy developed from differing opinions as to the effects of the human use of the leaf and products derived from it by combustion or other means. Pipe-smoking, chewing, and snuffing of tobacco were praised for pleasurable and reputed medicinal actions. At the same time, smoking was condemned as a foul-smelling, loathsome custom, harmful to the brain and lungs. The chief question was then as it is now: is the use of tobacco bad or good for health, or devoid of effects on health? Parallel with the increasing production and use of tobacco, especially with the constantly increasing smoking of cigarettes, the controversy has become more and more intense. Scientific attack upon the problems has increased proportionately. The design, scope and penetration of studies have improved, and the yield of significant results has been abundant.

The modern period of investigation of smoking and health is included within the past sixty-three years. In 1900 an increase in cancer of the lung was noted particularly by vital statisticians, and their data are usually taken as the starting point for studies on the possible relationship of smoking and other uses of tobacco to cancer of the lung and of certain other organs, to diseases of the heart and blood vessels (cardiovascular diseases in general; coronary artery disease in particular), and to the non-cancerous (non-neoplastic) diseases of the lower respiratory tract (especially chronic bronchitis and emphysema). The next important basic date for starting comparisons is 1930, when the definite trends in mortality and disease-incidence considered in this Report became more conspicuous. Since then a great variety of investigations have been carried out. Many of the chemical compounds in tobacco and in tobacco smoke have been isolated and tested. Numerous experimental studies in lower animals have been made by exposing them to smoke and to tars, gases and various constituents in tobacco and tobacco smoke. It is not feasible to submit human beings to

experiments that might produce cancers or other serious damage, or to expose them to possibly noxious agents over the prolonged periods under strictly controlled conditions that would be necessary for a valid test. Therefore, the main evidence of the effects of smoking and other uses of tobacco upon the health of human beings has been secured through clinical and pathological observations of conditions occurring in men, women and children in the course of their lives, and by the application of epidemiological and statistical methods by which a vast array of information has been assembled and analyzed.

Among the epidemiological methods which have been used in attempts to determine whether smoking and other uses of tobacco affect the health of man, two types have been particularly useful and have furnished information of the greatest value for the work of this Committee. These are (1) *retrospective studies* which deal with data from the personal histories and medical and mortality records of human individuals in groups; and (2) *prospective studies*, in which men and women are chosen randomly or from some special group, such as a profession, and are followed from the time of their entry into the study for an indefinite period, or until they die or are lost on account of other events.

Since 1939 there have been 29 retrospective studies of lung cancer alone which have varying degrees of completeness and validity. Following the publication of several notable retrospective studies in the years 1952–1956, the medical evidence tending to link cigarette smoking to cancer of the lung received particularly widespread attention. At this time, also, the critical counterattack upon retrospective studies and upon conclusions drawn from them was launched by unconvinced individuals and groups. The same types of criticism and skepticism have been, and are, marshalled against the methods, findings, and conclusions of the later prospective studies. They will be discussed further in Chapter 3, Criteria for Judgment, and in other chapters, especially Chapter 8, Mortality, and Chapter 9, Cancer.

During the decade 1950–1960, at various dates, statements based upon the accumulated evidence were issued by a number of organizations. These included the British Medical Research Council; the cancer societies of Denmark, Norway, Sweden, Finland, and the Netherlands; the American Cancer Society; the American Heart Association; the Joint Tuberculosis Council of Great Britain; and the Canadian National Department of Health and Welfare. The consensus, publicly declared, was that smoking is an important health hazard, particularly with respect to lung cancer and cardiovascular disease.

Early in 1954, the Tobacco Industry Research Committee (T.I.R.C.) was established by representatives of tobacco manufacturers, growers, and warehousemen to sponsor a program of research into questions of tobacco use and health. Since then, under a Scientific Director and a Scientific Advisory Board composed of nine scientists who maintain their respective institutional affiliations, the Tobacco Industry Research Committee has conducted a grants-in-aid program, collected information, and issued reports.

The U.S. Public Health Service first became officially engaged in an appraisal of the available data on smoking and health in June, 1956, when, under the instigation of the Surgeon General, a scientific Study Group on the subject was established jointly by the National Cancer Institute, the National Heart Institute, the American Cancer Society, and the American Heart Association. After appraising 16 independent studies carried on in five countries over a period of 18 years, this group concluded that there is a causal relationship between excessive smoking of cigarettes and lung cancer.

Impressed by the report of the Study Committee and by other new evidence, Surgeon General Leroy E. Burney issued a statement on July 12, 1957, reviewing the matter and declaring that: "The Public Health Service feels the weight of the evidence is increasingly pointing in one direction; that excessive smoking is one of the causative factors in lung cancer." Again, in a special article entitled "Smoking and Lung Cancer—A Statement of the Public Health Service," published in the Journal of the American Medical Association on November 28, 1959, Surgeon General Burney referred to his statement issued in 1957 and reiterated the belief of the Public Health Service that: "The weight of evidence at present implicates smoking as the principal factor in the increased incidence of lung cancer," and that: "Cigarette smoking particularly is associated with an increased chance of developing lung cancer." These quotations state the position of the Public Health Service taken in 1957 and 1959 on the question of smoking and health. That position has not changed in the succeeding years, during which several units of the Service conducted extensive investigations on smoking and air pollution, and the Service maintained a constant scrutiny of reports and publications in this field.

ESTABLISHMENT OF THE COMMITTEE

The immediate antecedents of the establishment of the Surgeon General's Advisory Committee on Smoking and Health began in mid-1961. On June 1 of that year, a letter was sent to the President of the United States, signed by the presidents of the American Cancer Society, the American Public Health Association, the American Heart Association, and the National Tuberculosis Association. It urged the formation of a Presidential commission to study the "widespread implications of the tobacco problem."

On January 4, 1962, representatives of the various organizations met with Surgeon General Luther L. Terry, who shortly thereafter proposed to the Secretary of Health, Education, and Welfare the formation of an advisory committee composed of "outstanding experts who would assess available knowledge in this area [smoking vs. health] and make appropriate recommendations . . ."

On April 16, the Surgeon General sent a more detailed proposal to the Secretary for the formation of the advisory group, calling for re-evaluation of the Public Health Service position taken by Dr. Burney in the Journal of the American Medical Association. Dr. Terry felt the need for a new look at the Service's position in the light of a number of significant developments since 1959 which emphasized the need for further action. He listed these as:

1. New studies indicating that smoking has major adverse health effects.
2. Representations from national voluntary health agencies for action on the part of the Service.
3. The recent study and report of the Royal College of Physicians of London.
4. Action of the Italian Government to forbid cigarette and tobacco advertising; curtailed advertising of cigarettes by Britain's major tobacco companies on TV; and a similar decision on the part of the Danish tobacco industry.
5. A proposal by Senator Maurine Neuberger that Congress create a commission to investigate the health effects of smoking.
6. A request for technical guidance by the Service from the Federal Trade Commission on labeling and advertising of tobacco products.
7. Evidence that medical opinion has shifted significantly against smoking.

The recent study and report cited by Surgeon General Terry was the highly important volume: "Smoking and Health—Summary and Report of the Royal College of Physicians of London on Smoking in Relation to Cancer of the Lung and Other Diseases." The Committee of the Royal College of Physicians dealing with these matters had been at its work of appraisal of data since April 1959. Its main conclusions, issued early in 1962, were: "Cigarette smoking is a cause of lung cancer and bronchitis, and probably contributes to the development of coronary heart disease and various other less common diseases. It delays healing of gastric and duodenal ulcers."

On June 7, 1962, the Surgeon General announced that he was establishing an expert committee to undertake a comprehensive review of all data on smoking and health. The President later in the same day at his press conference acknowledged the Surgeon General's action and approved it.

On July 24, 1962, the Surgeon General met with representatives of the American Cancer Society, the American College of Chest Physicians, the American Heart Association, the American Medical Association, the Tobacco Institute, Inc., the Food and Drug Administration, the National Tuberculosis Association, the Federal Trade Commission, and the President's Office of Science and Technology. At this meeting, it was agreed that the proposed work should be undertaken in two consecutive phases, as follows:

Phase I—An objective assessment of the nature and magnitude of the health hazard, to be made by an expert scientific advisory committee which would review critically all available data but would not conduct new research. This committee would produce and submit to the Súrgeon General a technical report containing evaluations and conclusions.

Phase II—Recommendations for actions were not to be a part of the Phase I committee's responsibility. No decisions on how Phase II would be conducted were to be made until the Phase I report was available. It was recognized that different competencies would be needed in the second phase and that many possible recommendations for action would extend beyond the health field and into the purview and competence of other Federal agencies.

The participants in the meeting of July 27 compiled a list of more than 150 scientists and physicians working in the fields of biology and medicine, with interests and competence in the broad range of medical sciences and with capacity to evaluate the elements and factors in the complex relationship between tobacco smoking and health. During the next month, these lists were screened by the representatives of organizations present at the July 27 meeting. Any organization could veto any of the names on the list, no reasons being required. Particular care was taken to eliminate the names of any persons who had taken a public position on the questions at issue. From the final list of names the Surgeon General selected ten men who agreed to serve on the Phase I committee, which was named *The Surgeon General's Advisory Committee on Smoking and Health.* The committee members, their positions, and their fields of competence are:

Stanhope Bayne-Jones, M.D., LL.d., (Retired), Former Dean, Yale School of Medicine (1935–40), former President, Joint Administrative Board, Cornell University, New York Hospital Medical Center (1947–52); former President, Society of American Bacteriologists (1929), and American Society of Pathology and Bacteriology (1940). Field: Nature and Causation of Disease in Human Populations.

Dr. Bayne-Jones served also as a special consultant to the Committee staff.

Walter J. Burdette, M.D., Ph. D., Head of Department of Surgery, University of Utah School of Medicine, Salt Lake City. Fields: Clinical & Experimental Surgery; Genetics.

William G. Cochran, M.A., Professor of Statistics, Harvard University. Field: Mathematical Statistics, with Special Application to Biological Problems.

Emmanuel Farber, M.D., Ph. D., Chairman, Department of Pathology, University of Pittsburgh. Field: Experimental and Clinical Pathology.

Louis F. Fieser, Ph. D., Sheldon Emory, Professor of Organic Chemistry, Harvard University. Field: Chemistry of Carcinogenic Hydrocarbons.

Jacob Furth, M.D., Professor of Pathology, Columbia University, and Director of Pathology Laboratories, Francis Delafield Hospital, New York, N.Y. Field: Cancer Biology.

John B. Hickam, M.D., Chairman, Department of Internal Medicine, University of Indiana, Indianapolis. Fields: Internal Medicine, Physiology of Cardiopulmonary Disease.

Charles LeMaistre, M.D., Professor of Internal Medicine, The University of Texas Southwestern Medical School, and Medical Director, Woodlawn Hospital, Dallas, Texas. Fields: Internal Medicine, Pulmonary Diseases, Preventive Medicine.

Leonard M. Schuman, M.D., Professor of Epidemiology, University of Minnesota School of Public Health, Minneapolis. Field: Health and Its Relationship to the Total Environment.

Maurice H. Seevers, M.D., Ph. D., Chairman, Department of Pharmacology, University of Michigan, Ann Arbor. Field: Pharmacology of Anesthesia and Habit-Forming Drugs.

Chairman: Luther L. Terry, M.D., Surgeon General of the United States Public Health Service.

Vice-Chairman: James M. Hundley, M.D., Assistant Surgeon General for Operations, United States Public Health Service.

Staff Director
Eugene H. Guthrie, M.D., M.P.H.
Public Health Service

Medical Coordinator
Peter V. V. Hamill, M.D., M.P.H.
Public Health Service

Chapter 2

Conduct of the Study

Chapter 2

CONDUCT OF THE STUDY

The work of the Surgeon General's Advisory Committee on Smoking and Health was undertaken, organized, and pursued with independence, a deep sense of responsibility, and with full appreciation of the national importance of the task. The Committee's constant desire was to carry out in its own way, with the best obtainable advice and cooperation from experts outside its membership, a thorough and objective review and evaluation of available information about the effects of the use of various forms of tobacco upon the health of human beings. It desired that the Report of its studies and judgments should be unquestionably the product of its labors and its authorship. With an enormous amount of assistance from 155 consultants, from members and associates of the supporting staff, and from several organizations and institutions, the Committee feels that a document of adequate scope, integrity, and individuality has been produced. It is emphasized, however, that the content and judgments of the Report are the sole responsibility of the Committee.

At the outset, the Surgeon General emphasized his respect for the freedom of the Committee to proceed with the study and to report as it saw fit, and he pledged all support possible from the United States Public Health Service. The Service, represented chiefly by his office, the National Institutes of Health, the National Library of Medicine, the Bureau of State Services, and the National Center for Health Statistics, furnished the able and devoted personnel that constituted the staff at the Committee's headquarters in Washington, and provided an extraordinary variety and volume of supplies, facilities and resources. In addition, the necessary financial support was made available by the Service.

It is the purpose of this section to present an outline of the important features of the manner in which the Committee conducted its study and composed this Report. A retrospective outline of procedures and events tends to convey an appearance of orderliness that did not pertain at all times. A plan was adopted at the first meeting of the Committee on November 9–10, 1962, but this had to be modified from time to time as new lines of inquiry led into unanticipated explorations. At first an encyclopedic approach was considered to deal with all aspects of the use of tobacco and the resulting effects, with all relevant aspects of air pollution, and all pertinent characteristics of the external and internal environments and make-up of human beings. It was soon found to be impracticable to attempt to do all of this in any reasonable length of time, and certainly not under the urgencies of the existing situation. The final plan was to give particular attention to the cores of problems of the relationship of uses of tobacco, especially the smoking of cigarettes, to the health of men and women, primarily in the United States, and

to deal with the material from both a general viewpoint and on the basis of disease categories.

As may be seen in a glance at the Table of Contents of this Report, the main topical divisions of the study were:

- Tobacco and tobacco smoke, chemical and physical characteristics (Chapter 6).
- Nicotine, pharmacology and toxicology (Chapter 7).
- Mortality, general and specific, according to age, sex, disease, and smoking habits, and other factors (Chapter 8).
- Cancer of the lungs and other organs; carcinogenesis; pathology, and epidemiology (Chapter 9).
- Non-neoplastic diseases of the respiratory tract, particularly chronic bronchitis and emphysema, with some consideration of the effects of air pollution (Chapter 10).
- Cardiovascular diseases, particularly coronary artery diseases (Chapter 11).
- Other conditions, a miscellany including gastric and duodenal ulcer, perinatal disorders, tobacco amblyopia, accidents (Chapter 12).
- Characterization of the tobacco habit and beneficial effects of tobacco (Chapter 13).
- Psycho-social aspects of smoking (Chapter 14).
- Morphological constitution of smokers (Chapter 15).

As the primary duty of the Committee was to assess information about smoking and health, a major general requirement was that of making the information available. That requirement was met in three ways. The first and most important was the bibliographic service provided by the National Library of Medicine. As the annotated monograph by Larson, Haag, and Silvette—compiled from more than 6,000 articles published in some 1,200 journals up to and largely into 1959—was available as a basic reference source, the National Library of Medicine was requested to compile a bibliography (by author and by subject) covering the world literature from 1958 to the present. In compliance with this request, the National Library of Medicine furnished the Committee bibliographies containing approximately 1100 titles. Fortunately, the Committee staff was housed in the National Library of Medicine on the grounds of the National Institutes of Health, and through this location had ready access to books and periodicals, as well as to scientists working in its field of interests. Modern apparatus for photo-reproduction of articles was used constantly to provide copies needed for study by members of the Committee. In addition, the members drew upon the libraries and bibliographic services of those institutions in which they held academic positions. A considerable volume of copies of reports and a number of special articles were received from a variety of additional sources.

All of the major companies manufacturing cigarettes and other tobacco products were invited to submit statements and any information pertinent to the inquiry. The replies which were received were taken into consideration by the Committee.

Through a system of contracts with individuals competent in certain fields, special reports were prepared for the use of the Committee. Through these sources much valuable information was obtained; some of it new and hitherto unpublished.

In addition to the special reports prepared under contracts, many conferences, seminar-like meetings, consultations, visits and correspondence made available to the Committee a large amount of material and a considerable amount of well-informed and well-reasoned opinion and advice.

To deal in depth and discrimination with the topics listed above, the Committee at its first meeting formed subcommittees with much overlapping in membership. These subcommittees were the main forces engaged in collection, analysis, and evaluation of data from published reports, contractual reports, discussions at conferences, and from some new prospective studies reprogrammed and carried out generously at the request of the Committee. These will be acknowledged more fully elsewhere in this Report. The first formulations of conclusions were made by these subcommittees, and these were submitted to the full Committee for revision and adoption after debate.

At the beginning, and until the Committee began to meet routinely in executive session, it had the advantage of attendance at its meetings of observers from other Federal agencies. There were representatives from the following agencies: Executive Office of the President of the United States, Federal Trade Commission, Department of Commerce, Department of Agriculture, and the Food and Drug Administration. Serving as more than observers and reporters to their agencies, when they were present or by written communication, they supplied the Committee with much useful information.

There were an uncounted number of meetings of subcommittees and other lesser gatherings. Between November 1962 and December 1963, the full Committee held nine sessions each lasting from two to four days in Washington or Bethesda. The main matters considered at the meetings in October, November, and December 1963 were the review and revision of chapters, critical scrutiny of conclusions, and the innumerable details of the composition and editing of this comprehensive Report.

Chapter 3

CRITERIA FOR JUDGMENT

In making critical appraisals of data and interpretations and in formulating its own conclusions, the Surgeon General's Advisory Committee on Smoking and Health—its individual members and its subcommittees and the Committee as a whole—made decisions or judgments at three levels. These levels were:

I. Judgment as to the validity of a publication or report. Entering into the making of this judgment were such elements as estimates of the competence and training of the investigator, the degree of freedom from bias, design and scope of the investigation, adequacy of facilities and resources, adequacy of controls.

II. Judgment as to the validity of the interpretations placed by investigators upon their observations and data, and as to the logic and justification of their conclusions.

III. Judgments necessary for the formulation of conclusions within the Committee.

The primary reviews, analyses and evaluations of publications and unpublished reports containing data, interpretations and conclusions of authors were made by individual members of the Committee and, in some instances, by consultants. Their statements were next reviewed and evaluated by a subcommittee. This was followed at an appropriate time by the Committee's critical consideration of a subcommittee's report, and by decisions as to the selection of material for inclusion in the drafts of the Report, together with drafts of the conclusions submitted by subcommittees. Finally, after repeated critical reviews of drafts of chapters, conclusions were formulated and adopted by the whole Committee, setting forth the considered judgment of the Committee.

It is not the intention of this section to present an essay on decision-making. Nor does it seem necessary to describe in detail the criteria used for making scientific judgments at each of the three levels mentioned above. All members of the Committee were schooled in the high standards and criteria implicit in making scientific assessments; if any member lacked even a small part of such schooling he received it in good measure from the strenuous debates that took place at consultations and at meetings of the subcommittees and the whole Committee.

Criteria of the Epidemiologic Method

It is advisable, however, to discuss briefly certain criteria which, although applicable to all judgments involved in this Report, were especially significant for judgments based upon the epidemiologic method. In this inquiry the

epidemiologic method was used extensively in the assessment of causal factors in the relationship of smoking to health among human beings upon whom direct experimentation could not be imposed. Clinical, pathological and experimental evidence was thoroughly considered and often served to suggest an hypothesis or confirm or contradict other findings. When coupled with the other data, results from the epidemiologic studies can provide the basis upon which judgments of causality may be made.

In carrying out studies through the use of this epidemiologic method, many factors, variables, and results of investigations must be considered to determine first whether an association actually exists between an attribute or agent and a disease. Judgment on this point is based upon indirect and direct measures of the suggested association. If it be shown that an association exists, then the question is asked: "Does the association have a causal significance?"

Statistical methods cannot establish proof of a causal relationship in an association. The causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability. To judge or evaluate the causal significance of the association between the attribute or agent and the disease, or effect upon health, a number of criteria must be utilized, no one of which is an all-sufficient basis for judgment. These criteria include:

a) The consistency of the association
b) The strength of the association
c) The specificity of the association
d) The temporal relationship of the association
e) The coherence of the association

These criteria were utilized in various sections of this Report. The most extensive and illuminating account of their utilization is to be found in Chapter 9 in the section entitled "Evaluation of the Association Between Smoking and Lung Cancer".

Causality

Various meanings and conceptions of the term *cause* were discussed vigorously at a number of meetings of the Committee and its subcommittees. These debates took place usually after data and reports had been studied and evaluated, and at the times when critical scrutiny was being given to conclusions and to the wording of conclusive statements. In addition, thoughts about causality in the realm of this inquiry were constantly and inevitably aroused in the minds of the members because they were preoccupied with the subject of their investigation—"Smoking and Health."

Without summarizing the more important concepts of causality that have determined human attitudes and actions from the days even before Aristotle, through the continuing era of observation and experiment, to the statistical certainties of the present atomic age, the point of view of the Committee with regard to causality and to the language used in this respect in this report may be stated briefly as follows:

1. The situation of smoking in relation to the health of mankind includes a host (variable man) and a complex agent (tobacco and its products, particularly those formed by combustion in smoking). The probe of this inquiry is into the effect, or non-effect, of components of the agent upon the tissues, organs, and various qualities of the host which might: a) improve his well-being, b) let him proceed normally, or c) injure his health in one way or another. To obtain information on these points the Committee did its best, with extensive aid, to examine all available sources of information in publications and reports and through consultation with well informed persons.

2. When a relationship or an association between smoking, or other uses of tobacco, and some condition in the host was noted, the significance of the association was assessed.

3. The characterization of the assessment called for a specific term. The chief terms considered were "factor," "determinant," and "cause." The Committee agreed that while a factor could be a source of variation, not all sources of variation are causes. It is recognized that often the coexistence of several factors is required for the occurrence of a disease, and that one of the factors may play a determinant role, i.e., without it the other factors (as genetic susceptibility) are impotent. Hormones in breast cancer can play such a determinant role. The word *cause* is the one in general usage in connection with matters considered in this study, and it is capable of conveying the notion of a significant, effectual, relationship between an agent and an associated disorder or disease in the host.

4. It should be said at once, however, that no member of this Committee used the word "cause" in an absolute sense in the area of this study. Although various disciplines and fields of scientific knowledge were represented among the membership, all members shared a common conception of the multiple etiology of biological processes. No member was so naive as to insist upon mono-etiology in pathological processes or in vital phenomena. All were thoroughly aware of the fact that there are series of events in occurrences and developments in these fields, and that the end results are the net effect of many actions and counteractions.

5. Granted that these complexities were recognized, it is to be noted clearly that the Committee's considered decision to use the words "a cause," or "a major cause," or "a significant cause," or "a causal association" in certain conclusions about smoking and health affirms their conviction.

Chapter 4

Summaries and Conclusions

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Chapter 4

This chapter is presented in two sections. Section A contains background information, the gist of the Committee's findings and conclusions on tobacco and health, and an assessment of the nature and magnitude of the health hazard. Section B presents all formal conclusions adopted by the Committee and selected comments abridged from the detailed Summaries that appear in each chapter of Part II of the Report. The full scope and depth of the Committee's inquiry may be comprehended only by study of the complete Report.

A. BACKGROUND AND HIGHLIGHTS

In previous studies, the use of tobacco, especially cigarette smoking, has been causally linked to several diseases. Such use has been associated with increased deaths from lung cancer and other diseases, notably coronary artery disease, chronic bronchitis, and emphysema. These widely reported findings, which have been the cause of much public concern over the past decade, have been accepted in many countries by official health agencies, medical associations, and voluntary health organizations.

The potential hazard is great because these diseases are major causes of death and disability. In 1962, over 500,000 people in the United States died of arteriosclerotic heart disease (principally coronary artery disease), 41,000 died of lung cancer, and 15,000 died of bronchitis and emphysema.

The numbers of deaths in some important disease categories that have been reported to have a relationship with tobacco use are shown in Table 1. This table presents one aspect of the size of the potential hazard; the degree of association with the use of tobacco will be discussed later.

Another cause for concern is that deaths from some of these diseases have been increasing with great rapidity over the past few decades.

Lung cancer deaths, less than 3,000 in 1930, increased to 18,000 in 1950. In the short period since 1955, deaths from lung cancer rose from less than 27,000 to the 1962 total of 41,000. This extraordinary rise has not been recorded for cancer of any other site. While part of the rising trend for lung cancer is attributable to improvements in diagnosis and the changing age-composition and size of the population, the evidence leaves little doubt that a true increase in lung cancer has taken place.

Deaths from arteriosclerotic, coronary, and degenerative heart disease rose from 273,000 in 1940, to 396,000 in 1950, and to 578,000 in 1962.

Reported deaths from chronic bronchitis and emphysema rose from 2,300 in 1945 to 15,000 in 1962.

The changing patterns and extent of tobacco use are a pertinent aspect of the tobacco-health problem.

TABLE 1.—*Deaths from selected disease categories, United States, 1962*

Cause of death*	Total	Males	Females
Degenerative and arteriosclerotic heart disease, including coronary disease (420, 422)	577, 918	348, 604	229, 314
Hypertensive heart disease (440-3)	62, 176	26, 654	35, 522
Cancer of lung (162-3)	41, 376	35, 312	6, 064
Cirrhosis of liver (581)	21, 824	14, 329	7, 495
Bronchitis and emphysema (502, 527.1)	15, 104	12, 937	2, 167
Stomach and duodenal ulcers (540-1)	12, 228	8, 836	3, 392
Cancer of bladder (181)	8, 081	5, 575	2, 506
Cancer of oral cavity (140-8)	6, 481	4, 920	1, 561
Cancer of esophagus (150)	5, 088	3, 973	1, 115
Cancer of larynx (161)	2, 417	2, 172	245
All above causes	752, 693	463, 312	289, 381
All other causes	1, 004, 027	531, 477	472, 550
All causes	1, 756, 720	994, 789	761, 931

*International Statistical Classification numbers in parentheses.

Nearly 70 million people in the United States consume tobacco regularly. Cigarette consumption in the United States has increased markedly since the turn of the Century, when per capita consumption was less than 50 cigarettes a year. Since 1910, when cigarette consumption per person (15 years and older) was 138, it rose to 1,365 in 1930, to 1,828 in 1940, to 3,322 in 1950, and to a peak of 3,986 in 1961. The 1955 Current Population Survey showed that 68 percent of the male population and 32.4 percent of the female population 18 years of age and over were regular smokers of cigarettes.

In contrast with this sharp increase in cigarette smoking, per capita use of tobacco in other forms has gone down. Per capita consumption of cigars declined from 117 in 1920 to 55 in 1962. Consumption of pipe tobacco, which reached a peak of 2½ lbs. per person in 1910, fell to a little more than half a pound per person in 1962. Use of chewing tobacco has declined from about four pounds per person in 1900 to half a pound in 1962.

The background for the Committee's study thus included much general information and findings from previous investigations which associated the increase in cigarette smoking with increased deaths in a number of major disease categories. It was in this setting that the Committee began its work to assess the nature and magnitude of the health hazard attributable to smoking.

KINDS OF EVIDENCE

In order to judge whether smoking and other tobacco uses are injurious to health or related to specific diseases, the Committee evaluated three main kinds of scientific evidence:

1. *Animal experiments.*—In numerous studies, animals have been exposed to tobacco smoke and tars, and to the various chemical compounds they contain. Seven of these compounds (polycyclic aromatic compounds) have been established as cancer-producing (carginogenic). Other substances in tobacco and smoke, though not carcinogenic themselves, promote cancer production or lower the threshold to a known carcinogen. Several toxic or irritant gases contained in tobacco smoke produce experimentally the kinds of non-cancerous damage seen in the tissues and cells of heavy smokers. This includes suppression of ciliary action that normally cleanses the trachea and bronchi, damage to the lung air sacs, and to mucous glands and goblet cells which produce mucus.

2. *Clinical and autopsy studies.*—Observations of thousands of patients and autopsy studies of smokers and non-smokers show that many kinds of damage to body functions and to organs, cells, and tissues occur more frequently and severely in smokers. Three kinds of cellular changes—loss of ciliated cells, thickening (more than two layers of basal cells), and presence of atypical cells—are much more common in the lining layer (epithelium) of the trachea and bronchi of cigarette smokers than of non-smokers. Some of the advanced lesions seen in the bronchi of cigarette smokers are probably premalignant. Cellular changes regularly found at autopsy in patients with chronic bronchitis are more often present in the bronchi of smokers than non-smokers. Pathological changes in the air sacs and other functional tissue of the lung (parenchyma) have a remarkably close association with past history of cigarette smoking.

3. *Population studies.*—Another kind of evidence regarding an association between smoking and disease comes from epidemiological studies.

In retrospective studies, the smoking histories of persons with a specified disease (for example, lung cancer) are compared with those of appropriate control groups without the disease. For lung cancer alone, 29 such retrospective studies have been made in recent years. Despite many variations in design and method, all but one (which dealt with females) showed that proportionately more cigarette smokers are found among the lung cancer patients than in the control populations without lung cancer.

Extensive retrospective studies of the prevalence of specific symptoms and signs—chronic cough, sputum production, breathlessness, chest illness, and decreased lung function—consistently show that these occur more often in cigarette smokers than in non-smokers. Some of these signs and symptoms are the clinical expressions of chronic bronchitis, and some are associated more with emphysema; in general, they increase with amount of smoking and decrease after cessation of smoking.

Another type of epidemiological evidence on the relation of smoking and mortality comes from seven prospective studies which have been conducted since 1951. In these studies, large numbers of men answered questions about their smoking or non-smoking habits. Death certificates have been obtained for those who died since entering the studies, permitting total death rates and death rates by cause to be computed for smokers of various types as well as for non-smokers. The prospective studies thus add several important dimensions to information on the smoking-health problem. Their data permit direct comparisons of the death rates of smokers and non-smokers, both overall and for individual causes of death, and indicate the strength of the association between smoking and specific diseases.

Each of these three lines of evidence was evaluated and then considered together in drawing conclusions. The Committee was aware that the mere establishment of a statistical association between the use of tobacco and a disease is not enough. The causal significance of the use of tobacco in relation to the disease is the crucial question. For such judgments all three

lines of evidence are essential, as discussed in more detail on pages 26–27 of this Chapter, and in Chapter 3.

The experimental, clinical, and pathological evidence, as well as data from population studies, is highlighted in Section B of this Chapter, which in turn refers the reader to specific places in Part II of the Report where this evidence is presented in detail.

In the paragraphs which follow, the Committee has chosen to summarize the results of the seven prospective population studies which, as noted above, constitute only one type of evidence. They illustrate the nature and potential magnitude of the smoking-health problem, and bring out a number of factors which are involved.

Evidence From the Combined Results of Prospective Studies

The Committee examined the seven prospective studies separately as well as their combined results. Considerable weight was attached to the consistency of findings among the several studies. However, to simplify presentation, only the combined results are highlighted here.

Of the 1,123,000 men who entered the seven prospective studies and who provided usable histories of smoking habits (and other characteristics such as age), 37,391 men died during the subsequent months or years of the studies. No analyses of data for females from prospective studies are presently available.

To permit ready comparison of the mortality experience of smokers and non-smokers, two concepts are widely used in the studies—excess deaths of smokers compared with non-smokers, and mortality ratio. After adjustments for differences in age and the number of cigarette smokers and non-smokers, an expected number of deaths of smokers is derived on the basis of deaths among non-smokers. Excess deaths are thus the number of actual (observed) deaths among smokers in excess of the number expected. The mortality ratio, for which the method of computation is described in Chapter 8, measures the relative death rates of smokers and non-smokers. If the age-adjusted death rates are the same, the mortality ratio will be 1.0; if the death rates of smokers are double those of non-smokers, the mortality ratio will be 2.0. (Expressed as a percentage, this example would be equivalent to a 100 percent increase.).

Table 2 presents the accumulated and combined data on 14 disease categories for which the mortality ratio of cigarette smokers to non-smokers was 1.5 or greater.

The mortality ratio for male cigarette smokers compared with non-smokers, for all causes of death taken together, is 1.68, representing a total death rate nearly 70 percent higher than for non-smokers. (This ratio includes death rates for diseases not listed in the table as well as for the 14 disease categories shown.)

In the combined results from the seven studies, the mortality ratio of cigarette smokers over non-smokers was particularly high for a number of diseases: cancer of the lung (10.8), bronchitis and emphysema (6.1), cancer of the larynx (5.4), oral cancer (4.1), cancer of the esophagus (3.4), peptic ulcer (2.8), and the group of other circulatory diseases (2.6). For coronary artery disease the mortality ratio was 1.7.

TABLE 2.[1]—*Expected and observed deaths for smokers of cigarettes only and mortality ratios in seven prospective studies*

Underlying cause of death	Expected deaths	Observed deaths	Mortality ratio
Cancer of lung (162-3) [2]	170.3	1,833	10.8
Bronchitis and emphysema (502, 521.1)	89.5	546	6.1
Cancer of larynx (161)	14.0	75	5.4
Oral cancer (140-8)	37.0	152	4.1
Cancer of esophagus (150)	33.7	113	3.4
Stomach and duodenal ulcers (540, 541)	105.1	294	2.8
Other circulatory diseases (451-68)	254.0	649	2.6
Cirrhosis of liver (581)	169.2	379	2.2
Cancer of bladder (181)	111.6	216	1.9
Coronary artery disease (420)	6,430.7	11,177	1.7
Other heart diseases (421-2, 430-4)	526.0	868	1.7
Hypertensive heart (440-3)	409.2	631	1.5
General arteriosclerosis (450)	210.7	310	1.5
Cancer of kidney (180)	79.0	120	1.5
All causes [3]	15,653.9	23,223	1.68

[1] Abridged from Table 26, Chapter 8, Mortality.
[2] International Statistical Classification numbers in parentheses.
[3] Includes all other causes of death as well as those listed above.

Expressed in percentage-form, this is equivalent to a statement that for coronary artery disease, the leading cause of death in this country, the death rate is 70 percent higher for cigarette smokers. For chronic bronchitis and emphysema, which are among the leading causes of severe disability, the death rate for cigarette smokers is 500 percent higher than for non-smokers. For lung cancer, the most frequent site of cancer in men, the death rate is nearly 1,000 percent higher.

Other Findings of the Prospective Studies

In general, the greater the number of cigarettes smoked daily, the higher the death rate. For men who smoke fewer than 10 cigarettes a day, according to the seven prospective studies, the death rate from all causes is about 40 percent higher than for non-smokers. For those who smoke from 10 to 19 cigarettes a day, it is about 70 percent higher than for non-smokers; for those who smoke 20 to 39 a day, 90 percent higher; and for those who smoke 40 or more, it is 120 percent higher.

Cigarette smokers who stopped smoking before enrolling in the seven studies have a death rate about 40 percent higher than non-smokers, as against 70 percent higher for current cigarette smokers. Men who began smoking before age 20 have a substantially higher death rate than those who began after age 25. Compared with non-smokers, the mortality risk of cigarette smokers, after adjustments for differences in age, increases with duration of smoking (number of years), and is higher in those who stopped after age 55 than for those who stopped at an earlier age.

In two studies which recorded the degree of inhalation, the mortality ratio for a given amount of smoking was greater for inhalers than for non-inhalers.

The ratio of the death rates of smokers to that of non-smokers is highest

at the earlier ages (40–50) represented in these studies, and declines with increasing age.

Possible relationships of death rates and other forms of tobacco use were also investigated in the seven studies. The death rates for men smoking less than 5 cigars a day are about the same as for non-smokers. For men smoking more than 5 cigars daily, death rates are slightly higher. There is some indication that these higher death rates occur primarily in men who have been smoking more than 30 years and who inhale the smoke to some degree. The death rates for pipe smokers are little if at all higher than for non-smokers, even for men who smoke 10 or more pipefuls a day and for men who have smoked pipes more than 30 years.

Excess Mortality

Several of the reports previously published on the prospective studies included a table showing the distribution of the excess number of deaths of cigarette smokers among the principal causes of death. The hazard must be measured not only by the mortality ratio of deaths in smokers and non-smokers, but also by the importance of a particular disease as a cause of death.

In all seven studies, coronary artery disease is the chief contributor to the excess number of deaths of cigarette smokers over non-smokers, with lung cancer uniformly in second place. For all seven studies combined, coronary artery disease (with a mortality ratio of 1.7) accounts for 45 percent of the excess deaths among cigarette smokers, whereas lung cancer (with a ratio of 10.8) accounts for 16 percent.

Some of the other categories of diseases that contribute to the higher death rates for cigarette smokers over non-smokers are diseases of the heart and blood vessels, other than coronary artery disease, 14 percent; cancer sites other than lung, 8 percent; and chronic bronchitis and emphysema, 4 percent.

Since these diseases as a group are responsible for more than 85 percent of the higher death rate among cigarette smokers, they are of particular interest to public health authorities and the medical profession.

Associations and Causality

The array of information from the prospective and retrospective studies of smokers and non-smokers clearly establishes an association between cigarette smoking and substantially higher death rates. The mortality ratios in Table 2 provide an approximate index of the relative strength of this association, for all causes of death and for 14 disease categories.

In this inquiry the epidemiologic method was used extensively in the assessment of causal factors in the relationship of smoking to health among human beings upon whom direct experimentation could not be imposed. Clinical, pathological, and experimental evidence was thoroughly considered and often served to suggest an hypothesis or confirm or contradict other findings. When coupled with the other data, results from the epidemiologic studies can provide the basis upon which judgments of causality may be made.

It is recognized that no simple cause-and-effect relationship is likely to exist between a complex product like tobacco smoke and a specific disease in the variable human organism. It is also recognized that often the coexistence of several factors is required for the occurrence of a disease, and that one of the factors may play a determinant role; that is, without it, the other factors (such as genetic susceptibility) seldom lead to the occurrence of the disease.

The Effects of Smoking: Principal Findings

Cigarette smoking is associated with a 70 percent increase in the age-specific death rates of males. The total number of excess deaths causally related to cigarette smoking in the U.S. population cannot be accurately estimated. In view of the continuing and mounting evidence from many sources, it is the judgment of the Committee that cigarette smoking contributes substantially to mortality from certain specific diseases and to the overall death rate.

Lung Cancer

Cigarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction.

The risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day, and is diminished by discontinuing smoking. In comparison with non-smokers, average male smokers of cigarettes have approximately a 9- to 10-fold risk of developing lung cancer and heavy smokers at least a 20-fold risk.

The risk of developing cancer of the lung for the combined group of pipe smokers, cigar smokers, and pipe and cigar smokers is greater than for non-smokers, but much less than for cigarette smokers.

Cigarette smoking is much more important than occupational exposures in the causation of lung cancer in the general population.

Chronic Bronchitis and Emphysema

Cigarette smoking is the most important of the causes of chronic bronchitis in the United States, and increases the risk of dying from chronic bronchitis and emphysema. A relationship exists between cigarette smoking and emphysema but it has not been established that the relationship is causal. Studies demonstrate that fatalities from this disease are infrequent among non-smokers.

For the bulk of the population of the United States, the relative importance of cigarette smoking as a cause of chronic broncho-pulmonary disease is much greater than atmospheric pollution or occupational exposures.

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Cardiovascular Diseases

It is established that male cigarette smokers have a higher death rate from coronary artery disease than non-smoking males. Although the causative role of cigarette smoking in deaths from coronary disease is not proven, the Committee considers it more prudent from the public health viewpoint to assume that the established association has causative meaning than to suspend judgment until no uncertainty remains.

Although a causal relationship has not been established, higher mortality of cigarette smokers is associated with many other cardiovascular diseases, including miscellaneous circulatory diseases, other heart diseases, hypertensive heart disease, and general arteriosclerosis.

Other Cancer Sites

Pipe smoking appears to be causally related to lip cancer. Cigarette smoking is a significant factor in the causation of cancer of the larynx. The evidence supports the belief that an association exists between tobacco use and cancer of the esophagus, and between cigarette smoking and cancer of the urinary bladder in men, but the data are not adequate to decide whether these relationships are causal. Data on an association between smoking and cancer of the stomach are contradictory and incomplete.

The Tobacco Habit and Nicotine

The habitual use of tobacco is related primarily to psychological and social drives, reinforced and perpetuated by the pharmacological actions of nicotine.

Social stimulation appears to play a major role in a young person's early and first experiments with smoking. No scientific evidence supports the popular hypothesis that smoking among adolescents is an expression of rebellion against authority. Individual stress appears to be associated more with fluctuations in the amount of smoking than with the prevalence of smoking. The overwhelming evidence indicates that smoking—its beginning, habituation, and occasional discontinuation—is to a very large extent psychologically and socially determined.

Nicotine is rapidly changed in the body to relatively inactive substances with low toxicity. The chronic toxicity of small doses of nicotine is low in experimental animals. These two facts, when taken in conjunction with the low mortality ratios of pipe and cigar smokers, indicate that the chronic toxicity of nicotine in quantities absorbed from smoking and other methods of tobacco use is very low and probably does not represent an important health hazard.

The significant beneficial effects of smoking occur primarily in the area of mental health, and the habit originates in a search for contentment. Since no means of measuring the quantity of these benefits is apparent, the Committee finds no basis for a judgment which would weigh benefits against hazards of smoking as it may apply to the general population.

The Committee's Judgment in Brief

On the basis of prolonged study and evaluation of many lines of converging evidence, the Committee makes the following judgment:

Cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action.

B. COMMENTS AND DETAILED CONCLUSIONS

(A Guide to Part II of the Report)

All conclusions formally adopted by the Committee are presented at the end of this section in bold-faced type for convenience of reference. In the interest of conciseness, the documentation and most of the discussion are omitted from this condensation. Together with the tables of contents which appear at the beginning of each chapter in Part II, it is intended as a guide to the Report.

Chemistry and Carcinogenicity of Tobacco and Tobacco Smoke

Condensates of tobacco smoke are carcinogenic when tested by application to the skin of mice and rabbits and by subcutaneous injection in rats (Chapter 9, pp. 143–145). Bronchogenic carcinoma has not been produced by the application of tobacco extracts, smoke, or condensates to the lung or the tracheobronchial tree of experimental animals with the possible exception of dogs (Chapter 9, p. 165).

Bronchogenic carcinoma has been produced in laboratory animals by the administration of polycyclic aromatic hydrocarbons, certain metals, radioactive substances, and viruses. The histopathologic characteristics of the tumors produced are similar to those observed in man and are predominantly of the squamous variety (Chapter 9, pp. 166–167).

Seven polycyclic hydrocarbon compounds isolated from cigarette smoke have been established to be carcinogenic in laboratory animals. The results of a number of assays for carcinogenicity of tobacco smoke tars present a puzzling anomaly: the total tar from cigarettes has many times the carcinogenic potency of benzo(a)pyrene present in the tar. The other carcinogens known to be present in tobacco smoke are, with the exception of dibenzo(a,i)pyrene, much less potent than benzo(a)pyrene and they are present in smaller amounts. Apparently, therefore, the whole is greater than the sum of the known parts. This discrepancy may possibly be due to the presence of cocarcinogens in tobacco smoke, and/or damage to mucus production and ciliary transport mechanism (Chapter 6, p. 61, Chapter 9, p. 144 and Chapter 10, pp. 267–269).

There is abundant evidence that cancer of the skin can be induced in man by industrial exposure to soots, coal tar, pitch, and mineral oils. All of these

contain various polycyclic aromatic hydrocarbons proven to be carcinogenic in many species of animals. Some of these hydrocarbons are also present in tobacco smoke. It is reasonable to assume that these can be carcinogenic for man also (Chapter 9, pp. 146–148).

Genetic factors play a significant role in the development of pulmonary adenomas in mice. It is possible that genetic factors can influence the smoking habit and the response in man to carcinogens in smoke. However, there is no evidence that they have played an appreciable role in the great increase of lung cancer in man since the beginning of this century (Chapter 9, p. 190).

Components of the gas phase of cigarette smoke have been shown to produce various undesirable effects on test animals or organs. One of these effects is suppression of ciliary transport activity, an important cleansing function in the trachea and bronchi (Chapter 6, p. 61 and Chapter 10, pp. 267–270).

Characterization of the Tobacco Habit

The habitual use of tobacco is related primarily to psychological and social drives, reinforced and perpetuated by the pharmacological actions of nicotine on the central nervous system. Nicotine-free tobacco or other plant materials do not satisfy the needs of those who acquire the tobacco habit (Chapter 13, p. 354).

The tobacco habit should be characterized as an habituation rather than an addiction. Discontinuation of smoking, although possessing the difficulties attendant upon extinction of any conditioned reflex, is accomplished best by reinforcing factors which interrupt the psychogenic drives. Nicotine substitutes or supplementary medications have not been proven to be of major benefit in breaking the habit (Chapter 13, p. 354).

Pathology and Morphology

Several types of epithelial changes are much more common in the trachea and bronchi of cigarette smokers, with or without lung cancer, than of non-smokers and of patients without lung cancer. These epithelial changes are (a) loss of cilia, (b) basal cell hyperplasia, and (c) appearance of atypical cells with irregular hyperchromatic nuclei. The degree of each of the epithelial changes in general increases with the number of cigarettes smoked. Extensive atypical changes have been seen most frequently in men who smoked two or more packs of cigarettes a day.

Women cigarette smokers, in general, have the same epithelial changes as men smokers. However, at given levels of cigarette use, women appear to show fewer atypical cells than do men. Older men smokers have more atypical cells than younger men smokers. Men who smoke either pipes or cigars have more epithelial changes than non-smokers, but have fewer changes than cigarette smokers consuming approximately the same amount of tobacco. Male ex-cigarette smokers have less hyperplasia and fewer atypical cells than current cigarette smokers.

It may be concluded, on the basis of human and experimental evidence, that some of the advanced epithelial hyperplastic lesions with many atypical cells, as seen in the bronchi of cigarette smokers, are probably premalignant (Chapter 9, pp. 167–173).

Typing of Tumors.—Squamous and oval-cell carcinomas (Group I of Kreyberg's classification) comprise the predominant types associated with the increase of lung cancer in the male population. In several studies, adenocarcinomas (Group II) have also shown a definite increase, although to a much lesser degree. The histological typing of lung cancer is reliable, but the use of the ratio of histological types as an index of the magnitude of increase in lung cancer is of limited value (Chapter 9, pp. 173–175).

Functional and Pathological Changes.—Cigarette smoke produces significant funtional alterations in the trachea, bronchus, and lung. Like several other agents, cigarette smoke can reduce or abolish ciliary motility in experimental animals. Postmortem examination of bronchi from smokers shows a decrease in the number of ciliated cells, shortening of the remaining cilia, and changes in goblet cells and mucous glands. The implication of these morphological observations is that functional impairment would result.

In animal experiments, cigarette smoke appears to affect the physical characteristics of the lung-lining layer and to impair alveolar (air sac) stability. Alveolar phagocytes ingest tobacco smoke components and assist in their removal from the lung. This phagocytic clearance mechanism breaks down under the stress of protracted high-level exposure to cigarette smoke, and smoke components accumulate in the lungs of experimental animals (Chapter 10, pp. 269–270).

The chronic effects of cigarette smoking upon pulmonary function are manifested mainly by a reduction in ventilatory function as measured by the forced expiratory volume (Chapter 10, pp. 289–292).

Histopathological alterations occur as a result of tobacco smoke exposure in the tracheobronchial tree and in the lung parenchyma of man. Changes regularly found in chronic bronchitis—increase in the number of goblet cells, and hypertrophy and hyperplasia of bronchial mucous glands—are more often present in the bronchi of smokers than non-smokers. Cigarette smoke produces significant functional alterations in the upper and lower airways to the lungs. Such alterations could be expected to interfere with the cleansing mechanisms of the lung.

Pathological changes in pulmonary parenchyma, such as rupture of alveolar septa (partitions of the air sacs) and fibrosis, have a remarkably close association with past history of cigarette smoking. These latter changes cannot be related with certainty to emphysema or other recognized diseases at the present time (Chapter 10, pp. 270–275).

Mortality

The death rate for smokers of cigarettes only, who were smoking at the time of entry into the particular prospective study, is about 70 percent higher than that for non-smokers. The death rates increase with the amount smoked. For groups of men smoking less than 10, 10–19, 20–39, and 40 cigarettes and over per day, respectively, the death rates are about 40 percent, 70 per-

cent, 90 percent, and 120 percent higher than for non-smokers. The ratio of the death rates of smokers to non-smokers is highest at the earlier ages (40–50) represented in these studies, and declines with increasing age. The same effect appears to hold for the ratio of the death rate of heavy smokers to that of light smokers. In the studies that provided this information, the mortality ratio of cigarette smokers to non-smokers was substantially higher for men who started to smoke under age 20 than for men who started after age 25. The mortality ratio was increased as the number of years of smoking increased. In two studies which recorded the degree of inhalation, the mortality ratio for a given amount of smoking was greater for inhalers than for non-inhalers. Cigarette smokers who had stopped smoking prior to enrollment in the study had mortality ratios about 1.4 as against 1.7 for current cigarette smokers. The mortality ratio of ex-cigarette smokers increased with the number of years of smoking and was higher for those who stopped after age 55 than for those who stopped at an earlier age (Chapter 8, p. 93).

The biases from non-response and from errors of measurement that are difficult to avoid in mass studies may have resulted in some over-estimation of the true mortality ratios for the complete populations. In our judgment, however, such biases can account for only a part of the elevation in mortality ratios found for cigarette smokers (Chapter 8, p. 96).

Death rates of cigar smokers are about the same as those of non-smokers for men smoking less than five cigars daily. For men smoking five or more cigars daily, death rates were slightly higher (9 percent to 27 percent) than for non-smokers in the four studies that gave this information. There is some indication that this higher death rate occurs primarily in men who have been smoking for more than 30 years and in men who stated that they inhaled the smoke to some degree. Death rates for current pipe smokers were little if at all higher than for non-smokers, even with men smoking 10 or more pipefuls per day and with men who had smoked pipes for more than 30 years. Ex-cigar and ex-pipe smokers, on the other hand, showed higher death rates than both non-smokers and current pipe or cigar smokers in four out of five studies (Chapter 8, p. 94). The explanation is not clear but may be that a substantial number of such smokers stopped because of illness.

Mortality by Cause of Death.—In the combined results from the seven prospective studies, the mortality ratio of cigarette smokers was particularly high for a number of diseases. There is a further group of diseases, including some of the most important chronic diseases, for which the mortality ratio for cigarette smokers lay between 1.2 and 2.0. The explanation of the moderate elevations in mortality ratios in this large group of causes is not clear. Part may be due to the sources of bias previously mentioned or to some constitutional and genetic difference between cigarette smokers and non-smokers. There is also the possibility that cigarette smoking has some general debilitating effect, although no medical evidence that clearly supports this hypothesis can be cited (Chapter 8, p. 105).

In all seven studies, coronary artery disease is the chief contributor to the excess number of deaths of cigarette smokers over non-smokers, with lung cancer uniformly in second place (Chapter 8, p. 108).

For cigar and pipe smokers combined, there was a suggestion of high mortality ratios for cancers of the mouth, esophagus, larynx and lung, and for stomach and duodenal ulcers. These ratios are, however, based on small numbers of deaths (Chapter 8, p. 107).

Cancer by Site

Lung Cancer

Cigarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction.

The risk of developing lung cancer increases with duration of smoking and the number of cigarettes smoked per day, and is diminished by discontinuing smoking.

The risk of developing cancer of the lung for the combined group of pipe smokers, cigar smokers, and pipe and cigar smokers, is greater than for non-smokers, but much less than for cigarette smokers. The data are insufficient to warrant a conclusion for each group individually (Chapter 9, p. 196).

Oral Cancer

The causal relationship of the smoking of pipes to the development of cancer of the lip appears to be established.

Although there are suggestions of relationships between cancer of other specific sites of the oral cavity and the several forms of tobacco use, their causal implications cannot at present be stated (Chapter 9, pp. 204–205).

Cancer of the Larynx

Evaluation of the evidence leads to the judgment that cigarette smoking is a significant factor in the causation of laryngeal cancer in the male (Chapter 9, p. 212).

Cancer of the Esophagus

The evidence on the tobacco-esophageal cancer relationship supports the belief that an association exists. However, the data are not adequate to decide whether the relationship is causal (Chapter 9, p. 218).

Cancer of the Urinary Bladder

Available data suggest an association between cigarette smoking and urinary bladder cancer in the male but are not sufficient to support a judgment on the causal significance of this association (Chapter 9, p. 225).

Stomach Cancer

No relationship has been established between tobacco use and stomach cancer (Chapter 9, p. 229).

Non-Neoplastic Respiratory Diseases, Particularly Chronic Bronchitis and Pulmonary Emphysema

Cigarette smoking is the most important of the causes of chronic bronchitis in the United States, and increases the risk of dying from chronic bronchitis.

A relationship exists between pulmonary emphysema and cigarette smoking but it has not been established that the relationship is causal. The smoking of cigarettes is associated with an increased risk of dying from pulmonary emphysema.

For the bulk of the population of the United States, the importance of cigarette smoking as a cause of chronic bronchopulmonary disease is much greater than that of atmospheric pollution or occupational exposures.

Cough, sputum production, or the two combined are consistently more frequent among cigarette smokers than among non-smokers.

Cigarette smoking is associated with a reduction in ventilatory function. Among males, cigarette smokers have a greater prevalence of breathlessness than non-smokers.

Cigarette smoking does not appear to cause asthma.

Although death certification shows that cigarette smokers have a moderately increased risk of death from influenza and pneumonia, an association of cigarette smoking and infectious diseases is not otherwise substantiated (Chapter 10, p. 302).

Cardiovascular Disease

Smoking and nicotine administration cause acute cardiovascular effects similar to those induced by stimulation of the autonomic nervous system, but these effects do not account well for the observed association between cigarette smoking and coronary disease. It is established that male cigarette smokers have a higher death rate from coronary disease than non-smoking males. The association of smoking with other cardiovascular disorders is less well established. If cigarette smoking actually caused the higher death rate from coronary disease, it would on this account be responsible for many deaths of middle-aged and elderly males in the United States. Other factors such as high blood pressure, high serum cholesterol, and excessive obesity are also known to be associated with an unusually high death rate from coronary disease. The causative role of these factors in coronary disease, though not proven, is suspected strongly enough to be a major reason for taking countermeasures against them. It is also more prudent to assume that the established association between cigarette smoking and coronary disease has causative meaning than to suspend judgment until no uncertainty remains (Chapter 11, p. 327).

Male cigarette smokers have a higher death rate from coronary artery disease than non-smoking males, but it is not clear that the association has causal significance.

Other Conditions

Peptic Ulcer

Epidemiological studies indicate an association between cigarette smoking and peptic ulcer which is greater for gastric than for duodenal ulcer (Chapter 12, p. 340).

Tobacco Amblyopia

Tobacco amblyopia (dimness of vision unexplained by an organic lesion) has been related to pipe and cigar smoking by clinical impressions. The association has not been substantiated by epidemiological or experimental studies (Chapter 12, p. 342).

Cirrhosis of the Liver

Increased mortality of smokers from cirrhosis of the liver has been shown in the prospective studies. The data are not sufficient to support a direct or causal association (Chapter 12, p. 342).

Maternal Smoking and Infant Birth Weight

Women who smoke cigarettes during pregnancy tend to have babies of lower birth weight.

Information is lacking on the mechanism by which this decrease in birth weight is produced.

It is not known whether this decrease in birth weight has any influence on the biological fitness of the newborn (Chapter 12, p. 343).

Smoking and Accidents

Smoking is associated with accidental deaths from fires in the home.

No conclusive information is available on the effects of smoking on traffic accidents (Chapter 12, p. 345).

Morphological Constitution of Smokers

The available evidence suggests the existence of some morphological differences between smokers and non-smokers, but is too meager to permit a conclusion (Chapter 15, p. 387).

A clear cut smoker's personality has not emerged from the results so far published. While smokers differ from non-smokers in a variety of characteristics, none of the studies has shown a single variable which is found solely in one group and is completely absent in another. Nor has any single variable been verified in a sufficiently large proportion of smokers and in sufficiently few non-smokers to consider it an "essential" aspect of smoking.

The overwhelming evidence points to the conclusion that smoking—its beginning, habituation, and occasional discontinuation—is to a large extent psychologically and socially determined. This does not rule out physiological factors, especially in respect to habituation, nor the existence of predisposing constitutional or hereditary factors (Chapter 14, p. 377).

PART II

Evidence of the Relation Between Smoking and Health