Reduced Tar and Nicotine Cigarettes: Smoking Behavior and Health (1982)

Pages
60

Size
5 x 9

ISBN
030932811X

Dean R. Gerstein and Peter K. Levison, Editors; Committee on Substance Abuse and Habitual Behavior; Commission on Behavioral and Social Sciences and Education; National Research Council

Reduced Tar and Nicotine Cigarettes: Smoking Behavior and Health

Dean R. Gerstein and Peter K. Levison, Editors

Committee on Substance Abuse and Habitual Behavior

Commission on Behavioral and Social Sciences and Education

National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1982

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

The National Research Council was established by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and of advising the federal government. The Council operates in accordance with general policies determined by the Academy under the authority of its congressional charter of 1863, which establishes the Academy as a private, nonprofit, self-governing membership corporation. The Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in the conduct of their services to the government, the public, and the scientific and engineering communities. It is administered jointly by both Academies and the Institute of Medicine. The National Academy of Engineering and the Institute of Medicine were established in 1964 and 1970, respectively, under the charter of the National Academy of Sciences.

Library of Congress Catalog Card Number 82-81147

International Standard Book Number 0-309-03246-0

Available from

NATIONAL ACADEMY PRESS
2101 Constitution Avenue, N.W.
Washington, D.C. 20418

Printed in the United States of America

COMMITTEE ON SUBSTANCE ABUSE AND HABITUAL BEHAVIOR

CH

LOUIS C. LASAGNA (Chair), Department of Pharmacology and Toxicology, University of Rochester
HOWARD S. BECKER, Department of Sociology, Northwestern University
PETER DEWS, Department of Psychiatry and Laboratory of Psychobiology, Harvard Medical School
JOHN L. FALK, Department of Psychology, Rutgers University
DANIEL X. FREEDMAN, Department of Psychiatry, University of Chicago
JEROME H. JAFFE, University of Connecticut School of Medicine and Veterans Administration Hospital, Newington, Connecticut
DENISE B. KANDEL, Department of Psychiatry, Columbia University, and New York State Psychiatric Institute, New York
JOHN KAPLAN, School of Law, Stanford University
GARDNER LINDZEY, Center for Advanced Study in the Behavioral Sciences, Stanford, California
GERALD McCLEARN, College of Human Development, Pennsylvania State University
CHARLES P. O'BRIEN, Drug Dependence Treatment Service, Veterans Administration Hospital, Philadelphia, Pennsylvania
JUDITH RODIN, Department of Psychology, Yale University
STANLEY SCHACHTER, Department of Psychology, Columbia University
THOMAS C. SCHELLING, John F. Kennedy School of Government, Harvard University
RICHARD L. SOLOMON, Department of Psychology, University of Pennsylvania
FRANK STANTON, New York, New York
ALBERT M. STUNKARD, Department of Psychiatry, University of Pennsylvania Hospital
RICHARD F. THOMPSON, Department of Psychology, Stanford University

PETER K. LEVISON, Study Director
DEAN R. GERSTEIN, Senior Research Associate
DEBORAH R. MALOFF, Research Associate
MARIE A. CLARK, Administrative Secretary

CONTENTS

PREFACE

Since the early 1900s, cigarette smoking has increased in popularity with relatively muted concern over its health effects or habituating properties. Reports of cancer risk based on hospital studies in the early 1950s and the landmark Surgeon General's report in 1964 induced many cigarette smokers to quit smoking entirely--but many others who tried to stop discovered the habit to be one not so easily broken. The persistence of smoking habits in those who wanted to quit and the great difficulties experienced by many others who finally stopped smoking only after repeated cycles of withdrawal, abstinence, and relapse led to the recognition of cigarette smoking as an addiction, at least for a substantial proportion of smokers.

The Committee on Substance Abuse and Habitual Behavior was formed within the National Research Council to examine similarities and differences among many kinds of firmly established habitual behavior patterns, principally but not exclusively involving chemical substances, and to see what common processes might be found to underlie compulsive, resistant habits that can endanger health and well-being. The committee's work has been sponsored by the National Institute on Drug Abuse (NIDA), which, in conjunction with its charter mission of research on and treatment and prevention of problems associated with narcotic drugs, was persuaded by the commonalities between habitual cigarette smoking and classical drug addictions to propose this major public health concern as an addictive process. In 1978, the committee and NIDA cosponsored a symposium entitled Cigarette Smoking as a Dependence Process, the

proceedings of which were published in 1979 as NIDA Research Monograph No. 23.

The committee members who participated in the symposium were especially interested in the hypothesis that habitual smoking reflects an addictive process involving the biological and behavioral effects of nicotine. Experimental studies of the quantity of smoking in relation to the nicotine content of cigarettes form a growing body of evidence suggesting that smokers who are given cigarettes yielding less nicotine (in standard mechanized assays that simulate smoking) than their usual ones smoke more of them. Such experimental findings might be especially important for persistent smokers in light of some major changes in the cigarette marketplace. First, measures of the average tar and nicotine yields of commercial cigarettes have declined dramatically since 1955. Second, some investigators have argued, with considerable support in public health circles and attendant publicity, that these lower yields represent a lessening of the health hazards of cigarette smoking (in short, that they amount to "less hazardous cigarettes"). Third, "light" and "low"-yield brands have been heavily promoted by cigarette manufacturers. This confluence of factors led the committee to form a subgroup to study the question of how tobacco products with reduced yields of nicotine, tar, or other components affect the health of those smokers who continue to use tobacco products.

The first draft of this study was discussed by the full committee and a number of consultants in a small conference in 1979. Initially the study sought to place equal emphasis on a range of alternatives to cessation of cigarette smoking, including pipes, cigars, "smokeless" tobacco for chewing or snuffing, and nicotine-bearing gum. However, the scarcity of useful epidemiological data on these alternatives to cigarettes and the commercial growth in demand for decreased-yield cigarettes, persuaded us to place the major emphasis of the study on cigarette smoking. The committee ended up synthesizing and drawing inferences from evidence on nicotine as the key addictive component of cigarette smoke, on the behavioral and health effects of reducing the standard yields of tar and nicotine in cigarettes, and on the consequences likely to result from the interaction between these two factors (addiction and yield reduction). In its survey of epidemiological studies, the committee was struck by the growth in death rates

INTRODUCTION AND CONCLUSIONS

Habitual cigarette smoking is hazardous to health. This is not only a scientific finding widely accepted by the biomedical research community; it has also become accepted as fact by a large majority of cigarette smokers. Mainly for this reason, more than 30 million of the 60 million habitual smokers in this country report having made serious but unsuccessful attempts to quit smoking. And more than 30 million others have in fact quit smoking since 1964 (U.S. Department of Health, Education, and Welfare, 1980; U.S. Department of Health and Human Services, 1981). Nonsmokers, especially young ones, are also aware of the hazards of cigarettes, and since 1975 fewer young people have started smoking them (U.S. Department of Health, Education, and Welfare, 1980).

Nevertheless, many people do not want to give up smoking cigarettes, and many people who want to quit still do not. Further complicating matters, tobacco has been an economic staple of a large region of the country for more than 250 years. Finally, cigarettes have acquired firm cultural associations, at times with social sophistication, individuality, or maturity, and such associations remain attractive to many people.

From this mixture of motives has come a movement for "reducing the risk" for those who continue to use tobacco. People can attempt such reductions in three principal ways. The first is by reducing the number of cigarettes smoked. The second is by taking tobacco in a different way than cigarettes--such as pipes, cigars, chewing tobacco, or snuff. The third is by smoking "less hazardous cigarettes." Although we comment on the first two methods, the focus of this report is on the third: first, because there are adequate scientific

reports to evaluate this method as a health strategy for smokers; second, because it has unquestionably been the major direction of consumer interest, commercial development, and governmental activity in this country in the past 25 years; and finally, because experiments with different types of cigarettes have provided the opportunity to assess the role of nicotine in the motivation to continue smoking.

The assumptions that have guided development of the less hazardous cigarette were outlined by Hammond et al. (1977:105):

> (1) Death rates from lung cancer, cancer of several other sites, coronary heart disease, and several other diseases increase with degree of exposure to cigarette smoke. (2) Many experimental studies have shown that material condensed from cigarette smoke (usually called "tar") is carcinogenic when applied to animals. (3) The known acute effects of nicotine upon the heart and circulatory system suggest that the nicotine content of cigarette smoke is partly, if not entirely, responsible for the fact that age-specific death rates are higher among cigarette smokers than among nonsmokers. (4) Therefore, it seems reasonable to suppose that if the tar and nicotine content of cigarette smoke were reduced, then the harm done per cigarette smoked would be correspondingly reduced.

Due in part to this kind of reasoning, the tar and nicotine (T/N) yields of commercially available cigarettes in the United States have declined markedly over the past 25 years. In 1955 the average cigarette sold in the United States yielded 43 mg. of tar and 2.8 mg. of nicotine (43/2.8) in standard tests. Almost no cigarettes yielded less than 30/2.0; the highest-yield brands were considerably higher; and virtually all cigarettes were unfiltered. In 1979 the average cigarette yielded about 15 mg. of tar and 1.0 mg. of nicotine; almost no cigarette yielded more than 30/1.8; and the tar and nicotine yields of readily available cigarettes ranged down to 0.5/0.01. The overall reduction has been achieved both by smokers' choosing the new, lower T/N brands and the steady reduction by cigarette companies of the T/N ratings of already

established brands (Owen, 1976; Gori, 1980; U.S. Department of Health and Human Services, 1981).

The less hazardous cigarette would seem to be the solution to a number of dilemmas. For the smoker who is both strongly attracted or habituated to continued smoking but also desires to reduce the hazard to his or her health, it offers the promise of compromise. For the manufacturers, reducing T/N has proved an important marketing tool to reach an increasingly health-conscious public and to reduce criticism in the biomedical community, without serious economic loss to interests dependent on tobacco sales. The less hazardous cigarette might be a compromise between the statutory commitments of the federal government to public health (and thus antismoking efforts) on one hand and to agriculture and other economic activity on the other.

The logic that lower T/N yields equal less harmful smoking seems simple and persuasive. But there are two ways in which this logic may be misleading. First, the measurements of T/N are performed, in the laboratories of the Federal Trade Commission (FTC) and others, by analyzing batches of smoke drawn by a machine that simulates smoking with a simple and unchanging program (Kozlowski et al., 1980; Kozlowski, 1981). Human smokers and their cigarettes, however, are neither simple nor unchanging. If lowering the T/N of cigarettes typically results in people's smoking more of them or smoking them differently, then the machine results may not predict the human results.

Second, there is the complexity of the product itself. Tobacco smoke contains several thousand distinct compounds (Guerin, 1980). While the particulate condensate we call tar is clearly carcinogenic, and pure nicotine has well-demonstrated effects on the cardiovascular system, the rated quantities of these two components (that is, the T/N yields given by the Federal Trade Commission and related methods) cannot give all the information relevant to the potential toxicity of cigarettes. In particular, these ratings do not take into account the yield of gases--such as carbon monoxide, hydrogen cyanide, and acrolein--in cigarette smoke, which may not parallel T/N yields as the cigarette is smoked. In addition, flavorings are added to tobacco to modify the taste for consumer satisfaction. As a rule these additives are not under the purview of federal regulation and are held as

industrial secrets. It is possible that some flavorings designed to offset reduced T/N taste may prove to be added risk factors.

A variety of studies has been published regarding the toxicity of cigarette smoke, the different ways smokers puff on cigarettes, and the effects in human subjects of smoking lower versus higher T/N cigarettes. Our report was undertaken largely to address the results of these studies, to try to distill from them some up-to-date advice to smokers, to the government, and to researchers concerning the degree to which alternatives to smoking cessation--prinicipally the use of less hazardous cigarettes--are protective of health. The body of this report is an examination of relevant findings and theories and recommendations for a research agenda.

From our review of data and concepts we have formulated some summary conclusions for smokers and for the government.

- Despite the adverse consequences for some people of quitting cigarette smoking, such as weight gain and psychological distress, we are convinced by the evidence that habitual cigarette smoking is unequivocally hazardous to health and that longevity can be enhanced by stopping. Smokers who want to reduce the health hazards from their cigarettes are best advised to quit smoking entirely.
- Short of cessation, reducing the intake of hazardous combustion products of cigarette smoking should reduce the health hazard. Switching to a lower tar and nicotine brand or cutting down the number of cigarettes smoked of the same brand could achieve this reduction, but the effects of changing the brand or the number of cigarettes smoked are complicated. For continuing smokers, exposure to the constituents of smoke and attendant risks depend not only on the content, construction, and number of cigarettes but also on the way they are smoked.
- Smokers have not been educated about the meaning of the T/N information that appears on packages of most "light" and "low"- yield

T/N brands as well as in advertising. These numbers derive from standard measurements on a calibrated smoking machine. The machine is set to smoke in a uniform way, whereas smokers exhibit many different patterns. There is no easy way to represent the variability of a smoking population when making such measurements. In addition to nicotine and tar, cigarette smoking delivers carbon monoxide and other toxic gases to the body, which are not currently measured. Therefore, the T/N yields may or may not correspond well to the actual hazard exposure of different smokers.

- There is evidence that many smokers respond to switching to lower-yield brands, at least in the short term, by altering their smoking patterns; they may increase their depth of inhalation, puff frequency, duration of holding smoke in the lungs, and/or number of cigarettes consumed. These changes tend to offset to some degree the expected reductions in nicotine and tar delivered by the new brands; the changes may also be difficult for the smoker to detect. Experimental evidence indicates that when such increases occur, smokers still may not absorb from the lower-yield brands all of the T/N previously absorbed from higher-yield brands. However, exposure to carbon monoxide and, by implication, to other gaseous components generally seems to stay about the same. While some large-scale studies have suggested small gains in health due to using lower T/N (or filter rather than nonfilter) cigarettes, other population-wide studies do not support this view. Thus, the evidence for switching to lower T/N cigarettes is doubtful.
- Many smokers may switch brands rather than quit smoking in the belief that their health gains will be essentially proportional to the reduction in rated T/N yield; or will be substantial; or that the lower-yield brand of their choice is virtually safe. In our judgment, the degree of benefit most smokers can expect from switching to lower T/N brands, if any, is small compared with the benefit of stopping smoking completely.

- Finally, the attempt to make cigarettes less hazardous by reducing their tar and nicotine yield is necessarily a crude approach, corresponding to the uncertainty of knowledge about the differential effects of the thousands of components of cigarette smoke and the difficulties in independently manipulating them. The weight of recent studies that we have reviewed supports the idea that nicotine dependence is a very important component of smoking behavior and that most heavy cigarette smokers, regardless of brand, tend to maintain high nicotine levels. For such smokers, studies should be conducted on the relative risks and benefits of tobacco products that deliver nicotine less encumbered by additional toxic compounds.

The basis for these conclusions is an assessment of two related bodies of findings, which are presented below: (1) epidemiological studies on the health consequences of cigarette smoking and (2) laboratory and field studies of smoking behavior involving detailed analyses of the quantity, frequency, and mechanisms of tobacco smoke inhalation. The epidemiological studies strongly support a monotonic dose/response relationship between the number of cigarettes smoked and the emergence of serious cardiovascular, pulmonary, and other diseases (U.S. Department of Health, Education, and Welfare, 1979). However, the studies do not as a whole substantiate the equation of lower T/N with healthier smokers. The laboratory and field studies of smoking generally but not uniformly show that a significant proportion of smokers who switch to lower T/N cigarettes change the way they smoke them so as to compensate partially for the reductions in T/N yields, thus making the reduction in actual T/N absorption by smokers less substantial than the reduction in T/N ratings based on the FTC smoking machine method. These studies also indicate that yields of other possibly harmful components of inhaled smoke, such as carbon monoxide, are not reflected by T/N ratings.

The review of these studies is followed by an assessment of current research needs on alternatives to smoking cessation.

THE HEALTH EFFECTS OF CIGARETTE SMOKING

EARLIER STUDIES

Habitual cigarette smoking is hazardous to health. Morbidity and mortality data from epidemiological studies have shown convincingly that there is a strong relationship between smoking and increased death rates, particularly from lung and other cancers and cardiovascular disease. The health prognoses for smokers and nonsmokers are so different that a middle-aged, male, pack-and-a-half-a-day cigarette smoker who began smoking in his teens has a life expectancy roughly one decade less than a man matched on a variety of relevant characteristics who has never smoked. Ex-smokers also gain a mortality advantage over continuing smokers: it begins soon after quitting and increases with years of abstinence up to 20 years, when the mortality of ex-smokers is indistinguishable from lifetime nonsmokers (U.S. Department of Health, Education, and Welfare, 1979).

It is more difficult to draw conclusions about the health differences between different sorts of smokers, beyond the well-confirmed proposition that smoking few cigarettes, other things being equal, is less harmful than smoking many. This has been demonstrated for the overall risk of death, the risk of death from cardiovascular diseases, and for the risk of developing and dying from neoplastic diseases of the respiratory system (U.S. Department of Health, Education, and Welfare, 1979).

In the largest prospective study, which initially enrolled 847,825 subjects, Hammond et al. report that, after statistically matching subgroups of smokers in their sample, "the adjusted number of [lung cancer]

deaths in low T/N smokers ranged from 81% to 88% of the adjusted number of deaths in high T/N smokers" (1977:107-108). The matching procedure was designed to hold the number of cigarettes smoked daily, among other variables, constant. Wynder and Stellman (1979), in a matched case/control study of patients with lung and larynx cancer, also reported statistically significant differences in favor of smokers of filter versus nonfilter cigarettes, with the number smoked daily held constant. Auerbach et al. (1979) examined sections of lung tissue from postmortem examinations of more than 200 smokers who died between 1955 and 1959 (deaths other than lung cancer) and a comparison group who died between 1970 and 1977. The number of cell anomalies, some of which the authors hypothesize could be precancerous, was far lower among those smoking similar numbers of cigarettes in the 1970-1977 group than the 1955-1959 group. The authors attribute this to the trend toward lower-yield commercial cigarettes.

A large prospective study in Scotland reported filter cigarettes and lower T/N yields to be associated with lower prevalence of respiratory illness but not with decreased death rates (Hawthorne and Fry, 1978). Another prospective study in Great Britain (Higgenbottam et al., 1980) found only small differences in lung function across varying T/N yields, differences that nearly vanished among smokers of more than one pack daily. A third British study (Wald, 1976) reported lower T/N levels to be correlated with reductions in pulmonary but not cardiovascular diseases. A recent report from the Framingham study (Castelli et al., 1981) found that smokers of nonfilter cigarettes had slightly lower coronary heart disease morbidity than smokers of filter cigarettes, which are generally lower in T/N yield.

Lee and Garfinkel reviewed these (except for Castelli et al.) and other epidemiological studies and concluded nevertheless that "smokers of filter (or low T/N) cigarettes have lower mortality than smokers of plain (or high T/N) cigarettes for those diseases most strongly associated with smoking . . ." (Lee and Garfinkel, 1980:23). This result occurs principally in studies in which the number of cigarettes smoked daily is statistically controlled, i.e., when smokers of 10-19 filter cigarettes daily are compared only with smokers of 10-19 nonfilter cigarettes; smokers of 20-29

filter cigarettes with smokers of 20-29 nonfilters; and so forth. Lee and Garfinkel note that this result would be somewhat misleading if in fact smokers of low T/N or filter cigarettes tended as a rule to smoke more cigarettes daily than smokers of high T/N or nonfilter cigarettes. To counter this difficulty, they cite Garfinkel's analysis of data that led him to conclude that "over a long period of time, people tend to smoke the same number of cigarettes a day regardless of tar and nicotine level" (Garfinkel, 1980:24). However, in this analysis, only one-third of continuing smokers said that they smoked the same number after 13 years, and small but consistent differences were seen in changes in the number of cigarettes smoked across time depending on T/N, even when the changes in T/N and the number of cigarettes smoked were collapsed into broad categories.

The overall consumption of T/N per capita among U.S. adults, based on the total numbers of cigarettes sold, their FTC machine-measured T/N ratings, and census population figures, is calculated to have declined by about half between 1955 and 1975, and most of this reduction occurred by 1966 (Wakeham, 1976). It seems to us that this reduction provides a natural experiment for evaluating the health effects of reduced-yield cigarettes on the adult U.S. population. Because of the long period needed for the development of morbidity and mortality differences, it may be too early to determine whether these changes in T/N yields were favorable for those who have smoked cigarettes only since 1965, i.e., principally smokers born after 1945. In addition, since 1975 there has been a notable increase in the sales of "ultra-low" T/N brands, i.e., those yielding less than 5 mg. of tar and 0.5 of nicotine. However, we should be able to detect the impact of the newer cigarette products through 1975 on smokers born before 1945, by analyzing appropriate trends in U.S. health statistics relative to available data on smoking patterns.

The largest share of morbidity and mortality attributable to smoking is due to its elevation of the risk of cardiovascular illness, including atherosclerosis, myocardial infarction, coronary heart disease, sudden cardiac death, and peripheral vascular disease (U.S. Department of Health, Education, and Welfare, 1979). Smoking is one of several major cardio-

vascular risk factors, which include such behavioral patterns as exercise, stress, and diet. The plurality of attributable risk factors complicates the detection of differences in risk among smokers of cigarettes with differing T/N. Moreover, the chances of dying from many of these disease have been reduced in recent years by declines in the incidence of several of the risk factors as well as better medical care.

A more easily analyzed health effect from the point of view of evaluating reduced T/N yield is cancer of the lungs and bronchi. There is no widespread behavioral risk factor for these cancers that is comparable, in either relative or absolute effect, to smoking cigarettes. Although the total burden of illness due to cardiovascular disease is many times larger, the loss due to these cancers is considerable--more than 100,000 new cases annually in the United States. Most of these cancers are attributable to cigarette smoking and most still lie beyond the reach of lifesaving medical intervention.

The following analysis, undertaken for this report, addresses the effect of reduced T/N yields on respiratory system cancer.

CHANGES IN DEATH RATES FROM RESPIRATORY SYSTEM CANCER IN THE UNITED STATES SINCE 1940

Among men between ages 25 and 65 in a given year, there has been a notable decline since 1955 in the proportion who are currently smoking. As of 1975 (the latest year that complete data for this analysis were available), there were about a fourth fewer cigarette smokers in each five-year age bracket than had been the case for men at the same ages 20 years before (see Figure 1). However, the proportion of the overall male population who were current heavy smokers (defined as more than a pack of cigarettes daily) did not decline during these years. Most of the drop-off has been due to the replacement of light smokers in the male population by nonsmokers. The proportion of current smokers who smoke heavily has therefore increased, while by 1975 nonsmokers had become the majority of men at every age.

The risk of death from lung cancer is 10 to 20 times greater among current heavy smokers than for their nonsmoking age-mates, accounting for between

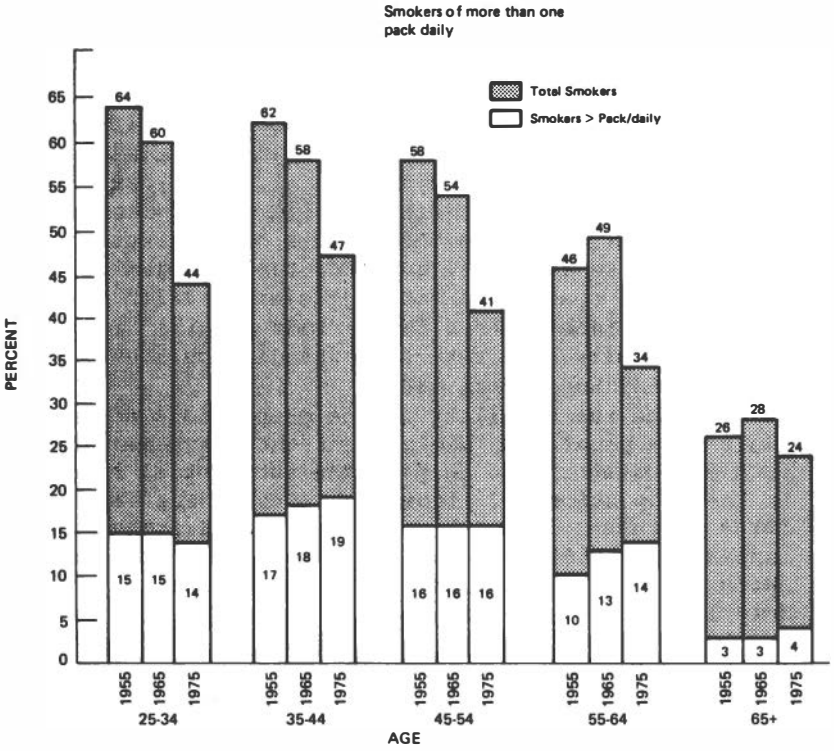

FIGURE 1 Estimated Prevalence of Current Cigarette Smoking by U.S. Men, 1955, 1965, 1975

Sources: Haenszel et al. (1956); Ahmed and Gleason (1970); USDHEW (1976, 1980).

one-half and two-thirds of all male lung cancer deaths (lighter smokers account for most of the remaining lung cancer deaths). Since heavy smokers have maintained their overall proportion of about one in six in the male population ages 25-65 and since these smokers account for the bulk of lung cancer deaths, we can use the annual age-specific death rates to see whether a discernible improvement in lung cancer mortality has occurred, as might be anticipated with the lower T/N cigarettes that have become available since 1955. It should be kept in mind that this is the one category of health effect for which the 1981 report of the Surgeon

General held open the possibility that lower T/N cigarettes might be relatively less hazardous (U.S. Department of Health and Human Services, 1981).

We have analyzed a data series on deaths due to respiratory system cancers (RSC), categories 160-165 in the ninth revision of the International Classification of Diseases. Most of the deaths in the data series are due to lung cancer (see Wynder et al., 1970; Enstrom and Godley, 1980). A small fraction of RSC deaths cannot be attributed to the effects of cigarette smoking; these data are, however, the best general indicator of changes in smoking-related health damage that is available across the periods of time necessary to this inquiry. We return to the difficulties of interpreting these data below.

Despite the stability in the proportions of the adult male population who are current heavy smokers in each age category and despite the substantial reductions in the proportions of lighter smokers, there have been large increases in death rates from respiratory system cancer since 1955 among men ages 35-65, and the rates among younger men begin to level off or fall slightly only after 1970 (see Figure 2). The overall increase has been on the order of 70 percent more RSC deaths per capita (males, age-specific) in 1975 than in 1955. These increases are at least partially attributable to two complicating factors: the steady rise in the prevalence of heavy smoking among these men prior to 1955 (Horn, 1977) and the fact that development of the more serious health effects of smoking generally requires periods of time. The conjunction of these factors makes the use of current or recent smoking patterns insufficient to sort out the RSC effects of cigarettes (Burch, 1980).

Based on surveys from the National Clearinghouse for Smoking and Health and others, Horn (1977) has published estimates of accumulated cigarettes smoked per capita in terms of total lifetime cigarette packs for virtually the same male age cohorts. Using these figures it is possible to construct an index of the relationship between lifetime cigarettes smoked and RSC deaths. The results of this calculation, reported in Table 1, can be thought of as roughly tracking the carcinogenicity of cigarettes as smoked by American men, controlling for the aggregate, lifetime numbers of

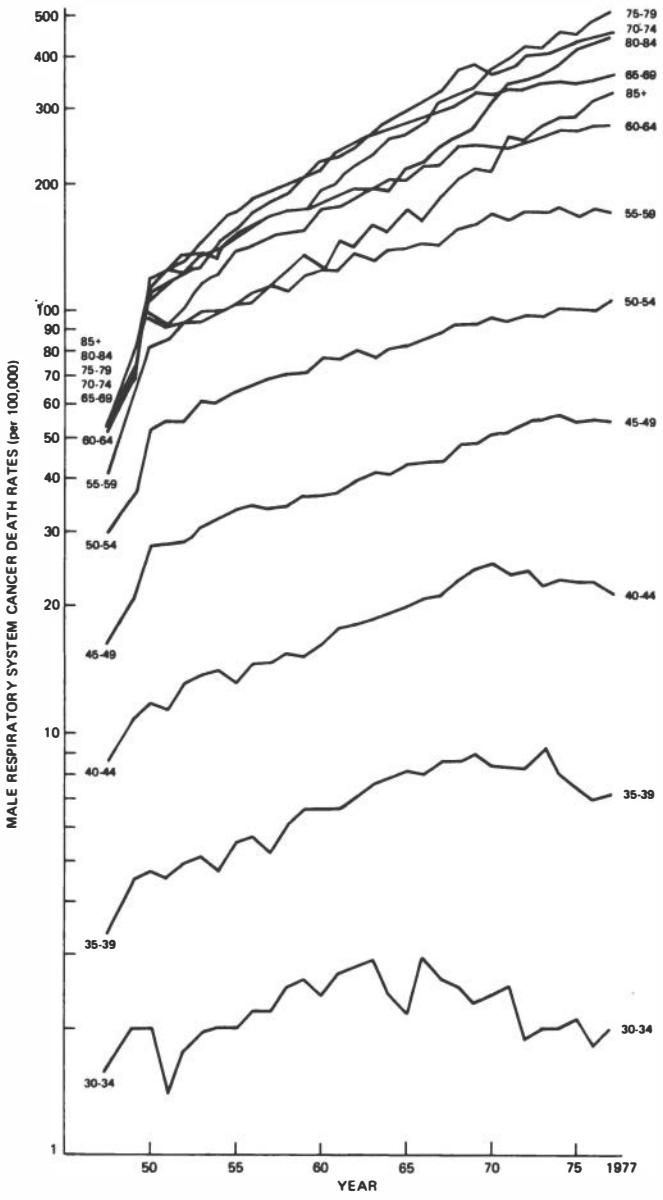

FIGURE 2 Male Respiratory System Cancer Death Rates per 100,000, 1940-1977

Source: U.S. Vital and Health Statistics (annual).

TABLE 1 Estimated U.S. Male Respiratory System Cancer Deaths Related to Accumulated Exposure to Cigarettes per One Billion Packs, by 5-Year Age Groups (35-64), 1955-1975

Age Group	1955	1960	1965	1970	1975
35-39	12	14	19	20	19
40-44	23	28	34	46	45
45-49	52	52	61	73	85
50-54	90	97	102	118	130
55-59	139	152	160	183	186
60-64	201	220	225	249	270

Sources: Death rates from U.S. Vital and Health Statistics for years shown; cigarette exposure estimates adapted from Horn (1977).

cigarettes they have smoked. The numbers in the "cells" result from computing the frequency of RSC deaths per 100,000 for the age groups and year (row and column) of each cell, then dividing this frequency by the average total lifetime cigarettes smoked by the men in that age group as of that year (Horn, 1977). The decimal points are uniformly adjusted to show the number of deaths that year per billion packs smoked up to that year.[1] The results of this set of calcula-

[1]Estimates of lifetime cigarette exposure like those compiled by Horn for men are not available for women, so a comparable analysis and resulting table cannot be offered. However, figures for female smoking prevalence and RSC death rates are reported in the appendix.

tions suggest that men died appreciably more often of RSC, pack for lifetime pack, in 1975 than in 1955, despite the massive switch during this intervening period from nonfilter to filter cigarettes and substantially lower T/N. There is a steady increase in RSC death rates from 1955 to 1970, which levels off for the youngest groups after 1970.

In interpreting the significance of Table 1, several caveats need to be introduced. (1) The estimates by Horn give equal weight to cigarettes smoked far in the past and ones smoked recently. (2) These estimates do not discriminate between alternative types of frequency distributions of cigarette smoking in the base population--that is, a hypothetical group of 100, all of whom smoked 10 cigarettes daily, would be counted the same as a group comprised of 50 nonsmokers and 50 smokers of 20 cigarettes daily. Our calculations thus assume a roughly linear dose-response relation, were other things held equal, between the number of cigarettes smoked and exposure risk for RSC death, when both are summed across the whole population (U.S. Department of Health and Human Services, 1982). (3) Roughly 20 percent of male RSC deaths in this period are probably not attributable to cigarette smoking.

In our judgment, the cumulative possible errors that might result from these complications are not very large across the ranges in the table and should affect the younger age-groups (below 50) little if at all. A more serious concern is that environmental factors other than cigarette smoking (Selikoff and Hammond, 1975; National Research Council, 1980) might have been increasing during the period covered, causing more RSC deaths among both smokers and nonsmokers, thus masking any decline due to reduced T/N yields. Although one study of trends in RSC mortality among nonsmokers (Enstrom, 1979) found evidence of an increase between 1958 and 1966-1968 among older men (but not among younger men or among women), other analyses (Doll and Peto, 1981; Garfinkel, 1981) discern no such trend.

We are left with the conclusion that, at least through 1975, cigarettes had not become appreciably less hazardous for men with respect to the aggregate risk of death from RSC between ages 35 and 65. There has in fact been a substantial and unexpected increase in RSC deaths per cigarette smoked, especially in the upper age brackets. We offer two main explanations for these results. One possibility that is consistent with

the inflections in the age-specific mortality trends is that packs of cigarettes were steadily increasing in carcinogenic risk until the 1950s, and since then they have maintained the same or a very slightly lower hazard. We might still be seeing the effects of the earlier increases due to decades-long delays in the process of carcinogenesis (though there is a counter-trend indicated by the steady reductions in relative RSC risk after quitting). Smokers who began smoking before 1950 would then still show increasing cancer mortality, while younger smokers would show a leveling off or a slight decline in per-pack cancer mortality in recent years. The second plausible inference from these data is that, in direct contradiction to the hopes of their proponents, the lower T/N cigarettes may have been more rather than less hazardous with respect to RSC for the millions of smokers who were accustomed to the earlier varieties, although no worse--or marginally better--for those who have no experience with the earlier high T/N brands. A third but much less persuasive (Doll and Peto, 1981) possibility is synergy between cigarette effects and something else, such as ambient air pollution, that may have been increasing during this period.

Whatever reasoning might explain the particular contours of Table 1, this analysis clearly shows that, with the data now available on trends in RSC mortality in the United States, it is not possible to credit lower T/N cigarettes up to 1975 with significantly improving the dismal picture of male RSC mortality.

SUMMARY

It was expected that the shift toward filter cigarettes and reduced T/N yields would be associated in the aggregate with reductions in disease and death, but an examination of respiratory system cancer trends in the general population does not confirm such an expectation through 1975. Older smokers (45+) are showing steadily higher RSC death rates, and there is at best a stabilization or a small decline among middle-aged or younger male populations in RSC per pack smoked. There are simply no data as yet relevant to smokers born since 1945.

While recent cigarette products may yield less weight of certain toxic materials per unit, the data do not as yet indicate that smoking these cigarettes has become generally or substantially less hazardous, at least as regards RSC mortality. This evidence supports the conclusion that smoking behavior is hazardous to health and that apparent changes in the machine-measured yields of T/N have not, in practice, turned out so far to hold notably less hazard.

SMOKING BEHAVIOR

Most of the studies mentioned in the previous section considered cigarettes along very simple lines. The number smoked and their relative T/N yield were taken as the sole independent variables relevant to the effects of smoking on the body. Most of the existing data on smoking and health are cast in the form of number and brand of cigarettes smoked and/or purchased. These data alone provide a rather puzzling picture, with matched-case studies pointing one way and general population studies pointing the other. In order to make sense of the situation, it is necessary to recognize some additional complexities of cigarettes and the smoking process.

The cigarette is a complex device with a variety of properties affecting the end product--smoke. The tobacco in different cigarettes may vary, among other ways, by variety, growing conditions, curing process, cut, and packing density. The tobacco may include varying proportions of stems, leaves, and resin, and an assortment of "flavoring" agents that are legally protected trade secrets. The properties of the paper (especially its porosity), the size and shape of the cigarette, and the type of filter all have a bearing on cigarette smoke. Filters can remove some portion of the particles and gases from the smoke; the porosity of the filter and the paper together determine how much air dilutes the smoke in each puff.

The public has become familiar with the labels on some cigarette packages and all cigarette advertising, which routinely specify the T/N yield of each cigarette. These index numbers represent quantities delivered into a smoking simulator. The labelled quantities are

averages per cigarette for batches of smoke "inhaled" by the machine, which is programmed to draw a 35-cc. volume of smoke in two seconds once a minute, until a certain point on each cigarette is reached. The machine takes from 8 to 13 "puffs" per cigarette, depending on the cigarette's length and burning rate (Kozlowski et al., 1980; Kozlowski, 1981).

Large differences are possible in the smoke that different smokers get from the same cigarette, or that one smoker gets at different times. Subtle changes in the velocity and depth of the puff affect the amount, temperature, and composition of the smoke delivered. Holding the type of cigarette constant, the amount of smoke going to the lungs depends on the depth of inhalation and the duration, number, and strength of the puffs taken. For example, Rawbone et al. (1978) found a low and nonsignificant correlation of 0.28 between amounts of smoke presented to the mouth and material absorbed into the lungs. These types of behavioral manipulation mean that smokers can draw roughly similar amounts of smoke from cigarettes with quite different T/N yields.

The T/N ratings can be likened to the estimates of gasoline mileage published by the Environmental Protection Agency as predictions of automobile performance. The exact exposure one gets from cigarettes depends on many individual factors.

There are additional considerations. In contrast to nicotine, which is a single compound, tar is a very complicated mixture of chemicals. The quantity (in milligrams) of this mixture of liquid particles, which collects in the smoking chamber (or the lungs), is a useful but imperfect measure of its toxicity. Broadly speaking, a monotonic relation is well established between the total quantity of tar deposited on living tissue and the likelihood of tumors developing on the site (U.S. Department of Health and Human Services, 1982). This general relationship includes considerable variation, both in individual response and in specific differences in tar content.

The acute pharmacological properties of nicotine are well established (Jaffe, 1980). It produces, among other actions, vasoconstriction, increased heart rate, and elevated blood pressure. Some degree of tolerance develops within a few hours to the effects on the heart; however, it remains possible, but not proven, that some cardiac disease is related to acute nicotine effects

(Wald et al., 1981). It is also possible but not established that chronic exposure might contribute to cardiovascular disorders such as peripheral artery disease. There has been at least one report (Bock, 1980) that nicotine is a cocarcinogen (increasing the effects of other agents) when tested in laboratory tissue assays. Epidemiological studies have not satisfactorily isolated the effects of chronic nicotine inhalation from the effects of other toxic constituents of tobacco.

The T/N ratings measure filterable, solid residues, but smoke also contains gases and volatile liquids. The best-known gaseous component is carbon monoxide (CO), and there is evidence implicating CO in promoting and aggravating cardiovascular disease (U.S. Department of Health and Human Services, 1981; National Research Council, 1977a). The gaseous phase contains a host of other toxic compounds as well, including potent carcinogens such as acrolein and benzo(a)pyrene (U.S. Department of Health and Human Services, 1981).

While nicotine and tar are highly correlated with each other, both residing in the particulate fraction of cigarette smoke, CO has a more variable relationship to either. Gori and Lynch (1976) have reported the highest correlations between CO and tar (r=.73) and nicotine (r=.50), respectively, using the smoking machine method. Jenkins et al. (1979) also found that CO levels decrease as T/N yields decrease on smoking machines. Taken as a whole, the smoking machine results indicate that when T/N deliveries are reduced by the method of more effective filtration, special blending of tobaccos, or related approaches that are directed toward the particulate phase, CO levels are not reduced and in some cases are increased. Diluting the smoke, by increasing the porosity of the cigarette paper or perforating the filter covering, affects both phases (Robinson and Forbes, 1975; Guerin, 1980). But these CO reductions can be at least partially reversed by increasing total puff volume, which correlates strongly with CO level (Fredericksen and Martin, 1979).

In some short-term experimental studies with small numbers of subjects, CO levels tend to decrease when smokers are given cigarettes with markedly lower T/N yields or with filters that dilute the smoke with air drawn through perforations in the paper (Turner et al., 1974; Ashton et al., 1979) This was not found to be

the case, however, in a field study by Jaffe et al. (1981). In comparing 196 daily smokers of cigarettes with widely different T/N yields, they found, except among the few smokers using "ultra-low" T/N cigarettes (0.1-0.2 mg. nicotine), that although CO levels were roughly but significantly correlated with daily cigarette consumption, there were no significant differences in expired CO relative to T/N content. Jaffe et al. (forthcoming) have replicated the CO result in a prospective study.

There are many other toxic constituents of cigarette smoke in both the gas and particulate phases, such as methane, hydrogen cyanide, and nitrosamines. It is, however, beyond the scope of this report to review them in further detail, especially since their relation to smoking behavior has not been studied. We can simply conclude that T/N yields, and even the number of cigarettes smoked, do not provide sufficient data about smoking behavior. While we need research to understand more fully the toxicological properties of cigarette smoke, we also need studies to understand more fully the factors that govern the behavior of smokers. To date, much of this research has involved a model of smoking that derives from the literature on drug dependence, focusing on nicotine.

THE NICOTINE COMPENSATION HYPOTHESIS

Cigarette smoking qualifies as a habit with most smokers--especially with heavy (20 cigarettes or more per day) ones. It has been proposed (Russell, 1976; Schachter, 1978) that such smokers can be called addicted and that one component of cigarette smoke, nicotine, is the critical element in this addiction. The case for nicotine as the primary substance that tobacco smokers seek is not proven, but the evidence is quite persuasive (e.g., Herning et al., 1981). There is as yet no evidence for a central role for any other component of cigarette smoke. Whether the term addiction is appropriate or not (see Jaffe, 1980; Gerstein, 1975; Levine, 1978), it is certainly worthwhile to investigate how smokers respond to changes in the composition of their usual tobacco smoke. One important model of such changes depends on the concept of compensation.

The compensation hypothesis proposes a control mechanism that, when it senses that the pharmacological level or effect of a constituent of smoke exceeds some limit, calls for no further intake. Conversely, when the pharmacological level or drug effect at some site in the body falls below some minimum, the mechanism impels intake. In the first instance the smoker puffs less or stops, and in the second, lights up or puffs more. As a result, smokers may maintain a relatively stable range or diurnal pattern of smoking. Intake may be adjusted by any or all of the features of smoking behavior, such as depth of inhalation, puff length, puff frequency, or number of cigarettes. This form of internal control of behavior may compete or coexist with other sources of control such as stimulus or schedule factors. The pharmacological effects of nicotine have thus far been the leading candidate for the internal control mechanism, although the hypothetical possibility of effects of other tobacco constituents has not been thoroughly ruled out.

If the nicotine hypothesis is correct, the pharmacology of nicotine helps to explain much of the behavior observed in the heavy cigarette smoker. Flue-cured tobacco, the kind principally used in cigarettes, yields relatively acidic smoke, in contrast to the more alkaline smoke from pipe and cigar tobaccos. Nicotine in an acidic medium is not well absorbed via the membranes of the mouth; it must be inhaled to be absorbed. Cigarette smoke is mild enough so that, with practice, the smoker usually tolerates the mild respiratory irritation. Once in the lung, nicotine passes very rapidly into the bloodstream, then to the heart, and a significant proportion is then sent relatively undiluted to the brain, where it moves quickly across the blood-brain barrier, being highly lipid-soluble. Nicotine absorbed from the lungs reaches the brain in about half the time and at a higher concentration than an intravenous dose in the arm (Russell, 1976). The process of transfer from lip to brain requires less than 10 seconds (Jaffe, 1980).

Nicotine is one of the shortest-acting of the common psychoactive drugs. It is destroyed rapidly in the liver. After repeated doses about half the nicotine in the blood is metabolized within 80 to 100 minutes. A very small percentage is excreted unchanged by the kidney, a percentage that increases significantly when

the urine is made acidic, as it often is under stressful conditions (see Schachter, 1978; Rosenberg et al., 1980).

Given the sharp and immediate transport of nicotine to the brain following each puff, it is not surprising that smokers are able to adjust the depth of puffing and inhalation to get the amount of nicotine that feels "right" even when the nominal nicotine content of the cigarette is radically altered. Nor is it surprising that, given the rapid destruction of nicotine in the body, most smokers who become dependent on its presence smoke at least one every hour during the waking day.

Adjustment for nicotine effects may not be very precise but may keep the effects within a range: between an upper boundary, where unpleasant "overdose" effects begin to occur, and a lower boundary, where pleasurable effects are not sufficient or withdrawal occurs (Herman and Kozlowski, 1979). Crossing either boundary does not necessarily mean that smoking always stops or starts; rather, the probability of an adjustment in smoking behavior increases. These probabilities are clearly affected by factors such as social setting, time of day, and access to cigarettes.

The term compensation has been used in the scientific literature on smoking to mean both the process by which smokers adjust their behavior to body levels of nicotine and the end state reached, i.e., the recovery of specific preferred or previous levels of smoke intake or of body nicotine levels. We use the term compensation to describe the tendency to adjust and the term recovery to mean that a former level has been reached.

Experiments have been designed to test the hypothesis that smoking can be thought of as a nicotine compensation process. The methods used include manipulating plasma nicotine by administering various doses of pure nicotine, by administering a nicotine antagonist, or by having subjects smoke cigarettes of differing nicotine yields and observing any consequent changes in smoking behavior. Most experimental studies to date (U.S. Department of Health and Human Services, 1981) support the existence of some degree of compensatory smoking for nicotine (and/or tobacco constituents correlated with it). In studies in which heavy smoker subjects are supplied on a blind basis with high versus low nicotine cigarettes, they generally smoke more of the low than of the high nicotine cigarettes; how many

more varies from study to study (Schachter, 1978). When subjects were "preloaded" with nicotine chewing gum or capsules, they smoked less than with placebo preloading (Kozlowski et al., 1975). Administration of a nicotine antagonist has been shown (Stolerman et al., 1973) to increase cigarette smoking; when nicotine excretion was increased by lowering urinary pH, smoking rates increased (Schachter et al., 1977); and intravenous nicotine tends to depress smoking rates (Lucchesi et al., 1967).

A few studies (Finnegan et al., 1945; Kumar et al., 1977) have not supported the compensation hypothesis, but a large majority do. It is important to note that most of the supporting studies demonstrate incomplete compensation, at least over a term of a few weeks or less. For example, in a crossover study with "low" T/N yield cigarettes rated at less than one-fourth as much nicotine as "high" ones, subjects on the average smoked only 25 percent more of the "low" cigarettes (Schachter, 1977). It is possible that this discrepancy may be partially explained by variations in the number of puffs and the depth and duration of inhalation. Large increments in nicotine delivery may be achieved by altering puffing behavior, even when the number of cigarettes remains constant. In a recent study Ashton et al. (1979) showed that smokers compensated so that their plasma nicotine was within two-thirds of the level yielded by their usual cigarettes when they switched to weaker brands. Learning to compensate efficiently may also require more time than most laboratory compensation studies provide.

Some epidemiological support for the nicotine compensation model can be drawn from consumption data for the smoking population. In recent decades, the nicotine content of individual brands of cigarettes in the United States has declined. One would expect at least a mild compensatory increase in the average number of cigarettes smoked, at least by long-term heavy smokers. In fact, such an increase can be seen for the years 1964-1975. As Figure 3 shows, the time series of average cigarette consumption per smoker for this period looks like an inverse function of the average nicotine yield of U.S. cigarettes. In other words, as nicotine yield per cigarette moved up or down, the number of cigarettes sold per smoker moved in the opposite direction, so that the total nicotine

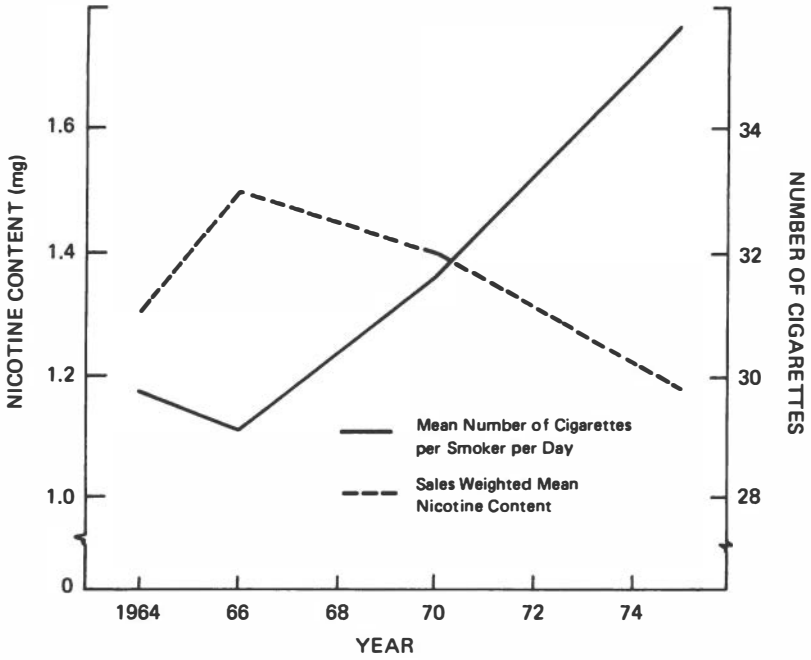

FIGURE 3 Average Weighted Nicotine Delivery and Mean Number of Cigarettes Smoked Per Smoker Per Day in the U.S., 1965-1976

Source: Schachter (1981).

yield stayed at roughly the same level. However, the selective drop-off in the proportion of lighter smokers affects these trends, so it is not warranted to relate these shifts exclusively to changes in nicotine levels.

Individual smokers exhibit wide differences in nicotine levels resulting from smoking. It can be presumed that individuals differ biologically, prior to significant use, in their sensitivity to nicotine effects, as with all other pharmacological agents; moreover, relative sensitivities may differ for different effects. New smokers may require some time to develop stable nicotine levels.

Stabilization of smoking patterns also depends on the extent to which increasing amounts of nicotine and probably other tobacco components are tolerated (Jaffe

1980). This process occurs in new smokers and perhaps in abstainers who have resumed smoking. Increases may stop when levels are reached that consistently result in unpleasant effects. There is no simple pharmacological answer to the question of why a smoker stabilizes at some relatively consistent level.

In principle, just as increasing the daily dose of tobacco probably increases the tolerance for unpleasant effects, so decreasing it might in time increase sensitivity to low doses of nicotine. Freedman and Fletcher (1976) found in a longitudinal study of smoking in natural situations that nicotine levels (determined by analyzing cigarette butts) stabilized at proportionally lower values when subjects switched to a lower-yield cigarette. However, from studies of people who are seeking to stop, it appears that at least some habitual smokers have lower limits of acceptable nicotine levels, below which they refuse to use milder cigarettes (Shapiro et al., 1971). It is commonly observed that habitual smokers often quickly return to their previous patterns following periods--even long ones--in which they have quit smoking but then resumed.

The value to an individual of lower T/N cigarettes and of other modes of reducing the dose of tobacco depends partially on how flexible the smoker's limits are. If the lower limit yields easily to downward adjustments, it should be practical to establish stable smoking at lower values. However, environmental factors--familiar situations, advertising, peer behavior, etc.--may be powerful obstacles or facilitators of change in concert with resistant biological mechanisms.

A NOTE ON CUTTING DOWN AND NEW SMOKERS

There has been little study of the psychological and physiological effects of simply cutting down without changing brands, although many individuals have adopted this control method and many clinical methods for smoking cessation use this technique as a transition to quitting altogether. In one experiment (Perlick, 1977), a group of heavy smokers was matched with a group composed mostly of formerly heavy smokers who were deliberately cutting down ("restrained smokers"). A control group of nonsmokers was also tested. In a

mock-experimental study of aircraft noise, these subjects rated the level of annoyance caused by simulated overflights while watching a television drama. The subjects had free access to either LOW T/N cigarettes, HIGH T/N cigarettes, or had NO cigarettes. The heavy smokers supplied with HIGH T/N and the nonsmokers recorded only half the annoyance levels of the "restrained smokers" and the heavy smokers supplied with LOW T/N. In a parallel finding, smoker subjects in the NO or LOW T/N condition ate twice as many jelly beans from a nearby jar as did HIGH T/N and nonsmoker subjects. In other studies, when compared either with continuing smokers or nonsmokers, deprived smokers have proven to be more irritable and anxious and less efficient at tasks requiring concentration, such as simulated driving tests (Heimstra et al., 1967; Nesbitt, 1973; Silverstein, 1976).

We have little information about the population that may be most affected by the availability of "light" and "low"-yield T/N cigarette brands: new smokers, especially adolescents and young adults. The perceived risks of entering a smoking career may be minimized by belief in the relative safety of lighter cigarettes. Yet there is virtually no evidence on how initial selection from among brands that vary widely in nicotine and other constituents affects long-term smoking patterns or their effects on health. There is also little evidence regarding the distribution of minimally acceptable strength of cigarettes in the new smoker population, a question that in part must relate to individual sensitivities to the components of tobacco smoke. In short, little as is known about the dynamics of smoking in established populations, even less is known about new smokers.

TOWARD A RESEARCH PROGRAM ON ALTERNATIVES

INTRODUCTION

The preceding sections of this report consider the problems facing the determined smoker whose dilemma is how to continue the habit with less risk. Unfortunately, we cannot advise the persistent smoker except to quit smoking entirely. More information on the relative toxicities of different constituents of tobacco smoking, the role of nicotine in promoting and maintaining smoking, the nature and consequences of compensatory smoking practices, and the relationship of these issues to rates of tobacco-associated diseases would be useful.

We propose a research agenda designed to clarify the effects of different tobacco-using alternatives, an agenda that can be put into effect without having to develop radical new technologies. By following existing research leads, standardizing methods and materials, and emphasizing questions related to alternatives to cessation, a focused research program should yield a clearer set of choices for the persistent smoker. This program does not directly address the basic questions of why people smoke and how smoking is a part of our social fabric; for these questions the time perspective may be decades. What we propose here is more short-range and focused in application.

This discussion of research begins with the cigarette, proceeds to smoking behavior and other forms of tobacco use, and ends with health effects. Following the narrative, there is a summary of the research recommendations annotated to reflect our judgments about their relative priority.

CIGARETTE RESEARCH AND DEVELOPMENT

Most studies on smoking have utilized the cigarettes available in the marketplace. Brands differ from country to country and manufacturers periodically change their composition, making comparisons between studies difficult. Chemical purity and the capacity to specify the doses used in an experiment are essential for research; it is crucial that studies of smoking have reproducible cigarette specifications. It is well within existing technical capacities to develop standardized cigarettes for research. A conference on needed research materials convening the major active investigators could outline specifications for these products. Once such cigarettes are available, scientists will be quick to employ them in research.

It is especially important to uncouple the nicotine and tar yields of cigarettes. In existing commercial brands the two are correlated at approximately 0.9, but there is no reason why nicotine cannot be varied independently of tar for research purposes. The degree to which particular smokers specifically seek nicotine could be clarified more readily if cigarettes with high or medium nicotine levels and low levels of "everything else" were standardized and used in appropriate studies. Increasing the nicotine content[2] (while holding the other toxins low) could result in the smoking of fewer cigarettes and perhaps less intensive puffing by nicotine-seeking smokers, so that the persistent smoker might receive less exposure to most of the other hazardous constituents in cigarettes (Russell, 1980). Possibly, however, with a reduction in the other noxious

[2]There seem to be no legal obstacles to adding nicotine to tobacco products. In the past, Jarvik and associates (Goldfarb et al., 1970) added nicotine to available tobaccos for experiments under an investigational drug license from the Food and Drug Administration. Our inquiries revealed that the Food and Drug Administration has no current jurisdiction over tobacco or nicotine; relevant authority lies with the Bureau of Alcohol, Tobacco, and Firearms of the Treasury Department, which has no restrictions on adding nicotine to tobacco products.

components, smokers might take in more nicotine than before. More information on the chronic effects of the doses of nicotine and other compounds delivered by such cigarettes is needed before any scientific judgment can be rendered on the health hazards of medium-nicotine, low-tar cigarettes.

Carbon monoxide appears to play a significant role in health effects and may even contribute to the maintenance of smoking behavior. Experimental cigarettes in which CO yield varies independently of nicotine and tar should also be developed.

An account of cigarette sales and composition of the products could be an important adjunct for epidemiological studies based on smoking in earlier periods. Most epidemiological analyses of smoking have included rather inadequate information about what was in the cigarettes people smoked. Intact samples of old cigarette brands by tobacco companies or private individuals might be obtained to expand this information (see Wald et al., 1981). Research to organize this information and make it available should be relatively inexpensive and valuable for illuminating existing findings or for new studies of the older smoking population.

DELIVERY AND ABSORPTION OF TOBACCO PRODUCTS

Research on the role of nicotine in the development and maintenance of smoking would be considerably advanced by the development of a quick and economical method for measuring plasma levels of nicotine and its metabolites. Most studies to date to assess the reinforcing properties of smoking have relied on such indirect measures as reports of the number of cigarettes smoked or observation of daily smoking patterns. Measuring nicotine effects within the brains of smoking subjects might be preferable, but measuring body levels of nicotine is the only practical method.

There are adequate analytic methods for determining the body level of carbon monoxide in expired air or as carboxyhemoglobin in the blood. However, more convenient methods of measuring body levels of other constituents of tobacco believed to be toxic in the doses present (e.g., acrolein, oxides of nitrogen) are needed.

The taste of cigarettes, a result of the natural constituents in tobacco smoke and of added flavors,

might be important in building preferences for different brands of cigarettes. Studies that manipulate olfactory and taste factors could help in the development of cigarettes that are low in toxicity but highly acceptable for taste-related reasons.

Individual differences in what people seek in smoking should be examined. One plausible hypothesis is that most heavy users (defined by number of cigarettes smoked) are addicted to nicotine and that many light users are primarily under the control of non-pharmacological reinforcers (Kozlowski, 1979). Among the latter, social approval, oral gratification, conditioned relaxation, and adjunctive behaviors have been proposed. Results of a pilot study (Russell and Feyerabend, 1978) suggest that individuals differ in their patterns of nicotine levels: there appear to be peak enhancers, who maximize brief, pleasurable episodes of fast nicotine absorption, and trough maintainers, who try to keep just above a minimum level of blood nicotine to avoid withdrawal effects. (A similar dichotomy was proposed for heroin addicts by McAuliffe and Gordon, 1974). The study of nicotine levels across patterns of smoking would help to establish a typology of smokers and identify the relative importance of nicotine in maintaining the habit (itself one dimension of the typology).

STANDARDIZED MEASURES OF SMOKING BEHAVIOR

The ways in which people smoke determine how much of the potentially hazardous contents of a cigarette actually reach them. Studies on smoking have often used the number of cigarettes consumed as the principal dependent variable. More recent studies of compensation include measures of a number of components of smoking behavior, such as puff intensity, volume, and duration, that affect what is finally absorbed into the lungs. However, studies vary widely in the measures and instrumentation used. It would be useful to establish working conventions on measures of smoking behavior and to develop relatively standard procedures and devices that could be efficiently used by investigators. There is sufficient agreement on the important segments of the smoking process to encourage some standardization of variables and methods.

It should be emphasized that measurement of body levels of smoke constituents will not serve as substitutes for measurements of smoking behavior. Smoking behavior patterns are unlikely to be strictly or perfectly dependent on body levels of nicotine, for example. Social conditions, previous habit patterns, taste, toxic side effects, etc. are all likely to contribute to smoking behavior and thus mediate between tobacco products and nicotine-related demand in smokers.

Data about "spontaneous" smoking behavior that is not strongly affected by situations calling forth attempts at control (e.g., clinical settings) or by elaborate measurement procedures are necessary in order to assess the validity of laboratory studies. Smoking behavior could be recorded in samples of smokers in natural settings, some of whom could also be laboratory subjects for comparison. Miniaturized instrumentation would be required for field studies because valid comparisons call for a minimum of intrusiveness to the subject. Miniaturized equipment might be installed, for example, in cigarette holders (Henningfield et al., 1980).

In the United States, the FTC's standard pattern for how a smoking machine puffs on a cigarette governs the current estimates of what brands of cigarettes deliver. As we have seen, any setting used to establish a single standard is more rigid than the behaviors of individual smokers. Reference standards that display how deliveries of different constituents change when smoking machine parameters change are needed for research (Kozlowski, 1981).

Dose-response experiments, in which the smoker uses a range of cigarettes from high-nicotine/low-tar to low-nicotine/high-tar, should demonstrate predictable changes in smoking behavior, tracking levels of nicotine, if the nicotine addiction hypothesis is correct. Also, anecdotal reports that very low cigarettes "aren't worth the effort" may suggest why compensation is not a completely orderly process (Russell, 1980); this conjecture should be tested. Dose-response studies should include attempts to uncouple taste from nicotine and to reveal whether substances other than nicotine are also functioning as reinforcers.

It is not known whether knowledge about compensation can help brand-switching smokers control their

tendencies to compensate. Inhibition of compensatory puffing may require such constant vigilance as to be impractical for most smokers. Self-control of smoking behavior may vary in response to situational factors. Highly focused activities like reading and problem solving may reduce awareness for the smoker attempting to control compensation; however, appropriate training may enable some smokers to achieve control. These questions should be investigated; they are amenable to testing using existing methods, in both the laboratory and the field.

STUDIES OF ALTERNATIVES

What are the prospects for commercial tobacco alternatives other than cigarettes? Pipes and cigars are older forms of smoking tobacco leaf than are cigarettes. There is evidence that inhalation of cigar smoke into the lungs bears risks comparable to inhalation of cigarette smoke. Most pipe and cigar smokers do not inhale, however, and have substantially lower health risks than cigarette smokers. Nevertheless, habitual cigarette users who adopt pipe or cigar smoking as an alternative to quitting may run continued higher risks from these alternatives because they find it difficult to suppress their habitual pattern of inhaling. Studies of inhalation among pipe and cigar smokers show uniformly higher smoke inhalation among those who are former or concurrent cigarette smokers than those who are not (U.S. Department of Health, Education, and Welfare, 1979).

Tobacco chewing and the use of snuff and nicotine chewing gum are possible alternatives for achieving some of the effects of tobacco by supplying nicotine while eliminating the numerous combustion products associated with smoking. Russell et al. have demonstrated that pinches of dry snuff can produce the same peak levels of plasma nicotine as do cigarettes. They have suggested that "snuff could save more lives and avoid more ill health than any other preventive measure likely to be available to developed nations, well into the twenty-first century" (Russell et al., 1980:475). While this statement is quite speculative (see Winn et al., 1981), the advantages and disadvantages of non-

smoking tobacco alternatives deserve serious attention. Study of these alternatives, including their health effects, their introduction in smoking cessation programs, and their relative nicotine delivery, should be initiated.

SMOKERS' RESPONSES TO EXISTING ALTERNATIVES

The research strategies discussed so far emphasize the analysis of the smoking process and the kinds of control required in the laboratory and the field. However, millions of smokers have already switched to lower T/N cigarettes, and significant numbers have switched to other forms of tobacco. It is important to find out what has guided these choices, how stable selections are, how new smokers are affected by the wider range of alternatives now available to them, and whether there are any patterns of switching that regularly lead to progressively less hazardous tobacco use or to cessation.

What people believe about the health risks associated with their choices of alternatives is important for understanding brand switching or adoption of other forms of tobacco ingestion. Careful surveys can provide much of this information. Questions should include to what extent switchers to "light" or "low"-yield brands or to pipes or cigars believe that their health is made more secure by their choice; whether they think that gains in health are proportional to the advertised T/N ratings of the lower-yield brands; how satisfying the alternatives they have selected are; and how much additional switching occurs after the initial choice, including reverting to their original brand preference.

As noted above, studies of clinic-based smoking cessation suggest that for many smokers there is a minimum nicotine level cigarette that is acceptable, below which they prefer no cigarette at all to a lower-strength alternative (Kozlowski, 1979). Survey data can reveal the extent of this effect outside the clinic.

There has been much discussion of peer pressures on adolescents and other determinants of the choice to smoke (e.g., U.S. Department of Health, Education, and Welfare, 1979), yet we know little about how particular brands are selected. Smokers who take up the habit today are faced with a quite different array of brand

choices from that available to the new smoker of two decades ago. We would like to know in what ways the merchandizing of modern cigarettes affects the induction of new smokers. For many smokers health warnings may have been effectively counteracted by beliefs that "light" or "low"-yield cigarettes are safe--not because such claims are found in cigarette advertising, but because the buyer concludes that a manufacturer who emphasizes lower levels of T/N must believe that such levels are safer. Conversely, the promotion of lower-yield cigarettes may be an effective warning to many people of the toxic, health-threatening nature of smoking.

Doubtless more individuals experiment with smoking in their childhood than become habitual users. There are many anecdotal reports of an early sickness experience in which an overdose of tobacco inhibited further interest in smoking. The legendary father who administered a five-cent cigar to the child caught smoking and required that it be smoked to the end possibly produced an effect that has been described in animal studies: conditioned taste aversions (Garcia et al., 1975). These reports give credence to the speculation that one extreme illness experience may produce a life-long nonsmoker (Garcia et al., 1955). Assuming that in the past these reactions have accounted for some people being nonsmokers, what are the effects of lower T/N on adoption of the habit in children today? It would be valuable to know whether initial experience with lower- rather than higher-yield cigarettes changes the likelihood of continued smoking by children.

The number of studies on the possibly harmful effects of attempts to reduce smoking should to be expanded. While the quitter usually experiences a period of intense craving for cigarettes, sometimes accompanied by physical withdrawal distress, the smoker who switches or cuts down may experience chronic abstinence effects. It is possible that these phenomena are more significant for the health and behavior of smokers than has been suspected. As noted above, preliminary evidence indicates that irritability, concentration, and eating patterns may be significantly affected. Individuals whose life patterns subject them to unusual levels of stress may be especially vulnerable to withdrawal effects. These possibilities are firm enough to call for laboratory and field studies.

Is the decision to switch to a lower strength brand the first step on the road to quitting? Encouraging or discouraging brand switching ought to be based in part on the relationship of switching to quitting. If it were true that all switchers soon quit, then we need not be concerned about the incidence or strength of compensation. However, it is likely that the more cigarettes smoked daily, the lower the probability of quitting. It is possible that the availablity of lower T/N cigarettes has encouraged continued smoking by some who might otherwise have quit. Epidemiological methods are available for providing contingent probabilities on the major alternative outcomes, but thus far investigators have not conducted the appropriate studies.

The use of pipes, cigars, chewing tobacco, snuff, and--when available--nicotine chewing gum probably differs according to smoking history. Research on heavy, moderate, and occasional cigarette smokers can assess the utility of noncigarette alternatives for reducing the user's cumulative dose from tobacco products. Natural histories of switching to these alternatives would seem to be a good starting point. Social and economic factors--acceptability, symbolism (e.g., pipe smoker = professor; tobacco chewer = cowboy), availability, and price--appear to play an important part in the current prevalence of each of these alternatives. Greatly increased use might occur if the health outcomes of switching to these options prove favorable relative to lighter cigarette alternatives and if the information is effectively communicated.

HEALTH EFFECTS

A major consideration in weighing the value of alternative tobacco products and uses is their effects on health. The kinds of epidemiological studies that have revealed risks of cancer, cardiovascular disease, and lung disorders have to be continued with specific attention to the smokers who are selecting various alternatives, including shifting cigarette brands. While shifts that actually reduce the absorption of nicotine, tar, and carbon monoxide are presumably desirable, the extent to which natural compensatory behaviors maintain previous levels of these substances

in the body, and hence diminish or eliminate the health gains, needs assessment, not only in the laboratory but also in naturalistic field studies.

Prospective and retrospective studies are necessary to track the symptom formation, morbidity, and mortality of different kinds of tobacco users. One approach is to compose panels of subjects whose health status is periodically measured in relation to what kinds of tobacco products they are consuming. Alternatives other than cigarettes should be included in these studies. Pipes and cigars may be as hazardous as cigarettes to the former cigarette smoker who continues to inhale the smoke; chewing tobacco and snuff may entail specific risks of mouth or nose cancers and other diseases. Nicotine chewing gum is now available on prescription in Canada; we should at least keep a close eye on Canadian studies.

Finally, data on sample populations to monitor absolute changes in morbidity and mortality across time are a critical element in the construction of scientific knowledge and public policy on smoking. Analyses of epidemiological data bases to assess changes over time in absolute rates of morbidity and mortality among types of smokers and among nonsmokers are very important. The major prospective and repeated time series mortality studies have not been updated since the early 1970s (Enstrom and Godley, 1980; Rogot and Murray, 1980; Garfinkel, 1981).

SPECIFIC RESEARCH RECOMMENDATIONS

This section is a summary list of the studies and development efforts we recommend in each of the categories we have discussed above. The recommendations are ordered by priority within each category. Asterisks are used to denote the studies with highest priority overall.

CIGARETTE RESEARCH AND DEVELOPMENT

- *We recommend developmental engineering to produce standardized experimental cigarettes for research. Such cigarettes should cover a range of different alternatives from high-nicotine/low-tar to low-nicotine/high-tar and should include the capacity to vary tastes (using standardized flavorings) and carbon monoxide independently of nicotine and tar.
- Historical studies should be undertaken to describe the construction and composition of cigarettes that were formerly available commercially. These findings and associated sales data would improve the interpretation of retrospective epidemiological studies on smoking.

DELIVERY AND ABSORPTION OF TOBACCO PRODUCTS

- *We recommend the refinement of techniques for measuring body levels of nicotine, gases, and other key residues of tobacco use. An

emphasis on economy, speed, and efficiency will encourage the use of such assays in most smoking experiments.

- *We recommend that studies test behavioral typologies of smokers (e.g., "peak enhancers" versus "trough maintainers") by measuring body levels of nicotine or other key components of smoke.
- Methods for more precise measurement of "taste" need to be developed.

STANDARDIZED MEASURES OF SMOKING BEHAVIOR

- *We recommend the standardization of apparatuses and procedures for measuring smoking behavior. This can be encouraged by convening a technical conference of major investigators.
- *We recommend that parametric studies on smoking machines be initiated to measure the delivery of nicotine, tar, and carbon monoxide so as to reflect a variety of puffing patterns rather than one arbitrary standard. It should be possible to develop standard tables displaying the data from these parametric studies for the entire range of available brands and, when they are available, experimental cigarettes.
- Improvements should be encouraged in both miniaturized equipment for field recording of smoking behavior, e.g., packaging instrumentation in cigarette holders, and in reliable, unobtrusive methods for recording smoking behavior, which have the same purposes as miniaturized instrumentation but trade off precision for flexibility.

TESTING THE ADDICTION MODEL

- *We recommend investigation of individual differences in what the smoker is seeking, especially in relation to nicotine reinforcement versus nonnicotine reinforcers. This includes studies to uncouple "taste" from nicotine and to determine whether taste preferences are conditioned reinforcers, i.e., they extinguish when not associated with nicotine.

- *We recommend continued studies on compensation for nicotine, using standardized experimental cigarettes with varied tar/nicotine ratios, and measuring changes in smoking behavior in relation to nicotine. Research should focus on the utility of cybernetic models of nicotine demand, with an emphasis on conditions for resetting the demand levels, such as prolonged intake of lower levels of nicotine. If other cigarette constituents prove to be significant reinforcers, studies of these factors should be encouraged as well.
- Researchers have yet to study whether and how knowledge of compensation and its health consequences can be used by the smoker (or by others in conjunction with the smoker) to inhibit compensatory smoking, and, conversely, what factors enhance "automatic" compensation.
- Research should be initiated to study the distribution of individual differences in sensitivity to nicotine's reinforcing and toxic effects in smokers and nonsmokers.
- Studies should be conducted of response cost factors (i.e., relatively unrewarded effort) that may lead to the extinction of smoking with very low nicotine-yielding cigarettes.
- The addiction model should be tested with tobacco products other than cigarettes, considering alternatives to delivery via the lungs for satisfying nicotine demand.

SMOKERS' RESPONSES TO EXISTING ALTERNATIVES

- *We recommend research to determine whether and how switching is a gateway to quitting or inhibits quitting.
- *We recommend studies on how beliefs about health risks associated with different alternatives affect choices, and on factors that shape these beliefs. This research ought to include surveys of attitudes toward "light" and "low"-yield cigarettes, pipes, cigars, and other alternatives; surveys to determine the role of T/N labels on perceptions of health risks, including the initial choices of new smokers; and natural history studies of brand switching.

- Studies of acute and chronic abstinence effects in nicotine withdrawal should be undertaken, including an assessment of the range of human actions that may be affected.
- The relative role of toxic side effects in discouraging the adoption of the smoking habit should be studied in relation to "low"-yield cigarettes.
- Natural histories of the adoption and use of pipes, cigars, chewing tobacco, and snuff as alternatives to cigarette smoking should be recorded.

HEALTH EFFECTS

- *We recommend the continued prospective and retrospective epidemiological study of the health effects of brand switching and yield reduction in cigarettes and other tobacco alternatives.

APPENDIX

Among women over 25, heavy smoking has increased dramatically since 1955, reaching at least double the 1955 levels in all age groups 25 years and older (see Figure 4). Concomitantly, respiratory system cancer death rates have increased two to four times the earlier levels (Figure 5). Thus, even if the minimum number of men (given the overall sales figures) were smoking the newer cigarettes, which have brought down the average T/N yield, the women who would then have been using them almost exclusively have shown no discernible improvement in this index. Figures 4 and 5 are strictly parallel to Figures 1 and 2 in the text, which describe trends in current cigarette smoking and respiratory system cancer among men. However, there are no available estimates of lifetime smoking exposure among women, as Horn (1977) has supplied for men, so we are unable to construct a parallel of Table 1 for women.

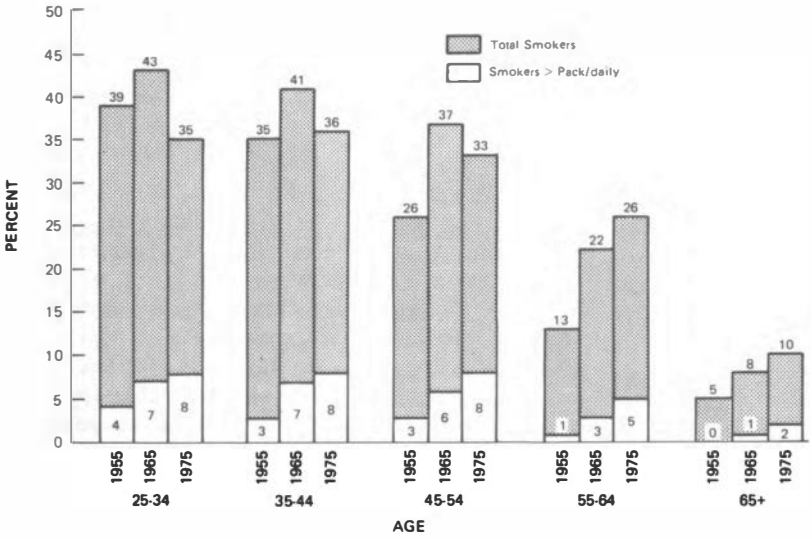

FIGURE 4 Estimated Prevalence of Current Cigarette Smoking by U.S. Women, 1955, 1965, 1975

Sources: Haenszel et al. (1956); Ahmed and Gleason (1970); USDHEW (1976, 1980).

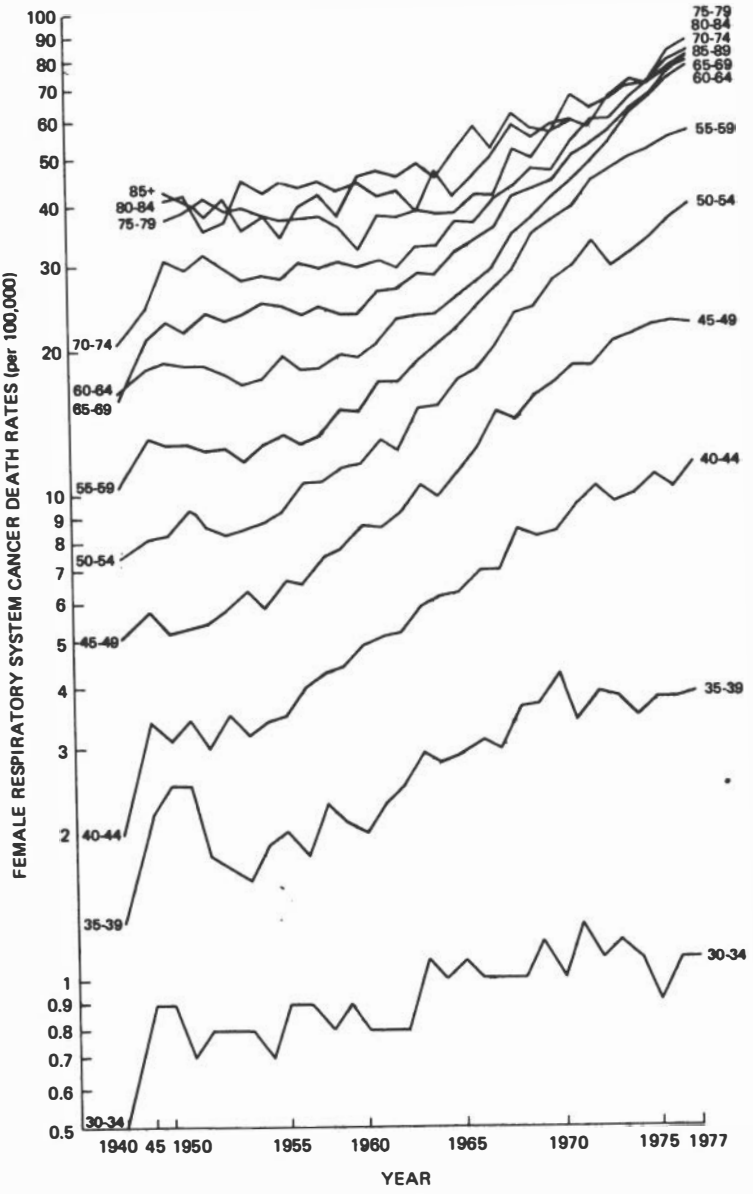

FIGURE 5 Female Respiratory System Cancer Death Rates per 100,000, 1940-1977

Source: U.S. Vital and Health Statistics (annual).

REFERENCES

Ahmed, P.I., and Gleason, G.A. (1970) Changes in Cigarette Smoking Habits between 1955 and 1966. Public Health Service Publication No. 1000, Series 10, No. 59, April 1970. Washington, D.C.: U.S. Government Printing Office.

Ashton, H., Stepney, B., and Thompson, J.W. (1979) Self-titration by cigarette smokers. British Medical Journal Aug 11:357-360.

Auerbach, O., Hammond, E.C., and Garfinkel, L. (1979) Changes in bronchial epithelium in relation to cigarette smoking, 1955-1960 vs. 1970-1977. New England Journal of Medicine 300(8):381-386.

Bock, F.G. (1980) Carcinogenic properties of nicotine. Pp. 129-140 in G.B. Gori and F.G. Bock, eds., A Safe Cigarette? Banbury Report no. 3. Cold Spring Harbor, N.Y.,: Cold Spring Harbor Laboratory.

Burch, P.R.J. (1980) Smoking and lung cancer. Tests of a causal hypothesis. Journal of Chronic Diseases 13:221-228.

Castelli, W.P., Dawber, T.R., Feinlieb, M., Garrison, R.J., McNamara, P.M., and Kannel, W.B. (1981) The filter cigarette and coronary heart disease: the Framingham study. Lancet (July 18):109-113.

Doll, R., and Peto, R. (1981) The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. Journal of the National Cancer Institute 66(6):1192-1308.

Enstrom, J.E. (1979) Rising lung cancer mortality among non-smokers. Journal of the National Cancer Institute 62(4):755-760.

Enstrom, J.E., and Godley, F.H. (1980) Cancer mortality among a representative sample of nonsmokers in the

United States during 1966-68. Journal of the National Cancer Institute 65(5):1175-1183.

Finnegan, J.K., Larson, P.S., and Haag, H.B. (1945) The role of nicotine in the cigarette habit. Science 102:94-96.

Frederiksen, L.W., and Martin, J.E. (1979) Carbon monoxide and smoking behavior. Addictive Behaviors 4:21-30.

Freedman, S., and Fletcher, C.M. (1976) Changes in smoking habits and cough in men smoking cigarettes with 30% NSM tobacco substitute. British Medical Journal 1:1427-1430.

Garcia, J., Kimeldorf, D.J., and Koelling, R.A. (1955) Conditioned aversion to saccharin resulting from exposure to gamma radiation. Science 122:157-158.

Garfinkel, L. (1980) Changes in number of cigarettes smoked compared to changes in tar and nicotine content over a 13-year period. Pp. 19-28 in G.B. Gori and F.G. Bock, eds., A Safe Cigarette? Banbury Report no. 3 pp. 19-28. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory.

Garfinkel, L. (1981) Trends in lung cancer mortality among non-smokers, and a note on passive smoking. Journal of the National Cancer Institute 66(6):1061-1066.

Gerstein, D.R. (1975) Heroin in Motion: A Working Paper in the Theory of Action. Unpublished doctoral dissertation, Department of Sociology, Harvard University.

Goldfarb, T.L., Jarvik, M.E., and Glick, S.D. (1970) Cigarette nicotine content as a determinant of human smoking behavior. Psychopharmacologia 17:89-93.

Gori, G.B. (1980) Less hazardous cigarettes: theory and practice. Pp. 251-279 in G.B. Gori and F.G. Bock, eds., A Safe Cigarette? Banbury Report no. 3. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory.

Gori, G.B., and Lynch, C.J. (1976) Toward less hazardous cigarettes: current advances. Journal of the American Medical Association 240(12): 1255-1259.

Guerin, M.R. (1980) Chemical composition of cigarette smoke. Pp. 191-204 in G.B. Gori and F.G. Bock, eds., A Safe Cigarette? Banbury Report no. 3. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory.

Haenszel, W., Shimkin, M.B., and Miller, H.S. (1956) Tobacco Smoking Patterns in the United States. Public Health Service Monograph No. 45; Public Health Service Publication No. 463. Washington, D.C.: U.S. Government Printing Office.

Hammond, E.C., Garfinkel, L., Seidman, H., and Lew, E.A. (1977) Some recent findings concerning cigarette smoking. Pp. 101-112 in H.H. Hiatt, J.D. Watson, and J.A. Winsten, eds., Origins of Human Cancer. Book A. Incidence of Cancer in Humans. Cold Spring Harbor Conferences on Cell Proliferation, Volume 4. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory.

Hawthorne, V.M., and Fry, J.S. (1978) Smoking and health: cardiorespiratory disease, mortality, and smoking behavior in west central Scotland. Journal of Epidemiology and Community Health 32:260-266.

Heimstra, N.W., Bancroft, N.R., and DeKock, A.R. (1967) Effects of smoking upon sustained performance in a simulated driving task. Annals of the New York Academy of Sciences 142:295-307.

Henningfield, J.H., Yingling, J., Griffiths, R.R., and Pickens, R. (1980) An inexpensive portable device for measuring puffing behavior by cigarette smokers. Pharmacology, Biochemistry, and Behavior 12:811-813.

Herman, C.P., and Kozlowski, L.T. (1979) Indulgence, excess, and restraint: perspectives on consummatory behavior in everyday life. Journal of Drug Issues 9(2):185-196.

Herning, R.I., Jones, R.T., Bachman, J., and Mines, A.H. (1981) Puff volume increases when low-nicotine cigarettes are smoked. British Medical Journal 283:187-189.

Higgenbottam, T., Shipley, M.J., Clark, T.J.H., and Rose, G. (1980) Lung function and symptoms of cigarette smokers related to tar yield and number of cigarettes smoked. Lancet (February 23):409-412.

Horn, D. (1977) The benefits of stopping smoking. Pp. 59-64 in J. Steinfeld, W. Griffiths, K. Ball, and R.M. Taylor, eds., Smoking and Health: Proceedings of the Third World Conference on Smoking and Health, New York City, June 2-3, 1975. Volume II: Health Consequences, Education, Cessation, and Governmental Action. DHEW Publication No. (NIH) 77-1413. Washington, D.C.: U.S. Government Printing Office.

Jaffe, J.H. (1980) Drug addiction and drug abuse. Pp. 535-584 in A.G. Gilman, L.S. Goodman, and A. Gilman, eds., The Pharmacological Basis of Therapeutics. Sixth edition. New York: Macmillan.

Jaffe, J.H., Kanzler, M., Friedman, L., Stunkard, A.J., and Vereby, K. (1981) Carbon monoxide and thiocyanate levels in low tar/nicotine smokers. Addictive Behaviors 6(4):337-343.

Jaffe, J.H., Kanzler, M., Freedman, L., and Kaplan, J. (1982) Money and health messages as incentives for smoking low tar/nicotine cigarettes: changes in consumption and exhaled carbon monoxide. British Journal of the Addictions 77:21-34.

Jenkins, R.A., Quincy, R.B., and Guerin, M.R. (1979) Selected Constituents in the Smokes of U.S. Commercial Cigarettes: "Tar," Nicotine, Carbon Monoxide, and Carbon Dioxide. Oak Ridge, Tenn.: Oak Ridge National Laboratories.

Kozlowski, L.T. (1979) Psychosocial influences on cigarette smoking. Pp. 97-125 in N. Krasnegor, ed., The Behavioral Aspects of Smoking. National Institute on Drug Abuse Research Monograph No. 26, DHEW Publication No. (ADM) 79-882. Washington, D.C.: U.S. Government Printing Office.

Kozlowski, L. (1981) Tar and nicotine delivery of cigarettes: what a difference a puff makes. Journal of the American Medical Association 245(2):158-159.

Kozlowski, L.T., Jarvik, M.E., and Gritz, E.R. (1975) Nicotine regulation and cigarette smoking. Clinical Pharmacology and Therapeutics 17:93-97.

Kozlowski, L.T., Rickert, W.S., Robinson, J.C., and Grunberg, N.E. (1980) Have tar and nicotine yields of cigarettes changed? Science 209:1551-1552.

Krasnegor, N., ed. (1979) Cigarette Smoking as a Dependence Process. Symposium proceedings. DHEW Publication no. (ADM) 79-800. Rockville, Md.: National Institute on Drug Abuse.

Kumar, R., Cooke, E.C., Lader, M.H., and Russell, M.A.H. (1977) Is nicotine important in tobacco smoking? Clinical Pharmacology and Therapeutics 21:520-529.

Lee, P.N., and Garfinkel, L. (1981) Mortality and type of cigarette smoked. Journal of Epidemiology and Community Health 35:16-22.

Levine, H.G. (1978) The discovery of addiction: changing conceptions of habitual drunkenness in America. Journal of Studies on Alcohol 39(1):143-177.

Lucchesi, B.R., Schuster, C.R., and Emley, G.S. (1967) The role of nicotine as a determinant of cigarette smoking frequency in man with observations of certain cardiovascular effects associated with the tobacco alkaloid. Clinical Pharmacology and Therapeutics 8:789-796.

McAuliffe, W.E., and Gordon, R.A. (1974) A test of Lindesmith's theory of addiction: the frequency of euphoria among long-term addicts. American Journal of Sociology 79(4):795-840.

National Research Council (1977) Carbon Monoxide. Subcommittee on Carbon Monoxide, Committee on Medical and Biological Effects of Environmental Pollutants. Washington, D.C.: National Academy of Sciences.

National Research Council (1980) The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980. Committee on Biological Effects of Ionizing Radiation. Washington, D.C.: National Academy Press.

Nesbitt, P.D. (1973) Smoking, physiological arousal, and emotional response. Journal of Personality and Social Psychology 25:137-145.

Owen, T.B. (1976) Tar and nicotine from U.S. cigarettes: trends over the past twenty years. Pp. 73-89 in E.L. Wynder, D. Hoffman, and G.B. Gori, eds., Smoking and Health: Proceedings of the Third World Conference on Smoking and Health, New York City, June 2-3, 1975: Volume I: Modifying the Risks for the Smoker. USDHEW Publication No. (NIH) 76-1221. Washington, D.C.: U.S. Government Printing Office.

Perlick, D. (1977) The Withdrawal Syndrome: Nicotine Addiction and the Effects of Stopping Smoking in Heavy and Light Smokers. Unpublished doctoral dissertation, Department of Psychology, Columbia University.

Rawbone, R.G., Murphy, K., Tate, M.E., and Kane, S.J. (1978) The analysis of smoking parameters: inhalation and absorption of tobacco smoke in studies of human smoking behavior. Pp. 171-194 in R.E. Thornton, ed., Smoking Behavior: Physiological and Psychological Influences. Edinburgh: Churchill Livingstone.

Robinson, J.C., and Forbes, W.F. (1975) The role of carbon monoxide in cigarette smoking. Archives of Environmental Health 30:425-434.

Rogot, E., and Murray, J.L. (1980) Smoking and causes of death among U.S. veterans: 16 years of observation. Public Health Reports 95(3):213-222.

Rosenberg, J., Benowitz, N.L., Jacob, P., and Wilson, M.K. (1980) Disposition kinetics and effects of intravenous nicotine. Clinical Pharmacology and Therapeutics 28:512-522.

Russell, M.A.H. (1976) Tobacco smoking and nicotine dependence. In R.J. Gibbins, Y. Israel, H. Kalant, R.E. Popham, W. Schmidt, and R.G. Smart, eds., Research Advances in Alcohol and Drug Problems, Volume 3. New Work: Wiley.

Russell, M.A.H. (1980) The case for medium-nicotine, low tar low-CO cigarettes. Pp. 297-308 in G.B. Gori and F.G. Bock, eds., A Safe Cigarette? Banbury Report no. 3. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory.

Russell, M.A.H., and Feyerabend, C. (1978) Cigarette smoking: a dependence on high-nicotine boli. Drug Metabolism Reviews 8(1):29-57.

Russell, M.A.H., Jarvis, M.J., and Feyerabend, C. (1980) A new age for snuff? Lancet (March 1): 474-475.

Schachter, S. (1977) Nicotine regulation in light and heavy smokers. Journal of Experimental Psychology (General) 106:5-12.

Schachter, S. (1978) Pharmacological and psychological determinants of smoking. Annals of Internal Medicine 88(1):104-114.

Schachter, S. (1981) Nicotine addiction and the withdrawal syndrome. Pp. 276-284 in Greenhalgh, Roger M., ed., Smoking and Arterial Disease. London: Pittman Medical.

Schachter, S., Silverstein, B., and Kozlowski, L.T. (1977) The effects of stress on cigarette smoking and urinary pH. Journal of Experimental Psychology (General) 106:24-30.

Selikoff, I.J., and Hammond, E.C. (1975) Multiple risk factors in environmental cancer. In J.E. Fraumeni, ed., Persons at High Risk of Cancer. New York: Academic Press.

Shapiro, D., Schwartz, G.E., Tursky, B., and Scheidman, S.R. (1971) Smoking on cue: a behavioral approach

to smoking reduction. Journal of Health and Social Behavior 12:108-113.

Silverstein, B. (1976) An Addiction Explanation of Cigarette-Induced Relaxation. Unpublished doctoral dissertation, Department of Psychology, Columbia University.

Stolerman, I.P., Goldfarb, T.L., Fink, R., and Jarvik, M.E. (1973) Influencing cigarette smoking with nicotine antagonists. Psychopharmacologia 28:247-259.

Turner, J.A.McM., Sillett, R.S., and Ball, K.P. (1974) Some effects of changing to low-tar and low-nicotine cigarettes. Lancet (2):737-739.

U.S. Bureau of the Census (annual) U.S. Vital and Health Statistics. Washington, D.C.: U.S. Government Printing Office.

U.S. Department of Health, Education, and Welfare (1976) Adult Use of Tobacco--1975. Issued jointly by the Prevention Branch, Division of Cancer Control and Rehabilitation, National Cancer Institute, and the Center for Disease Control. Washington, D.C.: U.S. Public Health Service.

U.S. Department of Health, Education, and Welfare (1979) Smoking and Health: A Report of the Surgeon General. Publication No. USDHEW (PHS) 79-50066. Supt. of Doc. no. 0-293-011. Washington, D.C: U.S. Government Printing Office.

U.S. Department of Health, Education, and Welfare (1980) Health, United States: 1979. Publication no. USDHEW (PHS) 80-1232. Supt. of Doc. no. 0-316-014. Washington, D.C.: U.S. Government Printing Office.

U.S. Department of Health and Human Services (1981) The Health Consequences of Smoking: The Changing Cigarette. A Report of the Surgeon General. Supt. of Doc. no. 017-002-00149-6. Washington, D.C.: U.S. Government Printing Office.

U.S. Department of Health and Human Services (1982) The Health Consequences of Smoking: Cancer. A Report of the Surgeon General. Publication no. DHHS (PHS) 82-50179. Washington, D.C.: U.S. Government Printing Office.

Wakeham, H. (1976) Sales weighted average tar and nicotine deliveries of U.S. cigarettes from 1957 to present. Pp. 151-152 in E.L. Wynder and S. Hecht, eds., Lung Cancer. UICC Technical Report Series,

Volume 25. Geneva: International Union Against Cancer.

Wald, N.J. (1976) Mortality from lung cancer and coronary heart disease in relation to changes in smoking habits. Lancet (January 17):136-138.

Wald, N., Doll, R., and Copeland, G. (1981) Trends in tar, nicotine, and carbon monoxide yields of UK cigarettes manufactured since 1934. British Medical Journal 282:763-765.

Wald, N.J., Idle, M., Boreham, J., Bailey, A., and Bunakis, H.V. (1981) Serum cotinine levels in pipe smokers: evidence against nicotine as cause of coronary heart disease. Lancet (Oct. 10):775-777.

Winn, D.M., Blot, W.J., Shy, C.M., Pickle, L.W., Toledo, A., and Fraumeni, J.F. (1981) Snuff dipping and oral cancer among women in the southern United States. New England Journal of Medicine 304(13):345-349.

Wynder, E.L. and Stellman, S.D. (1979) Impact of long-term cigarette usage on lung and larynx cancer risk: a case-control study. Journal of the National Cancer Institute 62(3):471-477.

Wynder, E.L., Mabuchi, K., and Beattie, Jr., E.J. (1970) The epidemiology of lung cancer: recent trends. Journal of the American Medical Association 213(1):2221-2228.