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FOR USE AFTER 10 A.M., APRIL 30, 1969

Statement of Thomas H. Brem, M.D., before the House Committee on Interstate and Foreign Commerce, April 30, 1969.

Dr. Brem is professor and chairman of the Department of Medicine, University of California School of Medicine, and director of Internal medicine of the Los Angeles County-USC Medical Center.

NEWS SUMMARY

Dr. Brem presents what he calls "a brief for objective reasoning in an important public issue that has become so beclouded in emotion, superstition, religion, morals and conviction as to be almost unrecognizable as a scientific problem."

Citing the major contentions of both proponents and opponents of the theory that cigarette smoking causes lung cancer, he says:

"Each side presents some highly persuasive, conflicting arguments, but neither can offer unequivocal scientific proof that smoking does or does not cause cancer of the lung."

"The crucial point in the whole debate centers on whether or not there has indeed been a true increase in incidence...we really do not know whether (it) is in fact increasing as cigarettes are increasingly consumed."

Dr. Brem states that the greatest rate of increase was between 1930 and 1935, diminishing in "almost every period" since then despite rising per capita cigarette consumption. This is "hardly consistent with the smoking-cancer theory," he says.

He calls for "continued and vigorous search for knowledge into the nature and true cause of human cancer," stating that meanwhile "the wise course is to hold sweeping judgments in abeyance."

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Statement of Thomas H. Brem, M.D.

I am Thomas H. Brem, M.D., a graduate of Johns Hopkins University School of Medicine in 1937. I have been on the faculties of Stanford University School of Medicine, University of California at Los Angeles, and am currently Professor and Chairman of the Department of Medicine in the University of Southern California School of Medicine and Director of Internal Medicine of the Los Angeles County - University of Southern California Medical Center.

I have been engaged in clinical medicine, research, medical education and administration in these fields for my whole professional life. My principal areas of interest have been in diseases of the heart, lungs, and liver, and in neoplasia, or cancer, in general. I have watched with interest the controversy over smoking and health and have followed fairly comprehensively the scientific literature and the reports of various concerned agencies and institutions. Although I have not contributed to this area of research, I have had considerable experience over the years in evaluating clinical and experimental evidence and in judging conclusions drawn from it as to their justification and logic.

I am very much aware that you have heard or read untold hours of testimony and debate on the relationship of smoking to cancer of the lung and other diseases, including the presentation of reams of statistical data and analyses, as well as a variety of strong opinions. I do not intend to produce additional evidence, but I do hope to review some of the conflicting claims and arguments with emotional detachment. I certainly present no brief for smoking, but I do present a brief for objective reasoning in an important public issue that has become so beclouded in emotion, superstition, religion, morals, and conviction as to be almost unrecognizable as a scientific problem.

The issue of the relationship of cancer of the lung to cigarette smoking revolves about two conflicting sets of arguments. That of the proponents of the causal relationship hypothesis involves essentially

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four contentions:

1. That there has been a striking increase in the incidence of lung cancer over the past forty to fifty years coincident with a similar increase in the per capita consumption of cigarettes.
2. That cancer of the lung is approximately ten times as frequent in cigarette smokers as it is in non-smokers.
3. That tobacco smoke condensates contain materials that have carcinogenic properties when applied to the skin of experimental animals.
4. That microscopic changes which are regarded by some pathologists as "pre-cancerous" are much more frequent in smokers than in non-smokers.

The opponents of the hypothesis present the following set of arguments:

1. That there is serious doubt that the great increase in reported lung cancer represents in fact a true increase in incidence of the disease.
2. That if there is some degree of increase in true incidence there are other equally, or even more, likely causes for it than smoking.
3. That cancer of the bronchi and lungs has not been produced in experimental animals by the application of tobacco smoke or its condensates.
4. That the microscopic changes seen in the bronchial lining of smokers, and to lesser extent in non smokers, have not been proved to be pre-cancerous, nor are they specific to smoking, and they do not have the same distribution in the bronchial system that cancers do.
5. That an uncontrolled statistical correlation cannot prove a cause and effect relationship.

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A tremendous body of literature relative to this problem has grown in the past decade or two, and massive accumulations and analyses of statistical data have been developed in efforts to substantiate or disprove the hypothesis. Virtually all of these studies and reports have been in reference to these points. Each side presents some highly persuasive, conflicting arguments, but neither can offer unequivocal scientific proof that smoking does or does not cause cancer of the lung.

The crucial point in the whole debate centers on whether or not there has indeed been a true increase in incidence in cancer of the lung, for, if in fact there has not, it is hardly logical to attribute cancer of the lung to the increased consumption of cigarettes over these decades.

From mortality tables it has been estimated that the incidence of cancer of the lung in white males increased twenty-six fold between 1914 and 1950, or eight fold between 1930 and 1960. The validity of these figures of course depends on the completeness and accuracy of diagnosis of lung cancer over this period. The mortality tables from which these figures are developed consist of the accumulation of causes of death (diagnosis) listed on death certificates by many thousands of individual practitioners of many varieties, from well trained, capable diagnosticians through country general practitioners, osteopaths, homeopaths, and others. They come in from all parts of the country--large cities with excellent diagnostic facilities to small hamlets with none. A large proportion of the diagnoses rests on clinical impressions, and relatively few, especially in the past, will have been substantiated by pathologic examination--biopsy or autopsy.

The clinical entity of carcinoma of the lung in the early part of this century was not widely known among the practicing medical profession. (Even such a common disorder as coronary occlusion or myocardial infarction was virtually unknown to clinicians prior to the 1920s.) Other diseases of the lungs, particularly tuberculosis and pneumonia were far more prevalent as causes of death than they are now, and both of them can, and often do, resemble lung cancer very closely. Even now sophisticated diagnostic techniques or postmortem examinations are often required to

differentiate between them. Furthermore, pneumonia is frequently present in the segment of the lung that is affected by cancer and only the effective therapy with modern antibiotics enables the patient to survive until the underlying cancer is suspected and special diagnostic procedures prove its presence.

A. G. Gilliam (1) of the Biometry and Epidemiology Branch of the National Cancer Institute has calculated that if only two per cent of the deaths in 1914 ascribed to non-cancerous diseases of the respiratory system had indeed been due to cancer of the lung, the increase in incidence of cancer of the lung between 1914 and 1955 would have been but four-fold instead of the claimed twenty-six fold. Evidence that he cites, relative to the confusion or misdiagnosis of tuberculosis for cancer in chest disease hospitals in recent times, makes a two per cent error in 1914 entirely plausible. My judgment would be that, considering the lack of access to competent medical care of a large proportion of our population, the lack of awareness of the disease by the practicing profession, and the imperfection of diagnostic techniques, a two per cent error in 1914 is a distinct underestimate. He goes on to state that if the diagnostic error were ten per cent in 1914 and gradually diminished over the years as medical care became increasingly available and diagnostic capabilities improved, to two per cent in 1950 there would be but a two-fold increase in incidence. There is, of course, no way of knowing what the error has been over the years, but the contention that the error in diagnosis, and hence reporting, was large five, and even three, decades ago is hardly assailable. Gilliam's conclusion is that "although there appears to have been a true increase in the incidence of carcinoma of the lung, and that it is still increasing, that the magnitude of the increase is nowhere near as great as recorded mortality suggests."

Certainly as the quantity and quality of medical care in any population increases, the incidence of recognition and reporting of any particular disease, especially those difficult to diagnose, is bound to increase. This circumstance obviously does not mean that the particular disease is necessarily increasing. Despite statistical analyses, there is no earthly way

of determining with any sort of accuracy or certainty in a rapidly changing and improving health care system whether a disease is indeed increasing in incidence or whether its recognition is. Hence we really do not know whether the true incidence of cancer of the lung is in fact increasing as cigarettes are increasingly consumed. There is some suggestion from the older, pre-cigarette era, based on large series of autopsies, that cancer of the lung then constituted about the same proportion of cancer of all sites as it does now. This would suggest there there has been no selective increase in cancer of the lung relative to cancer in general.

The report of the Advisory Committee to the Surgeon General of the USPHS entitled "Smoking and Health" (1964) states on page 135, "Lung cancer mortality has risen at a fairly constant rate since 1930." The authors of this section evidently were not aware of another publication of Gilliam's in 1961 (2). In this report entitled "Trends in Mortality Attributed to Carcinoma of the Lung" he states, "It is clear that, though the total death rate recorded for the white male population has increased throughout the period (1930-1958); there has been a regular decline in the rate at which this has occurred" and "It must be emphasized therefore that when considering trends in mortality, the rate at which a disease is rising or falling is of equal importance to the increase or decrease in actual rates. It is common practice to make dire predictions of the future position of cancer of the lung as a cause of death 'if present trends continue.' An important aspect of present trends in this country, which is generally ignored, is the declining rate of increase. If this feature of the trend continues, the disease will reach its peak among the white male population in the foreseeable future (1983) and then start to decline."

The fact that the rate of increase of cancer of the lung was greatest between 1930 and 1935, and has diminished in almost every period since 1935, despite the rising per capita consumption of cigarettes over these many years, is hardly consistent with the smoking-cancer theory. Certainly as smoking years and increasing consumption of cigarettes goes on year after year, logical consideration would dictate that with each passing year there would be a greater increase in lung cancer in any year

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than in the year before, if indeed smoking were a significant cause. The observed decline in the rate of increase of lung cancer is exactly what one would expect, however, if the reported increase were due to constantly improving detection of this disease--or of any other for that matter. That medical care has become increasingly available to our population over this span is undeniable. Likewise diagnostic techniques have improved tremendously. As long as good medical care becomes increasingly available to our population and diagnostic techniques improve, the reported incidence of cancer of the lung will inevitably increase, but as the diagnosed and reported incidence approaches the true incidence, there will be a steady decline in the yearly increase in reported incidence until a level state is reached.

I would offer the speculation that in the next few years, now that Medicare and Medicaid will make medical care more accessible to millions of previously medically deprived citizens, there may well be an increase for several years, rather than the current decline, in the yearly rate of increase in reported cancer of the lung.

Even if a part of the increase in reported cancer of the lung is real, and not simply apparent, to attribute it to smoking is speculative. Such things as the urbanization of our population, and increasing industrialization of our society, socio-economic levels and other factors have been statistically related to an increased risk of lung cancer. Also the vagaries in the incidence of cancer of any organ or site are not at all understood. During the period that lung cancer has appeared to increase so dramatically, the incidence of cancer of the stomach has decreased almost equally. Thirty years ago, when cancer of the stomach was of relatively high incidence, an eminent medical scientist attributed with conviction the rising incidence at the time to the increase in home barbecuing. He supported the hypothesis by demonstrating that the charred fat contained carcinogenic properties when applied to the skin of mice. One would hardly conclude that the subsequent decline in stomach cancer is due to a decrease in home barbecuing in this country. The fact is that we simply don't know what causes these rises and falls in frequency, but there

is always the temptation, even compulsion, to ascribe them to some sort of event that seems at least to be associated with the change.

The most persuasive evidence in favor of the smoking-cancer hypothesis is the repeated observation that lung cancer occurs in smokers much more frequently than in non-smokers, and that the incidence is related to the amount smoked. (In other diseases attributed to smoking, the difference is much less.) This ratio is cited over and over in the protagonists' debate. Although it is admitted that other differences in constitution, temperament, personality, living habits, economic level, and psychological attributes exist between smokers and non-smokers, these differences are dismissed rather lightly as being of minor consequence, relative to the difference in smoking patterns. This is of course a judgment based on statistical relationships in which only one of many variables is controlled. Opponents point out that despite this high ratio, only a very small proportion (probably less than two per cent) of heavy smokers over many years develops cancer of the lung. The incidence is even much lower for smoking women. If smoking were indeed an important cause of lung cancer, it is difficult to explain how ninety-eight per cent of smokers escape the disease. Again logic dictates that there must be something very different about these two per cent, other than their smoking habits. This difference has of course not been identified as to its nature. If the great "increase" in the incidence of cancer over the past four to five decades is indeed spurious, for which there is strong evidence, smoking can hardly be blamed, and other causes must be seriously considered for the differences in rates between smokers and non-smokers.

There are a number of other points of debate between the believers and the non-believers, each with varying degrees of merit. The inevitable conclusion that an unbiased person of reason would reach is that neither side has conclusive evidence for its position. My own opinion is that the evidence in favor of the hypothesis is weak, and the proponents have failed to answer satisfactorily a number of sharply conflicting observations, the most significant one being the persistently declining rate of increase of reported cases of lung cancer in the face of increasing per capita consumption of cigarettes.

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Medical history is replete with cherished beliefs based on uncontrolled observations and clinical impressions, which have subsequently been completely demolished when subjected to properly controlled clinical investigation. Only recently, for example, medical gospel held that the rupture of a peptic ulcer constituted the most urgent indication for immediate emergency surgery. We were taught, and virtually every physician fully believed, that the greater the number of hours that elapsed between perforation and the operation the less the chances of survival of the patient. Approximately twenty years ago a British surgeon treated a large group of such patients with conservative, non-surgical means with resulting lower mortality rates than in comparable groups treated surgically. This observation has led to a totally different approach to the management of perforated peptic ulcer.

A few years ago a wave of enthusiasm for a surgical procedure for angina pectoris swept the country. This was a relatively simple operation involving the ligation of the left internal mammary artery. The results in the relief of anginal pain were so impressive that the operation gained wide popularity until a Boston heart surgeon performed the crucial controlled experiment in which approximately half of his group of patients had the artery ligated and the other half had the skin incision made but no ligation. Analysis of the results clearly demonstrated that there was no significant difference whatever between the two groups. The popularity of the operation quickly faded, and virtually none are being performed today.

There are in medicine any number of similar examples of cherished beliefs based on uncontrolled clinical observations and supported by presumptive or circumstantial evidence which have been destroyed by objective scientific scrutiny.

The Report of the Advisory Commission to the Surgeon General of the United States Public Health Service on Smoking and Health states (p. 175)

that because the incidence of lung cancer is "relatively low" and the inherent difficulties in controlling environment, etc., of the large groups of young people over many years of smoking and not smoking renders a controlled experiment impossible. Therefore, we are told, we must make a judgment on precisely the kind of evidence that has been so fallible on so many occasions in the past. My contention would be that one should not feel under any compulsion to make a scientific judgment if the evidence does not warrant it. A person of true scientific discipline would never make a final judgment on the type of evidence presented in favor of the hypothesis.

What is really needed is not this kind of speculation based on uncontrolled statistical surveys, but rather continued and vigorous search for knowledge into the nature and true cause of human cancer. Knowledge is increasing rapidly in this area, and there is increasing likelihood that some of the answers at least will be forthcoming in the years ahead. Until this time the wise course is to hold sweeping judgments in abeyance.



Thomas H. Brem, M.D.

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Cancer of the Lung*			Cigarettes**		
Per cent increase per period			per capita per year		
		(White males)	(Non white males)		
1930-32	-	1933-35	10.2	20.8	1365
1933-35	-	1936-38	11.2	7.9	
1936-38	-	1939-41	8.7	11.4	1828
1939-41	-	1942-43	7	8.1	
1942-44	-	1945-47	8.8	13.7	
1945-47	-	1948-50	8.5	12.0	3322
1951-53	-	1954-56	6.6	7.7	
1954-56	-	1957-58	5	8.3	3888

* Gilliam, A. G., Cancer, 14: 622, 1961

** "Smoking and Health," Report of the Advisory Commission to the Surgeon General of the Public Health Service, 1964, p. 45.

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References

1. Gilliam, A. G.: Trends of mortality Attributed to Carcinoma of the Lung: Possible effects of Faulty Certification of Deaths to Other Respiratory Diseases. *Cancer*, 8: 1130, 1955.
2. Gilliam, A. G.: Trends of Mortality Attributed to Carcinoma of the Lung. *Cancer*, 14: 622, 1961.

CURRICULUM VITAE

A. PERSONAL INFORMATION

1. Name	Thomas Hamilton Brem
2. Business address	2025 Zonal Avenue, Los Angeles, California 90033
3. Business phone	CA. 5-1511, Ext. 230, 231
4. Home address	1310 Milan, South Pasadena, California 91030
5. Home phone	SY. 9-8694
6. Date of birth	October 3, 1910
7. Place of birth	Canal Zone, Panama
8. Citizenship	U.S.A.
9. Sex	Male
10. Marital status	Married
11. Wife's maiden name	Elizabeth Bloss
12. Number of children	Three

B. EDUCATION

1. High school	Fairfax High School, Los Angeles, graduated	1928
2. College	Stanford University	A.B. 1933
3. Medical School	Johns Hopkins University School of Medicine	M.D. 1937
4. Internship	Johns Hopkins Hospital	1937-1938
5. Residencies	Resident in Pathology, Stanford University	1938-1939
	Resident in Medicine - USC service Los Angeles County Hospital	1939-1942
6. Fellowships:	None	
7. Honors and awards	Alpha Omega Alpha (Alpha Chapter of AOA) Johns Hopkins University	
8. Licensure	California, Maryland	
9. Board certification	American Board of Internal Medicine	1946

C. PROFESSIONAL BACKGROUND

1. Academic appointments		
Assistant in Pathology	- Stanford University	1938-1939
Instructor in Medicine	- Univ. of Southern California	1939-1949
Assistant Clinical Professor of Medicine	- UCLA	1949-1951
Associate Clinical Professor of Medicine	- UCLA	1951-1953
Clinical Professor of Medicine	- UCLA	1953-1954
Professor of Medicine and Director of Clinical Teaching	- USC	1954-1955
Professor of Medicine and Co-Head of Dept. of Medicine	- USC	1955-1958
Chairman, Interim Administrative Committee (Acting Dean)	USC	1956-1958
Head, Department of Medicine, Univ. of Southern California		1958- present
2. Specific teaching responsibilities:		
Daily rounds with undergraduate students and house staff.		
Four regular clinical conferences per week		

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C. PROFESSIONAL BACKGROUND (Continued)

3. Specific administrative responsibilities

Chairman of Interim Administrative Committee	USC	1956-1958
Admissions Committee	USC	1956-1958
Public Relations Committee	USC	1958-1962
Board of Directors of L.A. County Attending Staff Association		1961-present
Medical Education and Curriculum Committee	USC	1963-present

4. Military service:

Medical Officer, A.U.S., in C.B.I. Theater Feb. 1942 - Dec. 1945

D. SOCIETY MEMBERSHIPS

1. Local:

Los Angeles County Medical Association
California Medical Association
Los Angeles Society of Internal Medicine - Secretary, 1951
Vice President 1952
President 1953
Los Angeles Academy of Medicine - Board of Governors 1954
President 1961
Los Angeles Heart Association - Board of Directors, 1947-1950
Long Beach Heart Association - Board of Directors 1951-1954
Pacific Interurban Clinical Club

2. National:

American Medical Association
American College of Physicians (Fellow)
American Board of Internal Medicine - Member 1955- present
Chairman 1963-1965
Residency Review Committee in Internal Medicine 1957-1965
Vice Chairman 1962-1963
Association of Professors of Medicine
Association of American Physicians
Western Association of Physicians Vice President 1965
Advisory Board for the Medical Specialties 1963
Vice President 1966-1968
President 1968-present

E. CONSULTANTSHIPS

1. Local: Area medical consultant to Veterans Administration
Editor-in-Chief, Audiodigest, 1959-present
2. National: Member of special Medical Advisory Group to
Veterans Administration, 1960-1965
Vice Chairman 1961-1964
Chairman 1964-1965
- California: Member of State Advisory Hospital Council, 1961-1968