



## AN OPEN LETTER TO DR. CLARENCE COOK LITTLE

by DAVID D. RUTSTEIN, M. D.

*Is there tangible evidence of a relationship between cigarette smoking and lung cancer? Eighteen studies conducted in five countries have shown that there is, but Dr. Clarence Cook Little, chairman of the Scientific Advisory Board to the Tobacco Industry Research Committee, asserts that three years of research by his group have "produced no evidence that cigarette smoking or other tobacco use contributes to the origin of lung cancer." DR. DAVID D. RUTSTEIN is head of the Preventive Medicine Department at the Harvard Medical School.*

DEAR DR. LITTLE:

As a professor of preventive medicine, I have been deeply concerned, as I know you have, by the constantly increasing death rate from lung cancer in the United States and in other parts of the world. Over 25,000 people in the United States die from lung cancer each year, and the number is increasing by about 2000 every year. This disease now kills more men than any other form of cancer.

What is the evidence that cigarette smoking is responsible for most of this increase? Eighteen studies in five countries show either that patients with lung cancer are predominantly cigarette smokers, or that cigarette smokers have more lung cancer than do non-smokers. All but one of these eighteen studies show that the more and the longer you smoke cigarettes (but not pipes and cigars), the more likely you are to get lung cancer. Depending on the amount and duration of the smoking, the rate of occurrence of lung cancer is from five to thirty-five times greater among cigarette smokers than among non-smokers. Most

important, in all of the medical literature there is not one study which shows no relationship between cigarette smoking and lung cancer. These results, it seems to me, are more than just "the opinion of a few statisticians," as you stated on last July 12.

There is another kind of evidence which links cigarette smoking to the development of lung cancer. Examination of the lungs of cigarette smokers under the microscope reveals precancerous changes. The extent of these abnormalities is directly proportional to the amount and duration of cigarette smoking. These changes were least common in the lungs of those who did not smoke cigarettes regularly and most common in the lungs of those dying of lung cancer.

There is a third but very weak kind of evidence which should be mentioned for completeness. Substances have been found in cigarette smoke which are similar in their chemical structure to compounds which produce cancer in animals. Actually, a few investigators have been able to

produce cancerous changes following application of such substances to the skin of mice. As a cancer research worker of many years experience, you know that evidence obtained on animals cannot be translated directly to man. You know that conclusive evidence on human lung cancer has to be obtained from observations on man. At present, therefore, these positive results in animal experiments add little to our understanding of human lung cancer.

You have consistently ignored or brushed off all of the human evidence whenever a statement relating cigarette smoking and lung cancer has been released to the press by a research worker, by the British government through its Medical Research Council, or by the Surgeon General of the United States Public Health Service speaking for the United States government. You have stated that there is nothing new, that the evidence is merely "statistical," and that no "cause and effect relationship has been demonstrated." Your statement troubles me because I had always thought that such evidence is valid; I had been taught to believe that it is essential for medical research workers to follow statistical principles in all their investigations. What is wrong with a statistical study? Do not statistical principles come into play whenever anything is counted in any scientific study, whether performed in the laboratory or in the field? Statistics are, after all, the rules by which things are counted, and it is impossible to do any experiment without counting up the results.

I don't know exactly what you mean by "cause." When you question the eighteen studies which show a relationship between cigarette smoking and lung cancer as being only "statistical," I think what you really mean is that these studies are not as well controlled as laboratory experiments. If we think about it, we realize that even in laboratory experiments, no matter how performed, the results are really nothing more than a statistical association between two events. The laboratory result becomes more valid if one can perform a series of experiments in sequence, because one can frequently rule out factors which may interfere with its interpretation.

On the other hand, in the study of epidemics of disease as they occur in a population, one can only observe what actually happens. This is as true for epidemics of influenza as it is for the present epidemic of lung cancer. This limitation does not deny the validity of the epidemiologic observation; it merely demands more care in interpretation. It requires analysis of the plan and results of each study and a comparison of the data of many studies planned along different lines. In the case of cigarette smoking and lung cancer,

one may get some reassurance from the unanimity of results from the many different approaches that were used in the eighteen studies. It is unlikely that all would have been affected in exactly the same way by extraneous factors. Moreover, these results are confirmed by the increase in precancerous lesions in the lungs of smokers.

In spite of possible limitations of the method of study, the control of many human plagues in the past has depended solely on the kind of information which you have criticized as being only "statistical." This was certainly true before the discovery of bacteria by Pasteur about 1860. Let's look at the record and see how it applies to the present situation.

In 1796, when Jenner recommended vaccination with cowpox for protection against smallpox, he did not know the "cause" of smallpox. He knew only that milkmaids who previously had cowpox had immunity against smallpox. This was purely a statistical association. The virus of smallpox was not discovered until the early 1900s — over a century after the disease had been brought under control in civilized countries. Would you have recommended that vaccination against this highly fatal and widespread disease should have been delayed for a century because the evidence for it was only "statistical" and because Jenner had not discovered the "cause" of the disease?

Again, in 1854, during an epidemic of cholera in London, John Snow recognized the statistical association between cases of cholera and the drinking of water supplied by one of London's many water companies. John Snow inferred from his observations that a noxious substance causing cholera must have been transmitted by the particular water company, although the "cause" of cholera was not to be clearly defined for another forty years. Would you have said that the recommendations of John Snow were not to be applied in London because he did not know the "cause" of cholera? Perhaps one cannot apply the same rules to cigarettes as one does to germs. But the Southwark and Vauxhall Company, which pumped the sewage of the Thames through its private water supply, was probably disturbed by the charge that its water was responsible for the cholera epidemic.

Other diseases, such as rabies in Scandinavia, have also been controlled without information as to "cause." Unfortunately the opposite is also true. For example, typhoid fever in Devonshire could have been prevented if Dr. William Budd's epidemiological observations had not been ridiculed by the clinicians of his time.

Remember, Dr. Little, I am not recommending that people be forbidden to smoke cigarettes. Fortunately, our citizens can make their own deci-

sions about matters such as these. But in a democracy, citizens have the right to be given the facts. They also must be protected by their government, as they were in a recent statement by the Surgeon General of the United States Public Health Service, against a smoke screen of irrelevant and confusing details.

In objecting to a public health program to diminish lung cancer by urging a decrease in cigarette smoking, you referred on July 12 to "variables in human habits, environmental and constitutional, such as biologic susceptibility to cancer, the effects of previous lung disease, hormonal influences and many other factors." These influences, as well as air pollution, are undoubtedly of some importance. But what do they have to do with the facts that the large majority of cases of lung cancer occur in cigarette smokers, that the longer and the more the individual smokes the more likely he is to have lung cancer, and that smokers have precancerous lesions in their lungs?

Actually, the evidence for the association between cigarette smoking and lung cancer is stronger than Jenner's evidence when he recommended vaccination against smallpox. This association is as strong as the basis for John Snow's recommendations for the control of cholera in London. Why do you insist that we find the "cause" of lung cancer before public health authorities be permitted to make any effort to control this disease?

I agree with you that further research must be carried on as intensively as possible so that we may completely control lung cancer and so that smokers can inhale their cigarettes in complete safety. At the same time, our citizens must be told clearly of the present risk of smoking any of the filtered or non-filtered cigarettes now available. But we must go even further. We must not limit our research on cigarette smoking to its relationship to lung cancer. As far back as 1938, Raymond Pearl of Johns Hopkins showed that non-smokers lived longer than smokers. Since that time, increasing evidence has been accumulating that other diseases, particularly coronary heart disease in young men, may be more common among

cigarette smokers than among non-smokers. It will be important to confirm or deny such relationships because a small increase in a very common illness like coronary disease may cause many deaths. And the people must be allowed to know.

The Tobacco Industry Research Committee is to be complimented on the large sum it has allocated for research on the relationship of smoking to lung cancer. This enlightened approach seems inconsistent with the committee's policy of blind opposition to any attempt at public health control of lung cancer. Shouldn't this committee take a cue from the experience of the liquor industry after Prohibition and at least counsel moderation in smoking?

Although I realize that your committee does not perform research, with your leadership it could aid in setting up an experiment to answer the crucial question: Will a decrease in cigarette smoking result in a concomitant decrease in the death rate from lung cancer? I am optimistic enough to believe that a study could be set up to answer this question. Volunteers could be randomly divided into two groups — one being urged to stop and the other to continue cigarette smoking. There will probably be enough difference in the smoking habits of the two groups to measure possible differences in the death rate from lung cancer.

The results of such an experiment would provide the basis for a continued public health program. The laboratory research on the basic mechanism of the disease would, of course, meanwhile be carried on.

In the meantime, Dr. Little, is there really any justification for your continuing to demand the discovery of the "cause" of lung cancer before we attempt to save human lives by recommending a decrease in cigarette smoking? Lung cancer is a serious disease which causes much suffering and cuts down people in the prime of life. Should not public health authorities immediately recommend the obvious remedy suggested by sound epidemiologic observation and confirmatory laboratory evidence? If not, why not?

DAVID D. RUTSTEIN, M.D