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## SMOKING AND LUNG CANCER: A REVIEW

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### Summary

Cigarette smoking is the most important known factor in the causation of lung cancer. The evidence supporting this statement is enormous and irrefutable. Efforts to reduce and eventually eliminate cigarette smoking throughout the world should be strongly endorsed by all nations. The task will be difficult, but it can and must be accomplished.

### Zusammenfassung

Zigarettenrauchen ist der bedeutendste bekannte Faktor bei der Verursachung des Lungenkrebses. Die Beweise für diese Feststellung sind umfangreich und unanfechtbar. Alle Länder sollten die weltweiten Anstrengungen unterstützen, die unternommen werden, um das Zigarettenrauchen zu vermindern und eventuell überhaupt auszuschalten. Diese Aufgabe wird schwierig sein; sie kann und muss sogar erfüllt werden.

Tobacco came to Europe from the Americas. It was introduced to Zurich by Konrad Gesner less than 75 years after the sailors of Christopher Columbus first observed the "Indians" of Hispanola performing the act of smoking (1). It is appropriate that an American addressing a Swiss Medical Society on the subject of smoking and lung cancer begins by apologizing. On the other hand, the flag of that magnificent humanitarian organization known as the Red Cross has the same configuration as the Swiss flag, but with the color scheme reversed. The Red Cross helped foster the smoking habit in the Americas by supplying our soldiers and

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Professor of Medicine, Mayo Medical School, Rochester, Minnesota USA This investigation was supported in part by U.S. Public Health Service Research Contract No. CB-53-886 from the National Institutes of Health. sailors with cigarettes during World War I. The Swiss are not responsible for the lung cancer pandemic that followed, but it is an interesting historical note.

With the great economic depression that followed World War I came awareness that the increasing frequency of lung cancer might be smoking-related. In 1936 FLECKSEDER described a study in which 94 percent of patients with cancer of the lung were heavy smokers (2). Other pioneering reports linking tabacco smoking and lung cancer were those of MULLER in 1939, OCHSNER and DEBAKEY in 1941, SCHAIRER and SCHOENIGER in 1943, and WANDER and GRAHAM, LEV IN and associates, and DOLL and HILL, all in 1950 (3-8). A 1953 editorial in the New England Journal of Medicine stated that the evidence associating cigarette smoking and lung cancer was "so strong as to be considered proof within the everyday meaning of the word." (9).

In 1962 the Royal College of Physicians of London published its superb, concise report, "Smoking and Health", and I joined the rapidly growing ranks of physicians who were exsmokers (10). Two years later came the more voluminous report of the Advisory Committee to the Surgeon General of the U.S. Public Health Service, which delivered the strong recommendation that "cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action." (11).

There have been follow-up publications to both of these reports, each follow-up providing additional evidence that cigarette smoking is a causative factor in lung cancer (12-22). These and similar publications the world over have sealed the indictment against smoking. To be sure, cigarette smoking is not the sole cause of lung cancer. Occupational, geographical, environmental, nutritional and familial factors all play a role (23). Certain industrial carcinogens, including the halo ethers cause high risks in extremely small exposed populations. Other less potent agents, such as asbestos and atmospheric pollution, have a greater impact because larger numbers of persons are exposed, but the impact of that great "personal pollutant", cigarette smoking, is far greater than anything else, because of the vast distribution of the exposure. It also acts synergistically with other etiologic substances. The studies of TOKUHATA and LILIENFELD on the familial aggregation of lung cancer have been widely discussed, and more recently the possible roles of aryl hydrocarbon hydroxylase (AHH) inducibility and vitamin A and its analogs in chemical carcinogenesis have received considerable attention (24-26). Again, the influence of cigarette smoking is much stronger, and again there is synergism. We have observed increased AHH inducibility in smokers. There is a definite dose, time, age and "tar" content relationship between cigarette smoking and lung cancer (27, 28). Those who begin smoking at an early age, those who inhale large amounts of tobacco smake (and tobacco "tar") and those who smake many years all have a

much greater risk of developing lung cancer (29). However, it is also recognized that this risk diminishes after cessation of smoking (30). There is evidence that cigarettes with a low "tar" content may be somewhat less harmful, but this is difficult to evaluate, in view of the multiplicity of carcinogens contained in tobacco smoke (31). Moreover, there exists the possibility that a "less harmful" cigarette, while decreasing the risk of lung cancer, might inadvertently increase the risk of developing another disease, such as myocardial infarction or emphysema. The search for a "less harmful" cigarette should continue, but at present the only "safe" smoking pattern is that employed by the Seventh Day Adventists, the Mormons, the Sikhs and Parsees of India and other groups who do not smoke at all (1). Histologic studies of the bronchial epithelium of smokers have correlated increasing intensity and duration of smoking with a progression from normal ciliated epithelium to basal cell hyperplasia to squamous metaplasia with increasing degrees of cellular atypia and ultimately to squamous carcinoma (32). In ex-smokers abnormalities less than frank carcinoma seem capable of regressing (33).

Not everyone who smokes develops lung cancer, but the relationship seems to be growing stronger. Lung cancer was once considered to be primarily a disease of men, but in the United States the lung cancer incidence and death rates are now rising much faster among women and parallel increased cigarette consumption by women (29). At one time it was thought that adenocarcinoma of the lung, particularly in women, was not smoking-related (34). Current evidence not only indicates that it is, but also that increased cigarette smoking by women may be an important reason for the increasing overall frequency of adenocarcinoma compared to other cell-types of lung cancer (35). If ever an "experimental model" were needed to demonstrate that smoking can and does cause lung cancer, that model is the American female cigarette smoker.

The precise mechanism by which inhaled tobacco smoke induces lung cancer has not yet been defined. All that can be stated with certainty now is that cigarette smoking is by far the most important of the known causes. Today this fact is common knowledge. It is no longer seriously challenged by any organization except, of course, the tobacco industry. Why, then, should there be any need for another discussion of smoking and lung cancer? The answer is that despite the massive amount of data clearly documenting the cause and effect relationship between smoking and lung cancer, both continue their global increase (36). The proportion of lung cancers attributable to smoking varies in different countries. In the United States the proportion has been estimated to be 80 percent (29). In the emerging nations, where the full impact of cigarette smoking has not yet been felt, the proportion is undoubtedly lower now. However, the increasing rates of cigarette smoking in these nations (where tobacco producers present it as a symbol of progress) suggest that there will be a significant increase in future lung cancers, with a corresponding increase in the proportion attributable to smoking.

In the United States there has been a decline in recent years in cigarette smoking among adults. This has been largely among men, particularly those who are health professionals. Unfortunately, the trend among adolescents, especially girls, is just the opposite. There are still more than 50 million U.S. smokers, and the percapita consumption of cigarettes remains the world's highest, 2'750 annually, or nearly 8 per day for every man, woman and child (36). It has been predicted that there will be more than 100'000 new cases of lung cancer in the United States during 1978 and more than 90'000 lung cancer deaths (29). Nearly 74'000 of these deaths could have been prevented.

Reduction of cigarette smoking presents many problems, and there is no simple solution. The physician should always inquire about the patient's smoking habits. The patient should be informed about the risks of smoking and the benefits of cessation. The patient should also be strongly advised against smoking and be actively assisted in his or her attempts to stop. This is the minimum amount that should be done for the patient.

In the Public Health sector there should be a concerted an continuous effort by governmental agencies, advertising and communications media, health professionals, behavioral scientists, voluntary health agencies, public and private anti-smoking consultants and clinics, and exemplars at all levels. The tobacco interests are wise, capable, unscrupulous and extremely powerful. If a government derives considerable revenue from tobacco products or if a legislator or other public official is influenced by those who produce cigarettes or grow tobacco, it will be extremely difficult to reduce smoking.

Nevertheless, all of these tasks must be vigorously and steadily pursued. The alternative is a mounting toll of lives lost to lung cancer and other smoking-related diseases, and this is unthinkable.

### Abstract

The lung cancer pandemic continues at an ever-increasing pace. The disease is the leading cancer killer among men, and its frequency among women is accelerating rapidly. While particularly prevalent in the United Kingdom and other nations of Western Europe, as well as Finland, the U.S.S.R., and the U.S.A. and Canada, it is also on the rise in most other areas of the world. Japan is currently in the midst of a burgeoning incidence rate.

The prognosis for lung cancer remains dismal. The current 5-year survival rate is 10 percent or less, although if the disease is detected and treated while still in the localized stage, survivorship might be increased to 30 percent or more. This is no cause for elation, but it is encouraging when the frequency of lung cancer is considered.

Thus the enormity of the problem of lung cancer demands that all possible methods for reducing its incidence be addressed and implemented as expeditiously as possible. Reasons for past failures to control the disease must be candidly and conscientiously reviewed and critically reappraised. Unless this is done with boldness, optimism and enthusiasm, there will be little chance of successfully combatting this dread disease.

Lung cancer is a largely preventable disease. More than eighty percent of all cases in the U.S.A. are related to tobacco smoking alone. Familial, environmental and occupational factors also play an etiologic role, and have received considerable attention, but they are distinctly less important than the great personal pollutant, tobacco smoke.

Reduction of cigarette smoking cannot be accomplished by any single measure. This fact has been emphasized repeatedly, two of the most recent communications being "Smoking <u>or</u> Health", The Third Report from the Royal College of Physicians of London and the Report of the National Commission on Smoking and Public Policy to the Board of Directors of the American Cancer Society. The problem requires a strong, concerted effort by governmental agencies, advertising and communications media, health professionals, behavioral scientists, volunteer health agencies, public and private anti-smoking consultants and clinics, and exemplars at all levels.

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