

# Cigarette Smoking and Lung Cancer

Richard G. Lynch, MD

Originally published in *The ASIP Bulletin*, Volume 6, Issue 2 - June 2003

## MILESTONES

Auerbach O, Gere JB, Forman JB, Petrick TG, Smolin HJ, Muehsam GE, Kassouny DY, Stout AP: **Changes in the bronchial epithelium in relation to smoking and cancer of the lung.** *New England Journal of Medicine* 1957, 256:97-104

Auerbach O, Stout AP, Hammond EC, Garfinkel L: **Changes in bronchial epithelium in relation to cigarette smoking and in relation to lung cancer.** *New England Journal of Medicine* 1961, 265:254-267



Oscar Auerbach

In these milestone articles published in the *New England Journal of Medicine* (NEJM), Oscar Auerbach and colleagues presented incontrovertible evidence linking cigarette smoking to the development of lung cancer in humans. The data presented in these publications resulted from a systematic, comprehensive and extraordinarily labor-intensive histopathological analysis of many hundreds of lungs obtained at autopsy. Dr. Auerbach was a pathologist at the Veterans Administration Hospital in East Orange, New Jersey and Professor of Pathology at New York Medical College. In the decades prior to Auerbach's publications, epidemiological studies implicated cigarette smoking as an etiological agent in human lung cancer, a conclusion that was strongly supported by experiments conducted in laboratory animals. Nonetheless, the potential health hazard of cigarette smoking was a very controversial subject during the post-World War II years. Various interest groups challenged both the relevance to humans of experiments conducted in laboratory animals and the conclusiveness of population studies that showed statistical links between lung cancer and patterns of cigarette usage.

The Auerbach experimental protocol involved histological examination of samples taken from 208 specific sites of each tracheobronchial tree. All slides were coded and groups of slides from smokers and non-smokers were mixed and randomized so that the pathologist who examined the slides was totally ignorant of the clinical and smoking history of the patient. Individual lungs were scored for qualitative and quantitative mucosal alterations that included the loss of cilia, the presence of epithelial hyperplasia, and the occurrence of cytologic alterations that today would be categorized as degrees of atypia and dysplasia. It was well known from experimental studies that application of a carcinogen to a tissue caused cellular hyperplasia, metaplasia and nuclear and cytoplasmic atypia during the period before

a tumor appeared. In designing their extensive sampling protocol Auerbach and colleagues assumed that if inhaled cigarette smoke contained a carcinogenic substance it would likely be widely distributed over the inner surfaces of the tracheobronchial tree and that cellular injury would also be widely distributed. They reasoned that if inhaled cigarette smoke was a major cause of lung cancer it would be expected that in smokers who died of lung cancer the remaining bronchial epithelium would manifest evidence of mucosal injury including hyperplasia, metaplasia and preneoplastic cytologic changes. They reasoned further that similar changes would occur in the bronchial epithelium of patients who died of other causes, but who had been heavy smokers. The data published in the NEJM in 1957<sup>1</sup> was a status report of Auerbach's large ongoing study and the 1961 NEJM article<sup>2</sup> extended and refined the original observations. Auerbach had collected over 1500 tracheobronchial trees at autopsy and the results presented in each of the milestone articles reflected the microscopic examination of over 20,000 randomized and coded slides. The data from this enormous undertaking clearly showed that the frequency and severity of cellular alterations in the lungs were directly related to the extent and length of cigarette smoking by the patient. The lungs from non-smoking patients contained far fewer cellular alterations and these were always of a much lower grade than the lesions found in the lungs of smokers. There was excellent agreement between pathologists in scoring the slides for mucosal cell alterations.

During the 1950's the steady rise in number of deaths from lung cancer in the United States and in European countries – a pattern that had been noted as early as 1900 – and the increasing number of epidemiological studies implicating cigarette smoking as an etiologic factor in lung cancer led to a growing consensus by private and public health agencies in North America and Europe that cigarette smoking was a major cause of lung cancer.

Public declarations and policy statements by

such organizations as the American Cancer Society and the British Medical Research Council triggered counterarguments from individuals, groups and the tobacco industry who were critical of retrospective and population-based studies and skeptical about drawing conclusions from them. Auerbach's studies moved the cigarette smoking - lung cancer controversy beyond an argument that was based on a statistical association. The extensive histopathologic analysis of individual lungs from many hundreds of patients, coupled with a thoroughly documented clinical and smoking history for each patient, allowed Auerbach to conclude in the 1961 NEJM paper<sup>2</sup>: "In our opinion the histologic evidence from this study greatly strengthens the already overwhelming body of epidemiologic evidence that cigarette smoking is a major factor in the causation of bronchogenic carcinoma."

The tremendous public health impact of the studies by Auerbach and colleagues is evident in the very prominent position they were given in the Report of the Advisory Committee to the Surgeon General of the Public Health Service<sup>3</sup> and the very influential role they played in the subsequent actions taken by the Surgeon General regarding labeling and advertising of tobacco products. Auerbach's work is a powerful example of the societal benefits that have come from investigations conducted with tissues obtained at autopsy, a resource that, unfortunately, is progressively disappearing.

#### References

1. Auerbach O, Gere JB, Forman JB, Petrick TG, Smolin HJ, Muehsam GE, Kassouny DY, Stout AP: *N Eng J Med* 1957, 256:97-104
2. Auerbach O, Stout AP, Hammond EC, Garfinkel L: *N Eng J Med* 1961, 265:254-267
3. *Publication No. 1103*, U. S. Surgeon General's Advisory Committee on Smoking and Health, Public Health Service, U.S. Department of Health, Education and Welfare, 1964