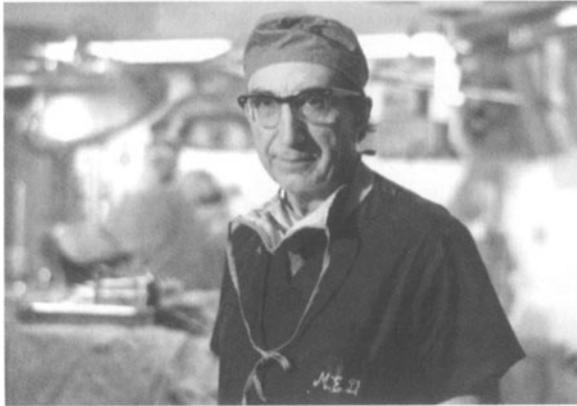


Carcinoma of the Lung and Tobacco Smoking: A Historical Perspective

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In 1933, Evarts Graham and J. J. Singer reported the first successful case of pneumonectomy for carcinoma of the lung (1). This occurred in the era of pioneering developments in thoracic surgery, and this announcement had an electrifying effect among those surgeons working in this field. The announcement of this successful surgical procedure for carcinoma of the lung was all the more exciting because the procedure had resulted in dismal failure in all eight previously reported cases (2). Historically, the first successful surgical treatment for any condition, particularly one that had been inevitably fatal, has always had a stimulating effect in encouraging surgeons to adopt the procedure promptly.

Accordingly, my chief, Dr. Alton Ochsner, like a few other pioneering thoracic surgeons, immediately developed an intense interest in this problem. We began a systematic search in the wards and clinics at the Charity Hospital in New Orleans for possible candidates. Indeed, Dr. Ochsner made arrangements through his friend, Professor Warren Cole, for me to obtain a training fellowship in endoscopy with Professor Paul Hollinger in Chicago. After my return from Chicago, I performed all the diagnostic tracheobronchial and esophageal endoscopic procedures in our Department of Surgery.

As is often the case in medicine, once a therapeutic technique becomes successful and available, the condition requiring this treatment suddenly becomes more common. Dur-

ing a little more than 20 years after the report of unsuccessful surgical treatment for carcinoma of the lung in 1911, only eight surgical procedures were performed, whereas during the five years after Dr. Graham reported his successful case, the procedure was performed in 77 cases.

Of interest is the relative rarity of this disease before Dr. Graham's report and its relative frequency after his report. In 1846, Hasse stated, in the chapter, "Cancerous Tumors in the Respiratory Organs," in *An Anatomical Description of the Diseases of the Organs of the Circulation and Respiration*: "The lungs are less prone than most other organs to cancerous disease ... [and] the diagnosis of a malady so rare as the present one, necessarily remained obscure" (3). He was able to collect only 22 published cases. In 1912, Adler was able to collect 374 cases of carcinoma of the lung and stated: "On one point, however, there is nearly complete consensus of opinion and that is that primary malignant neoplasms of the lung are among the rarest forms of disease." (4)

Within a few years of the 1933 report by Graham and Singer, and as a consequence of our and other investigators' efforts to find patients requiring surgical treatment, this concept of the rarity of the disease, then considered almost a museum curiosity, was radically altered. Suddenly, the disease had become common. In a 1939 publication, we were able to report 79 cases of total pneumonectomy for carcinoma of the lung with presentation of our own experience of seven cases (2). The following year, we were able to report on 136 published cases and present our own experience with 19 cases. Our concern is well expressed in an article we published in 1941 (6). We stated:

The present widespread interest and increasing attention devoted to primary carcinoma of the lung are thoroughly deserved. Any disease entity that rises from almost complete obscurity to one of the foremost subjects of the day in the relatively short period of a few decades demands serious consideration. At the beginning of this century, pri-

mary carcinoma of the lung was considered a museum curiosity. At the present time it is one of the most frequent primary malignancies of the body. Such a phenomenal rise to prominence immediately presents an intriguing challenge to the zetetic medical mind.

Dr. Ochsner, with his keen intellect and inquisitive nature, eagerly accepted this challenge. In our discussions of this matter, certain questions arose. First, was this increase in pulmonary carcinoma in recent years apparent or real? Second, if real, what is the explanation for it? To help answer these questions, I was assigned the task of a thorough review of publications on the subject. This was accomplished in our article published in 1941, in which more than 400 references are cited (7). A review of reported postmortem studies over several decades from numerous institutions in this country and in Europe showed that the incidence of carcinoma of the lung was absolutely increasing. For example, in 1929, Weller found that of the first 1,000 autopsies at the University of Michigan Hospital, carcinoma of the lung occurred in 0.1%; in the second 1,000 autopsies, this incidence had increased to 0.5%; and in the next 450 cases, it had increased to 0.8% (8). In the Department of Pathology at the University of Leipzig, Assmann found that the incidence of carcinoma of the lung in all autopsies from 1900 to 1906 was 0.67% and that 5.01% of all carcinomas were pulmonary (9). From 1919 to 1922, these respective figures had increased significantly to 1.54% and 9.17%. In our own review of the mortality statistics on all persons in the United States, we reported an actual increase in the number of deaths from cancer of the lung, as well as a significant increase in the death rate per 100,000 of population from 1.1 in 1920 to 3.6 in 1936 (7).

On this basis, we became convinced that there was a relatively recent real and rapid increase in the occurrence of carcinoma of the lung. We then addressed the obvious question: Why this significant increase in this form of malignancy? In our own review of publications, we found that a number of theories were advanced to explain this increase, including the influenza epidemic of 1918 (owing to the presence of metaplasia as a precancerous lesion in the bronchial mucosa of persons dying from influenza), other specific and non-specific lung infections, and the inhalation of irritating gases such as war gas, exhaust gas of combustion motors, and silicosis (7).

After reviewing these various theories and explanations, we focused our attention on tobacco smoking as the more reasonable and likely cause for the relatively recent increase in this disease, to a large extent because of our observation that virtually all the patients with this disease whom we studied, with the exception of two women, had been heavy cigarette smokers for more than two decades. We first made

this connection in our article published in 1939: "In our opinion the increase in smoking with the universal custom of inhaling is probably a responsible factor, since inhaled smoke, constantly repeated over a long period of time, undoubtedly is a source of chronic irritation to the bronchial mucosa" (2). In this connection, we were aware that during World War I, the tobacco companies made packages of cigarettes freely available to soldiers, and tobacco smoking, especially with cigarettes, rapidly became fashionable. Thus, with two decades of widespread smoking in the population, the time seemed ripe for the chronic irritation of the tracheobronchial mucosa to begin its oncogenic effect.

Our conviction about the causal relation of tobacco was supported by certain previous reports that we found in our search of previous publications. As early as 1923, Fahr expressed the opinion that the increase in the incidence of pulmonary carcinoma was due to the increased incidence of cigarette smoking (10). In 1929, Lickint also believed that the inhalation of tobacco smoke was a responsible factor in the increase in bronchogenic carcinoma (11). In 1927, Tylecote stated: "In almost every case I have seen and known of, the patient has been a regular smoker, generally of cigarettes," an observation similar to our experience (12). In 1932, McNally stated that the tar of cigarette smoke may account for the recorded increase of cancer of the lung (13).

A number of studies have demonstrated experimentally the irritating carcinogenic effects of tobacco. Although nicotine has been chiefly considered by many investigators, Roffo, at the University Institute for Experimental Medicine and for the Study of the Treatment of Cancer in Buenos Aires, reported his conviction in 1930 that the carcinogenic agent in tobacco responsible for the development of pulmonary carcinoma is tobacco tar, which is produced as a result of the burning of the tobacco, rather than the nicotine (14). He was able to produce tumors in 100% of cases when the tar was applied to the surface of the ear of rabbits. Particularly significant was Roffo's conviction that on the basis of his clinical observations of 78,000 patients treated at his Institute in Buenos Aires, tobacco was the most important factor.

I was asked recently by a media organization producing a documentary on tobacco smoking, which had found our first articles published in 1939, why no one paid any attention to our opinion on the causal relation of tobacco smoking to carcinoma of the lung. I had some difficulty answering that question, but on further reflection made an effort to do so. For one thing, the zeitgeist of that period virtually encouraged smoking. It was considered fashionable. In all the movies of that time, all the actors and actresses smoked. At medical meetings, most doctors were smoking; in fact, there was always a heavy haze of smoke in the meeting rooms and conference halls.

For another reason, the relation of smoking and the development of carcinoma of the lung was not immediately apparent, since it may take several decades of habitual smoking before the malignancy occurs. Since at that time most physicians smoked and could not observe any immediate deleterious effects, they were skeptical of the hypothesis and reluctant to accept even the possibility of such a relation. This is well exemplified by the critical and almost derisive comments of Dr. Evarts Graham, a highly respected thoracic surgeon of that time. At a surgical meeting, Dr. Ochsner presented our experience with carcinoma of the lung, and in support of our opinion regarding the causal relation of smoking, presented a slide of a graph demonstrating the progressive increase in cancer of the lung over a 12-year period and a graph demonstrating a parallel increase in the production of tobacco during that same period. In his discussion of Dr. Ochsner's presentation, Dr. Graham stated that we would have obtained the same parallelism by a graph of the production of nylon stockings. He was later converted to the belief that there was a causal relation between tobacco smoking and cancer of the lung, but tragically, his conversion was too late for his own health, since he subsequently died of cancer of the lung.

It was, finally, gratifying to have our conviction on the causal relation between tobacco smoking and cancer of the lung vindicated by the Surgeon General's Report in 1964— some 25 years after we published our report (15). It is also gratifying that the medical community has now embraced the concept that tobacco smoking is a serious health hazard and is generally committed to its prevention. Finally, it is most gratifying to observe the public recognition of this hazard, as reflected by no-smoking policies in public buildings, hospitals, schools, and airplanes. It is important to continue these efforts to educate the public, especially children and teenagers, about the health hazards of tobacco smoking, and, indeed, about the use of any kind of tobacco.

References

1. Graham EA, Singer JJ. Successful removal of an entire lung for carcinoma of bronchus. *JAMA* 1933; 101:371.
2. Ochsner A, DeBaakey M. Primary pulmonary malignancy: Treatment by total pneumonectomy; analysis of 79 collected cases and presentation of 7 personal cases. *Surg Gynecol Obstet* 1939; 68:435-451.
3. Hasse CE. Cancerous tumors in the respiratory organs. In: Swaine WE ed. *An Anatomical Description of the Diseases of the Organs of the Circulation and Respiration*. London, England: Sydeham Society; 1846: 370-375.
4. Adler I. *Primary Malignant Growths of the Lung and Bronchi*. New York, NY: Longmans, Green & Company; 1912.
5. Ochsner A, DeBaakey M. Surgical considerations of primary carcinoma of the lung: Review of the literature and report of 19 cases. *Surgery* 1940; 8:992-1023.
6. Ochsner A, DeBaakey M. Primary carcinoma of the lung. *New Orleans M & SJ* 1941; 93:387-394.
7. Ochsner A, DeBaakey M. Carcinoma of the lung. *Arch Surg* 1941; 42:209-258.
8. Weller CV. Pathology of primary carcinoma of the lung. *Arch Path* 1929; 7:478.
9. Assmann H. Zur frage der pathogenese und zur klinik des brochialkarzinoms. *Med Klin* 1924; 20:1757 and 1796.
10. Fahr A, in discussion on Teutschlaender. *Brochialkrebs. Verhandl d deutsch Path Gesellsch* 1923; 19:191.
11. Lickint F. Tabak und tabakrauch als ätiologischer faktor des carcinoms. *Ztschr f Krebsforsch*. 1929; 30:349.
12. Tylecote FE. Cancer of the lung. *Lancet* 1927; 2:256.
13. McNally WD. The tar in cigarette smoke and its possible effects. *Am J Cancer* 1932; 16:1502-1514.
14. Roffo AH. Leocoplasia tab quica experimental. *Bol Inst de Med Expe para el Estud y Trat del Cancer*. 1930; 7:501.
15. U.S. Department of Health, Education and Welfare. *Public Health Service Publication No. 1103. Smoking and Health*. Washington, D.C.: U.S. Government Printing Office, 1964.