Oncology

12

Oscar Auerbach

The discovery of a causative link between cigarette smoking and lung cancer is one of the twentieth-century medicine's greatest triumphs. It was a tale that took over 20 years to unfold, beginning with epidemiological studies in Germany, the United States, and Great Britain in the 1930s, 1940s, and 1950s. Richard Doll and Tony Bradford Hill are perhaps the best known of these early investigators [1, 2]. Despite their persuasive epidemiological findings, there was resistance from the tobacco industry and others, who argued that epidemiological associations failed to show any causative explanation. Data concerning possible mechanisms were based on animal studies, which were considered to be of limited relevance. Even Doll and Bradford at first thought the rise in lung cancer rates could be explained by air pollution.

The next stage in demonstrating a connection between tobacco and lung cancer began with Oscar Auerbach (1905–1997), a pathologist whose work is regarded as a major milestone in investigative pathology, ranked alongside the discoveries of smallpox vaccination and prevention of hospital sepsis [3] (Fig. 12.1). Auerbach neither completed high school nor undergraduate school, but was accepted into New York Homeopathic Medical College on the strength of passing its entrance exams. He qualified in 1929 and went to work at Halloran Hospital and Sea View, a tuberculosis hospital on Staten Island. He subsequently accepted a position in the Veterans Administration, where he conducted seminal work on lung cancer. For 12 years, Auerbach held a faculty position in the department of pathology at NYMC, and then in his later years at the New Jersey Medical School. His teaching left an impression on at least one student, Arthur Topilow, who recalled that in 1964 at NYMC, Auerbach asked all the assembled students to refrain from smoking in his class, whereupon several walked out of the room. In the words of Topilow, who forever gave up smoking after the lecture, they "missed a ground-breaking presentation" [4].

Auerbach was known as a tireless researcher who adhered to impeccable standards. He was extraordinarily productive: while most of his colleagues examined 200 slides a day, Auerbach examined 2,000 [5]. Auerbach published two articles in the *New England Journal of Medicine*, which appeared in 1957 and 1961. The first report showed that among 117 deceased veterans, there was an increased degree of tissue change in proportion to the extent of smoking, as obtained from the medical history [6]. Auerbach's study was the first to examine this relationship directly by tissue histology and to relate it to patterns of smoking. In a second report [7], he extended his earlier findings in a larger sample and answered

Fig. 12.1 Oscar Auerbach. Pathologist known for demonstrating a clear link between smoking and lung cancer (Image in the public domain, by courtesy of National Library of Medicine)

J. Davidson, *A Century of Homeopaths*,
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an important methodological criticism of his previous report that concerned possible misclassification of the abnormal tissue findings. In this second paper, Auerbach concluded that "the histological evidence from this study greatly strengthens the already overwhelming body of epidemiological evidence that cigarette smoking is a major factor in the causation of bronchogenic carcinoma." An accompanying editorial in the journal seemed to agree with their conclusions [8]. In each study, Auerbach obtained over 200 samples from each subject, to represent the entire tracheobronchial tree – a monumental accomplishment. All of his ratings were conducted without knowledge of any other details about the patient, which had been coded separately.

In demonstrating a clear association between cellular change in the lungs and extent of smoking, Auerbach moved the debate about cancer and smoking beyond population statistics into the realm of tissue pathology, directly examined.

The impact of Auerbach's work cannot be overestimated. Lynch notes the "tremendous public health impact" of his studies, which were given prominence in the 1964 surgeon-general's report on tobacco that did so much to shape tobacco regulations on labeling and advertising.

Charles Cameron

Charles S. Cameron (1908–1998) was a 1935 Hahnemann graduate who later became an expert in the diagnosis and treatment of cancer (Fig. 12.2). He subsequently became dean of Hahnemann, where he shepherded a troubled institution away from its homeopathic past towards a future highly ranked allopathic medical school. Cameron was the first Hahnemann graduate to complete an internship at the prestigious Philadelphia General Hospital, where he developed an interest in cancer [9]. This led him to a Rockefeller Fellowship at Sloan-Kettering from 1938 to 1942 and then four war years in the Navy. From there, Cameron was appointed medical and scientific director and vice-president of the American Cancer Society (ACS). In addition, he served on the National Cancer Institute Study Section, and later as a member of the AMA National Board of Medical Examiners. Cameron authored a best-selling book *The Truth About Cancer*. He was a champion of public education about the disease, the need for early detection and treatment, and a strong advocate of the Pap smear before it was accepted as a standard screening test for cervical cancer. Another of Cameron's legacies was the journal *CA – A Cancer Journal for Clinicians* – which he founded in 1950 and which is still going strong 62 years later. As Cameron wrote in the first issue, the journal was designed to "condense authentic information about diagnosis, treatment, control, and research" for busy clinicians [10]. *CA* is the now most widely circulated oncology journal in the world, with a circulation of approximately 84,000. *CA* reaches a wide and diverse group of professionals and continues to fulfill Cameron's original vision of presenting information to these professionals about cancer prevention, early detection, treatment, palliation, advocacy issues, and quality-of-life topics. For his work with the ACS and for his book, Cameron has been acknowledged as a father of the national campaign against cancer (Fig. 12.3).

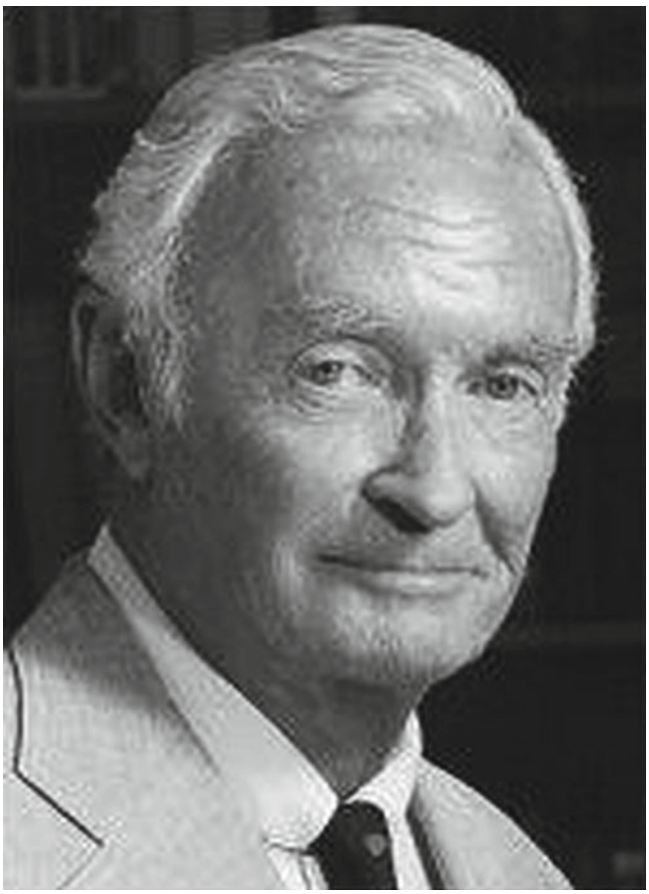

Fig. 12.2 Charles Cameron. Dean of Hahnemann Medical College and pioneer in cancer medicine (By permission, *CA: Cancer Journal for Clinicians*)

In 1956, Cameron was recruited back to Hahnemann as Dean of the College and later as president and chairman of the board of trustees. Notwithstanding the ups, downs, and conflicts that are an inevitable part of institutional change, under Cameron's leadership, the Hahnemann ship stabilized and prospered on its voyage to respectability as an orthodox medical school. As one who was trained in, and familiar with, homeopathy, Cameron wrote some perceptive accounts of the specialty and of its founder, Samuel Hahnemann (see Chap. 2) [11–13].

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Statement of Dr. Charles S. Cameron
Medical and Scientific Director

The report of Doctors Hammond and Horn, and the exhibit summarizing their report are the first published data based on the large-scale survey of smoking practice among some 187,000 healthy men. The first of its kind ever attempted, it is being carried out with the assistance of 22,000 volunteers in 394 counties scattered throughout the United States, and is now in the 29th month. The correlation of the smoking practices of these many thousands of subjects - recorded while they were alive and in good health - with the causes of their deaths as they occur has provided important information in advance of the time schedule originally estimated. Furthermore, it is information so clearly valid - beyond any question of statistical error - that it appeared to warrant publication at this time. While the observed correlation between heavy cigarette smoking and the likelihood of death from cancer of the lung and from cardiovascular disease was perhaps not astonishing, the degree of that relationship was. In addition, deaths from forms of cancer other than the lung appear to be associated with heavy cigarette smoking, thus opening up new considerations of the mode of action of the carcinogen, if any, contained in tobacco smoke.

Personally I am not convinced that the Hammond-Horn theory of cause and effect relationship between heavy cigarette smoking and increased susceptibility to death from cancer in general is as yet entirely proved. One cannot at this time exclude the possibility that heavy cigarette smoking and the tendency to cancer are both expressions of a more fundamental cause of a constitutional or hormonal nature.

Whatever interpretation is put on the evidence brought forth by this study, the data themselves and the methodology employed to get them are sound. The results appear to be of first importance in consideration of the changing death rates of the past 25 years. If further validated, they point the way to the means of still further lengthening man's life-span.

June 17, 1954

Fig. 12.3 Letter from Charles Cameron to the American Cancer Society, June 17, 1954, regarding the association between tobacco smoking and lung cancer (Image by permission John W. Hill Papers, Wisconsin Historical Society Archives)

Howard W. Nowell

Homeopathy basked in warm sunshine in 1913, when the national press gave extensive coverage to research from the Evans Memorial Institute purporting to have identified a cause of cancer. The chief investigator of this study was Howard Wilbert Nowell (1872–1940), a 1911 graduate of Boston University who was appointed to the faculty as instructor of pathology (Fig. 12.4). He gained quick promotion and was granted extensive research support at Evans. Nowell surrounded himself with experienced collaborators, including Allen Rowe, J Emmons Briggs, and William H. Watters, as well as receiving administrative support from Drs. Sutherland, Richardson, and Mann, all of BUSM; he was also granted the services of two research assistants.

Nowell conducted extensive experiments on rabbits, into which he injected material from human carcinoma. The rabbits in turn developed tumors microscopically and macroscopically similar in character to the human tumor. He then injected into healthy rabbits serum obtained from those with tumors and found that antibodies were produced in the former group. In a third step, Nowell then injected into healthy rabbits a mixture of the tumor-inducing substance and antitumor antibodies. This last set of experiments demonstrated that tumors did not develop and led Nowell to consider the possibility that serum containing these antibodies would either prevent the development of human cancer or treat it when established. The results of Nowell's research, which had taken 3 years, were first presented at the 73rd Annual Meeting of the Massachusetts Homeopathic Society in April 8, 1913, and were extensively covered in the *New York Times* of April 20 that year [14]. Nowell wasted no time in testing his serum in humans with cancer, having administered it within a few weeks to 50 patients, many of whom noted a rapid reduction in pain such that they could lower the dose of their opiate analgesics [15]. In a third article about Nowell within a 2-month period, the newspaper quoted Nowell as saying "This work has progressed further than we had any idea it would go. In experimental work time has to elapse, and usually a long time, before definite results can be ascertained." The article reported that Nowell's experiments have been so successful that the Evans administration increased his laboratory space and personnel [16]. The senior administrators at Boston University Medical School hailed Nowell's work as groundbreaking.

What then became of Nowell and his work is unclear. His animal studies led to the logical next step of administering his "cancer antiserum" to patients with the disease, and Nowell commenced a highly ambitious 600-patient program, the ultimate outcome of which was negative [17]. Nowell seems to have left Evans rather sooner than might have been expected given the spectacular promise of his initial work. By 1915, he had relinquished his faculty appointment in pathology and in 1917 was elected a fellow of the American Public Health Association, somewhat of a change in direction for such a promising pathologist. His name appeared again in the American Public Health Association Yearbook of 1930–1931.

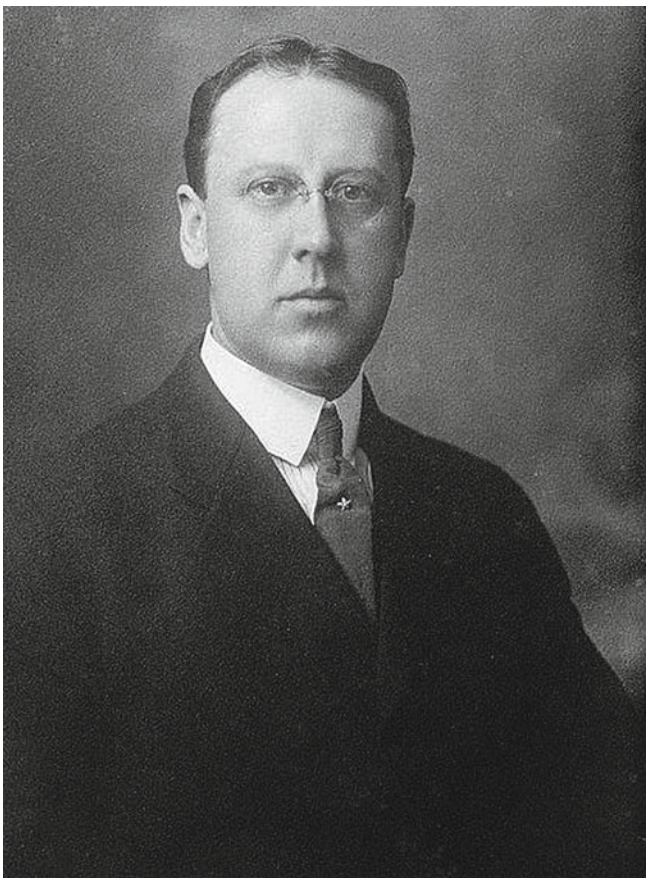

Fig. 12.4 Howard W. Nowell. Pathologist at Evans Institute who thought he had found a cause for cancer (Image in the public domain)

There are, however, some useful lessons to be learned from Nowell's work. (1) Firstly, Nowell and his associates were appropriately restrained about their findings; amidst all the excitement and intense press coverage, they took pains to explain that results of the initial animal studies should not be construed as providing a cure for cancer. (2) Secondly, in selecting patients for this new treatment, Nowell's team required either that the accepted treatment (i.e., surgery) must have been first tried or that patients were considered too high of a surgical risk and thus have few options left. In other words, they wisely adhered to the principle of balancing risk and potential benefit, by not exposing patients to a new treatment with all its possible side effects and unknown efficacy, unless they have received customary treatment or were unsuitable for it. (3) Nowell established an oversight board to guide the study and to select subjects, whose diagnosis of cancer had to be confirmed by the five-physician oversight panel. These moves were farsighted for the time and accord with the requirements of today's clinical trials.

Ita Wegman

Ita Wegman (1876–1943) was born into a Dutch colonial family in Karawang, Java, which was then part of the Dutch East Indies, where she resided until 1900 (Fig. 12.5). Wegman returned to Europe to study physical education and methods of massage based on Swedish massage. A biographical summary [18] of Wegman's life reveals that between 1906 and 1911 she studied medicine at the University of Zurich, and thereafter practiced gynecology. Wegman was profoundly influenced by the ideas of Rudolf Steiner, who became her mentor, friend, and, ultimately, her patient in his terminal illness. Early in Wegman's medical career, Steiner suggested that mistletoe (or *Viscum album* L, to give its botanical name) might be a useful treatment for cancer, and together they worked on its preparation as a medicinal agent. Between 1917 and 1920, Wegman used mistletoe in her Zurich practice. By 1922, commercial formulations of the drug were being made by the pharmaceutical company Weleda AG (under the name of "Iscador"™), and other companies have since followed suit. In 1921, Wegman set up a clinic near Basel, which still thrives today. Her initial work in cancer has stimulated further activity, much of which is carried out at the Lukas Clinic, a second AM center, established in 1963 in Arlesheim.

The research on mistletoe in cancer has been extensive, and while debate still continues about the extent of its therapeutic effect, there is good evidence that it has antitumor and anti-metastatic properties in animal experiments [19]. What is not in doubt, however, is the fact that mistletoe is now widely used in Central Europe. In 2007, for example, mistletoe products accounted for 23 % of all chemotherapy agents sold in Germany [20]. An extensive body of information on mistletoe is available at the National Cancer Institute website [21] and elsewhere [22].

Wegman was not a homeopath in the strict sense of the word, but is known for her collaboration with Steiner in introducing anthroposophical medicine (AM) as a new system [23]. AM incorporates homeopathy into its practice and more importantly perhaps has assimilated a basic principle underlying homeopathy, namely, that medicinal potency remains into highly diluted material [24, pp. 259–261]. The earliest research in AM, conducted by Kolisko in 1922, sought "to examine the behavio[u]r of matter on the way to and beyond the boundary of its ponderable existence" [24, p. 526]. AM and homeopathy can rightfully be seen as medical cousins.

Mistletoe is available in different strengths, including a homeopathic preparation of 30X, although for the most part, it is used at conventional doses, with initial doses being on the low side and then increased up to a point of side effects [25].

Wegman's other activities included the development of rhythmical massage, curative education for the disabled, and the AM movement in general. She was a cofounder of Weleda pharmaceuticals, which has grown into a global organization over the past 90 years. The worldwide Camphill School movement was begun by her pupil, Karl Konig. Wegman established a number of AM clinics in Europe, the best known being the clinic in Arlesheim, Switzerland, which is now named after her.

Fig. 12.5 Ita Wegman. Founder of anthroposophical medicine and advocate of mistletoe for cancer (Image in the public domain)

Edward Cronin Lowe

In 1933, the pathologist Edward Cronin Lowe (1880–1958) reported the development of a test to diagnose cancer. This publication appeared in the *British Medical Journal* and quickly generated correspondence and an attempt at replication by another group. Unfortunately this second study failed to support any value to the Cronin Lowe test, which eventually was abandoned. Lowe is better known for his work in influenza, as described in Chap. 13.

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