

CONFERENCE  
*on*  
BIOLOGY OF CUTANEOUS CANCER



FEBRUARY 1963

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**The First International Conference on  
The Biology of Cutaneous Cancer**

**Sponsored by  
The Skin and Cancer Hospital  
Department of Dermatology  
Temple University School of Medicine  
and  
The Committee on Geographic Pathology  
Unio Internationalis Contra Cancrum  
Held April 6 to April 11, 1962  
Philadelphia, Pennsylvania**

***Cochairmen:***

**Frederick Urbach, *M.D.*, and  
Harold L. Stewart, *M.D.***

**A Merck Sharp & Dohme Medical Research Conference**

**Edited by  
Frederick Urbach, *M.D.***

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## FOREWORD TO THE FIRST CONFERENCE ON THE BIOLOGY OF CUTANEOUS CANCER<sup>1</sup>

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The First Conference on the Biology of Cutaneous Cancer grew out of an idea generated independently and nearly simultaneously in two places separated by more than 6,000 miles—Philadelphia and Tokyo. In Philadelphia in the fall of 1960, Dr. Frederick Urbach and Dr. Carroll F. Burgoon, Jr., of the Temple University Skin and Cancer Hospital, conceived the idea of a conference on skin cancer, with international participation, to bring together dermatologists and experimentalists for exchange of ideas and for planning future studies. They wrote to a number of investigators in this country and abroad and asked them to explore the possibility and submit suggestions and plans. The replies professed a real enthusiasm and contained many excellent comments. With this encouragement, the organizers arranged for a conference to be held in 1962 near the spring meeting place of the American Association for Cancer Research. In Tokyo, on October 15, 1960, on the last day of a symposium held by the Committee on Geographic Pathology of the International Union Against Cancer, R. E. J. ten Seldam, Professor of Pathology at the University of Western Australia and cochairman of the newly established Subcommittee on Geographic Pathology for the Pacific Area, suggested that cutaneous cancer be the subject of the first scientific gathering of that group. It was as clear from the data presented to participants of the symposium in Tokyo, as it was to those at the Conference in Philadelphia, that the pattern of cutaneous cancer in different parts of the world showed remarkable differences that should be thoroughly investigated. To hold such a meeting presented difficulties, not the least of which was financial. As so often happens, the areas of the world with the most challenging scientific problems possess few or no funds to support such studies or finance a symposium to plan for future investigations.

Finally, the two groups became aware of their common interest, and the present Conference was the result. These proceedings abundantly

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<sup>1</sup> Presented at The Conference on Biology of Cutaneous Cancer, Philadelphia, Penna., April 6-11, 1962.

<sup>2</sup> National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

demonstrate the happy blend of disciplines and talents that this amalgamation brought together. They attest to the conviction reached in Tokyo that the pattern of cutaneous cancer varies remarkably in different regions of the world, and its proper study requires international cooperation. The present Conference has given opportunity for many stimulating and fertile discussions which can lay the groundwork for the design of joint undertakings in geographic pathology and dermatologic research. A practical solution for some of the problems discussed may hopefully follow this joint effort. Investigators from widely scattered communities have brought into perspective the variations in the prevalence and site distribution of cutaneous cancers within their world-wide distribution. These variations cannot be by chance alone but must result from causes that we can hope to disclose if scientists on the spot pursue their investigations with vigor. The Conference increased our understanding of some obscure points, but at the same time, it revealed how many large and important areas of total ignorance exist. Nevertheless, our experience with skin cancer in the past has taught us optimism. We are indebted to studies of skin cancer for much of the knowledge we now possess about cancers in general. Skin cancer was the first cancer for which a cause was demonstrated—soot, 1775. The cause of cancer of another site was not discovered for more than 100 years; it was not until 1879 that lung cancers in Schneeberg miners were shown to be caused by ionizing radiation. In the intervening years knowledge had accumulated about four other causes for skin cancer in human beings—arsenic in 1822, crude wax from coal in 1875, and coal tar and shale oil in 1876. To these causes others were added in succession; among them ultraviolet light, creosote, X rays, shale oil, mineral oil lubricants, and crude anthracene, all of which may cause skin cancer in man when applied directly to the skin.

Of cancers with known causes that physicians see in their daily practice, skin cancer ranks first by a large margin. On the experimental side, our early knowledge about cancer research grew out of the laboratory investigations of Yamagiwa and Ichikawa who followed up the shrewd clinical observations that had been made earlier on skin cancer induced by coal tar. With this past history we have every reason to be optimistic and feel confident that the peculiar variations in histologic type and site distribution of skin cancers revealed by this Conference will yield important information on etiology. With this as a guide, the initiation of vigorous investigations by the participants should reveal new knowledge of inestimable value.

This Conference represents a landmark in the progress of dermatology. Its proceedings give us the latest information on the clinical and pathologic manifestations of cutaneous cancer in man and the research accomplishments from animal experimentation. The speakers have emphasized the practicability of studies on skin cancer and the success to be gained by focusing the attention of experienced investigators on the subject. If the geographic approach is to realize its full potentialities, it needs the support of scientists from many disciplines. Now is the time to carry

out the investigations discussed at the Conference because the improvements in living conditions and other unforeseen changes all over the world will abolish our present opportunities for such enterprises. The publication of the proceedings that follow should convince everyone that we have an important and urgent duty to learn all we can about the biology of skin cancer and its geographic variations while the opportunities last.



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## PERCIVALL POTT'S CONTRIBUTION TO CANCER RESEARCH<sup>1</sup>

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WHEN PERCIVALL POTT was 62 years old he had practiced and taught surgery for 39 years. In that year of his life, 1775, he sent to his publisher a small book containing 5 surgical papers, one of which was an article (*see* pp. 7-13) on cancer of the scrotum (1). Historically this was the beginning of cancer research because Percivall Pott probed beyond the immediate problem of the surgical treatment of scrotal cancer into the question of etiology. He found that scrotal cancer occurred almost exclusively in chimney sweeps and ascribed its origin to contact with soot. As Pott wrote: "The disease in these people seems to derive its origin from a lodgment of soot in the rugae of the scrotum." Thus he identified the first carcinogen known to man. Not only did his discovery have practical applications for cancer prevention, but it began a chain of inquiry into the cause of cancer that a century and a half later led to the elucidation and identification of carcinogenic hydrocarbons, and the rich harvest of knowledge that has resulted from the study of chemical carcinogenesis.

The recognition of soot as a carcinogen developed from a thoughtful inquiry, and only fleeting indications of Pott's own thoughts are found in the article—for Percivall Pott, as James Earle wrote: ". . . studiously avoided reference to obscure and general principles—and preferred reasoning by analogy and induction from established facts . . ." (2). It is not often appreciated that cancer was accurately diagnosed 187 years ago, particularly when the science of cellular pathology had not been developed, but the clinical description of the progression of scrotal cancer in chimney sweeps, written by Pott, leaves no doubt concerning the accuracy of the diagnosis. Further, scrotal cancer in chimney sweeps was not the usual form of cancer and Pott pointed this out quite clearly: ". . . all this makes it (at first) a very different case from a cancer which appears in an elderly man whose fluids are become acrimonious from time, as well as other causes, or from the same kind of complaint in women who have ceased to menstruate."

<sup>1</sup> Presented at The Conference on Biology of Cutaneous Cancer, Philadelphia, Penna., April 6-11, 1962.

<sup>2</sup> National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

Pott was impressed with other clinical aspects of chimney sweeps' scrotal cancer and wrote: "I never saw it under the age of puberty,<sup>3</sup> which is I suppose one reason why it is generally taken both by patient and surgeon for venereal, and being treated with mercurials, is thereby soon much exasperated." Mercurial therapy, the chief treatment for venereal diseases, was applied locally as an ointment. Pott probably observed these unresponsive patients with scrotal lesions were all chimney sweeps by trade. He noted that the chimney sweeps themselves referred to the scrotal lesion as a "soot wart," and it is reasonable to assume that his attention was directed more to the idea of a disease associated with a specific occupation—a concept not unknown to him, for he refers in scholarly manner to Ramazini's book "de morbis artificum," the Colic of Poitou, and the disorders of white lead workers. This scholarly method was important, for it provided a new approach: Scrotal cancers were in some way connected with the occupation of the patient.

Pott was a scholar though he had only 9 years of formal education before his apprenticeship to the surgeon Edward Nourse (2). Sir James Earle wrote of his father-in-law: "He often said he began to teach when he had much to learn; and as he was not actuated by that opinionative wisdom which sometimes attends advanced life, after all his study and experience he confessed that he still retained a long list of inquirenda." Pott's epitaph reads: "The labours of the ancients were familiar to him; he scorned to teach a science of which he had not traced the growth" (2). On the same subject, Sir James Earle said, "Mr. Pott always professed great value and respect for the early writers on the art and perused their voluminous works with great diligence and sagacity."

Strengthened by evidence and by the precedent of other occupational diseases, Pott must have then continued his inquiry beyond the environs of his usual routine. While older members of the lucrative chimney sweeps' trade had contact with soot in many different ways, such as sifting and preparing soot for sale, the most intimate contact was that of the small boy who climbed the tortuous, narrow English chimneys. Since Percivall Pott was aware of the abuse of these children (he vividly described their "singularly hard fate"), it can be assumed that *some* time about 187 years ago he observed chimney sweeps at work. He must have been struck by seeing soot in the rugae of their scrotums, and then in that 18th century moment have perceived for the first time a process which we now speak of as "chemical carcinogenesis."

The recognition of soot as a carcinogen was a monumental step in our knowledge of carcinogenesis and Pott's paper presented just this idea to his contemporaries, for they immediately began to see the principle involved in other circumstances. Benjamin Bell in 1794 (3) wrote: "This variety of cancer appears obviously to be produced by soot, for it

<sup>3</sup> James Earle later showed Pott an 8-year-old apprentice chimney sweep with a scrotal cancer (2).

is found that besides chimney sweeps those who are employed in manufactures in which soot enters as an ingredient are occasionally seized with it." In 1808 James Earle recorded the history of Allan Spragg, a 49-year-old gardener who developed an epithelioma on the dorsum of his left hand. This gardener had spread soot in his garden one spring 5 years before to kill slugs. He carried the soot in a pot that was hung over his left hand; the handle rubbed spilled soot onto his wrist. Earle grasped the point that skin cancer elsewhere than in the scrotum might be caused by soot. Henry Earle, a grandson of Percivall Pott, found "some exceptions to the rules" of his grandfather (4). He agreed that the "peculiar stimulus" soot caused scrotal cancer, but it was not the only factor; he said that the frequency in chimney sweeps was not great, considering how many were exposed. Earle suggested that a ". . . constitutional predisposition is required which renders the individual susceptible to the action of the soot." He strengthened the idea with facts; scrotal cancer sometimes favored "different branches of the same family at a particular period of their lives." Heredity in cancer was not a new subject, for John Hunter discussed this question in 1787 in his *Lectures on the Principles of Surgery* (5).

Further, Henry Earle had difficulty in understanding why individuals as children were exposed to soot and then developed cancer after the age of 30. By 1823, soot cancer in chimney sweeps was provoking new questions that today would be debated in terms of genetic factors predisposing to cancer, the latent period of carcinogenesis, etc.

Chimney sweeps' cancer was considered by Astley Cooper, T. B. Curling (6), and James Paget (7). Curling took up Henry Earle's concept of the individual predisposition and hereditary background. He described a sailor with a scrotal cancer in the fifth decade of life. The sailor had been "brought up as a sweep" but had been to sea for the 19 years preceding the appearance of the neoplasm and during this time had no contact with soot. In 1856 James Paget raised many new questions about scrotal cancer. He described precancerous changes, but, concerning soot, said, "I suspect that the true influence of the soot in this disease is not that its continued contact determines the growth of cancers but (at least in part) that it produces a state of skin which provides an apt locality for epithelial cancer in persons of cancerous diathesis."

In 1892 Henry Butlin reinvestigated in detail the subject of scrotal cancer in chimney sweeps (8). Though a century had passed since Pott's death, new facts had come to light and old ones, such as the continuing appearance of scrotal cancer in chimney sweeps still remained.

The expanding Industrial Revolution had brought an increased need for lubricating oils for machines. Prior to 1850, machines were lubricated with animal oils. With the rise of the mineral oil industry and after the reports of Volkmann in 1875 (9) and Bell in 1876 (10) on the occurrence

of scrotal cancer in the tar, paraffin, and shale oil workers, Butlin recognized other crude carcinogens for the scrotum. He also recognized a few other unpleasant facts: "We who live in large cities swallow and inhale soot every day in greater or less quantity. We accept the position, grumblingly no doubt, still we accept it; we know that our great smoke fogs make many people ill, and that they kill a certain number with acute disease. But it is possible that we owe far more than this to the influence of *floating soot* and that a part of the increase in the occurrence of that awful disease, cancer, of which the national statistics tell so striking a tale, is due to the daily contact of soot with areas of the lining of the mucous membrane, or to the entrance of soot into some one or other of the internal organs, in which the conditions are favorable to its action." This complaint about increasing deaths from cancer was dated July 9, 1892!

Butlin brought out an important concept from his review. There were several types of carcinogens for man: soot, tar, paraffin, and certain mineral oils, and he raised an important question: If these agents could cause cancer on the skin, might they not also cause cancer internally? In this century great additions to our knowledge of carcinogens for man have been published by Henry (11) and by a participant in this Conference, Wilhelm Hueper (12).

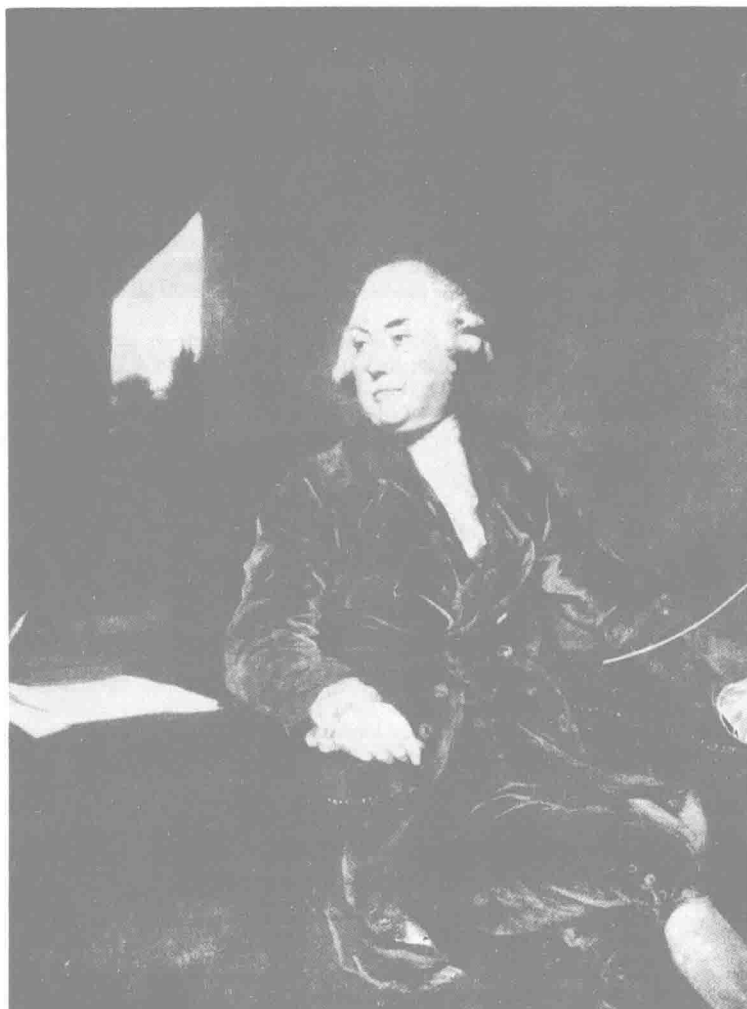
Pott's contribution is being extended in another way and the realizations of this work may be the most important of all. For tar, soot, and crude mineral oils induce cancers not only in man but also in many other species. The historic achievement in 1915 of Yamagiwa and Ichikawa is well known [see Bibliography in (13)]. Passey in 1922 extracted from soot a potent carcinogen for mice (14). The brilliant series of experiments of Kennaway, Heiger, Mayneord, Cook, and Hewitt from 1922 to 1935 led finally to the identification of many active principles of several crude products. Sir Ernest Kennaway described the historic development of these important experiments in 1955 (15).

All these experimental techniques and agents have led to a new order of investigation which relates to the all-important question of how these chemicals transform normal cells to neoplastic ones. But most of all, experimental evidence has given irrefutable validity to the speculation of Butlin that the agents which cause cancer on the skin can also induce cancer internally. The mechanism of action of soot or its active ingredient is not understood, even after 187 years of enormous, technological development, and the easiest, most effective method to control scrotal soot cancer is the same as that available to Percivall Pott and his contemporaries: *prevention by avoidance of contact*. It is remarkable that Percivall Pott did not suggest this method.

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Percivall Pott (1714-1788)

Portrait by Sir Joshua Reynolds (1784)

This painting now hangs in St. Bartholomew's Hospital, London, where Percivall Pott was a surgeon, and is reproduced here by permission of the Governors of the Hospital.