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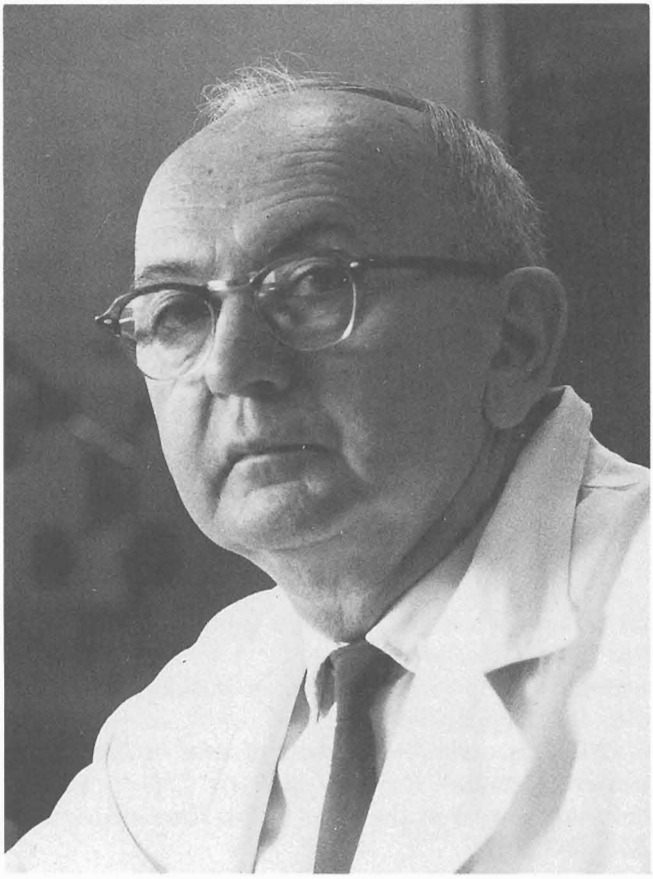
JACOB FURTH

1896—1979

A Biographical Memoir by

SIDNEY WEINHOUSE AND JOHN J. FURTH

Biographical Memoir



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JACOB FURTH

September 20, 1896–July 23, 1979

BY SIDNEY WEINHOUSE AND JOHN J. FURTH

THE TWENTIETH CENTURY has witnessed the phenomenal growth of medical science, and cancer research in particular has advanced from a field of descriptive anatomy to a flourishing, sophisticated biological discipline, pregnant with insights directed toward understanding and control of one of humankind's misfortunes. One of the leaders who helped to transform cancer research to a true scientific endeavor was Jacob Furth. In a career of fifty-seven years he contributed to diverse fields of cancer biology and experimental pathology. He was responsible for major advances in immunology, leukemia and radiation, and viral carcinogenesis. His pioneering work on hormonal effects in tumor development added new dimensions to our understanding of how tumors proliferate.

Jacob Furth was born in the city of Miscolcz, then part of the Austro-Hungarian Empire, in 1896. His father, Jonas, had seven children, four of whom died as infants. Jacob was the next to the youngest. His mother, Jetti Sussman, died when he was three. His father remarried Roza Farkas, and they had four more children. Roza was a simple woman and a devoted mother to both her children and her stepchildren. Jacob was particularly close to one brother, Lajos, with whom he played soccer and chess. Lajos came to the

United States in 1941, and they remained close until his death in 1969.

Jetti's children were all talented. One sister, Margit, wrote first-rate novels and poetry (in Hungarian). Jacob pondered whether to go into medicine or law. He chose medicine over law because, as he put it, "Lawyers can be hired to prove not only the right, but also that the wrong was right."[1]

This was at the outbreak of World War I; after his first year, having been captured in the first major battle in which his unit was engaged, Jacob spent three years in Russian military prisons. He returned to Hungary as part of a prisoner exchange and completed his medical training in 1921. His experiences as a prisoner during the turmoil of the Bolshevik Revolution, which extended into Hungary on his return, have been recounted by Murray Angevine.[2]

It was in Prague that Jacob met Olga Berthauer, a medical student at the Czech University, while he was attending the German University. She was to come to the United States a year after Jacob. The immigration authorities were reluctant to let her stay (as a single woman). However, they were married the next day, and, upon presentation of the marriage certificate, the immigration authorities relented. She was to be collaborator, colleague, homemaker, and confidant for over fifty years. Although maintaining a career, first as a pediatrician and later in school health, Olga's devotion to Jacob was complete. Without hesitation she gave up good jobs when he moved. She was good at her vocation, always able to get a good job in the new city (except Boston, for Massachusetts would not license a graduate of a foreign medical school). Her last job was with the School Health Department of New York City, a position she held until the mandatory retirement age of eighty. She died April 21, 1988.

EARLY YEARS IN RESEARCH, 1918–32

Jacob had an inquiring mind and a love of learning that attracted him to research, even while a medical student. Under the guidance of Edmund Weil, one of several great scientists who, he acknowledged, had an important influence on his career, Jacob began research in microbiology and immunology, directed to whether bacterial species could be characterized antigenically. This work required keeping open plates for one or two weeks in search of mutants, and these were subject to fungal contamination. In his autobiographical essay,[1] Jacob wryly confessed his chagrin at his presumption that the "damned fungi were preventing growth of the bacteria by depriving them of essential nutrients. The possibility that the fungi secreted a bactericidal substance did not cross my mind." He also regretted that he did not write up or follow up on work he started at that time on bacteriophage, just discovered by D'Herelle, recalling the statement by his dean and department chairman Oscar Bail that "this may be the greatest discovery of our period." However, a lasting contribution of the period was Jacob's introduction of the agar plate, which has now become standard practice in microbiology.

A turning point in Jacob's career was the sudden death of his mentor, Edmund Weil, and his senior associate, F. Breinl, from typhus, and his own illness and recovery from the same disease. Facing the dilemma of whether to choose a career in clinical research or stay in the laboratory, and weighing his future in postwar Europe, Jacob accepted an offer from Eugene L. Opie of the Henry Phipps Institute of the University of Pennsylvania in Philadelphia. He remained there for two productive years, 1924–26, working on acid-fast organisms and their antigens.

Jacob acknowledged with gratitude (naming one of his

twin sons Eugene) the profound influence of Opie and an outstanding group of young scientists on his career. During his two years at the Phipps Institute he established immunologic relationships among acid-fast organisms, the antigenicity of microbial lipids, and at the suggestion of Opie he confirmed the observation of Zinnser that new antigens could be created by heat.

This last work caught the interest of Karl Landsteiner, the discoverer of the blood groups, who invited Jacob to the Rockefeller Institute as his assistant. His two years there, from 1926 to 1928, were a profound learning experience. From Landsteiner and daily contact with other great scholars at the institute, Jacob learned both the philosophy and strategies of research. It was at the institute that he was introduced to the cancer problem by the brilliant work of Peyton Rous, James Murphy, and especially Alexis Carrel, through whom he was introduced to tissue culture, a tool he used continuously in his future work.

With Landsteiner he attempted to transform saprophytic vibrios to cholera vibrios and to transform Drosophila strains. They chose the wrong organism. It was Avery who several years later successfully transformed pneumococcal strains, thereby revealing the hereditary role of DNA!

Under Landsteiner's instruction Jacob demonstrated differences in the blood groups among the anthropoid apes, and Landsteiner asked him to stay on to take on Philip Levine's work on minor blood subgroups. Restless to do independent work, however, Jacob accepted an offer in 1928 from Opie to return to the Phipps Institute in Philadelphia. A return to this institution was not without some regret. In his autobiographical essay[1] he points out ruefully, "Now that Philip Levine has attained greatness by the discovery of the Rh factor . . . I see what I have missed."

Opie had accepted a generous grant from E. Mallinkrodt, Jr., for experimental work on leukemia and placed Jacob in charge. It was here that Jacob began a long, wide-ranging, and uniquely productive study on leukemia, for which he received widespread recognition. He frequently expressed his gratitude to Mr. Mallinkrodt, who required no reports and even kept his support anonymous until 1957, when he relented on Opie's urging.

Jacob took two independent approaches simultaneously. One was to obtain leukemic mouse strains. He succeeded by inbreeding mice in which leukemia occurred spontaneously or was induced by radiation. One strain, the AKR mouse, carries a leukemia virus and has become one of the most common and widely used animals in many diverse experimental studies. The second approach was to attempt to isolate viruses from the various types of leukoses then available. Five leukosis viruses were isolated and studied, one of which was the fowl neurolymphomatosis virus, the agent of Marek's disease, an economic scourge of the poultry industry until its conquest by a vaccine in 1970.

Other notable findings of this period were the transmission of avian leukosis by blood-sucking insects, the occurrence of high concentrations of leukemia virus in the serum of leukemic chickens, and the viral nature of the common venereal sarcoma of dogs, transmitted through copulation.

It was in Philadelphia that Jacob's twin sons were born. He somehow found time to be a good father. Both sons emulated him and became physicians. One is now in North Carolina, the chairman of the Department of Medicine at East Carolina Medical School, and the other, a coauthor of this memoir, is a professor of pathology at the University of Pennsylvania in Philadelphia.

CORNELL, 1932–47

When Opie assumed chairmanship of the Department of Pathology at Cornell Medical College in New York in 1932, Jacob joined him as assistant professor of pathology. Acquainted with New York through his prior two years at the Rockefeller Institute, Jacob found the atmosphere exhilarating. Angevine, his colleague and sometime collaborator at Cornell, has succinctly described this period:

> The days spent at Cornell were among the happiest of J.F.'s career. The conditions and environment were ideal for investigation with fine, well-equipped laboratories, space for animals, a loyal and efficient technical staff, and adequate financial support.[2]

Angevine goes on,

> Initially, when full time was available for the studies on leukemia, [Jacob] was like a human dynamo, working so continuously and relentlessly that although he frequently appeared fatigued, his pace seldom slackened. He seemed to thrive in the midst of the restless activity and ferment of New York City, which served as a catalyst for his boundless energy. His enthusiastic approach to every problem attracted bright young men to his laboratory, most of whom worked hard and completed an *arbeit*. He was also strongly convinced of the value of student participation in research; perhaps this stemmed from his own experience as a student.

Jacob's fifteen years at Cornell were very productive. With Cole and Boon in the early forties he demonstrated important genetic factors in the heritability of leukemia in mice, and in cross-breeding experiments they showed that in some instances the influences of the low leukemia strain predominated, whereas in others the high leukemia strain predominated. He (and others) also showed that heritability was not due to a maternal "milk factor," as it was with high and low mammary tumor strains.

A role of the thymus in leukemia was shown by work with McEndy and Boon. In the high leukemia AK strain, removal of the thymus, a primary site in this strain, lowered the incidence from 78 to 11 percent. Removal of the spleen had no effect, and the effect of thymectomy was not inherited, since the offspring of thymectomized mice had the same high incidence as the high leukemia grandparent. Thymectomy also lowered the incidence of methylcholanthrene-induced leukemia but had no effect on the growth of grafted leukemic cells, which grow equally in high and low leukemic mice.

During his period at Cornell Jacob received support not only from the Mallinkrodt Fund but also from the Lady Tata Memorial Trust, the International Cancer Research Foundation, the Jane Coffin Childs Fund, and the Anna Fuller Fund.

Although research remained his foremost interest, Jacob enthusiastically entered into the other elements of the academic triad, teaching and service. Also in his mind was the tenuous nature of full-time research, particularly at that time. He was in a pathology department and felt he had to become a "compleat" pathologist. He took a minisabbatical to Vienna to learn anatomical pathology from Masters.

One of Jacob's major responsibilities was teaching experimental pathology, then a requirement for medical students, who had the choice of spending two semesters on an investigative study proposed by either the staff or the student. He derived much satisfaction in having indoctrinated future physicians in the methods and spirit of research and in some instances having encouraged students toward research careers. Additional wartime responsibilities as acting chairman of the department when Opie retired and other staff members left for wartime service drew

him further away from research. He regretted this hiatus in his leukemia studies, causing loss in momentum to other investigators. Much of his most important work on viral causation of leukemia, such as genetic inheritance of the virus causing leukemia in AK mice, went unreported. Another important contribution inadequately reported during the pressure of wartime responsibilities were the effects of thymectomy in preventing viral expression and the use of thymus extracts to activate viral expression. This work, however, marked the beginning of a major career effort, to be described later, on the role of host factors in cancer development.

As recognition came and he advanced to full professorship, Jacob became increasingly in demand as a consultant and as a member of committees dealing with the evaluation of research projects and policies for such agencies as the Armed Forces Institute of Pathology, the Atomic Energy Commission, the National Institutes of Health, and the American Cancer Society. As a sometime member with him on such panels, the senior author of this biography saw firsthand how well Jacob performed in these roles. He was a superb adviser on these bodies—forthright in his opinions, backed always by adequate documentation; they were invariably the well-thought, considered, and eminently fair views of an erudite scientist well versed in biomedical science. These same qualities made for extremely effective service on editorial boards for a number of journals such as *Blood, Cancer Research, Journal of the National Cancer Institute,* and others, to which he gave much time and effort.

Jacob modestly attributed his productivity at Cornell to

> . . . a good student body, associates and assistants. We reported on the individuality of various types of leukemia in mice; their transmission by a single cell; a method for preservation of living cells by slow freezing (with

C. Breedis); the genetics of spontaneous leukemia (with R. Cole); the role of the thymus in leukemogenesis; the individuality of the monocytes, histiocytes and microglia cells (with H. Dunning) and their relation to reticulum cell sarcoma; differentiation of leukemia and leukemoid reactions (with W. A. Barnes); and the possibilities of experimental therapy of leukemias (with L. Reiner and C. Flory). We also expanded the list of different viruses causing leukemias and sarcomas, and indicated the essential identity of mouse and human leukemias and the neoplastic character of both. . . . The two years Elvin Kabat spent with us at Cornell were highly productive. In addition to work on high-speed sedimentation of leukemia viruses, the histochemical identification of alkaline phosphatases, and the localization of alkaline phosphatase (with C. Breedis) in the proximal convoluted tubules of the kidney led us to identify the site of nephrotoxic agents such as the mercurial compounds, then used in the therapy of syphilis.[1]

A SHORT STAY IN DALLAS, 1947–49

Disappointed at being passed over for chairmanship of the Pathology Department at Cornell after Opie's retirement, Jacob left to join the Veterans Administration Hospital in Dallas, Texas, in 1947. The Dallas position also carried an academic appointment at Southwestern Medical College, but several unforeseen setbacks made this position much less desirable than he had anticipated. Though accepted wholeheartedly by the faculty, the dean (a retired general of the Army Medical Corps) refused to appoint Jacob to a full professorship, a rank he held at Cornell; nor would the dean allow him to accept any of the research grants from the foundations that supported him in New York. (It would be hard to imagine any of today's deans conducting such an act of self-immolation.)

Although a heavy service load severely handicapped Jacob's research, notable observations were still made. With T. Bali he observed some remarkable changes in radiation-induced ovarian tumors, and he isolated a highly functional mast cell tumor.

When the Veterans Administration abolished its regional organization, a better opportunity arose in 1949 to chair a department in one of its university-based hospitals. At the same time, however, Jacob received a cordial invitation from Alexander Hollaender to join the Biology Division of Oak Ridge National Laboratory. He accepted on the advice of Shields Warren, a statesman of U.S. science who at the time was head of the Atomic Energy Commission Biology Division, and thus ended a seventeen-year period of broad-based pathology to return once again to the laboratory.

RADIATION BIOLOGY AT OAK RIDGE, 1950–54

Jacob had already contributed to radiation carcinogenesis with x-ray induction of leukemia in mice back in 1929, the induction of ovarian tumors as late radiation effects, and some attempts at γ-ray therapy of experimental leukemia. Enthusiastically plunging into the newly developing area of radiation biology, Jacob greatly expanded his perceptions by taking a course in radiation physics. Aided and guided by members of the Biology Division, he entered a renewed surge of research accomplishment in a highly charged atmosphere, of the same type that had nourished and sustained him at Cornell. A unique experiment in which he took part at Oak Ridge was a massive study of radiation effects on mice, resulting from an experimental explosion of an atomic bomb (Operation Greenhouse). As Shields Warren wrote,

> Jacob was the recipient of large numbers of mice, survivors from a Pacific nuclear test, placed with various degrees of shielding along radii from the point of explosion. He had the foresight to follow these animals to the time of their natural death. As a result of these studies, much new information was developed about the late effects of radiation, about biological dosimetry, and about the similarity of certain radiation effects to those of aging. The meticulous care with which these animals were kept free of

epizootics and the painstaking observations on them, pre and postmortem, became a milestone in radiobiological research.[2]

The hitherto puzzling cause of the anemia associated with acute death from radiation occupied much of Jacob's attention during this period. This problem was solved by the discovery, with Storey, Wish, and others that erythrocytes enter the lymph ducts owing to radiation-induced destruction of platelets. Within minutes after platelet perfusion, the bloody lymph clears. With amusement Jacob described his difficulty in getting this important observation accepted by a prestigious journal.[1] This work led to the effective use of platelet perfusion in platelet deficiency disorders.

At Oak Ridge Jacob's senior associate was Arthur C. Upton. Among his various collaborations there, Jacob acknowledged that "in studies of radiation-induced leukemias of various types and the relative biological efficiency of diverse types of radiations, my senior associate, A. Upton, did a 'lion's share' of the work."[1] This collaboration, extending long beyond Jacob's tenure at Oak Ridge, resulted in many publications on detailed mechanisms of radiation-induced carcinogenesis and influences thereon of hormonal manipulation. As Upton has stated, "His name has become legend here. His intensity, devotion to science and impatience with imperfection are recalled vividly by all who knew him. My admiration for J.F. and my debt to him as my mentor are boundless."[2]

This period was especially notable for the beginning of Jacob's perhaps most important contributions—the role of hormones in neoplasia, a field in which he subsequently devoted most of his scientific efforts. Endocrine tumors had been observed in Operation Greenhouse. It also had been observed by Gorbman that radiation from ^{131}iodine

induced pituitary tumors in mice. Further investigation with Burnett and others led to the finding of a thyroid-pituitary axis whose manipulation could produce at will either thyroid or pituitary tumors.

HARVARD AND THE CHILDREN'S CANCER RESEARCH FOUNDATION, 1954–59

Despite the productivity of these Oak Ridge years, Jacob yearned for a more academic atmosphere and in 1950 welcomed an invitation by Sidney Farber to join him as associate director and chairman of the experimental pathology section of the Children's Cancer Research Foundation in Boston, supported by the so-called Jimmy Fund, named after a young cancer victim cured by chemotherapy. These were also fruitful years of research, which Jacob modestly attributed "to the fame of Harvard, which . . . channeled to my laboratories guest investigators from . . . Australia, England, Israel, India, Japan, . . . and the U.S.",[2] and the unparalleled opportunity of collaborating with the many talented members of Harvard's faculty.

With Paul Hagen, the transplantable mastocytoma that Jacob had developed earlier was shown to produce heparin, serotonin, and histamine, a striking example of a transplantable tumor that retains considerable functional activity. Other notable Harvard faculty who contributed materially to Jacob's investigations of endocrine neoplasms were Jean Mayer on the obesity-inducing adrenotropic tumors, and Gregory Pincus and Eric Bloch on the steroids formed by these tumors. Several of the guest investigators—Donald Metcalf, now head of the Walter and Eliza Hall Institute of Melbourne, Australia; Nechama Haran-Ghera of the Weizmann Institute, Rehovot, Israel; Kelly Clifton, now at the University of Wisconsin; Gordon Sato, now at the W. Alton Jones Cell Science Center, Lake Placid; and Untae Kim of the

Roswell Park Memorial Institute, Buffalo—are among the current leaders in cancer research.

Gordon Sato was inspired by Jacob to develop completely defined media for cell culture to dissect the endocrine factors in cell growth in vivo being explored by Jacob. He acknowledged his debt by dedicating to Jacob Furth a conference on the "Growth of Cells in Hormonally-Defined Media."[7]

TWO YEARS IN BUFFALO

In 1959, approaching the Harvard retirement age, and with his hitherto cordial relationship with Sidney Farber having become strained, Jacob let it be known that he would like to move and so accepted an invitation from the Roswell Park Memorial Institute in Buffalo. Along with continuing unfinished work begun at Harvard, he was encouraged by Theodore Hauschka to examine chromosomal abnormalities in relation to hormone dependence of neoplasms.

In Buffalo a young Japanese pathologist, Kenjiro Yokoro, came to work with Jacob as a visiting scientist. Their association continued through the next seventeen years and included Yokoro's students and colleagues. Their appreciation was demonstrated by cordial receptions accorded Jacob (and Olga) on two lecture tours to Japan, the last one a year before he died.

THE FINAL YEARS, COLUMBIA, 1961–79

After two years in Buffalo, Jacob was invited by Alfred Gellhorn, then director of the Institute of Cancer Research, and Donald McKay, chairman of the Pathology Department at Columbia University's College of Physicians and Surgeons, to join the pathology department and to head the pathology department at the Francis Delafield Hospital, Columbia's cancer center. Despite his age of sixty-five,

Jacob was warmly welcomed, and with youthful vigor he once again engaged in the broad responsibilities of service and teaching. However, he soon gave these up to concentrate on research and terminated his position at the Delafield Hospital to join the newly formed Institute of Cancer Research, an independent unit of Columbia University, headed by the late Sol Spiegelman. Here Jacob's research focused directly on the induction and properties of endocrine neoplasms, particularly of the thyroid, pituitary, and mammary glands, and on the role of the thymus gland on viral induction of leukemia. During this period, and after his retirement at age seventy, Jacob wrote a number of thoughtful essays on his conceptions of the neoplastic process.[3-6]

Jacob never really retired. His life was his work, except for several hobbies. In his Cornell years, when he lived in Pelham, he gardened, specializing in dahlias. He was interested in stocks and dabbled in the market—always long term; he would never buy and sell for the quick return. He consulted a broker and subscribed to several investment publications but made his own decisions. Overall they were excellent ones and on his death it was his investments, not his retirement pay, that left his wife financially secure.

One investment Jacob sold was some General Motors stock—to buy a farm in Surry, Maine. He thought he would spend the summers there and work at the house or at the Jackson Laboratory in Bar Harbor, about a forty-five-minute drive by car. He never spent more than a few weeks a summer there, often accompanied by colleagues. His children would visit him with their children and what with his frequent moves it became the family home. He called the place "Jake's folly," but it turned out to be his best investment. He died in Surry on July 23, 1979.

The previous day Jacob had attended a meeting at the Jackson Lab, visiting with old friends. This day, as was his

custom, he spent the morning working on his latest manuscript. He then went out in the yard to pick up some brush that his son John had scattered about. After about an hour of yardwork he laid down to take a nap, also his custom. He never woke up.

The following tribute by Gordon Sato, abridged here, appeared in the proceedings of a 1982 Cold Spring Harbor conference dedicated to Jacob:

> Great artists and great scientists tend to be identified with more than one masterwork. Furth developed the first experimental leukemia system in mammals. This work involved the derivation of the AKR and RF mouse strains, the unequivocal demonstration that the experimental disease was analogous to human disease, and the transmission of leukemia with a single cell, the first demonstration that neoplasia can be monoclonal in nature. He demonstrated the necessity of the thymus in the genesis of lymphocytic leukemia and also defined the spectrum of neoplasms resulting from a specific virus infection in fowl, the role of genetics in the spectrum, and the incidence of neoplasms in mice following ionizing radiation. He also pioneered in cryopreservation of mammalian cells. Furth's interest in endocrine carcinogenesis was stimulated by the ovarian neoplasms that occurred in his early radiation studies, and this ultimately led to the investigation of radiation and hormone-induced functional pituitary tumors. The concept of conditioned and autonomous neoplasia emerged during these studies, a major insight into the importance of physiological feedback regulation in oncogenesis. Furth employed endocrine neoplasms as indwelling hormone sources in studies of normal and pathological growth, and he gave freely of his unique functional tumor cell lines to others for study *in vivo* and in culture. Perhaps the most important of his endocrine work was the establishment of the pivotal role of prolactin in mammary growth, differentiation, and neoplasia.[7]

Perhaps the greatest and most lasting influence of Jacob Furth has been on the crucial role of host factors in the induction and maintenance of tumors. Early on he recognized that the tumor and its host comprise a dynamic duo, in which the host and its regulatory mechanisms are pitted against the unremitting progression of tumors toward au-

tonomy and invasiveness. Foremost among the host factors are the hormones, and their interplay with each other and the tumor was Jacob's main research interest in the latter part of his career. Several examples from his classical studies with model endocrine systems illustrate how these systems interact.

Mammary tumors in rats produced by oral administration of chemical carcinogens, such as 3-methylcholanthrene, are responsive to the presence of the ovary and pituitary gland. Kim and Furth showed that if these organs are removed, the tumors regress, but they can be restored to growth even after months of dormancy by implanting a pituitary tumor secreting a hormone that stimulates mammary growth. If rats are given subcarcinogenic doses of either radiation or methylcholanthrene, or if mice are given a subcarcinogenic injection of milk containing a mammary tumor virus, no tumors occur. However, if the carcinogen is supplemented by mammatrophic growth-stimulating hormone, which is itself noncarcinogenic, mammary tumors arise. This promotional effect of hormones, Jacob concluded, is likely relevant to humans, where we are continuously exposed to small subcarcinogenic doses of multiple carcinogens.

Jacob thus amassed an impressive body of evidence for the hypothesis that hormonal imbalances caused by either overproduction of growth-enhancing hormones or underproduction of growth-restraining factors can lead to abnormal cell proliferation. Such growths are generally dependent on or responsive to the hormone that affects its behavior and can regress partially or completely if the imbalance is corrected. However, when to the hormonal imbalance there is added an alteration to the genome that removes intrinsic restraints on proliferation, autonomy ensues, leading to loss of hormone dependency and un-

controlled cell proliferation. This genomic alteration may occur first, causing the initiation of autonomous tumor development, or may be induced by cellular proliferation, thereby leading to the commonly observed gradual sequential progression resulting in partial and ultimately complete autonomy of growth.

Jacob was prominent in a host of professional activities. He was elected to the National Academy of Sciences in 1974 and was a member of its Advisory Committee to the Atomic Bomb Casualty Commission. He was on the Surgeon General's Advisory Committee on Smoking and Health, the Public Health Service's Advisory Committee on Tumor Viruses, and the Committee on Radiation of the Department of Health. He was president of the American Association for Cancer Research and the American Society of Experimental Pathology. He was a fellow of the American Academy of the Arts and Sciences and held honorary memberships in the Endocrinology Society of Chile, the Cancer Society of Peru, and the Pan American Medical Association (diplomate member).

Among his awards and honors were the Gold Medal of the American Medical Association, 1932; the Rosenthal Award of the American Association for the Advancement of Science, 1957; the Bertner Foundation Award from M. D. Anderson Hospital and Tumor Institute, 1958; the Robert Roesler de Villiers Award, 1959; the G. H. A. Clowes Award and Lectureship of the American Association for Cancer Research, 1962; the Semmelweiss Medal and Lectureship, 1962; an honorary doctor of science from the University of Pennsylvania, 1968; the Alessandro Pascoli Prize, 1973; and the Rous-Whipple Award of the American Association of Pathologists and Bacteriologists, 1974.

Jacob was a thoughtful statesman of science, with extraordinary vision that enabled him to see the process of

cancer induction in its formidable complexity. With singular talent, a keen intellect, an inquiring and analytical mind, and experimental skill, he was able to unify otherwise disparate data to explain the development and maintenance of the cellular proliferation of cancer in terms of the operation of extrinsic and intrinsic factors. Our conceptions of cancer induction were broadened greatly in the decade following Jacob's death in 1979 with the discovery of a host of proto-oncogenes whose activation by various mechanisms leads to abnormal cell proliferation. The essential correctness of Jacob's views has been confirmed by the further discovery that the activated oncogenes encode a number of growth-promoting hormones and their cellular receptors.

Jacob brought to experimental pathology a high degree of scholarship, an appreciation of the contributions of the basic sciences to the understanding of disease, and an attitude of humility in the face of what still needs to be learned about life's processes.

His legacy is captured in the words of Henry Wadsworth Longfellow:

> When a great man dies, for years beyond our ken,
> The light he leaves behind him, lies upon the paths of men.

NOTES

The authors depended for this memoir on material in the following publications and are indebted to Arthur C. Upton for assistance.

1. Jacob Furth, "The Making and Missing of Discoveries: An Autobiographical Essay," *Cancer Research*, 36(1976):871–80.

2. Murray Angevine, "Significant Events in the Life of Jacob Furth," *Cancer Research*, 26(1966):351–56.

3. Jacob Furth, "Influence of Host Factors on the Growth of Neoplastic Cells. The G.H.A. Clowes Memorial Lecture," *Cancer Research*, 23(1963):21–34.

4. Jacob Furth, "Pituitary cybernetics and neoplasia," in *The Harvey Lectures*, Ser. 63 (New York: Academic Press, 1969):47–71.

5. Jacob Furth, "Hormones as Etiologic Agents in Neoplasia," in *Cancer: A Comprehensive Treatise*, vol. 1, ed. F. F. Becker (1975):75–120.

6. Jacob Furth, "A Meeting of Ways in Cancer Research: Thoughts on the Evolution and Nature of Neoplasms," *Cancer Research*, 19(1959): 241–58.

7. In *Cold Spring Harbor Conferences on Cell Proliferation*, eds. G. H. Sato, A. B. Pardee, and D. A. Sirbasku, vol. 9, (1982):xxix.

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