Chapter 15

Arthur Purdy Stout

(1885–1967)

"It is impossible to do intelligent surgery without a thorough understanding of the pathology of the disease at hand, and it is equally impossible to make an intelligent interpretation of pathology without understanding its clinical implications." (1952)[630]

Arthur Purdy Stout was born in Manhattan on 30 November 1885, the fourth son of Julia Frances Purdy (1844–1922) and Joseph S. Stout (1844–1904). He had three brothers, Newton (1868–), Andrew (1872–), and Joe (1875–). He was baptized in the Methodist Episcopal church (then at 60th Street and Madison Avenue), of which his father was the treasurer. On his mother's side, he was the grandson of Dr. Alfred Seaman Purdy (1808–1886), a general practitioner who attended his daughter at Arthur's birth. His paternal grandfather, of Dutch-English provenance, was a banker.

In the 67th Street dwelling, Arthur's childhood was spent mostly in the company of adults: his parents and three brothers, the youngest ten years his senior. His father was glad to leave the education of his youngest son in the hands of his deeply religious wife. His mother, chronically in frail health, frequently entrusted the child to the care of her nieces, who were very kind to him. Thus he stayed away from home for long periods of time (Fig. 15-1). Naturally shy and reserved, the child had an active imagination. He found it interesting to live in a fantasy world of his own with imaginary difficulties and dangers he could overcome painlessly.[630]

In 1896 cousins named Shedden took him on a fifteen-month visit to Europe. He spent a good part of this time as a student at the Seelig Institute of Vevey (Vaud), Switzerland, where he learned to speak and study in French. He lodged at the Pensionat Bellerive where he practiced his language skills on other guests. He took hikes in the mountains, visited Chamonix, and saw a demonstration of X rays as well as an exhibit of trained fleas at the International Exposition of Geneva in 1897. The trip included a visit to Florence, where he admired the great masters, as well as a stay in Paris. He later reflected that this early trip had broadened his interest in history, the arts, and foreign people and lands.

On his return from Europe, Arthur was enlisted as a day student at the semi-military Berkeley School not far from home. He remained painfully shy and spent much of his time in the family library with "a collection of handsomely bound books that no one else reads."[630] His paternal ancestors were hard-headed financiers, and his three brothers joined the Wall Street brokerage firm founded by their father. His maternal ancestors and relatives seemed more interested in the arts, medicine, and broader aspects of life. He greatly admired and loved his mother, "the only person who thought that I amounted to anything."[630]

In 1899, at age fourteen, Arthur was sent away to a boarding school in Pomphret, Connecticut. To the introspective boy, the Pomphret School was a terrifying place. He was a good student. One of his teachers introduced him to the beauties of Latin poetry, and Stout long remembered him. He read Horace and Virgil and studied Greek on his own. However, he did not play any sports. He was "different" and consequently unpopular. His summer vacations were spent with various relatives, mostly at his grandfather's estate in Bernardsville, New Jersey.

In the fall of 1903, Stout entered Yale University. He was an average student and did not participate in extracurricular activities. He was not admitted to the fraternity to which all his brothers belonged: a definite family humiliation. Yet he longed to achieve, to be recognized, to excel. He also wished to be popular with girls, but could not learn to dance and was too tongue-tied. He rated himself a "complete flop."[630]

Fig. 15-1. Young Arthur Purdy Stout, age five (around 1890). (Courtesy of Julia Frances Stout.)

At the time he entered college, Stout's father died. Arthur reflected that the only thing they had done together was an occasional game of tennis. While at Yale, he lived in New Haven, whereas his brothers, two of them married, lived at home with their mother. He secretly renounced religion, for it required an act of faith of which he was not capable, but he kept his decision to himself to avoid hurting his mother's feelings. He did not become an atheist, he said, for that would have meant a change of religions. He gained an appreciation of the "unfair advantage" that was his by accident of birth, and decided to devote himself to a life of service. He fell in love and became engaged to a young lady who promptly talked him out of his budding intention to study medicine, as it would not lead to wealth. Fortunately, although he suffered emotionally, their engagement was broken, and he gradually regained his intention of becoming a physician.

In the third year of college, Stout made close friendships with three congenial classmates: Amasa Mather (1884–1920) of Cleveland, Hervey Perrin (1885–1962) of Indianapolis, and Gilbert Little Shark (1885–1908) of Saginaw. All sons of affluent fathers, they planned a fifteen-month trip around the world to follow graduation. Stout studied Japanese history and started to collect literature on China. Their elaborate preparations included a variety of equipment, medicines, and letters to consular officials. One item was overlooked: no one suggested vaccination.

Early in July 1907, Am, Gil, Scurvy, and Purdy left Seattle and disembarked seventeen days later in Yokohama. Avoiding big hotels and large urban centers, they enjoyed contact with ordinary Japanese people and their customs. Stout and Perrin left their friends in Japan and proceeded by sea to Shanghai. There they made detailed preparations to undertake a 3,600 mile trek to Bhamo in Burma. With a retinue of translator, cook, and servants, they gathered considerable supplies and beasts of burden. Attired in Chinese clothes (Fig. 15-2) to avoid being conspicuous, they proceeded along the Yangtze River, through its three monumental gorges, sometimes perilously pulled upstream from the banks by as many as fifty coolies, and eventually reached Chunking. They roughed the remaining 2,000 miles, weathering a snowstorm in the mountainous country of western Yün-Nan. At Yünan-Fu, Perrin decided to detour toward Tonkin, taking the cook with him. Stout continued, depending on canned sardines and local foods.

Meanwhile, Stark and Mather visited Peking, Mongolia, Formosa, Borneo, Java, and Malaysia. Since Stout was late in arriving in Bhamo, Stark advanced on the road to China and encountered him ministering to the sick at a border village.[598] Perrin was recalled home, and the three remaining travelers met in Mandalay and later in Calcutta. Stout then teamed with Stark to extend their adventure to Darjeeling and to Sikkim at the foot of the Himalayas, continuing to Delhi and Udaipur. Reunited in Bombay, Stark opted for a visit to Ceylon, while Stout and Mather went to Kasmir. They agreed to meet again in three weeks. Aboard the ship to Ceylon, Stark developed a severe case of smallpox and was put ashore in Mangalore, where his friends rejoined him on the day he died, 20 March 1908. He was summarily cremated. Stark's parents and sisters received the sad news by cablegram in Saginaw. Stout took custody of his friend's ashes for later delivery to his family. Subdued by the tragedy, Stout went to Aden and thence to Germany and home (subj. note 15.1). Many years later, Stout kept a cherished memory of this youthful adventure: sunrise on Yokohama harbor, starlit nights in the mountains of the Yün-Nan, olive gold sunsets on the lower Yangtze, and the earthly paradise of Kashmir.[630]

Stout's collection of literature on China kept growing through contacts established with book brokers at home and abroad. His interest brought him to be elected a Fellow of the Royal Geographical Society. In a scholarly article published by the Geographical Society of Philalelphia he displayed his vast knowl-

edge of the Yün-Nan.[610] Years later he decided to dispose of his valuable collection, probably second to none in the United States. Yale University was not interested. The New York Public Library agreed to take only those items not already on their shelves: a total of 578 books and 136 pamphlets.

On completing his world tour, Stout presented his credentials, paid the admissions fee, and was perfunctorily admitted as a freshman student to the College of Physicians and Surgeons (P and S) of Columbia University. In retrospect he thought he might have been inspired to enter medicine by his grandfather, Alfred S. Purdy, an 1831 graduate of P and S and one of the founders of the New York Academy of Medicine. His only previous experience in medicine had been as a patient, convalescing from typhoid fever at the Presbyterian Hospital. He had witnessed the teaching rounds and bedside instruction, and endured repeated palpations of his spleen by students. Perhaps the demands put on him to help the sick during his long trek in China also awakened his feelings of compassion and satisfaction in being of service.

Medical students were not required to, and for the most part did not, attend faculty lectures. They secured their instruction from private tutors ("quiz masters"), who lectured them at night on materia medica, medicine, and surgery for a fee of one hundred dollars. This system assured the students of eventual internship. The principal activity of first year students was the dissection of cadavers under the guidance of instructors who repeatedly questioned them. One of these instructors was Hugh Auchincloss, who took an interest in Stout and invited him to the out-patient department of the Roosevelt Hospital (subj. note 15.2). Stout spent the summer months there, and Auchincloss introduced him to the recently created laboratory of surgical pathology.

Joseph Augustus Blake (1864–1937), professor of surgery, had asked William Cogswell Clarke (1872–1943) to teach a course of surgery for second year medical students. Clarke thought it was wrong to teach surgery as a purely technical art and that it should be related to pathology. Theophil Mitchell Prudden (1849–1924), professor of pathology, provided Clarke with a small room in his department for the study of surgical specimens. It was to this room that Stout was brought in the summer of 1909 by Auchincloss, who worked there while Clarke was on vacation. Shortly afterward, Clarke assumed direction of the surgical research laboratory, also created by Blake for dog surgery. Thus, the surgical pathology and experimental surgery laboratories were fused. This led to the creation of a fourth-year elective course on surgery for medical students. Clarke added a classmate, John F. McWhorter, to his staff along with a most capable technician, Mamie O'Brien.

Clarke was an excellent teacher who used the Socratic method of leading students to find the right answers to his questions. His second-year course on surgical principles was very popular, and Stout attended. "Bill gave me early inspiration and enthusiasm," wrote Stout, who spent his second summer in the laboratory. By then a penthouse had been built on the roof of the medical school, with facilities for animal experimentation and a good-sized surgical pathology laboratory. In 1911 the College of Physicians and Surgeons became affiliated with the Presbyterian Hospital. The merger gave Columbia University the right to choose the chiefs of services at the hospital.

As a medical student, Stout gained self-confidence. He was among the highest ten students of his class and became a prosector of anatomy. He was elected to membership in the Alpha Omega Alpha Honor Society and president of the Omega club. He managed to spend a short vacation in 1910 climbing the snow-capped rim of Mexico's Popocatepetl and

Fig. 15-2. Stout, right, in Chinese attire at the Yün-Nan (1908) with Chinese translator and guide. (Courtesy of Raffaele Lattes, M.D.)

visiting the isthmus of Panama, where he met William Crawford Gorgas (1854–1920). Having decided on a future course in surgical pathology, Stout gained well-deserved peace of mind.

Towards the end of his fourth year, in May 1912, Stout took the highly competitive written and oral examinations offered jointly by three New York hospitals for the selection of interns. Top contestants had a choice of service. Stout ended in second place and chose the Roosevelt Hospital's surgical service under Charles Howard Peck (1870–1927). He skipped the formal commencement exercises of his class and took a few weeks to go hiking in Switzerland before starting his internship.

The new intern was thrown into duties for which he had no preparation.[630] Internship was hard work and an intense challenge to resourcefulness. The intern recorded histories and obtained specimens for the laboratory. He had to administer general anesthesia, mostly ether or gas, to all his ward patients who underwent surgical interventions. He was also expected to treat casualties arriving in the crowded emergency room. His immediate supervisor, the house surgeon, could be called for guidance or help, but was busy elsewhere most of the time. There was an admirable *esprit de corps* between interns and nurses. No intern could venture into a ward without a nurse coming promptly to provide support and assistance. Interns were off duty every other evening after 6 p.m. and every other Sunday after 12 noon.

Stout spent the second half of his first year as an intern in the hospital laboratory of pathology where he gained experience in frozen sections. As a second-year intern, he was often assigned to assist in surgical interventions and writing surgical reports in longhand. Once a week, there were grand rounds with presentations of cases, reviews of treatments, complications, etc. During the last six months, he was house surgeon (chief resident).

One misty morning in August 1913, the White Mountain Express was stalled in Willingford, Connecticut, when another express train plowed into it. Jane Stoddart (1891–1955), a trained nurse from Toronto, was trapped between an upper and lower berth of the pullman car and was brought into the Roosevelt Hospital with a fractured pelvis. She remained in the hospital several months. When discharged, she was engaged to the house surgeon, Dr. Arthur P. Stout.

The College of Physicians and Surgeons offered Stout a position in the Department of Surgery, but first he had other important business to take care of. As planned, his fianceé preceded him to Paris. He joined her, and on 22 June 1914 they were married in the City of Light. He had planned to see certain surgical services in Germany and Austria, but during their visit to Scandinavia the first World War broke out. They retreated to England and were back in New York by September.

The newlyweds settled themselves in a six-room apartment at 150 East 72nd Street, obliging Stout to give up his collection of books on China. His father had left him an endowment of three thousand dollars a year, so they could live well enough to afford even a maid. Stout credited his forebears with the additional endowment of enough business sense to preserve his inheritance. He also credited his wife's Scottish ancestry and frugality for their continuing ability to live within their means. Traveling abroad was to be their only luxury. On 30 October 1916, Julia Frances Stout was born. "Frinda" was to be the Stouts' only child.

Stout accepted a dual appointment as instructor in surgery and assistant attending surgical pathologist at the Presbyterian Hospital.[340] He was expected to lecture on surgery to second year students, to work in the outpatient department, and to help Clarke with reporting on surgical specimens. To meet these obligations, he commuted daily from the Hospital at Park Avenue and 70th Street to the medical school at 59th Street, where the pathology laboratory had been expanded to a two-story building connected with the operating rooms.

Since his second year in medical school, Stout had a fascination with neoplasia. He thought he had discovered a rare tumor of the appendix only to find it was a well-known carcinoid. In 1917 he wrote on tumor-like lesions of the epidydimus for presentation to the New York Pathological Society. He also reported the first case of retroperitoneal ganglioneuroma in the American literature.[611,613] In addition, he made a review of all cases of cancer that had been treated at the Presbyterian Hospital.

As the U.S. entered the war, First Lieutenant Stout was shipped to Liverpool and promptly to the war front in France. Under night flares and the constant rumbling of guns, a chateau was hastily converted into a hospital for American casualties at Crépy-en-Valois. For the rest of his life, he kept the heart-rending memory of mangled bodies and wasted youth. When the Armistice came, he had to wait long to be evacuated. Finally, the *S.S. Alfonso XIII* brought him from the Gironde to the U.S. and, five days after his return in May 1919, he was discharged.

James Ewing published his *Neoplastic Diseases* in 1919. From it Stout learned of numerous tumors he had never seen. He was particularly appreciative of the book's thorough bibliographic references. The dominant theme was histopathology, and tumors of the same organ could be found in different chapters. It was a time when pathologists gave their retrospec-

tive conclusions in the court of the autopsy room, and looked down on the examinations of mere fragments of anatomy.[340] Stout, unencumbered by time-consuming autopsies (pathology of the dead), concentrated on the prospective responsibilities of biopsy diagnosis and thorough examination of surgical specimens (pathology of the living). His aim was not only to judge the adequacy of the excision and character of the lesion, but also to record the metastasizing ability of malignant tumors and to relate findings to eventual outcomes. He also was to establish criteria of operability for the protean variety of malignant tumors and their response to irradiation.

In 1921 Allen Oldfather Whipple (1881–1963) became professor of surgery at Columbia University and introduced important innovations. Auchincloss was made head of one of the two surgical services and changes were also made in the staffs of surgical subspecialties. Wilder Graves Penfield (1891–1976), a Rhodes Scholar with a future in neurosurgery, was given a floor of the surgical pathology annex, which he converted into a laboratory of neuropathology. Penfield had spent time in Madrid with Pío del Rio-Hortega (1882–1945), and he brought George Frederick Laidlaw,[B] an ingenious researcher who had worked with Pierre Masson,[B] in Montreal. Penfield and Laidlaw introduced Stout to the secrets of silver staining and did original work with dopa and other special stains.

Under the new administration, Stout withdrew from his work as a surgeon in the outpatient department. He devoted time to attending rounds in the departments of dermatology, gynecology, and otolaryngology, gathering clinical information of value in the interpretation of surgical specimens. Penfield invited Stout to become a co-founder of the Halstead Club, an organization that grew to be a national society. At meetings of their group in various places, Stout was to meet Churchill, Wangensteen, Ravdin, and other leading surgical authorities of the nation. Laidlaw introduced him to Masson, with whom he was to have a fruitful interchange for many years.

Bill Clarke was a gregarious and charismatic man with a great interest in people. His main interest was in teaching, and he was willing to leave the surgical pathology work to Stout. Clarke had a restless and inquiring mind with original ideas on the principles of surgery as applied to "dynamic" pathology. His ambition was to put these ideas in book form. Unable to articulate his thoughts, he sought the help of his young associate who was willing to contribute his effort. However, Clarke was somewhat inconsistent and kept shifting his views, causing repeated revisions. After years of effort during which Stout had written little for himself, he realized this could be an endless task. In a moment of frustration,

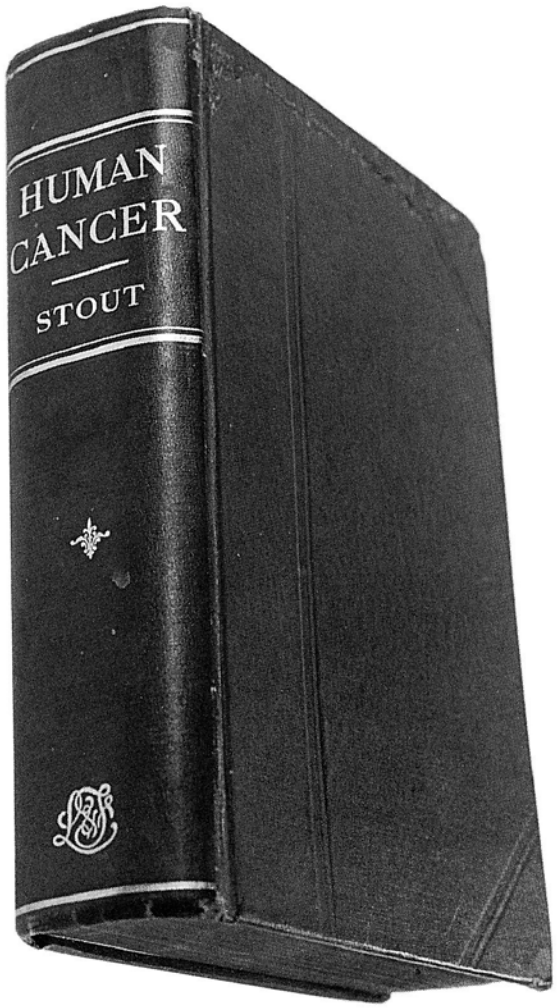

Fig. 15-3. Stout's book, 1933.

he told Clarke they both lacked the scientific foundation and ability to convey the philosophical subtleties of surgery in lucid English. Although they remained friends and collaborators, their intimacy was never the same.[630]

Gradually, Stout formed his own plans to write a book on cancer, organized so that all tumors of one organ would be found together with comprehensive clinical information provided. He had collected references, reprints, and illustrations. On summer vacation in New Canaan and Bermuda, he began to write notes for his book.

Plans for consolidation of the medical school and medical center at Washington Heights finally came to fruition. Clarke and Stout worked out designs for the ample animal quarters and experimental operating rooms on the sixteenth floor of the new building. Clarke was appointed professor of experimental surgery, and attracted to the laboratory a brilliant young lady, Virginia Frantz,[B] who was willing to take over

some of the teaching and to help him with his book. The laboratory staff was enriched by two remarkable technologists of Russian origin: Helen Gregory and Nina Kuroff.

Clarke intended to retire early but agreed to stay an extra year to allow Stout to go on sabbatical. In the summer of 1928, Stout, Jane, and twelve-year-old Frinda were off to France. In Paris the Stouts took quarters in fashionable Neuilly, within walking distance of the Bois de Boulogne. At the medical school on the rue des Ecoles, Stout was welcomed by Gustave Roussy (1874–1948) and his able associate, Roger Leroux (1892–1950). They made available to him the rich school library. Stout spent hours of every morning in the library and took lunch in the quaint small restaurants of the neighborhood. In the late afternoons, he enjoyed the long bus ride through the city to the Place de Roule in Neuilly. There he sat like a *petit bourgeois* at a sidewalk cafe for a glass of beer *(un demi de blonde),* then walked home for dinner with his family. On weekends he played tennis with Frinda in the Bois.

Loaded with abstracts, notes, and references, Stout moved his family to the Riviera in fall 1928. In Cannes they took four rooms at the Hôtel des Orangers. One of the rooms had a view of the sea and was reserved for several hours of daily writing. There he completed about one-third of his text. Late in the spring, they visited San Juan de Luz and returned to Paris.

Back in New York, Stout took charge of the department of surgical pathology, and with Frantz, faced the service demands made on it. He was to make two other summer visits to France before finishing his book. With the text completed, he prepared the index and went to Philadelphia to deliver it personally to the publisher. He waived royalties in exchange for permission to add illustrations. In 1932, *Human Cancer* was published (Fig. 15-3). The book found wide acceptance among clinicians, because in addition to pathology, it provided information on etiology, symptomatology, and treatment. Stout had become aware that some malignant tumors were not undifferentiated or spent their potential in multiplication, and that the diagnostic differentiation between benign and malignant often needed to take clinical facts into consideration. He acknowledged that tumor nomenclature was confusing due to various concepts of cell origin. He would later recognize that he overemphasized the role of chronic inflammation in the etiology of tumors and was under the impression that malignant tumors arose from benign ones. The book included discussion of the suitability of surgery or radiotherapy as applied to the various manifestations of neoplasia.

Unquestionably, Stout's success as a surgical pathologist was in part due to his friendly relationship with a variety of professionals who provided clinical information when they sought his advice. Cornelius Godfrey Coakley (1862–1934) offered him an unusual opportunity to study lesions of the oral cavity.[616] With James Albert Corscaden (1881–1964), he wrote on sarcomas of the uterus.[105] With Maurice Lenz (1890–1974),[B] he observed the effects of radiotherapy on cancer of the pharynx and larynx.[417] With Ross Golden (1889–1975), he made a study of superficially spreading carcinomas of the stomach.

One of the activities of the laboratory introduced by Clarke was the *in vitro* studies of embryos carried out by McWhorter as well as the studies of tissue culture. Margaret Murray[B] was brought to the laboratory in 1930 to work on a special project on the tissue absorption of calcium. After the project was finished, she remained in the laboratory. Murray was well acquainted with normal tissues in culture and, with Stout, was to collaborate fruitfully in important contributions to the histogenesis of tumors.[470]

The American Association for Research in Nervous and Mental Diseases extended to Stout, two years in advance, an invitation to participate in its 1935 annual meeting. The assigned subject was tumors of the peripheral nerves. The casual invitation was to have significant consequences. With ample time for preparation, Stout began by reading every available paper on the subject from the world literature. He then reviewed all of the cases accumulated in the files. His methodology led him to divide his subject into three parts: 1) benign solitary nerve tumors, 2) tumors of the neuro-myo-arterial glomus, and 3) malignant tumors of the peripheral nerves.[615,617,619]

Benign tumors of the peripheral nerves were thought to arise from the nerve sheath, but opinions were divided on whether the Schwann cell or the fibroblast was the cell of origin. After proper semantic consultation, Stout proposed to call them neurilemomas, a neutral term indicating only that they arose from the nerve sheath.[619] The malignant tumors of deep-seated nerves, Ewing's neurogenic sarcomas, Stout designated as fibrosarcomas of nerves. In work he was to do later with Margaret Murray, he further clarified the origins of these tumors.[633,634,700]

At the 1949 Cancer Seminar of Colorado Springs, a case of tumor of the parotid was presented and diagnosed by Stout as oxyphilic adenoma. The young pathologist who had submitted the case dared to stand up and state that on slides he had previously submitted to Stout, he had received a diagnosis of malignant mixed tumor. Unaffected by the alleged contradiction, Stout made no comment but took note. On his return to New York he examined the earlier

slides, and wrote a note to be added to the proceedings, stating that indeed, he had made a previous diagnosis of malignant tumor on the evidence submitted.[11] At the same Cancer Seminar, Stout had explained that the word neurilemoma (with only one m beginning the fourth syllable) was derived from the Greek *eilema*, as in the French *neurilème,* having nothing to do with the word "dilemma."[19]

Mrs. Stout was suffering from upper respiratory difficulties for which a dry climate was recommended. Stout drove his family along a southern route to Arizona, where their daughter registered at the university. He returned to New York on a Golden Eagle bus: it took four days. In the spring, he went to Arizona by bus and drove his family back home.

The opportunity arose for Stout to take another sabbatical year of study in Europe. He asked Laidlaw and Haagensen to make his scheduled presentation to the American Association, and in the summer of 1935 left with his family on the *S.S. Grispholm* which took them to Göteborg. After testing their ability to drive on the left side of the road, they proceeded through charming small towns and beautiful country to Stockholm. At the Radiumhemmet, his host was Hugo Ahlbom (1900–1952),[B] who had just completed his remarkable monograph on salivary gland tumors and with whom he made daily rounds. He also attended the gynecological clinic of James Ernest Heyman (1882–1956), and spent time in the laboratory with Lars Santesson. He also visited Hildweg Begstrand, pathologist to the Sabbastberg Hospital.

Following the short Swedish summer, the Stout family crossed the Kattegat on a ferry and continued by road through Denmark, Germany, and France. In the Rhône valley, their gourmet tastes delighted in the excellent cuisine and wines to match. They spent the autumn and winter visiting the French and Italian Rivieras. In the spring, Stout spent six weeks on a visit to the Fondation Curie in Paris. He met Antoine Lacassagne and Henri Coutard. He borrowed a microscope from Simeon Theodore Cantril (1908–1959),[B] an American receiving training in radiotherapy as a foreign *stagier.* He made it a point to examine every slide in the laboratory that had been diagnosed as lymphoepithelioma. He concluded that they constituted a variety of reticulum-cell sarcomas. He attended follow-up clinics of patients of the department of roentgentherapy conducted by J.A. del Regato.[630]

In London Stout met Sir Ernest Laurence Kennaway (1881–1958), who had done original work with carcinogenic hydrocarbons at the Royal Cancer Hospital. He spent many hours in the laboratory where Miss Hawkley presented him with rare tumors of the peripheral nerves. He also visited the West End Neurological Hospital and examined the rare neuropathological specimens of Carnegie-Dickson. His interest in tissue culture also brought him to the Strangeways Laboratories in Cambridge to visit the brilliant Honor Fell. After a look at Devonshire and Bournemouth, the family returned home.

His second sabbatical had not been one of hard work, but he felt satisfied by what he had learned and by contacts made with knowledgeable colleagues. He came back with renewed interest in the nature of complex tumors of the peripheral nerves: the enigma kept stirring in his mind. He decided to extend his methodology to the study of other tumors of interest to him. In the decade after his return, he was to make his most important contributions to the understanding of a variety of tumors. Interest in glomus tumors led Stout to study the painful subcutaneous neoplasms, of which leiomyomas were the most common.[620] He wrote on the embryonic nature of perianal cysts. He studied Bowen's disease of the skin and Paget's disease of the nipple, concluding that the latter was always associated with cancer of the breast.[621]

Margaret Murray found that no matter what the differentiation of a tumor *in vivo,* it reproduced *in vitro* the character of its cell of origin with sufficient precision to identify its fundamental nature. Reporting on eleven cases of neuro-myo-epithelial glomus, Murray and Stout found Masson's epithelioid cells to be actual pericytes and thus, mesenchymal neoplasms which they called hemangioperi-cytomas.[632] Further study of subcutaneous leiomyomas established that they often arose from the walls of veins and suggested for them the name vascular leiomyomas.[539]

With the development of thoracic surgery, types of tumors previously considered as pulmonary, primary, or metastatic were recognized as originating from the pleura.[360] They had been assumed to arise from vessels, myoblasts, fibroblasts, etc. Stout and Murray established that the cell of origin had characteristics of the mesothelium and suggested mesothelioma as the proper designation.[627,633]

Dorothy Hansine Andersen (1900–), pathologist of the Babies Hospital, offered Stout an unusual opportunity to study a variety of pediatric tumors, a field in which he also left his imprint. Studying a series of eighteen tumors of various sites occurring often in children, Stout designated them as hemangioendotheliomas.[623] His study of mesenchymal tumors, mesenchymomas of childhood, is a classic.[128]

During the second World War, Stout served in the Office of Price Administration (O.P.A.), receiving requests for extra food or fuel and making decisions as to their worth. Serving his faculty in the accelerated medical school program, he concluded that passing or not passing an examination was far from a reliable

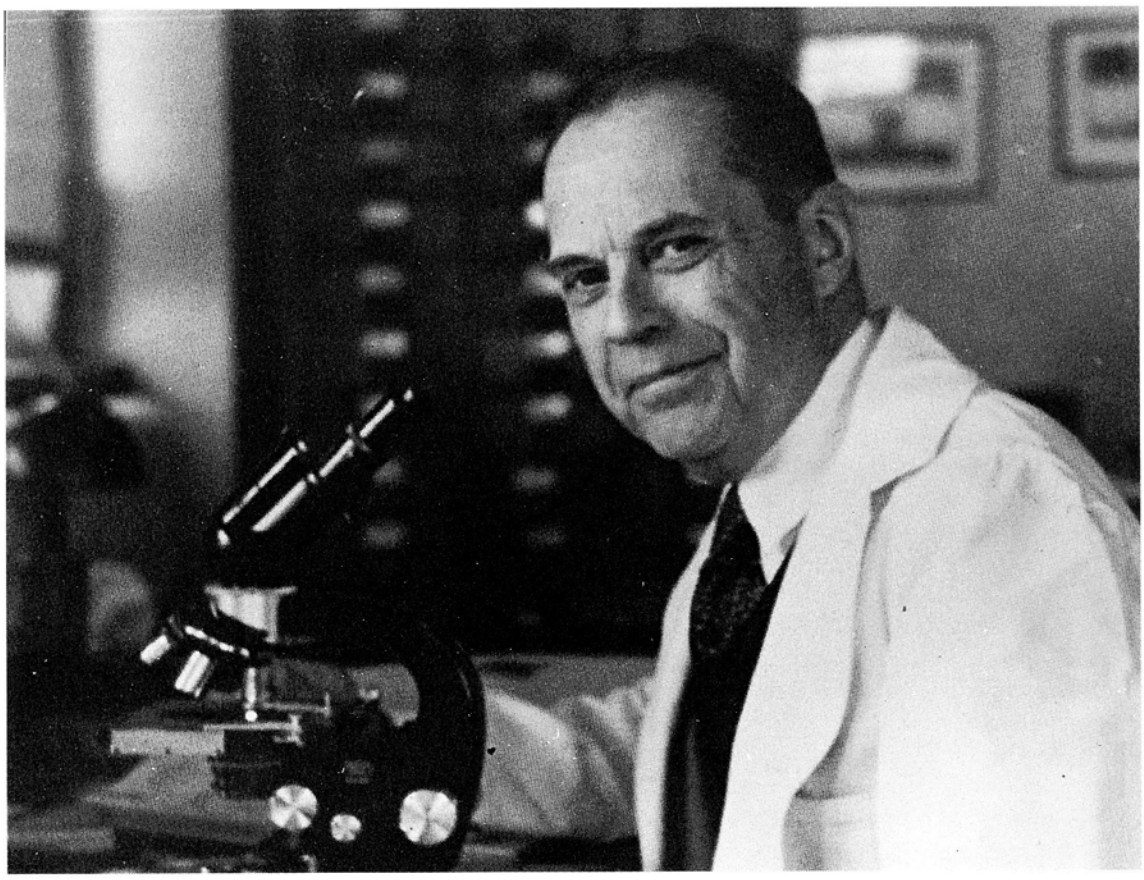

Fig. 15-4. Professor Emeritus of Surgery (1954).

measure of intelligence, ability, and honesty of purpose.

Cushman D. Haagensen (1900–) undertook with Stout a thorough retrospective study of patients with cancer of the breast examined or treated at the Presbyterian Hospital. They sought to identify signs present preoperatively that were associated with eventual surgical failure.[254,255] With minor variations, Haagensen and Stout's "criteria of inoperability" has long been adopted in clinical practice. R. P. Hill and Stout also wrote a comprehensive study of sarcomas of the breast. Haagensen and Stout collaborated in a study of ninety-five cases of synovial sarcoma.[256]

The burden of the surgical pathology work was shared by Stout and Frantz. Haagensen held the position of resident while on a Crocker Foundation project. Frederick Mervin Smith (1899–1974), also a surgeon, was resident for two years followed by J. Vardanman Cockrell (1912–). Theodore Philip Eberhard (1904–1960), and Vincent Patrick Collins (1912–), both later radiation oncologists, were also residents in surgical pathology. In addition there were innumerable surgical residents who volunteered for a minimum of three months or as long as two years. Stout was aware that these physicians benefited personally but that their experience in surgical pathology was not extended to others in medical training. He felt it was preferable to offer supplemental training in surgical pathology to those already trained in general pathology and likely to establish training programs in pathology. Alvin Otis Severance (1902–), Robert Pelley Hill (1913–), Robert Chisolm Horn, Jr. (1913–1976), and Raffaele Lattes (1918–)[B] were the earlier residents with a background in pathology to serve in the department. They were followed by William Louis Lehman (1918–), Peter Max Marcuse (1914–), Phillip Thomas Flynn (1916–), Saul Kay (1914–), Dorothea Georgia Worcester (1922–), Jane Lester (1915–1978), John Warren Pickren (1922–1984), Stanley Ronald Opler (1922–1965), Frank Vellios (1922–), Robert Stoy Totten (1912–1974), and Michael Walter Heinemann, Jr. (1917–).

Graduate training of surgical pathologists received special attention from Stout.[622] Besides describing gross specimens and microscopic appearance, students were expected to familiarize themselves with the clinical details of the cases and, to complement that purpose, attend surgical rounds.

They were also expected to attend the weekly Neoplasm Clinic, at which histopathology was discussed along with indications for treatment from surgeons and radiotherapists. Stout prepared a two-hour conference at which he discussed in depth the nature, character, and treatment of a variety of rare entities from his own files. This weekly conference at P and S, dubbed "lumps and bumps" by Virginia Frantz, was widely attended for many years.

Stout lamented that in medical schools and large medical centers, surgical pathology was splintered into various surgical sub-specialties and was practiced by retired surgeons with no background in general pathology and little knowledge of neoplasia. He felt strongly that collective discussions of the histopathology of tumors helped disseminate knowledge of oncology among practicing pathologists. The New York Pathological Society held several slide conferences under Ewing, Stout, and Fred Waldorf Stewart (1894–).[B] With the help of Severance, Stout extended such conferences first to Texas and later to Columbia, Missouri; to Birmingham; to Nashville; to Alexandria, Virginia; to Milwaukee; and to Los Angeles. He was also guest pathologist at two Colorado Springs Cancer Seminars and, for many years, participated in others by mail.

At the fourth International Congress of Cancer held in St. Louis in 1946, the suggestion was made that an atlas of tumor pathology should be published to serve as a guide in the recognition of tumors. The National Research Council accepted the challenge and appointed a subcommittee, of which Stout was a member, to assign the writing of illustrated fascicles on tumor pathology. Stout himself was assigned four such publications and started to work immediately. Others were less prompt, and some never finished their assignment. A few fascicles were published, and when funds were no longer available, the Armed Forces Institute of Pathology, to which Stout became consultant in 1948, assumed responsibility for continuing the project and devoted considerable effort to its achievement. Stout's first fascicle on the subject of tumors of the peripheral nerves was the first published in 1948. His second one, on tumors of the soft tissues, appeared in 1953.[625]

William Louis Lehman, a former resident who had once been considered as a successor to Stout, took the initiative and with Severance, Collins, Haagensen, Horn, Lattes, Asa Beach, and John P. Heaney, founded the Arthur Purdy Stout Club on 14 June 1947. Stout liked the opportunity of meeting periodically with former associates and held at each annual meeting a slide conference that was the height of each event. Annual meetings were held in New York, Philadelphia, and St. Louis. In 1956 the "club" became the "society," which today gathers not only his students, but a host of over 250 surgical pathologists.

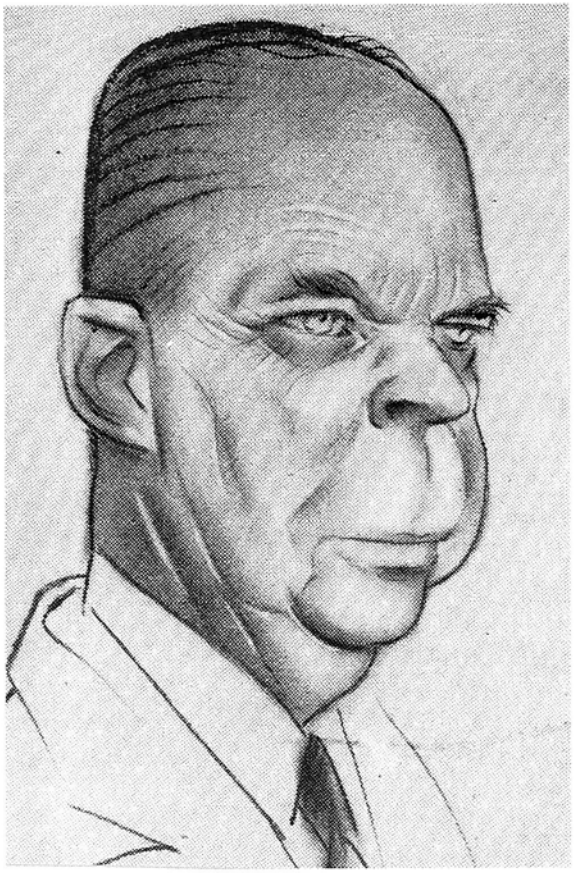

Fig. 15-5. Charcoal caricature of Stout by Cabral (Mexico, 1952).

The first National Cancer Conference took place in Memphis, Tennessee, in 1949. Stout collaborated with the American Cancer Society and the National Cancer Institute, sponsors of the event, participating in planning and at the sessions of the program. He also served in the study sections of the NCI and various committees of the ACS, in particular the subcommittee in charge of awarding fellowships for training in the various oncologic disciplines.

An important part of Stout's activities, known only to those closely associated with him, were the numerous consultations he received from countless pathologists. In 1951 the flow of consultations had risen to over six hundred from thirty-four states and nineteen foreign countries. He gave this task the best of his time and serious attention. To avoid clerical errors, he himself unwrapped all incoming packages addressed to him, labeled the slides, and gave them accession numbers in the department's books. He never issued a brief diagnostic opinion: for each slide submitted, he dictated a thorough description and

discussion, giving appropriate references to the literature. In this fashion, he contributed greatly to the education of countless pathologists in the privacy of their interrelation. A copy of his report, kept in the department's files with the slides, provided a rich resource for future students and researchers. To comply with the increasing demands of these consultations, he went to his laboratory on Saturday and Sunday mornings. Often, he typed his own reports.

In 1951 Stout reached the age of retirement from the department of surgery. His associate, Raffaele Lattes,[B] was appointed as his successor. Stout was named professor of pathology and was permitted to keep a desk where he continued to do his consultant work (Fig. 15-4). The municipality of New York had agreed to build a cancer hospital on the university's ground with a staff to be chosen by the P and S faculty. Mayor Fiorello La Guardia (1882–1947) had hoped to name it the Florence Nightingale Hospital. Plans were delayed by the war, and it was subsequently decided to name the new hospital after a former professor of pathology, Francis Delafield (1841– 1915). The opening of the hospital coincided with Stout's retirement, and he was appointed head of the Delafield department of pathology. The new department, much at variance from the parent institution, gathered all aspects of pathology (clinical, experimental, surgical, and postmortems) under one administrative jurisdiction. Stout was fortunate to find a willing, eager, and devoted collaborator in Edith E. Sproul (1907–), who took responsibility for the operation of the department, leaving Stout to continue his activity in surgical pathology and the education of residents in this aspect of their work. He had great hopes for this institution as an outstanding cancer center, to which end he collaborated with Haagensen, Lenz, Joseph John McDonald (1895–1955), Gray Huntington Twombly (1905–), Alfred Gelhorn (1913–), and Perry Burrers Hudson (1917–).

In anticipation of his retirement and while on vacation in the Laurentian Mountains in August 1950, Stout started to write a series of autobiographical notes. He was to continue this project on the 8th Avenue subway, on the high seas, at Cannes, and in Turin. The notes include details of his education and training, travels, family, etc. It also contains his own judgment of his work and that of his associates. After his retirement, he made an annual addition, listing professional engagements and publications; he kept it up until 1962. His secretaries, Frances Maxwell and later, Kitty Sorensen, typed the episodic script through the years. The typewritten version of his handwritten notes consists of 427 pages and contains an introduction he wrote for it. "Perhaps the most illuminating thing about me," he wrote, "is that I have written this at all."[630] He added that perhaps after his death, the manuscript might be turned over to a member of the Arthur Purdy Stout Society. The original of these typewritten notes is to be found in the manuscript division of the Columbia University Health Sciences Library. A copy has graciously been made available to the author by the APS Society.

Henry Azar has given us a vivid description of the famous Delafield noon conference held by Stout four times a week for fifteen years.[17] With associates and residents seated along a rectangular table in front of their individual microscopes, the proceedings were started by Stout's voice order: "shoot." Slides of current cases were offered to him, then passed around to others. He would ask for opinions as to whether the lesion was reactive or neoplastic. If neoplastic, he would then ask whether it was benign or malignant, to him the paramount question. Then came discussions of tissue of origin and considerations of treatment of choice. At this point, he would display his clinical insight and his thorough familiarity with the literature. An occasional difficult case ("a lulu") was discussed at length. The closing number ("coup de grace") was the presentation of a case ("an unknown"), usually from Stout's consultation file. Twice a month, he held a similar conference at the Veterans Hospital of Orange County, New Jersey, to which a resident would usually accompany him and provide transportation.

In 1952 the American Radium Society offered Stout the Janeway Medal with its northern mythological allegory. In November 1952, Stout conducted a seminar in Mexico City to celebrate the founding of the Sociedad Mexicana de Patología, where he was the subject of the trenchant charcoal of Cabral, the famous Mexican caricaturist (Fig. 15-5).

In 1954 Stout reached the age of retirement from the P and S department of pathology and also as head of the department of pathology of the Delafield. He was then made emeritus professor of surgery and consultant to the Delafield (Fig. 15-6). He continued his work as before. He mused that he could take the cut in salary and appreciated the emeritus status entitling him to an office and a half-time secretary. He resigned from various positions and membership in societies and clubs, and only retained membership in the Century Association. Although he failed to attend the annual meeting of the Halstead Society, his colleagues elected him president. He continued to attend the annual meetings of the APS Club and accepted only short engagements outside of New York. He continued to keep up with an increasing number of consultations.

A New Yorker by birth and inclination, Stout had a lifetime love affair with Central Park. He had always lived near it. In the days of horsedrawn vehicles and electric cars, he had played there as a child on

Arthur Purdy Stout.

Fig. 15-6. Arthur Purdy Stout.

Fig. 15-7. Stout with Alvin O. Severance (1957) at Palisades. (Courtesy of Raffaele Lattes, M.D.)

roller skates and bicycle. He had sledded on its snow and, some winters, ice skated on its ponds. He loved the park's trees and knew its birds. In its paths he dreamed the dreams of his youth. Once, as a young man wearing his Sunday best, he ran to seize the bridle of a galloping horse that would not heed his mistress' rein. He tore his trousers, but kept a secret pride in his chivalrous exploit. To him, the park was like "an old friend."[630]

In the spring and summer of 1954, Stout suffered from a rare condition causing pain in his muscles, diagnosed as myositis. This required taking aspirin and, eventually, meticorten. In 1954 he was elected a Fellow of the American College of Surgeons and received the Cleveland Medal of the New York Cancer Society. In the early morning, over the years, Stout walked the three miles from East 72nd Street across the southern part of the park to Columbus Circle on the west side, where he took the 8th Avenue subway. In the late afternoon he did it in reverse to return home for dinner with his wife and daughter, either at home or at a nearby restaurant.

Jane Stout had never been in good health. She developed ever more frequent symptoms of coronary insufficiency and in 1955 died in her third coronary infarct. Stout wrote that theirs had been forty years of harmonious marital life.[630] Unmarried, Frinda, whose apartment was on the same floor as his, assumed the domestic chores and continued to provide company for her father. Interested in widely different cultural areas, they were nevertheless congenial and friendly companions. An aloof and reserved young lady, she was interested in the arts and composed serious music. She wrote a ballet that was performed in Shreveport and San Antonio by a professional company. Frinda favored the company of artists. To please her, Stout spent vacations in Nantucket and in Rockport, Maine (Fig. 15-7).

Perry Hudson made an original study of perineal biopsies of the prostate in elderly asymptomatic individuals. Stout cooperated in this study and with Hudson co-authored a beautifully-illustrated atlas of prostate surgery. He was consultant on an experimental study by E. T. Oppenheimer on the production of sarcomas by implantation of plastic materials. He did considerable work with Oscar Auerbach (1905–) on an interesting study of the entire bronchial tree of smokers as observed at autopsy. Stout maintained a lifetime interest in the great variety of lesions and neoplasms of fibroblasts.[612] He divided them into three groups: 1) the hyperplasias, 2) the fibromatosis, and 3) the fibrosarcomas. He recognized the risks of assigning a case to any of these categories.[628] To the first group belong the nasopharyngeal fibromas, the myositis, and the fascitis: benign lesions which may be diagnosed as malignant. The fibromatosis, a term introduced by Stout, include the palmar fibrosis (Dupuytren's), plantar fibrosis, penile fibrosis (Peyronie's), and an important but difficult and rapidly growing manifestation, juvenile fibromatosis which may be indistinguishable microscopically from fibrosarcoma.[626] He pointed out that a diagnosis of fibrosarcoma should be the result of a thoroughly responsible exclusionary study.[625,629]

Mesenchymal tumors in children also became one of Stout's main interests.[128] In collaboration with Delafield residents, he published an average of twelve papers a year. With Shirley L. Kauffman (1924–), he wrote on extra-skeletal osteosarcomas, mesotheliomas, and congenital mesenchymomas. With Kaity Yanopoulos (1929–), he wrote on smooth cell tumors of the mesentery, and with Artemis Damaskinidon-Nash (1928–) on malignant mesenchymomas. With pediatrician Marrin E. Leber (1939–) he wrote on benign mesenchymoma and with Elfriede C. Kohout-Dutz (1926–) on glomus tumors. By 1963 the number of consultations entered into his files rose to 1150 from 47 states and 30 foreign nations.

Henry Azar, one of Stout's most distinguished students, tells us that it is possible to note from his writings and seminar discussions the unfolding of certain principles of surgical pathology now generally accepted:[17] that collagen fibers may be produced by cells other than fibroblasts, which he called "facultative" fibroblasts (mesothelial cells, histiocytes, Schwann cells, and an occasional lipoblast); that a variety of fibroblastic proliferations may simulate fibrosarcoma; that mixed tumors, often designated by hyphenated names, are derivatives of pluripotential mesenchymal cells that should be called mesenchymomas; that the benign or malignant character of gastrointestinal smooth cell tumors may be difficult

to ascertain; and that hemangiopericytomas are probably tumors of the contractile perivascular smooth muscle.

Stout considered Harvey Perrin, who shared his adventure in the Yün-Nan, as his best friend. Devoted to different professions, they seldom met. Perrin, the last of his three companions, died in California in 1962. Stout obviously had affectionate concern for his associates and students. Many of them were physically and intellectually attractive women, and some openly admitted loving him, but he was always detached. He wrote that he had lost the art of friendship, and was afraid to cultivate the affection of those associated with him for fear of breaking the emotional balance he needed to concentrate on his work.[630] The three loves of his life in succession were his mother, his wife, and his daughter.

In the spring of 1965, Stout suffered an attack of pneumonia and lost some weight. He also had some cervical aches attributed to osteoarthritis. "It is in its insidious and indolent onset," had written Stout, "that lies the tragedy of cancer."[619] Indeed! A roentgenogram of the spine revealed the presence of osteoblastic lesions, and a biopsy of the prostate proved the presence of adenocarcinoma. Regretfully, he declined an invitation to be the guest pathologist of a 1965 Colorado Springs Cancer Seminar on pediatric tumors. However, he examined the slides of the fifteen problem cases and submitted by mail his careful discussion and diagnosis of each. In his cover letter, he casually revealed his predicament and the fact that he was pain-free under estrogen. In the spring of 1966, he was hospitalized for an orchiectomy. He remained for five weeks, during which time a microscope was brought to his room to allow some pragmatic distraction, and he was frequently visited by friends and residents.

Stout continued to conduct the Delafield noon conferences thanks to the offering of friendly transportation. In June 1967, the Arthur Purdy Stout Society met in New York under the presidency of Alvin Severance. Lattes took charge of the careful arrangements. Obviously flattered by the adulation, Stout made a summary of his contributions and gladly boasted that because of his work on fibromatosis, many a youthful limb had been spared. His health progressively decayed and, on 20 December 1967, Arthur Purdy Stout died. He made a generous bequest to the Arthur Purdy Stout Society of Surgical Pathology, according to Dr. William L. Lehman.

A man of average physical stature, thinning black hair, high forehead, and rather large facial features, Stout exhibited an intensely fixed look with a discreet smile always about to break on his lips. He was a kind, charmingly simple, courteous, and dignified gentleman. "He worked," said Virginia Frantz, "at what would have been a killing pace to any of his colleagues."[247] A scholarly scientist devoted to ideals of service and education, he was forceful in argument, prudently critical, calm, and deceptively mild. "He was an exceptional teacher," wrote Lattes, "with high respect and compassion for human life, absolutely scientific and professionally honest."[411] Innovative and effective, he kept a kindly interest in the progress of his younger associates. "He had a profound and lasting effect on my professional life," wrote Edith Sproul. "The years spent in association with him were the most rewarding of my career." "He was never too busy to deny his help," wrote Philip Flynn. "He was a teacher-friend with the attributes of a true patriarch," wrote Azar. "His genius would have been a lesser influence but for the humane qualities that distinguished him."[17] "Each one of his publications," wrote Masson, "is a model of its kind, a monograph providing a well documented history of the subject carefully crediting his predecessors, providing impeccable illustrations, offering a point of departure for future work, in clear and elegant style."[417] "It is rare to find a pathologist," wrote Sharon Whelan Weiss, "whose ideas are so sound and pervasive as to influence our thinking decades after his writing."[654] He called himself an "oncological surgical pathologist."[630] He was widely recognized as the world's undisputed doyen of tumor pathologists.

Subject Notes

15.1 In his autobiographic notes, Stout refers to his youthful adventure as a leisurely pilgrimage.[630] He gives the names of his companions and records Stark's death, but left few other details of their odyssey. Those given in this article are taken from Stark's long letters to his family and from his travel diary, published by his father.[598] This rare gem of a book contains candid observations on Japan, China, Mongolia, Formosa, Java, Borneo, Malaysia, and India early in the century. Stark was an unusually gifted writer at this early age, with extraordinary ability and great powers of observation.

15.2 Hugh Auchincloss, Sr. (1878–1947) had great interest and experience with cancer of the breast. Impressed by the frequent incurability of mammary cancer, he postulated for earlier diagnosis: every young woman should be taught to intentionally feel for lumps in her breasts *once a month for her lifetime*.[16] The importance of self-examination was later emphasized by Haagensen in a film by the American Cancer Society.