A Century of Pathology at Yale: Personal Reflections

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This history is largely about the players on the stage of the Yale Pathology Department acting out their roles as observed by the author in over a half-century as a member of the department and as associate dean of the medical school.

INTRODUCTION

The modern department of pathology at the Yale University School of Medicine was established by a thirty-four-year-old associate professor of pathology from The Johns Hopkins University named Milton C. Winternitz (Figures 1 and 5) [1] who had trained under the legendary pathologist William H. Welch [2]. Welch had worked in the laboratories of Koch and Cohnheim in Europe and had brought back the excitement of scientific discovery to The Johns Hopkins University, where he became dean of its School of Medicine. Because Winternitz was Jewish, Welch advised him that he could not be promoted to full professor at Hopkins, since, at the time, one had to be white, male, Protestant, and preferably rich, to occupy leadership positions in medicine. On the other hand, Welch found the contributions from Yale’s School of Medicine to be barren and uninspiring.

WINTERNITZ AS DEAN AND PATHOLOGIST

George Blumer, dean of the Yale University School of Medicine, invited Winternitz to come to Yale, which he did, becoming the first Brady Professor of Pathology and dean in 1917. Through his mentor, Welch, Winternitz was the direct inheritor of the European renaissance in pathology. The pathology department was housed in the Brady Memorial Building, for which the Brady family provided funds in 1914. Winternitz was a five-foot, three-inch dynamo, who rolled up his sleeves and flexed his muscles while lecturing.

Medical education and the Yale Plan

Winternitz agreed with Simon Flexner, author of the Flexner report of 1910 [3], that Yale needed a full-time faculty, more basic science, more laboratories and an endowment. Less than half the medical schools in the United States met the standards of Flexner’s report and managed to survive [4]. Winternitz set about getting a better curriculum, better students, more money, laboratories and fewer didactic lectures. In 1922, the chairman of the curriculum committee said that the Yale student had become the "defenseless recipient of an overwhelming mass of facts which he may or may not be able to correlate" [5]. Winternitz recommended that required courses be reduced by over 1200 hours, and electives substituted. This was the start of what became known as the Yale Plan, which also incorporated a required researched-based thesis, so that students could learn methods of

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investigation and the value of research [5]. In 1932, Winternitz accepted passage of the National Board examinations as a requirement to enter the third year. Over the years, “The Yale System” has repeatedly been reaffirmed by the Yale faculty (albeit with significant changes).

Pathology research

The great flu pandemic of 1918-1919 filled the New Haven Hospital with hundreds of patients, of whom many died and were autopsied. The pathology findings were discussed by Winternitz in a book he published in 1921 [6]. It contains line drawings of neoplastic-like proliferation of pneumocytes, which caused him to predict a great increase in lung cancer. This is a good example of being right for the wrong reason. During World War II, he wrote on mechanisms involved in shock and its therapy. After the war, he advised returning members of the Armed Forces what special areas to pursue.

Neuropathology: Zimmerman and Cushing

Winternitz sent Harry Zimmerman (Figure 2), a resident in pathology in 1927-1929, to study neuropathology under Walter Spielmeyer in Munich. When he returned in 1930, he established the first neuropathology section in the United States at Yale.

Years later, Zimmerman was asked by the president of Yeshiva University in New York to help build a medical school. Zimmerman required that it be non-parochial, and wanted to name it after Albert Einstein. He obtained an interview with Einstein through a friend in January 1953, and persuaded Einstein to lend his name to the new school. When Einstein died in 1955, Zimmerman did the autopsy. He was passionately devoted to students and their learning, and contributed to the field of pathology as editor of the *American Journal of Pathology*; in 1981 he received the “Gold-Headed Cane” of the American Association of Pathology.
Harvey Cushing, chief of surgery at the Peter Bent Brigham Hospital in Boston, was subject to mandatory retirement at the age of sixty-three. John Fulton, professor of physiology at Yale, persuaded him to come to Yale as Sterling Professor of Neurology. Cushing brought with him his collection of 2000 brain tumors as well as his long-time collaborator, Louise Eisenhardt. She organized the collection along with Percival Bailey, and they co-founded the Brain Tumor Registry. Later, when more space was needed in Brady, the Cushing brain collection was moved to basement of Harkness Dormitory, which became the “Brain Room.” Recently, efforts have been made to refurbish these materials.

Cushing had suffered paralysis of the legs during World War II, which he thought was viral-induced. When he died in 1939, Zimmerman autopsied him and found the cause to have been thrombosis of the aorta below the renal arteries.

Cushing was a collector of medical books, and his book collection, together with those of Fulton and Arnold Klebs of Switzerland were presented to Yale’s new medical library, thus beginning the Historical Medical Library at Yale.

**HARRY S.N. GREENE AND PATHOLOGY AT YALE**

During World War II, Yale’s School of Medicine was involved in the 39th General Hospital in the Solomon Islands. Back home, Winternitz brought Harry S.N. Greene (Figure 3) to Yale because of his work on tissue transplantation. Greene implanted bits of tissue into the anterior chamber of rabbits’ eyes. He exploited this model in several ways: he believed that embryonic tissue would grow and differentiate in this anatomic site. In a variation of the Ascheim-Zondek test, he reasoned that if embryonic ovarian tissue were transplanted to the anterior chamber, one need not sacrifice the animal injected with the
urine of a putatively pregnant woman (as a source of HCG); one had only to look the animal in the eye to see whether ovulation was induced.

In addition to embryonic tissue, Greene found that malignant tissue would grow in the eye. Since carcinoma in situ and occult carcinoma did not survive transfer, he believed truly malignant cells were not present in these conditions. Also, since lymphomas, myelosarcomas and leukemia did not survive such transfers, he concluded that they, too, were not neoplastic diseases.

He implied that pathologists, on the whole, were lazy and perhaps even dishonest; he even compared them to WPA workers as recipients of official "make-work" charity. In 1944, such statements caused a considerable uproar [7]. G.H. Twombley replied:

(\text{The pathologist}) is the primary person one relies on. He cannot be dishonest because his dishonesty is so quickly discovered. If we had to wait two or three months for the results of transplantation to tell whether or not a woman has cancer of the breast, the results from therapy would be very poor. A good pathologist ought to be able to diagnose cancer in at least ninety out of one-hundred cases. Morphological research may be very dead, but the work that the morphological pathologist does is anything but dead. [7]

Jacob Furth opposed Greene’s views and noted that leukemia cells could be passed on to new hosts almost indefinitely, which could be done with immature, normal cells. "This is certainly autonomy" [7].

Greene succeeded Winternitz as chairman of pathology, despite the fact that he did not believe pathologists contributed anything, and would not bring them into his department. He dressed in operating room garb, and delighted in taking unconventional positions. He
lost no opportunity in putting down Republicans, and could be even more insulting. He referred to visiting attorney Melvin Belli as “Bell-E,” and when Belli protested, Greene said when “spaghetti” was pronounced “spaghett-eye,” he would call him Belli [8]. When I once asked him why he came to Yale, Greene said he liked to open the window and smell skunk. Of course, stories about him abounded, and his reputation always attracted an overflow crowd when he spoke in Fitkin Amphitheater.

For example, Greene took a position contrary to the mounting evidence that smoking was contributing to lung cancer. He had, he said, taken some of the “crud” from his pipe and put it in the subcutaneous tissue of a rabbit, along with some embryonic tissue. Since no cancer resulted, it indicated that the tobacco residue was not carcinogenic. The attribution of the rise of lung cancer to the rise of cigarette smoking was, he said, a parallel phenomenon. Since there was a simultaneous rise in the wearing of nylon stockings, one might say this was the cause of lung cancer [9].

His behavior at times could be outrageous. He liked to tell the story of the time he did not want a secretary the administration sent over. When she came in, he was holding an open umbrella while sitting with his bare feet up on his desk. Over the door to his office was the sentence: *Hic Locus Est Ubi Mors Gaudet Succurrere Vitae* (In this place death rejoices in helping life), which is now prominently displayed in the new mortuary.

**PATHOLOGY AND THE VA SYSTEM**

As the war drew to a close, a system of “Dean’s Committee Hospitals” was established under the impetus of Generals Hawley and Bradley to coordinate interactions between medical schools and Veterans Administration hospitals. The medical school

![Figure 4. Milton C. Winternitz.](image-url)
would be responsible for the medical aspects, and the VA for the administration. The
Newington (Connecticut) VA Hospital, built in 1925, thirty-five miles from Yale, was
accepted by dean Francis Blake as an affiliated hospital until a new VA Hospital could be
constructed adjacent to the medical school. However, it became clear that parking would
be a problem with this plan, so the Yale-owned Winchester property in West Haven,
Connecticut, was sold to the Veterans' Administration as the site for the new hospital. That
sale, together with other gifts, provided the money that Yale needed for its own post-war
construction program. The new West Haven VA Hospital was designed to be a 500 bed
general hospital and a 400-bed tuberculosis hospital. It was to be built of glazed yellow
Ohio brick, but Connecticut Senator McMahon demanded that it be built of good, red
Connecticut brick. Since such good brick, however, was not available due to the post-war
construction boom, brick that was literally half-baked was used [10].

When the new VA Hospital opened in Newington in 1946, young physicians, demo-
ibilized from the Armed Forces in large numbers, were eager to resume their training, and
most lived in Quonset huts erected on the grounds. I was among these, and became chief
of laboratory services in March, 1947, responsible for all anatomic and clinical pathology
functions, one of twenty-two certified pathologists in the state. Medical-legal work, how-
ever, was handled by a coroner, a political appointee who spent as little state money as
possible. Connecticut was an easy state in which to get away with murder, requiring some-
thing like a dagger sticking out of the back to launch an investigation. Across the country,
new hospitals were being constructed with the assistance of federal money, opening up
many positions for young pathologists.

POST-WAR PATHOLOGY AT YALE

After the war, Averill Liebow (Figure 5) returned as assistant professor of pathology.
He was a great admirer of Winternitz, whom he physically resembled. He brought back
from Japan a Samurai sword, and at an exuberant post-war Christmas party, Liebow hoist-
ed up Winternitz, who used the sword to carve his initials on the panel over the entrance
to the Beaumont Room [11], where they still remain. Liebow became a consultant to the
new pathology department at Newington VA Hospital while he ran the teaching programs
at Yale and directed the autopsies. These were presented in great detail in what he called
the “organ recital,” with no blood in sight.

This was the era of the classic clinicopathologic conference, and the flowering of
“CPC-manship.” Students eagerly read the Cabot cases published each week in the New
England Journal of Medicine. John Peters, the John Slade Ely Professor of Medicine,
noted for running all chemical tests in duplicate, would regularly attend the CPCs and be
pleased to say that the patients had died in perfect metabolic balance. Liebow published
the first Armed Forces Institute of Pathology Fascicle on Tumors of the Lower Respiratory
Tract [12] in 1952 at the behest of Winternitz, who had retired from the Yale faculty in
1950 and moved to Washington and the National Research Council. This work started
Liebow on his career in pulmonary disease, for which he became recognized as the pre-
mier pulmonary pathologist in the United States. He was particularly well-known for his
introduction of a series of pneumonias, which he called “usual interstitial pneumonia”
(UIP), “desquamative interstitial pneumonia” (DIP), “lymphoid interstitial pneumonia”
(LIP) and “proteinosis” [13]. He rose rapidly in the academy to become John Slade Ely
Professor of Pathology. He was famous for knowing every student’s name and the name of
their families. Liebow had zero tolerance for poor presentations, charging the resident five
cents for every “uh” uttered while searching for a word (this has been succeeded by “you
know”). He worked long hours and expected the same of the house officers, some of whom
found it hard to work under this difficult and critical, but fair, preceptor. Liebow's research involved the preparation of plastic casts of lung vessels in different diseases, color pictures of which appeared in the American Journal of Pathology and Bacteriology. He was ably assisted in this work by the department artist, Armin Hemberger, who did accurate drawings and paintings. In 1948, Liebow published a study on the accuracy of cytologic diagnosis of sputum and bronchial secretions, controlled by surgical specimens [14]. The pathology department now makes an annual teaching award in his name. It has been awarded to Rosai, Flynn, Smith, Carter and Carcangi.

Another returnee from World War II was Gerald Klatskin who had served in the China-Burma-India Theater. Winternitz advised Klatskin to get a biopsy needle with which to get material to study liver disease. Since Klatskin had little knowledge of pathology, he spent several hours a week with me at the Newington VA Hospital studying these biopsies. Together we wrote several papers on fat deposition in cirrhosis and on liver granulomas [15]. I found a small adenocarcinoma at the porta hepatis which piqued Klatskin's interest. He subsequently published a description of what has become known as the Klatskin tumor. He established the first liver study unit in the country, with an invaluable collection of pictures with accompanying clinical detail, which formed the basis of his posthumous Histopathology of the Liver [16], edited by his former student Harold Conn. His studies of alcoholic cirrhosis, however, did not deter his appreciation of very dry martinis, for which he kept glasses in the freezer. Klatskin was the David Page Smith Professor of Medicine when he had to retire at the age of sixty-eight, then mandatory. He became greatly disabled by macular degeneration, which is why Conn had to edit his book.

Figure 5. Averill Liebow.
In 1953, the Yale School of Medicine incorporated two new services into the Department of Pathology. The Grace Hospital, which had started as a homeopathic hospital, was well supported by private patients, and attended by Yale private physicians. When the old building was condemned because of deterioration, a new wing was built adjacent to the Yale School of Medicine for the private physicians to house their patients; thus, the Grace-New Haven Hospital came into being. Another returning veteran took responsibility for surgical pathology in the private Memorial Wing of the Yale Hospital. William Barris (Barry) McAllister, who had served in Egypt, was an attending physician at Newington VA Hospital as well as the surgical pathologist in the Memorial Wing. He had very good relations with the clinicians who came to discuss their cases, and an annual lectureship was established in his honor.

In 1953, the West Haven VA Hospital was completed, and I was assigned to be Chief of the laboratory service. The first patient was admitted to the TB Building in April of that year. However, since successful antibiotic therapy had been introduced, TB sanatoria around the state were closing, and the number of patients admitted to the TB Building continued to fall. The first patient was admitted in the fall of 1953 to the General Medical and Surgical Building, where all laboratory functions were carried out except for TB bacteriology. The TB laboratory became a national center for mycobacterial identification.

When opening ceremonies were held at the West Haven VA Hospital, they were attended by luminaries such as Vice-Admiral Boone, who had been President Truman’s physician. On this occasion, I observed John Peters sitting in a corner, holding a glass in his hand, and looking rather disconsolate. When I asked him what was troubling him, he pointed to the glass and said, “Punch without punch.”

The West Haven VA Hospital developed its own approved four-year training program in pathology. This program included both clinical and anatomic pathology. Residents at Yale who had completed two years of anatomic pathology transferred to the West Haven VA Hospital for two years of clinical pathology training, which was not organized at Yale.

There were twenty-seven separate clinical laboratories at Yale. Blood iodine measurements were done in pharmacology, renal function tests in Frank Epstein’s laboratory, liver function tests in Klatskin’s laboratory, both in the department of internal medicine, and there was a separate laboratory for pediatric bacteriology. David Seligson, from Philadelphia, was invited to consolidate these disparate labs into a single clinical pathology laboratory. He applied for certification in clinical chemistry and was made a Diplomate of the National Boards on a “grandfather” clause. We arranged to have the VA residents rotate through his chemistry section for six months to learn the more labor intensive belt-line analytic system he used in contrast to the autoanalyzer system I had installed at the VA in 1958, and which proved to be a very successful technological advance.

Integration of the VA Hospital with the Yale School of Medicine proceeded rapidly, except for pathology services. Greene refused to allow Yale residents to rotate through the VA for training; instead, he sent them there to do autopsies at a specified charge of $75 per autopsy. We protested that it would be unfair to the clinical services for pathology alone to remain unintegrated. At the next Dean’s Committee meeting, Paul Beeson, chair of the department of internal medicine, said the situation was intolerable, that integration was a contract between Yale and the VA as institutions, and that individual services had no choice. He regarded the VA as a “pearl beyond price,” which was allowing a great increase in staff and in clinical and research opportunities. After the Dean’s Committee meeting, integration of pathology occurred.

In the meantime, because of the decline in the number of hospitalized TB patients, the TB building simply became known as Building No. 2, and it housed an intermediate service for patients needing prolonged hospitalization. The TB morgue was converted into an
electron microscope suite, and any TB autopsy was done in the morgue in the General Medical and Surgical Building.

Although Greene was chair of pathology, he had little interest in surgical pathology. Because of Greene's attitude, surgical pathology at Yale, headed by Wilhelm Albrink, had a poor reputation. For example, Howard Spiro, head of gastroenterology, sent his biopsies to the VA for interpretation. When Greene was unable to obtain a full professorship for Albrink, he managed to help Albrink gain the chair of pathology at West Virginia.

Greene, who was accustomed to going to Maine in the summer for a fishing vacation, suffered a stroke from which he did not fully recover in 1968. At this time, he offered the position of professor of anatomic pathology to Robert Hutter, an excellent pathologist at Sloan-Kettering Memorial Hospital. Shortly thereafter, Greene suffered another stroke, and died in February 1969, leaving Hutter to come to Yale without any written guarantee of his duties. Levin Waters, another professor in the department, opposed Hutter's having authority over the autopsy and cytopathology services, demanding that Hutter's domain be restricted to surgical pathology [17].

PATHOLOGY AFTER HARRY S.N. GREENE

Meanwhile, a new chair had to be found, and a search committee, headed by Philip Bondy, recommended Baruj Benacerraf, an internationally-known immunologist. Many members of the pathology department were strongly opposed to having an immunologist as chair, and Benacerraf accepted a position at Harvard within a few days of Yale's offer. Lewis Thomas (Figure 6) was subsequently recruited, coming from New York University where he was chairman of internal medicine and dean of the School of

Figure 6. Lewis Thomas.
England Journal of Medicine. He recognized that medical knowledge and treatment would be frozen in time without research, and he referred to symptomatic treatment alone as “half-way” medicine. He was a prize-winning author, famous for his writings, first published in the *New England Journal of Medicine* [18]. Thomas arrived at Yale shortly after Hutter, who was running a first-rate surgical pathology service. Hutter still insisted that Greene had committed Yale to make him director of pathologic anatomy. Since Hutter had no written confirmation of this agreement, however, Thomas agreed with Waters that Hutter’s work should be limited to surgical pathology; Hutter promptly left. He was temporarily replaced by Peter Hukill and Romeo Vidone, and subsequently John Cornog, an early advocate of the use of electron microscopy in pathology.

Upon the retirement of Fritz Redlich as dean of the School of Medicine, Thomas was asked by Yale President Kingman Brewster to take the deanship. Thomas was reluctant, but agreed to do so if he could also retain his post as chair of pathology and to continue his research, which he was conducting at Wood’s Hole. During his short tenure as dean, Thomas succeeded, together with Russell Barnett, in bringing George Palade from the Rockefeller University to Yale; while at Yale, Palade was awarded the Nobel Prize for his seminal work in electron microscopy. Palade’s wife and well-known cell biologist, Marilyn Farquhar, became a member of the pathology department. Thomas also presided over the founding of a new department of human genetics.

In 1971, Thomas was offered the position of Director of Sloan-Kettering Memorial Hospital in New York. He decided he could have a greater influence on the course of medicine there. Upon his departure, both the deanship and the chair of pathology were left open. The deanship was filled by Robert Berliner, recruited from the NIH. The appointment to the Brady Chair in Pathology went to Vincent Marchesi, whom Thomas brought into the department because of his work on red cell membranes. Marchesi had been a Public Health Service Officer at NIH when he discovered spectrin, the main protein comprising the red cell cytoskeleton, genetic mutations of which appeared to account for hereditary elliptocytosis and spherocytosis. This work had earned him a Parke-Davis award for outstanding research in basic cellular mechanisms of disease.

At the same time John Cornog stepped down as director of surgical pathology, and I chaired a search committee to bring a new director of anatomic pathology to Yale [19]. Darryl Carter from Johns Hopkins, who had co-authored the second edition of the AFIP *Tumors of the Lower Respiratory Tract* [20], was chosen but elected to direct only surgical pathology. He later stepped down from that position and was temporarily replaced by Kenneth Barwick. During Carter’s sabbatical that followed, he wrote a successful book on breast tumors [21] then returned to do surgical pathology. Autopsy pathology had been declining throughout the western world for many years for many reasons including the proliferation of technological techniques, the cost, the long delays, the fear of lawsuits, the lack of payment (not compensated by third-party payers) and lack of research grants. Most pathologists, it seems, would prefer to do something else. Walker Smith, a disciple of Liebow, was in charge of autopsy pathology and also director of the residency program in pathology.

Under the leadership of Thomas and Marchesi, the pathology department became strongly committed to research in immunology, which had previously been scorned. Its first prominent research work was represented by Richard Gershon. Having lost neuropathology to neurosurgery, and most of dermatopathology to dermatology, pathologic anatomy needed strong leadership, and Juan Rosai was brought from Minnesota to be the director of anatomic pathology as well as of the residency program.
RECENT DEVELOPMENTS

Because of increased specialized knowledge, surgical pathology was compartmentalized by organ systems, with a particularly heavy load in areas such as gastroenterology and gynecologic pathology. A section of fine needle aspirations has been introduced recently as well.

With help from the Howard Hughes Medical Institute and Herbert Boyer, the construction of a new building devoted to basic biomedical research, the Boyer Center for Molecular Medicine, was completed and Marchesi was named its director. These laboratories are directly connected by a bridge to the pathology department. Marchesi was mentor to Jon Morrow, who succeeded him as chair of pathology, which has been modernized and computerized. New research laboratories have been built as well as a new morgue to house the autopsy service. A Decedent Affairs Office has been organized, to increase the efficiency of handling autopsies, which remain an important part of teaching. Rosai has gone to Sloan-Kettering Memorial Hospital to be its director of pathology, and he has been replaced by José Costa, who is vice-chair of pathology, deputy director of the Yale Comprehensive Cancer Center and director of critical technologies.

The department of pathology at Yale is poised to enter the twenty-first century with one leg strongly planted in pathologic anatomy and a second leg in molecular biology, joined together in the body of pathology.

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