Chapter 20

The Clinical Laboratories (Chemistry and Hematology)

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The clinical laboratories (Clinical Chemistry and Hematology) at the Massachusetts General Hospital (MGH) originated with individual physicians interested in specific diseases for which biological and therapeutic clues began to emerge from laboratory tests. Over time, custom tests developed for specific patients were repeated for patients with similar symptoms; in this way laboratory tests progressively moved from research to patient care.

The chemistry laboratory at MGH has a long history. It began as a central facility but was quickly accompanied by a group of independent specialty laboratories such as the Thyroid, Endocrine and Metabolism, Blood Gases, and Lipid Laboratories, which led to a decentralized and complex set of separate facilities. On the other hand, there is little mention of hematology as a laboratory science until the middle of the twentieth century. For much of their history, therefore, the clinical laboratories were not recognized as a unique specialty or operation: even as late as the middle of the second half of the twentieth century, the clinical laboratories were not identified as a separate and distinct service. The last two decades have witnessed progressive consolidations, resulting in centralization of laboratory services, although the recent emergence of point-of-care testing has moved some testing back to the bedside. As a result, the present configuration is primarily that of a single large Core Laboratory in the department of Pathology, performing millions of tests per year with a menu of over 1,500 different tests (including those sent to outside reference laboratories), and with oversight of all point-of-care testing as well. This chapter traces the transition from the earliest documented times to the present day.

The Early Years

Clinical laboratories had a minimal role in the early years of the hospital: "For the first seventy-five years of its life there was nothing really worthy [of] the name of a laboratory. Important work was carried out in a hole-and-corner way" (1). Even by 1872 the laboratory measured only approximately 6 by 10 feet. Located on the ground floor of the Bulfinch Building, it was described as a "small dark room used as a laboratory where specimens of urine were taken for analysis" (2) (figure 20.1). Testing was performed by the house pupils (medical students) as part of their training.

In 1851 Dr. John Bacon Jr. was appointed the first Chemist-Microscopist for the hospital. He had graduated from Harvard Medical School (HMS) in the class of 1840, and he was known from his early years as a gentleman with a bent for mechanics. While in Europe after graduation, he developed an interest in chemistry. Upon his return, he quickly built a career around analytic techniques. He was known for maintaining an organized private laboratory with the highest quality reagents, and his primary expertise was

preparing specimens for crystal identification. Dr. Bacon's appointment to the MGH staff allowed him to expand his activities and his reputation as an authority on analytic chemistry (1). In making this appointment, the Trustees were recognizing the early contributions of chemistry and microscopy to clinical practice and research: "Microscopy and organic chemistry are now considered legitimate specialties and a few among our most promising and intelligent medical men devote themselves entirely to these interesting studies" (1). Even after Dr. Bacon established a formal laboratory at the MGH, however, many physicians continued to do their own laboratory work for their patients.

In the mid-1860s the roles of Chemist and Microscopist were divided, and Dr. Bacon's title changed to Chemist. He served in this role until 1863, when he resigned because of illness and his growing workload at HMS as Professor of Chemistry. He died in Boston in 1881, at the age of 64. From 1863 to 1897 the role of Chemist changed to that of Consultant in Chemistry. The next two Consultants in Chemistry (chapter 1), Dr. James C. White (1863–1872) and Dr. Edward S. Wood (1872–1905), also had responsibilities at HMS.

In 1893 the laboratories were described as "a little den fitted up under the front steps, and unfit for human occupation; partly in the nurses' rooms connected with the wards; partly at the Medical School, a mile away; partly at the pathological room in the department of out-patients" (1). In 1896 the new Clinico-Pathological Laboratory (chapter 3) was established in the Allen Street Building and included a chemistry laboratory on the third floor. A separate house officer's laboratory for patient testing was located on the second floor. The first annual report from the laboratory describes the facility as a model laboratory for providing training opportunities. Dr. Franz Pfaff (chapter 3) was appointed Chemist in 1897 and put in charge of the Chemistry Laboratory in 1898, but much of the laboratory work was still performed by house officers.

In the early 1890s Drs. William Gannett and Richard C. Cabot (house officer from 1893 to

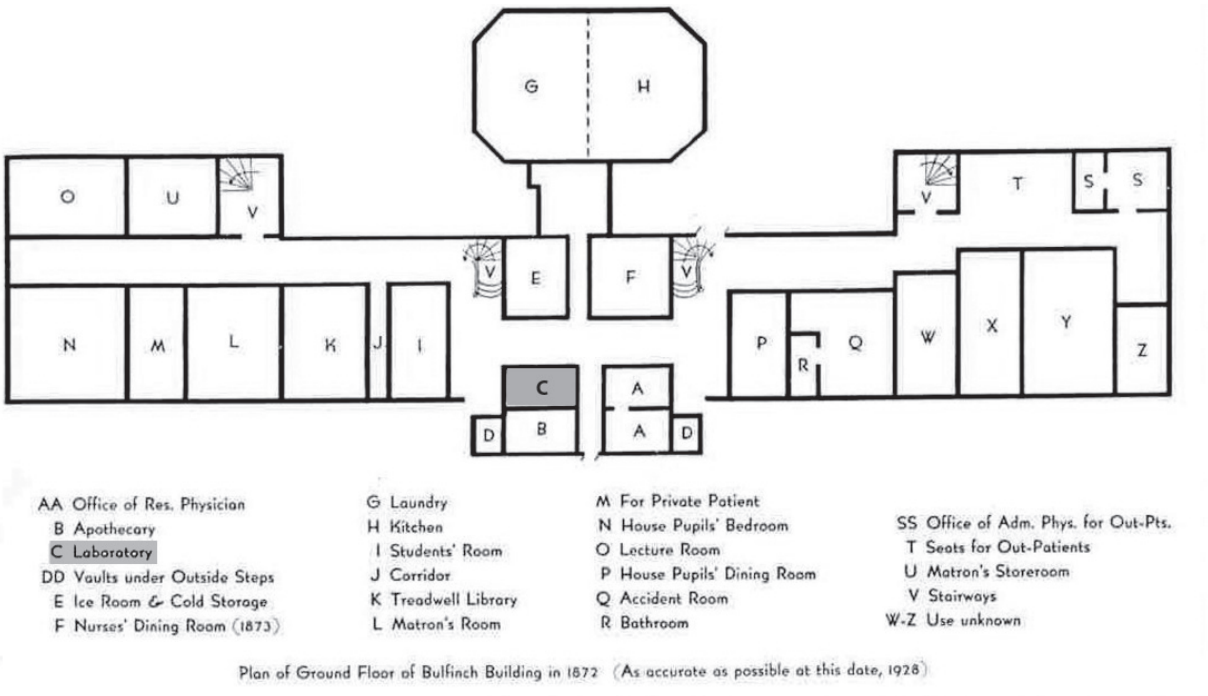

Figure 20.1 *Bulfinch Building floor plan, 1872, with the laboratory (C) highlighted*

1894) started their work in the field of hematology (considered a medical specialty that included examination of blood for malarial parasites) by counting white cells in their patients' blood specimens. William Gannett (chapter 1) was born in Boston in 1853, a descendent of John Winslow, one of the leaders of Plymouth Colony. He entered HMS in 1874 and was the first student to extend his studies to a fourth year for postgraduate work. During this year Gannett worked as an assistant to physicians at the MGH. He joined the MGH as a house pupil and received his medical degree in 1879, officially joining the MGH Medical Service after his graduation. He first spent a year in Vienna studying pathology, and then returned to MGH in 1882 to start his career as an Assistant in Pathology and Visiting Physician. At HMS, Dr. Gannett was responsible for the laboratory work in pathological histology. Between 1882 and 1891 he also served as Pathologist at Boston City Hospital and Carney Hospital. Dr. Gannett was an accomplished and highly regarded diagnostician, and he continued seeing and consulting on patients in addition to his laboratory work.

Richard C. Cabot (chapter 24) worked on blood pathology in collaboration with Dr. James Homer Wright. Dr. Wright's research included hematology (chapter 4), and the Wright stain is still used today. In 1894, Dr. Cabot was the first recipient of the Dalton Scholarship and continued his work on the "minute examination of blood." During this time, he discovered red cell inclusions associated with certain anemias and disorders of erythropoiesis that are now termed Cabot rings. His first book, *A Guide to the Clinical Examination of the Blood for Diagnostic Purposes,* was published in 1886.

Dr. Cabot's career highlights the uncertainty of the role of laboratory testing in clinical diagnosis. He rejected an offer to serve as the first bacteriologist of the hospital in favor of a position in the Outpatient Clinic. Nonetheless, he was an early proponent of providing a specific diagnosis to the patient and of using laboratory data to monitor a patient's progress. In 1907 he wrote:

> When I see statements of blood counts which tell us, for example, that the patient had 5,633 leucocytes to the cubic millimeter, I cannot help making two comments. First, that the degree of accuracy to which the statement pretends is wholly useless; and second, that it is only the pretense of accuracy after all. It is pseudo-science and not science. Now, if there is one thing which we who try to do scientific work should avoid more than another, it is, I think this pseudo-scientific pretension—the appearance of accuracy expressed in figures and diagrams, when there is no such accuracy in fact. All blood counts should end with at least two zeros, usually three.
>
> There should be no diagnoses made merely in the laboratory, and none merely at the bedside, unless what are called "laboratory methods" are carried out, as they may be carried out, at the bedside. (3)

In the early twentieth century, therefore, the role of the laboratory in the clinical diagnosis was still in question. Most physicians, like Dr. Cabot, emphasized the power of observation and overall medical knowledge; information from the laboratory only provided confirmation of the diagnosis.

Typical Laboratory Workflow: Early Twentieth Century

Laboratory specimens were usually collected by interns in the first six months of their training. Urinalysis and blood counts were performed in the ward laboratory under the supervision of the laboratory leadership ("point-of-care testing," in today's lexicon). Orders for blood counts were sent to the central laboratory. An intern was assigned to collect the samples and perform the counts. In the central laboratory, urgent (stat) tests were performed by interns on a rotating basis. By today's standards, the process for reporting and archiving test results was cumbersome

and labor-intensive. Results were handwritten on a requisition form and forwarded to a clerk, who stamped them with a unique specimen number. Each patient had an index card, and the clerk typed the specimen number on the card so that all the laboratory activity for the patient was available in one location. Then the clerk typed the report in triplicate: one copy was sent to the physician responsible for the patient, one copy was filed by test name, and one copy was filed by diagnosis. This filing system made correlation studies of laboratory results to specific diagnoses easier to complete.

During this period funding for the laboratory came from private donations. Usually, private patients were charged an extra fee of up to $10 to cover the laboratory costs. Although initially used as a model for training, over time the laboratory became an important part of the diagnostic process: its purpose was to provide routine laboratory assessments on urine and blood for the patients in the wards. The test menu was limited to urinalysis, hemoglobin, and white blood cell counts. Urinalysis was considered an important test for "practical medical work." Dr. Wright observed in the first annual report (1898) that each admission had at least one urinalysis and often more than one. During this time, Dr. Wright hired an assistant to perform basic duties in the laboratory and to prepare special diets for the patients.

The Flexner Report, Otto Folin, and the Emergence of Modern Clinical Chemistry

The Flexner Report, released in 1910, was intended to reform medical education. An additional effect of the report was the development of clinical chemistry as an integral yet independent medical discipline; hematology, however, remained a part of Medicine, both as a clinical discipline and as a science. One of the debates in the reorganization of HMS and Harvard University was the placement and scope of chemistry. At the center of the debate was whether chemistry should be considered a pure science or an applied branch of physiological chemistry. Also disputed was who should teach the subject: physicians with knowledge of chemistry or chemists with medical knowledge. As the entrance requirements for medical school were tightened and included undergraduate studies, students came with a broader scientific background and an increasing variety of specialties they wished to study. The discussion extended into the medical school and the hospital, where the value of laboratory data was balanced against the value of the bedside diagnostic skills of the physician. The overall consensus was that laboratory information was an added benefit for the physician. As a result, laboratories in the wards continued to operate, but interns were scheduled to work directly under a physician rather than performing tests as time allowed. In 1910 the Board of Trustees approved the addition of two laboratory assistants to the staff of the hospital. Thus, a new profession of medical technology was introduced to the MGH: "We expect in the future to pay laboratory workers enough to attract men of the first ability, as modern medicine has become so dependent for its success upon laboratory work" (4). The perception of the role of the laboratory had begun to change, and by 1918 Dr. Max Kahn, Director of Laboratories at Beth Israel Hospital in New York City, wrote: "Treatment, in so far as it can do good, is nowadays directly proportional to the amount of laboratory work. Given the diagnosis, it is a simple matter to treat—if treatment is possible—any case. The rub is in ascertaining the diagnosis" (5).

In 1917 the hospital created formal space for the Medical Laboratory on the first floor of the Bulfinch Building: six rooms with space for 12 workers. The laboratory was not viewed as an independent department, but rather was used by individuals who were interested in pursuing clinical investigation in their professional development. In this model, tests were developed in

conjunction with the services or clinics. The tests performed there were technically complex; routine tests were performed on the second floor. After World War I work was done on blood gases (Dr. A. V. Bock, supervised by Professor L. J. Henderson), blood disorders (Dr. George Minot), thyroid disease (a collaboration with the Medicine and Surgical Services and the X-Ray Department), and analysis of blood and urine chemistries in diabetes and kidney disease (Dr. Reginald Fitz, son of Dr. Reginald Heber Fitz, chapter 2). The Medical Laboratory was also used for microbiology investigations.

Along with the growth of the hospital's inpatient service, its outpatient activities continued to increase: by 1917 there were over 200,000 visits in the Outpatient Department (6). Disease-specific clinics opened and included services for diabetes, blood disease, and thyroid and cardiac disorders. Hospital staff to support the outpatient service included laboratory technicians, and laboratory testing was included within each clinic. In this regard, laboratory testing was growing quickly but was dispersed among many different clinics and disciplines.

A product of this laboratory evolution was Dr. Otto Folin, who moved the science of chemistry into the clinical chemistry laboratory (figures 20.2 and 20.3, and see figure 3.5). He had come to the United States from Sweden in 1882 and received his doctorate in biochemistry from the University of Chicago in 1898, which he described as "the wild and wooly west of science" (7). When he graduated there was little demand for college-educated biochemists, and so he spent time studying in Germany, where the science of biochemistry had already been incorporated into the study of physiology. While in Germany, Dr. Folin continued his interest in the metabolism of nitrogen and had the opportunity to be exposed to hospital patients while at the Pathological Institute of the Charité Hospital in Berlin. Returning to the United States, however, he struggled to find a career that leveraged the

Figure 20.2 *Otto Folin*

analytic skills he had so carefully developed. He filled the gap teaching at West Virginia University and working in rudimentary basement laboratories. In 1900 his work was rewarded with an appointment as a research chemist at the McLean Hospital for the Insane, the psychiatric division of the MGH. Edward Cowles, the Superintendent of McLean, had a long-term goal to build a psychiatric research laboratory, and the laboratory created for Dr. Folin was one of the first in the United States. In the usual medical model of the day, patients were selected for inclusion in Folin's studies on the basis of markers of mental illness in urine. His early work was directed to refining the analytical techniques that would quickly develop into the basic tools of a clinical chemistry laboratory. His research in colorimetry during that time produced methods to quantify the amount of creatinine and creatine in urine using alkaline picrates. The first studies quickly disproved the then-current belief that there was a difference between the urine chemistry of normal

individuals and of psychiatric patients. Dr. Folin expanded his research and concentrated on the chemistry of urine and its relationship to diet. In 1902 he began early studies on ammonia in blood. Because there was little in the way of a commercial market for laboratory equipment or chemicals at the time, he had to develop his own analytical devices and reagents before beginning his experiments. Dr. Folin subsequently developed procedures to purify creatinine from urine and invented a preservative solution for collecting 24-hour urines.

In 1907 Dr. Folin was recruited to Harvard with an appointment as Assistant Professor and head of the Department of Biochemistry at HMS. In this role he was the first nonphysician on the faculty. This move was somewhat controversial, as the medical school and university struggled to respond to the failures in training described in the Flexner Report. While serving as an effective department chair, Folin was also known as a gifted teacher and taught first-year medical students. He continued his work training students in the laboratory. It was said that Dr. Folin was quick to add humor to any setting, including tricking his students into believing he performed the long-obsolete urine taste test to detect sugar in the diagnosis of diabetes mellitus! He was well known for correcting students with the comment "With all the mistakes you've already made, this one is inconsequential" (7). Within a few years, he was promoted to full Professor.

Dr. Folin created a nationally recognized department that began producing the next generation of biochemists. Among them was Hsien Wu, who collaborated with Dr. Folin to develop a relatively simple analysis for blood glucose that would become the standard method for glucose testing well into the twentieth century. Wu was born in 1893 in Foochow, China. He was sent to

Figure 20.3 *Otto Folin in his laboratory at McLean Hospital*

college in the United States in 1911 and enrolled at the Massachusetts Institute of Technology to study naval architecture, but he soon changed his major to chemistry with a minor in biology. Wu's graduate work was in organic chemistry, and in 1917 he entered the doctoral program under Dr. Folin. The two men quickly became friends and collaborators. Their first paper together, "A System of Blood Analysis," was published in 1917 in the *Journal of Biological Chemistry* (8). Dr. Wu left Harvard in 1920 to return to China, becoming the head of the Department of Biochemistry at Peking Union Medical College, the youngest department chair at the time. He expanded his work on methods for analyzing blood, including deproteinization and labeled antigens. He also continued the teaching legacy of his mentor Otto Folin and incorporated Western teaching and scientific methods in China. In 1952 a heart attack restricted Dr. Wu's academic and research activities. He returned to Brookline, Massachusetts, to start a second career by studying mathematics and using these skills to analyze data from radioisotope patterns, authoring three more publications before his death in 1959 (9).

Another of Dr. Folin's notable trainees was Dr. Willey Denis, a pioneer in her own right as one of the first women to have a career in biochemistry and the first woman to be appointed to the MGH staff (figure 20.4; chapter 3). She came to the field following the same path as Dr. Folin, via the University of Chicago, where she completed her doctoral work in chemistry. In a six-month stay at Harvard in 1910, she completed early investigations on the application of Folin's urine analytic methods to blood analyses that resulted in three publications. In 1911 Dr. Denis returned to Harvard as a research assistant, and in 1913 she moved to the MGH, though still within Dr. Folin's program. She and Folin were given laboratory space in the Power House; he was appointed Chemist and she was made Assistant Chemist. By moving to the MGH, they had direct access to patients to further their biochemical investigations. Dr. Joseph Aub observed: "By 1915 blood chemistry was being done extensively in the very good chemical laboratory that Willey Denis ran, and I remember her feeling of dissatisfaction with the medical House Officers who, she said, did not have enough scientific interest to allow her to accumulate specimens. She said the dermatologists were the ones who really cooperated with her" (1). "Throughout Denis' sojourn at Harvard and at the Massachusetts General Hospital, she was not forced into a woman's role, except in title; her collaboration with Folin was a matter of choice and mutual esteem" (10). By 1917 she was managing her own research projects. With access to patients, Folin and Denis could continue their work studying patients with nephritis. A significant by-product of their studies was establishing normal values for blood creatinine and creatine. They also added turbidimetric methods for studying protein to their established colorimetric techniques. Their collaborative work resulted in 73

Figure 20.4 *Willey Denis*

publications between 1910 and 1920 (18). In 1920, after she left the MGH to take a faculty position at Tulane University in New Orleans (chapter 3), Dr. Denis further modified the method for the analysis of protein in cerebrospinal fluid. She died in New Orleans in 1929.

Developments in Clinical Chemistry and Hematology, 1900–1930

Under Dr. Folin's leadership and as the discipline of clinical chemistry emerged, test menus began to expand at the MGH. Additional tests by 1907 included urinalysis (to distinguish at least seven different types of nephritis), analysis of urinary calculi, and "examinations of organs for the presence of exudates, transudate, etc." Pharmacological investigations also interfaced with clinical chemistry. For example, the Chemistry Laboratory test menu in the early 1900s included assays for both lead and arsenic: these tests were not performed to investigate heavy metal poisoning but, rather, to monitor the therapeutic use of the metals and the patient's progress.

Pharmacological laboratory tests were one of the interests of the chemist Dr. William Boos, who worked collaboratively with his colleagues in the Medicine Service on cases with pharmacology questions to produce new assays (chapter 3). Dr. Boos graduated from Harvard in 1894, spent a year in graduate study in Germany, and returned to Boston and became an Instructor in Chemistry at Harvard beginning in 1896. He graduated from HMS in 1901 and was appointed to the staff at MGH as a house physician. Like many talented physicians, he was encouraged to study abroad, and he spent four years as a research student at the University of Strasbourg Pharmacological Institute studying biological chemistry and internal medicine. In 1906 he returned to Boston to launch his career, rejoining the MGH staff as the Director of the Biochemical Lab and consulting in internal medicine.

In 1910, Dr. Boos designed a tool for administering Salvarsan ("606") intravenously. Using both hospital and private patients, he developed an assay for urinary arsenic levels to predict the amount of 606 circulating in the blood. He demonstrated that four doses provided the greatest benefit for the treatment of syphilis. Using the same technique, Dr. Boos developed methods to study alcohol levels in postmortem cases of acute alcoholism. In 1910 James Homer Wright reported a case of an elderly man with chronic heart disease who was admitted to the hospital; his urine laboratory results showed no sugar and a specific gravity of 1.070. The medical staff approached Dr. Boos for additional laboratory information. He identified the problem as magnesium poisoning. Having seen three other cases with similar characteristics, he began to study the absorption of magnesium. By 1910 he also perfected the biuret reaction for albumin and associated the presence of tryptic "ferments" in the stool as a measure of pancreatic disease. One significant test still performed by the "pups" (students) on the Medical Service was the opsonic index. This test was used as a measure of the activity of opsonins—chemicals thought to be important in phagocytosis. The test was performed by comparing the number of organisms phagocytized in normal and infected patients. It was used for diagnosis, determining acuity, and measuring the efficacy of vaccines. It aided the treatment of a variety of diseases, including tuberculosis, erysipelas, puerperal fever, and scarlet fever.

By 1915 the laboratory service had expanded sufficiently to begin reporting test volumes to the hospital. Dr. Willey Denis reported that the number of tests performed was 531, a significant increase from the 102 reported in 1914. One of the highest-volume tests was the colloidal gold test on spinal fluid. Dr. Thomas Cunningham (a house pupil on the Medical Service in 1918) recalled, "We sent so many bloods for blood chemistries to the chemistry laboratory that they protested vigorously about it" (1). The chemistry test menu

included nonprotein nitrogen, uric acid, glucose, urea (blood urea nitrogen), and creatinin (creatinine). Calcium and phosphorus had just been introduced as routine tests. Hemoglobin assays were completed using the Tallqvist scale. With the growth in the number and types of laboratory tests, "the early laboratory space was perhaps bizarre, and certainly disseminated" (1). In a 1916 report, when the test volume had reached 1,060, Dr. Denis described additions to the test menu: measuring the daily output of urine sugar and ammonia in diabetics and the reticulocyte count for the diagnosis of pernicious anemia and bone marrow status. The "pups" continued to perform the complete blood counts.

In association with the rapid development of new techniques, new clinics and laboratories emerged in the hospital. For instance, in 1912 Dr. Boos had developed a method to measure urine pH in the evaluation of renal function; he made more than 2,500 observations in this study; he then extended his studies to blood as physicians became interested in controlling pH in patients with metabolic disease. With such techniques in hand, Dr. James H. Means opened the Metabolic Laboratory in 1913. Dr. David Edsall, Chief of Medicine, quickly identified Dr. Means as one of several talented interns with the potential to help launch a research program for MGH. The first step was to gain expertise from leading authorities in the United States and Europe. When Dr. Means returned from his travels to MGH in 1913, Dr. Edsall created the laboratory for Dr. Means to pursue his interest in metabolism. Means's early work was pure research, but he quickly moved to more clinically oriented studies on the thyroid and metabolism, including development of the basal metabolism test for diagnosing and monitoring patients with thyroid disease. In 1925 before his move to become Dean at HMS, Dr. Edsall created Ward 4, the research ward that included laboratories to support the unit's activities. Dr. Means was appointed Chief of Medical Services, and his research team included Drs. Joseph Aub and Fuller Albright. The Diabetic Clinic opened in 1916 with the "hearty cooperation" of the Chemistry Laboratory (1). In 1917 the Medical Laboratory was established; its primary function was to support clinical investigations, including the practical use of blood gas assays. The laboratory was used by the clinic for monitoring and treatment of patients with unique or interesting diseases. By the mid-1920s the resident on each service was appointed a full-time lab worker. The clinics for epilepsy and rickets contributed to new blood chemistry tests, including blood pH and vitamin assays. The laboratory operations increased to the point that the costs were recognized in a change in the hospital rates. In 1928 "there was another increase in admission charges so that adults over 16 years were charged 75 cents for the first visit and 50 cents for a subsequent visit. . . . This increase was made to help pay the expense of the laboratory work, which had grown a great deal" (1).

Laboratory-based hematology also emerged during this period as a distinct discipline at the hospital. The process of collecting blood specimens by venipuncture for laboratory testing was complicated and viewed by many as a surgical procedure. To facilitate the collection of specimens, house pupils used a technique to collect blood from the ear lobe into a small curved tube (1). This development enhanced the study of blood cells and facilitated the growth of hematology as a discipline. For example, Dr. Wright began early studies in the value of quality control in the development of his stain to study cell morphology. Drs. Roger Lee and Paul Dudley White developed the coagulation time test in Dr. Wright's laboratory.

At this time, Dr. George Minot began his work on coagulation, hemophilia, and anemias (figure 20.5). His laboratory was in the basement of the Bulfinch Building, and all patients with blood disorders were referred to him for his detailed review of their blood smears. He had been born in Boston in 1885 and had a long

lineage in Boston medicine; his grandmother was the daughter of James Jackson, cofounder of the MGH. He studied at Harvard and received his medical degree in 1912. While in medical school, Minot worked in an outpatient clinic staffed by HMS faculty and began his diagnostic career by distinguishing pernicious anemia from congenital hemolytic anemia. His HMS instructors included Drs. Otto Folin and Walter B. Cannon. When Minot enrolled in a hematology elective taught by Dr. James Homer Wright, his interest and career in hematology was sealed. Dr. Minot joined the staff at MGH as a house pupil for the Medicine Service in 1912. He continued to explore the link between nutrition and anemia and became interested in the study of blood films in these patients. When he completed his year as house pupil, Minot joined the ranks of junior faculty and then went to Johns Hopkins to continue his work and develop his skills. During his tenure at Hopkins, his basic research contributed to the preparation of heparin from livers.

In 1915 Minot returned to Boston as an Assistant in Medicine at MGH and Assistant in Chemistry at HMS. Dr. Minot, along with other notable junior faculty such as Drs. James Means and Paul Dudley White, operated in the medical model of using science to understand and treat disease. Minot found space to set up a microscope in the "inner sanctum of the hospital's irascible pathologist, Dr. Wright" (11). During World War I he consulted on cases of anemia in ammunition factory workers, and after the war he received a joint appointment at the Huntington Hospital, where he had an opportunity to continue his study of blood disorders. In 1921 Minot was diagnosed with diabetes. At the time the only treatment consisted of severe diet restrictions. When insulin was discovered in 1922, Dr. Elliott Joslin, Minot's physician, was able to obtain it in sufficient quantity to allow Minot to continue his work, which culminated in the 1926 publication of the effect of the use of liver to treat pernicious anemia (work that resulted in the 1934 Nobel Prize in Physiology or Medicine). In 1923, Dr. Minot left MGH and was appointed the Chief of the Medical Service at the Huntington Hospital. Despite an active clinical and research career, he managed to mentor students, often by writing notes on recent publications that related to their work. By the time he reached his mid-fifties, the complications from his diabetes started to restrict his activities, and in 1947 he suffered a debilitating stroke, which kept him in a wheelchair for the rest of his life. After the stroke, he resigned from his formal positions but followed his staff and their research on an informal basis until his death in 1950. His seminal work played an important part in establishing the disciplines of clinical and laboratory hematology.

Figure 20.5 *George Minot*

Fuller Albright and the Emergence of Laboratory Endocrinology

Fuller Albright was born in 1899 and graduated from Harvard College in 1919 and HMS in 1924 (figure 20.6). After graduation, Dr. Albright,

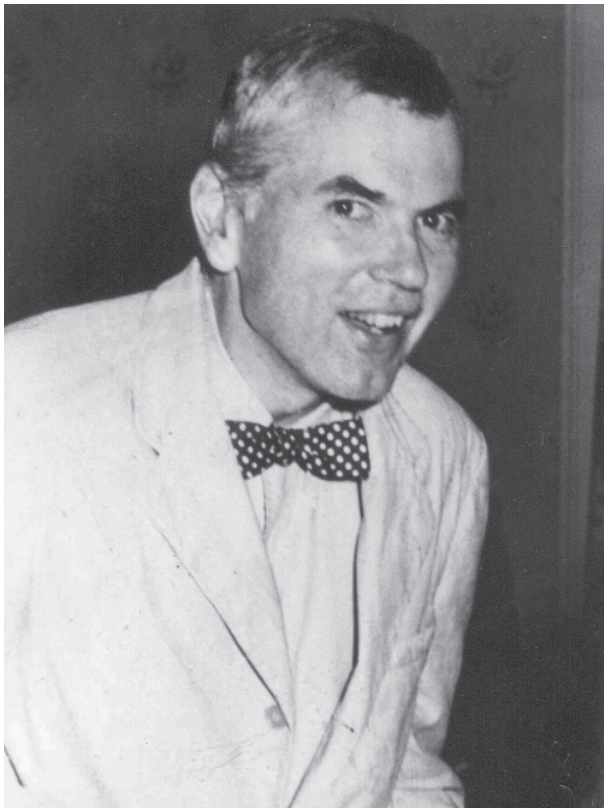

Figure 20.6 *Fuller Albright*

intrigued by recent scientific discoveries in biochemistry and physiology, focused his career on combining direct patient care with investigation of the endocrine system. His first interest was the metabolism of calcium. He spent time at Johns Hopkins with his lifelong friend and collaborator, John E. Howard; their collaboration was so close and spontaneous that they frequently could not attribute ideas to one or the other. After returning to MGH, he used the information from his clinical work to determine his research into diseases that had not been previously defined. Much of his patient work was performed in the Metabolism Unit (Ward 4), where he worked closely with Dr. Means (12, 13). His investigations led to one of the first descriptions of hyperparathyroidism, and the work in his Stone Clinic provided some of the earliest descriptions and treatments for kidney stones. Perhaps his most notable work bears his name: Albright's syndrome—which includes early-onset puberty in girls, bone cysts, and changes in skin pigmentation. Dr. Albright's work in the research lab produced analyses that developed into some of the basic endocrine test menu of today: gonadotropins in urine, sex hormones, and parathyroid hormones. In the mid-1930s Fuller Albright began to develop the early signs of Parkinson's disease. Despite progression of the disease and with the devoted assistance of his wife, Albright continued his work on Cushing syndrome, the use of estrogen to control ovulation, and the harmful effects of steroids. He is remembered for his many trips to the Pathology department to review histology and for his unlimited enthusiasm for his work and for life in general. Dr. Alexander Leaf, Chief of Medicine 1966–1981, recalled: "One day he was joined by a young aggressive foreign visitor in attendance at one of his clinics. In the course of the discussion regarding one of the patients seen on that occasion, the visitor reprimanded Dr. Albright for not having read the visitor's writings on the subject. Whereupon Dr. Albright humbly apologized for his negligence but added, 'I hardly have time to read my own' " (12). After unsuccessful experimental surgery in 1956, Fuller Albright remained in a coma until his death in 1969.

The 1930s, 1940s, and 1950s

In the 1930s the laboratory operations were distributed between the second floor of the Phillips House (private patients), with one unsupervised technician, and the second floor of the Baker Building, which opened in 1930 with three technicians and a supervising physician. The laboratory technicians covered the two operations as the level of activity warranted. The Phillips laboratory consolidated with the Baker Laboratory in 1933 to conserve space and resources. The test menu for these laboratories was limited to hematology. This was due in part to the instability of the hematology specimens. Without effective anticoagulant additives, the cell counts and smears had to be performed on fresh specimens.

The laboratory supported the Consultation (Diagnostic) Clinic and helped produce blood grouping sera for the Blood Bank. In 1933 the laboratory was opened on weekends for the first time, on Saturday afternoons and Sunday mornings. By the end of the decade there were small laboratories in the Emergency Department, the Outpatient Department, the White Building (for surgical patients), and the Vincent Burnham Building for the obstetrical patients. Despite the addition of laboratory technicians, the house pupils were still expected to perform laboratory tests. The growth in laboratory testing responsibilities led to the decision to increase the number of house pupils to 67, which resulted in a ratio to patients of 1 to 10 (down from 1 to 15 in 1900). In the same year the laboratory in the Operating Room/Anesthesia Department raised $1,500 in private donations to help defray expenses. In their individual specialty labs, significant work was done on the development of new laboratory assays for parathyroid hormone (Dr. Joseph Aub), sex hormones (Dr. Fuller Albright), thyroid hormones (Dr. James Means), and anemias (Dr. George Minot) (figures 20.5, 20.6, and 20.7).

By the mid-1930s there were three types of laboratory in the hospital: the clinical laboratories for patient care, research laboratories, and disease- or organ-oriented laboratories that integrated research and clinical care. In 1937 the General Executive Council approved a report recommending a reorganization of the "routine laboratories," which resulted in the consolidation of the clinical laboratories into Pathology administration. Dr. Francis Hunter, responsible for the Baker and Phillips laboratories, was appointed the Clinical Pathologist. Hunter graduated from Harvard in 1919 and HMS in 1924. From there, he joined the MGH staff as well as the Massachusetts Eye and Ear Infirmary as a consultant physician and pathologist. He was viewed as an expert in X-ray safety, and during World War II he helped maintain the war records of MGH personnel.

For 1938 Dr. Tracy Mallory, the Chief of Pathology, reported a significant growth in the Chemistry Laboratory: its annual volume had reached 18,886 tests. He stated, "In spite of this marked growth, there has, unfortunately been no increase in the amount of space for the Chemistry Laboratory until last year when I succeeded in getting a very small additional corner of space" (1). The Chemistry Laboratory had expanded that year to accommodate new equipment (calorimeter, microscope, and a balance) necessary for the 30 percent growth expected with the opening of the Baker and White buildings.

In the 1940s there was continued innovation in technology and tests in the laboratories. Despite the growth, the Baker Laboratory had a reduction in personnel. It continued to operate with a menu of total protein, hematocrit, and hemoglobin in cooperation with the Medical staff. The annual report of 1944 offers a proposal for new laboratory space for all the routine laboratories, citing the advantage of collaboration and consultation. In the late 1940s Dr. Hunter perfected the use of spectrophotometric methods for quantitative assays and eliminated interference caused by turbidity. Despite the interest in consolidation, two new laboratories opened: the Enzyme Laboratory of Dr. Fritz Lipmann (who won the Nobel Prize in 1953 for his work on coenzyme A) on Bulfinch 3 and the Anesthesia Laboratory on White 4.

With the continued development of new technologies in the 1950s, the scope of the clinical laboratories grew. The model did not change, however: tests were performed in specialized laboratories defined by specific clinical disciplines. Resident training included chemistry and hematology (through the Medicine Service) and was provided not only for Medicine residents, but also for physicians interested in a career in clinical pathology.

Dr. Hunter died in 1954 at the age of 57, having directed the large clinical laboratories at MGH for 17 years. At this time the Hematology Laboratories were temporarily assigned to

Dr. Charles DuToit, the Director of Chemistry. Hospital leadership decided that hematology was developing into a unique specialty and appointed Dr. William Beck as Director of the Baker Laboratory and the new Hematology Unit. Dr. Beck was recruited from New York University to the MGH in 1957; his interest was hematology, with a focus in biochemical research. At MGH he continued his work on vitamin B12, DNA synthesis, and pernicious anemia. When the Harvard–MIT Health Sciences and Technology program started, Dr. Beck was named the Director of the Hematology course. At the same time, Dr. Beck directed the Hematology Program at HMS. He continued his work and teaching even after being diagnosed with pancreatic cancer, until his death in 2007 (14).

Under Dr. Beck's direction the Hematology Laboratories became the service laboratory and were known as the Clinical Laboratories. Most of the laboratory work in Hematology was still performed by the medical students and interns as part of their patient care responsibilities. The experience of doing cell counts and urinalysis was viewed as a valuable part of their training as physicians. Dr. Beck recalled, "The weary house officer would return to a dismal, crowded laboratory after his other work was finished" (15).

Dr. DuToit continued as the Director of the Chemistry Laboratory on the fourth floor of the Domestic Building, and G. Margaret Rourke was the lead technologist of a staff of 12 technologists. Methods included protein electrophoresis (one of the earliest uses of electrophoresis in the country) and flame photometry. Though the model of disease-based research combined with a clinical laboratory for esoteric tests continued (for example, in the 1950s the Immunology and Allergy Unit opened, along with the requisite laboratory dedicated to developing and performing tests for patients with immunological disorders), the Chemistry Laboratory provided support to all clinical services, performing the basic routine tests. In 1955 the first automated technology, the Technicon AutoAnalyzer, was implemented. Each of these early platforms performed one electrolyte assay using automated sampling and continuous flow. The hospital also opened a one-year laboratory training program for 10 students from Simmons College that included rotations in Pathology, Medicine, Bacteriology, and the Blood Bank.

The 1960s and 1970s, and the Beginning of Computerization and Automation

The 1960s saw rapid growth in the laboratories. The test volume grew from 259,553 tests per year in 1960 to 745,358 in 1970 (the first year that cumulative statistics were produced by the computer). This was attributed to increased utilization in the Outpatient Department, since few beds were added to the hospital during this time.

In the early 1960s MGH clinical services convinced the hospital leadership to eliminate laboratory work from the house staff's responsibilities and transfer it to dedicated laboratory staff. The Surgical Service started the transition, and the Medicine Service followed. This significant change did not affect the specialty laboratories still active in the services. Dr. Myron Laver joined the Surgical Service during this time and opened the Blood Gas Laboratory to support the growing interest in laboratory assessment of respiratory status during and after surgery. Dr. Laver designed and built many of the early blood gas analyzers. As the anesthesiologists noted in a history of their department, the "perfected accuracy and speed in providing serial blood gas analyses . . . enabled physicians to follow rapidly changing clinical situations" (15). In its first year the Blood Gas Laboratory performed 3,000 tests. The initial plan was to have the Chemistry Laboratory staff the Blood Gas Laboratory, but the leadership of the Chemistry Laboratory was not interested in developing that part of the specialty (J. Flood, personal communication, 2010). The Thyroid Laboratory opened in the Bulfinch basement and

performed thyroid-stimulating hormone (TSH) and thyroxine binding pre-albumin testing at no charge to the patient. Dr. Lot Page in the Hypertension Clinic developed the renin assay. The Cardiac Unit (and laboratory) opened in 1965 under the direction of Dr. Paul Dudley White. In that laboratory Dr. Edgar Haber developed an assay for digoxin.

In 1961 Dr. Sidney Rieder was appointed the Director of Chemistry. His appointment was in Medicine rather than Pathology. Dr. Rieder came to the MGH from the Department of Biochemistry at Yale University School of Medicine. While there, he had worked with Dr. Irwin A. Rose, who went on to receive the 2004 Nobel Prize in Chemistry (16). In his autobiographical note for the Nobel Prize, Dr. Rose recognized Dr. Rieder as one of many who had helped him solve problems in his early years of biochemical research (17). There were two head technologists to manage the growing volume: Olive Holmes and Mary Zervas. With the volume expanding by 20 percent each year, the Chemistry Laboratory implemented a four-channel AutoAnalyzer and added a third head technologist. There were about 40 technologists in the Chemistry Laboratory, and

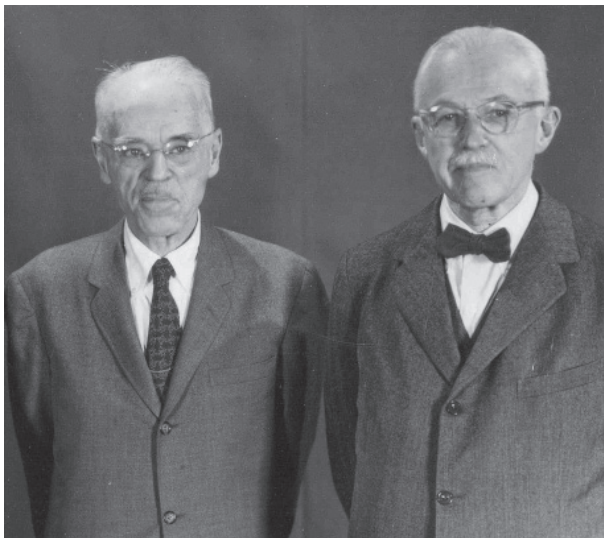

Figure 20.7 *Paul Dudley White (left) and James Howard Means*

it operated around the clock throughout the year. Routine samples were accepted Monday through Saturday from 9:00 A.M. to 5:30 P.M. In 1965 the Chemistry Laboratory had a menu of 130 tests, most of which were offered 24 hours a day; there were five AutoAnalyzers and an enzyme analyzer in the laboratory, most running at 50 percent capacity.

In 1965 the MGH chemistry laboratories performed over 1,000,000 procedures, an increase of 70 percent in five years. Physicians were responsible for completing the laboratory requisitions; specimens were collected according to the requirements of the laboratory performing the procedure and hand-delivered to the laboratory by a messenger service. The samples were recorded in a logbook, and the tests scheduled by the laboratory technician. Up to 32 color-coded test worksheets and up to 90 total pages were transcribed by the laboratory technicians every day. Test results were manually transcribed from each worksheet onto the original multipart requisition. The original requisition was sorted and returned to the patient unit, a second copy was filed for billing, and a third copy was saved in the laboratory for five months. Requisitions were sent back to units via dispatch at 3:30 P.M. and 6:30 P.M. The laboratory scheduled its testing activity on the basis of the number of specimens delivered to the laboratory on any given day. Although tests were performed continuously throughout the day, the results were not sent back to the unit until after 5:00 P.M. Although the laboratory was open 24 hours a day, only emergency specimens were accepted after 5:30 P.M. This schedule was frequently abused; Dr. Rieder reported, "On Saturday 20% of the slips coming to the Chemistry Laboratory bore the red sticker indicating that they were emergencies." He cited an example of one of the house officers who got up at 5:30 and aroused his patients, secured blood, marked them all with red slips, and got them down to the laboratory. When the house officer was asked about the necessity of this, it became clear that many of

these were not emergencies. "This example only points out one fact of what is a very large problem," Dr. Rieder observed (18).

In 1966 the Gray Building opened, and new space on the second floor housed the Hematology, Special Hematology, and Coagulation Laboratories. In the same year Medicine completed the transition of laboratory tests being performed by technicians rather than house staff. This move was accelerated with the introduction of the Coulter S automated cell counters, which required training to operate. The service levels of the Hematology Laboratories varied greatly, and differences in the menus on the automated cell counters introduced confusion. This was further complicated by the decision to eliminate the order "CBC" (complete blood count), because each laboratory performed a different panel. (The Baker Laboratory CBC included a white blood count, hemoglobin, and cell differential, whereas the CBC of some of the other laboratories included a hematocrit instead of hemoglobin.) Consequently, it was difficult for physicians to follow the course of a patient's care. The ease of ordering a CBC test was also identified as the cause for the volume increase in daily CBC orders on long-term patients. Ordering the individual analytes as opposed to a panel was presumed to add clarity—one of the earliest efforts at managing laboratory test utilization in the hospital. The Special Hematology Laboratory performed vitamin B12, folic acid, and leukocyte alkaline phosphatase.

In 1967 the growth in the volume of available laboratory data and the emergence of new laboratory regulations required improved ways to make this information available to providers. Dr. Octo Barnett was recruited in 1962 by Dr. Robert Ebert, the Chief of Medicine, who believed "the enormous information transmittal problems involved in the practice of medicine in a large hospital might be simplified, and the availability of data upon which medical practice is based might be improved by the computers" (15). Dr. Barnett was recruited to develop computerized systems for processing patient information. This was a joint project with an outside consulting firm and was funded through the National Institutes of Health. Dr. Barnett was a trained cardiologist with a particular interest in the applications of computers to medicine. Using data that included patient medical and personal information to develop computer systems was controversial. He started by identifying areas of the clinical operation in which clear information flow was a priority to the physicians providing care, and the laboratories were identified as a prime opportunity. One of his earliest efforts resulted in COSTAR (Computer Stored Ambulatory Record), developed in the MGH Laboratory for Computer Science; it was one of the first laboratory systems in the country. There were many benefits; for example, following the introduction of computer systems, it was reported that "in some areas of the hospital, the turnaround time from drawing of blood samples to the report is less than an hour" (15). The information system included several automated quality assurance thresholds, including delta-checks and abnormal flags that prompted the technician to verify the result before release. Chemistry and Microbiology were the early adapters, followed by Hematology, Blood Bank, Pathology, the acute care laboratories, and various specialty laboratories.

By 1970 the MGH laboratory information system was one of the largest in the country and was adapted by other institutions. The system had several functions, including worksheets, patient inquiries, results reporting, billing, and statistics. The first computer application was used for internal laboratory operations only, and the second phase expanded to include manual result entry (eliminating many handwritten test results) and cumulative reports. The last phase included accumulation and manipulation of data and interfacing of laboratory instruments to the laboratory information system. The scale of the task soon exceeded the technical capabilities of the available computer programming languages. Dr.

Barnett and his team then developed MUMPS (MGH Utility Multi-Programming System) to accommodate multiple users. Dr. Barnett wrote:

> The major finding of this evaluation is that the principle impact of automation in the chemistry laboratory has been to increase its capacity and make it unnecessary either to hire more manpower or to reorganize the system in order to handle a rapidly increasing load. Two indices of success of this system are important, although both are subjective. The first is the dependency of the hospital operation on the function of the system (the chemistry laboratory director is convinced that his laboratory would have been in absolute crisis by now were it not for the computer system) and the willingness of the hospital administration to both purchase a computer system and support the continuing operational costs out of patient care charges. (19)

Even with the introduction of computers, the majority of the laboratory work was performed on paper. The paper requisitions were color-coded to facilitate deliveries to the correct specialty laboratory. The Clinical Laboratories (Hematology) had five unique locations: Baker, Bulfinch, Burnham, Outpatient Department, and White 6. The proliferation of test requisitions can be illustrated by a consideration of the Clinical Laboratories to develop a special requisition for prothrombin time because the secretaries were spending too much time on the 200 samples received each day. Dr. Rieder was a strong proponent of computer solutions and felt that this would all be solved by computerization.

The Coagulation Laboratory was also growing, having taken over the prothrombin time test from the Chemistry Laboratory and the histamine test from a research laboratory. The laboratory encouraged use of the partial thromboplastin time (PTT) as a screening test over clotting time. Coagulation testing moved from the Baker Laboratory to new space created on Gray 2. The menu now included the thromboplastin generation test, thrombin time, fibrinolysis, fibrin solubility in urea, euglobinlysis time, and factor assays.

In 1968 the Chemistry Laboratory moved to the fourth floor of the Gray Building with a staff of 60 employees. There was also a separate Blood Gas Laboratory on White 4 that offered rapid turnaround time and callback of test results to the patient location. The Blood Gas Laboratory also introduced an interesting billing structure: the patient was charged $10 per sample, with a maximum of $25 per day.

By 1969 automation was expanding in both Chemistry and Hematology. Chemistry began releasing the first automated laboratory reports: consolidated reports printed from the computer to replace handwritten results on a requisition. There were frequent communications to the units emphasizing the need for legible requisitions and full information. In an attempt to improve quality of care, laboratory leadership considered rejecting specimens received without a medical record number. Atomic absorption and automated enzyme assays were added to the Chemistry menu. The Hematology Laboratory was processing 500 specimens a day, and a Coulter B instrument was acquired to automate the platelet assay. All the laboratories performing hematology tests moved to space on Gray 2 and merged with the Coagulation Laboratory. Virtually all the satellite hematology laboratories were closed, with the exception of a laboratory in the Emergency Department.

The tradition of setting up autonomous specialized laboratory services continued in the 1970s. A new admitting area opened in 1971, supported by a dedicated laboratory. In Endocrinology, Dr. Farahe Maloof introduced the most sensitive TSH assay available at the time. The Endocrine Unit also began performing parathyroid hormone tests using the relatively recent immunoassay techniques. A new Intensive Care Unit opened on Gray 3A, supported by a new Blood Gas Laboratory. By the middle of the decade the Blood Gas

Laboratories performed over 100,000 tests per year. During the 1970s laboratory medicine at the national level was progressively moving toward more formal systems for quality control and quality assurance. The MGH Chemistry Laboratory implemented a semi-automated quality control statistical package in the mid-1970s.

In 1975 Dr. Leonard Ellman was appointed director of the Hematology Laboratories (also known as the Clinical Laboratories at that time). Dr. Ellman had been Chief of the Hematology Unit in Medicine since 1971. He continued the teaching activities of the unit and expanded the clinical Hematology Service. Dr. Ellman continued as Director of the Hematology Laboratories following the 1977 merger to form the Hematology-Oncology Unit in Medicine.

The laboratory associated with the Immunology and Allergy Unit, dedicated to developing and performing tests for patients with immunological disorders, also grew. Under the leadership of Dr. Francis Cabot Lowell in the 1960s and early 1970s and Dr. Kurt Bloch following 1976, many new assays of the immune system were developed. Dr. Bloch was recruited to be the Chief of the new Immunology and Allergy Unit, and he combined his work in rheumatology on the Medical Service with the developing field of immunology. As Dr. Alexander Leaf, the Chief of Medicine, observed: "With the strengths of the Pathology Department in immunology, close relationships have developed with that department, although occasional jurisdictional disputes have surfaced regarding teaching roles and territory with respect to certain clinical immunologic tests" (15).

The Modern Clinical Laboratories

In the 1980s economic issues prompted a consideration of efficiency and consolidation of laboratory services. One of the earliest changes resulted in the closure of the Gray 3A laboratory. But in the late 1980s there began a more progressive trend of laboratory consolidation and centralization of laboratory management under the department of Pathology. Over the next two decades this process transformed the clinical laboratories from a group of autonomous specialized testing facilities into a coordinated division of Pathology responsible for providing comprehensive laboratory services. The initiating event was the decision by the hospital in 1988 to recruit a Director of Clinical Laboratories. Following a national search, Dr. Michael Laposata was recruited from the University of Pennsylvania to become the first Director of Clinical Laboratories at the MGH (figure 20.8).

Dr. Laposata received his M.D. and Ph.D. from Johns Hopkins University School of Medicine and completed a postdoctoral research fellowship and residency in Laboratory Medicine (Clinical Pathology) at Washington University School of Medicine in St. Louis. He took his first faculty position at the University of Pennsylvania School in 1985, where he was an Assistant

Figure 20.8 *Michael Laposata*

Professor and Director of the hospital's Coagulation Laboratory. In 1989 he became Director of Clinical Laboratories at the MGH and was appointed to the faculty at HMS, where, as a dynamic teacher, he eventually became a full Professor of Pathology. Laposata's clinical focus was in blood coagulation, and his research focused on fatty acids and their metabolites.

At the time of Dr. Laposata's recruitment, the clinical laboratories were scattered across the MGH campus, and many laboratories were directed by physicians from medical specialties outside Pathology (see table 1); little attention was given to coordinating clinical laboratory services within the hospital. Several laboratories were not computerized and still relied on handwritten paper records. In laboratories that did have computer systems, there was a mixture of homegrown and customized commercial systems that could not be networked into a single laboratory information system. Soon after his arrival, Dr. Laposata began working with colleagues to craft a strategic vision for the clinical laboratories, emphasizing the emerging role of laboratory medicine as a distinct specialty within Pathology. Highlights of this vision included:

1. Consolidation of the management of the clinical laboratories under Pathology
2. Development of a formalized Clinical Pathology resident training program
3. Development of formalized laboratory-based consultative services to support MGH physicians in the selection and interpretation of laboratory tests
4. Implementation of modern instrumentation and laboratory information systems.

Dr. Laposata created an overall coordinating administrative position within the Clinical Pathology Division and hired Donna MacMillan in 1994 to fill the role. MacMillan's undergraduate work was as a medical technologist, and she has an MBA in Health Management from Boston University. Her areas of interest include regulatory compliance, process improvement, and quality and safety. Beginning in 2004, her role expanded to cover Anatomic Pathology as well, as Director of Operations for the Pathology department.

Table 1. Individual Clinical Laboratories and Their Departmental Affiliations in 1988

Laboratory	*Department Affiliation of Director*
Clinical Chemistry	Hospital Administration
Acute Care Laboratory	Cardiac Anesthesia
Pediatric Microchemistry	Pediatrics
Reproductive Endocrine Laboratory	Endocrinology (Medicine)
Thyroid Endocrine Laboratory	Endocrinology (Medicine)
Gastrointestinal Laboratory	Gastroenterology (Medicine)
Diabetes Laboratory	Endocrinology (Medicine)
Clinical Immunology	Allergy/Immunology (Medicine)
Neurochemistry Laboratory	Pediatrics
Hematology	Hospital Administration/ Hematology-Oncology
Microbiology	Hospital Administration/ Infectious Diseases
Blood Transfusion Services	Surgery
Phlebotomy/Transport	Hospital Administration

Over the ensuing decade, nearly all clinical laboratories were sequentially consolidated, which ultimately resulted in the configuration that exists today (table 2). The first consolidation occurred in 1990 and involved the Pediatric Microchemistry Laboratory and the Acute Care Laboratory; this consolidation was a logical move because both laboratories provided whole blood testing for blood gases and electrolytes and other tests relevant to acute care settings (adult intensive care units, cardiac surgery, and the pediatric intensive care unit). In 1997 the largest consolidation occurred, combining Clinical Chemistry, Thyroid Endocrine, the new Acute Care

Laboratory, Reproductive Endocrine, and the Lipid Laboratory, which led to the formation of a full service chemistry-immunochemistry laboratory on Gray 5. In subsequent years other laboratories consolidated into this operation, including the Gastrointestinal Laboratory, the Neurochemistry Laboratory, and the Clinical Immunology Laboratory. Another major transformative event occurred in 1999 when a single commercial laboratory information system (Sunquest) was implemented by Dr. James Flood. Dr. Flood had received his B.A. and his Ph.D. in Analytical Chemistry from Lehigh University. After clinical chemistry training with Drs. George Bowers and Robert McComb at Hartford Hospital, he joined MGH as Assistant Director of the Chemistry Laboratory in 1980. In 1984 he became Director of the Chemistry Laboratory. His research interests include analytical toxicology, automation, and computer applications in the clinical laboratory.

The new information system replaced five obsolete legacy systems that could not be networked: for the first time all of the major clinical laboratories were united on a single laboratory information system. Finally, in perhaps the largest consolidation to date, the Clinical Chemistry Laboratory was combined with the Hematology Laboratory, which moved from Gray 2 to Gray 5 in 2006. This event marked the physical creation of the current Core Laboratory on Gray 5; for the first time, all the major testing laboratories, including Chemistry, Hematology, and Microbiology, were located in one contiguous space on Gray-Jackson 5. It also brought to a close the decadelong process of creating a single consolidated laboratory supported by a modern laboratory information system.

Dr. Kent B. Lewandrowski was the first Core Laboratory Director and also served as the Associate Chief of Pathology. Dr. Lewandrowski received his M.D. from the University of Massachusetts Medical School, completed his residency in Anatomic and Clinical Pathology at the MGH, and joined the faculty in 1991, serving in various leadership capacities in the clinical laboratories and being appointed Associate Chief of Pathology and Director of Clinical Services (combining anatomic and clinical pathology) in 2006. His research interests include studies on critical care/point-of-care testing and pancreatic pathology. Along with Dr. James Flood, the Director of Clinical Chemistry, he oversaw most of the many consolidations that ultimately resulted in the formation of the Core Laboratory. When Dr. Lewandrowski assumed oversight of all departmental clinical operations in 2007, Dr. Anand Dighe became the Director of the Core Laboratory. Dr. Dighe had received his undergraduate degree from the Massachusetts Institute of Technology and his M.D. and Ph.D. degrees

Table 2: Configuration of the MGH Pathology Clinical Laboratories (ca. 2011)

Laboratory	*Comment*
Core Laboratory	The Core Laboratory on Gray 5 represents the final organization of a number of individual laboratories including clinical chemistry, hematology, thyroid endocrine, reproductive endocrine, lipid laboratory, gastrointestinal laboratory, pediatric microchemistry, acute care, clinical immunology, and neurochemistry
Microbiology	Includes bacteriology, virology, molecular microbiology, parasitology, serology, mycobacteriology, and mycology
Diabetes Laboratory	Performs specialized testing related to diabetes mellitus
Blood Transfusion Services	Includes the blood donor service and blood transfusion services
Laboratory Support Services	Includes phlebotomy, some transport services, and a centralized phone service (4-LABS)
Point-of-Care Testing	Provides oversight of bedside testing performed by physicians and nurses across MGH campus

from Washington University in St. Louis. He then spent six years in the information technology industry. After completing clinical pathology residency training at the MGH, he joined the faculty and is currently Director of the Core Laboratory and Associate Director of Pathology Informatics. His research interests include the application of information technology to the laboratory testing process, from test ordering to test interpretation.

The next major advance in the Core Laboratory occurred in 2010 with the implementation of a fully automated chemistry-immunochemistry system. This system uses a track method and robotics to move specimen tubes through the laboratory. The automated "line" includes instrumentation to perform specimen processing, including centrifugation, decapping of tubes, and aliquoting of daughter specimen tubes, followed by analysis on consolidated instrument platforms. Another major innovation led by Dr. Dighe in 2009 was the development of a computer interface between the Sunquest laboratory information system and the hospital provider order entry system. This interface eliminated the need for handwritten paper requisitions and permitted specimen tubes to be labeled with bar codes directly on the inpatient care units.

Dr. Laposata also developed laboratory consultative services, the first such service being a coagulation consult service run by clinical pathologists that provided laboratory interpretations on complex coagulation abnormalities and also assisted physicians in test selection. Other laboratory-based consultative services included clinical immunology (protein electrophoresis and antinuclear antibodies), hemoglobin electrophoresis, and toxicology. In 2008 Dr. Laposata left the MGH to become the Executive Vice Chair of Pathology and Professor of Medicine at Vanderbilt University School of Medicine.

With the appointment of Dr. David Louis as Chief of the MGH Pathology Service in 2006 (chapter 25), the Division of Laboratory Medicine was combined with the Division of Anatomic Pathology into a single administrative Clinical Services Division led by Kent Lewandrowski.

The growth of the Core Lab and its subspecialties led to an expansion of the faculty as well, as the Core Lab faculty grew to six members in addition to Drs. Dighe and Flood (in alphabetical order): Drs. John Higgins, Elizabeth Lee-Lewandrowski, Mandakolathur Murali, Patrick Sluss, Aliyah Sohani, and Elizabeth Van Cott (figure 20.9). Dr. Higgins graduated from HMS in 2004 and came to the MGH in 2009 as an Assistant Professor of Systems Biology and Assistant Pathologist. He serves as a Clinical Consultant to the Hematology Lab, and his academic work is in the mathematical modeling of human disease processes and in population dynamics of red and white blood cells and blood flow in vaso-occlusive disorders. Dr. Lee-Lewandrowski received her Ph.D. in chemistry from Brown University in 1986 and served as a postdoctoral fellow in clinical chemistry at Hartford Hospital and at the Center for Blood Research in Boston. She received an M.P.H. in Health Care Management from the Harvard School of Public Health in 1993 and joined the staff of the MGH in 1999. She is an Assistant in Chemistry, Assistant Professor at HMS, and Codirector of the Clinical Research Core Laboratory. Her scientific interests include the evaluation of rapid point-of-care technologies and outcomes studies of new diagnostic technologies. Dr. Murali came to the MGH in 2002 after serving on the faculty of SUNY Brooklyn in Medicine and Allergy/Immunology and SUNY Stony Brook as the Training Program Director in Allergy/Immunology. At the MGH he has a dual role in the Allergy/Immunology division and Pathology, where he is Director of the Immunology Laboratory in the Core Lab. His clinical interests are in immunodeficiency diseases, urticaria, and monoclonal gammopathies. Dr. Sluss came to the MGH in 1991 to study reproductive endocrinology, direct the Immunoassay Core Research Lab,

Figure 20.9 *MGH Core Laboratory, 2010. Seated, left to right: Elizabeth Lee-Lewandrowski, Aliyah Sohani, Donna MacMillan. Standing: Patrick Sluss, Elizabeth Van Cott, John Higgins, Mandakolathur Murali, Anand Dighe, Kent Lewandrowski, James Flood.*

and manage the Medicine laboratory for infertility testing. He is an Associate Professor at HMS with academic interests in biomarker discovery and development, and he is the Codirector of the Clinical Research Core Laboratory and the MGH Director of the Partners' Biorepository for Medical Discovery. He also serves as the Assistant Director for the immunodiagnostics test menu in the Core Laboratory. Dr. Sohani graduated from HMS and came to MGH Pathology as a resident in 2001. She was appointed to the staff in 2007 and serves as the Director of the Hematology Lab and is interested in hematopathology, laboratory hematology, and coagulation (thus overlapping the traditional domains of anatomical and clinical pathology), and the delivery of pathology services in resource-challenged settings. Dr. Van Cott graduated from HMS and was appointed to the MGH Pathology staff in 1997, after completing her residency at MGH. She is the Director of the Coagulation Lab within the Core Labs. She provides a consult service for patients with coagulation disorders, including individualized test interpretations for complex coagulation cases.

Another major development in the clinical laboratory services of the MGH during the 1990–2010 period was the emergence of bedside laboratory testing performed by physicians and nurses throughout the hospital and outpatient clinics (point-of-care testing, or POCT). Limited forms of POCT had existed for decades at the MGH, including testing for fecal occult blood and dipstick urinalysis. Indeed, as described earlier, laboratory testing performed by physicians and house staff was the norm in the early years of the hospital. The growth of POCT was initially catalyzed

by the introduction of bedside glucose testing for the routine management of patients with diabetes mellitus. The use of hand-held bedside glucose meters rapidly spread throughout the hospital in the early 1990s, becoming a standard of care. Over the ensuing two decades, POCT expanded and by 2009 approximately 650,000 tests per year were being performed at the point of care; there were 26 tests on the menu. One area where the MGH became a recognized national leader was in Emergency Department (ED) POCT. In 2001 a satellite laboratory was established in the ED to provide rapid on-site testing to improve ED efficiency, reduce ED length of stay, and increase the number of patients who could be sent home directly from the ED, thus avoiding unnecessary admissions. The ED Laboratory was the first in the country to perform rapid whole blood cardiac marker testing for the evaluation of patients with acute coronary syndromes.

In 2011 tests are ordered online in the Physician Order Entry (POE) system. The orders are placed in the laboratory information system (LIS) and given an accession number, and labels are printed on the patient units. The labels indicate the specimen tube type, patient demographics, and laboratory tests to be performed. When the specimens are collected by the unit staff, the labels are placed on the containers and they are sent to the laboratory. Laboratory staff acknowledge receipt of the specimens in the LIS and place them on the automation line for processing and analysis. The automated line captures quality control data and patient test results, followed by validation and release to the patient electronic medical record (EMR).

In summary, the years from 1990 to 2010 witnessed a transformation in the MGH clinical laboratories. Starting from a group of isolated specialized laboratories with no administrative coordination, the clinical laboratories were integrated into a single division within Pathology and consolidated into a contiguous facility on Gray 5 with a common laboratory information system and highly automated instrumentation. The focus of the laboratories has also changed from small facilities providing services to a select group of specialists to an organization that provides comprehensive laboratory services across the MGH campus.

Conclusion

The history of the clinical laboratories at the MGH is remarkable and mirrors the evolution of medicine over the past two centuries. Early endeavors in the laboratory resulted from the intellectual interests of a select group of physicians who were beginning to apply scientific principles to the understanding of human disease. This was followed by investigators in translational medicine seeking to apply scientific discoveries to the practical diagnosis and treatment of disease. And the most recent phase involved physicians specifically trained in laboratory medicine transforming the laboratories into a coordinated and efficient hospital system.

Despite the dramatic changes that have occurred over the years in laboratory operations, some things remain unchanged to this day. For example, although the CBC and urinalysis have been automated, cell differentials and urine sediments, even after image analysis, still require the expertise of a trained medical technologist for review. Changes in technology have also produced new specialties in the medical technology profession, including informatics, automation, molecular diagnostics, and operations. Undoubtedly the future will produce more changes, further evolution, and progressive improvements in the ability of the clinical laboratory to improve patient care.

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