At the beginning of the 20th century, therapeutic agents were still relatively few, and many common diseases that are easily cured today were still considered life-threatening. As improvements were made in diagnostic techniques and new drugs were discovered, the laboratory galvanized the authority of medicine by endowing it with the ability to identify and cure disease. Clinical labs began to evolve into permanent institutions within U.S. hospitals as new diagnostic tools were derived from advances in physics. These included radioactive isotopes, electrophoresis, microspectrophotometry, the electroencephalogram and electromyogram. Other techniques such as ventriculography, intracardiac catheterization and tomography greatly extended the physician’s understanding of body function.

In 1840, the only laboratory the average European physician was likely to have used was that of a pharmacist; but by 1900, a host of laboratory types emerged, including physiological laboratories, pharmaceutical and pharmacologic laboratories, as well as forensic, public health, and microbiological laboratories. The lab, in one form or another, became an “obligatory passage point” for researchers who wanted to make new discoveries.

Microbiology
Developments in microbiology attested to the link between the diagnosis and treatment of disease. The arrival of antibiotics and sulfonamides was especially important in curing

**Timeline**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tr>
<td>1899</td>
<td>American Society for Microbiology is founded.</td>
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<td>1900</td>
<td>F.G. Hopkins discovers tryptophan; Otto Folin becomes the first full-time clinical biochemist (in its modern sense) in the U.S.</td>
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<td>1902</td>
<td>The DuBoscq visual colorimeter is first introduced into clinical laboratories.</td>
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<td>1903</td>
<td>Ayer Clinical Laboratory is established at Pennsylvania Hospital, designed by Simon Flexner for work with patients.</td>
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<td>1904</td>
<td>Christian Bohr discovers the reciprocal relationship between pH and oxygen content of hemoglobin (Bohr effect); M. Beijerinck obtains the first pure culture of the sulfur-oxidizing bacterium <em>Thiobacillus thioparus</em>; the first ultraviolet lamps and the first practical photoelectric cell are invented.</td>
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<tr>
<td>1905</td>
<td>H.J. Bechtold discovers immunodiffusion.</td>
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<td>1906</td>
<td>American Hospital Association is formed from the Association of Hospital Superintendents of the U.S. and Canada.</td>
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<tr>
<td>1908</td>
<td>Todd and Sanford publish the first edition of <em>Diagnosis by Laboratory Methods</em>.</td>
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**The history of the laboratory continues: Advances made in the laboratory eradicate life-threatening illnesses, and laboratorians establish their own identities and societies.**
many previously fatal diseases.

The accidental discovery of penicillin by Sir Alexander Fleming (1881–1955) in 1928 was paramount in initiating the antibiotic era. The Scottish scientist had been studying the natural bacterial action of the blood and antibacterial substances that would not be toxic to animals. While working on the influenza virus, he observed a mold that had accidentally developed on a staphylococcus culture plate. Around the mold was a bacteria-free circle. Fleming experimented with the mold and found it could prevent growth of staphylococci, even when diluted 800 times.

Later, Gerhard Johannes Paul Domagk (1895–1964), a German anatomic pathologist and bacteriologist, discovered that a red dye called prontosil rubrum protected laboratory animals from lethal doses of staphylococci and hemolytic streptococci. Prontosil was a derivative of sulfanilamide. Domagk was not convinced the substance would be equally effective in humans, but when his daughter became very sick with a streptococcal infection, he gave her a dose of prontosil in desperation. She made a complete recovery, but these results were not divulged until 1935 when other clinicians had tested the new drug on patients. Domagk’s discovery of the antibacterial action of the sulphonamides gave medicine and surgery a new weapon against many infectious diseases.

Clinical chemistry
There were many outstanding biochemists of the time. One who conferred a repertoire of tests to the laboratory was Otto Folin, a Swedish professor of biological chemistry at Harvard (1907). Between 1904 and 1922, Folin developed quantitative analytical methods for several urine analytes including urea, ammonia, creatinine, uric acid, total nitrogen, phosphorus, chloride, total sulfate and acidity. He also attempted to measure blood ammonia and introduced Jaffe’s alkaline picate method for creatinine. Folin showed the effect of uricosuric drugs on blood and uric acid levels in gout; introduced the colorimetric method for measuring epinephrine; and published the first normal values for uric acid, nonprotein nitrogen (NPN), and protein in blood. Folin is also responsible for establishing the relationship of uric acid, NPN and blood urea nitrogen to renal function. The Folin Cicalteau reagent, among others developed by Folin, is still used today for protein determinations.

Blood banking
New discoveries about the biochemical nature of blood made possible the transfusion of blood between humans, which greatly advanced the success rate of surgery. By the early 1940s, blood banking was established in the United States.

In 1900, the Viennese pathologist Karl Landsteiner (1868–1943) discovered the concept of the human blood
enzymology; refractometry is first used in clinical labs for the determination of protein in urine; ASCP issues its first medical technologist certification to P.H. Adams for Ft. Wayne, IN; Beckman Instruments is founded.

1932 Cherry and Crandall develop the clinical laboratory method for serum lipase activity; American Society of Clinical Laboratory Technicians, precursor of the American Society for Medical Technology, is founded.

1934 Commercial development of the electron microscope takes place.

1935 Beckman Instruments Co. introduces the first pH meter; ASCP Board of Registry first requires a college degree for medical technologist certification.

1937 First hospital-based blood bank is established at Cook County Hospital, Chicago, IL; ASCP and its Board of Registry officially oppose state licensure of medical technologists.

1938 Somogyi develops 2 major clinical laboratory methods for serum and urine amylase activity; Gutman develops the first assay for acid phosphatase.

1939 Conway and Cook develop the first clinical laboratory method for blood ammonia; American Medical Technologists is founded.

1940 Visual colorimeters begin to be replaced by photoelectric colorimeters in clinical labs; RCA demonstrates the first commercial electron microscope.


1943 Penicillin is successfully used in therapy.

1944 William Sunderman applies refractometry of proteins in the clinical lab.

1945 S. Borgstrom develops the whole blood clotting time test; itemized charges for hospital services are begun.

1946 The Vacutainer evacuated serum collection tube is introduced by Becton Dickinson Co.; Arne Tiselius separates proteins by chromatography; College of American Pathologists is founded.

1947 Edwin Land develops the Polaroid camera; American Association of Blood Banks is founded.

1948 American Association of Clinical Chemistry is founded.

1950 R.S. Yalow and S. Berson develop radioimmunooas-
types and the following year, described the ABO blood group. Accounts of previously unsuccessful blood transfusions from animals to humans reported that the foreign blood corpuscles were clumped and broken up in the human blood vessels, thus liberating hemoglobin. Landsteiner reported a similar reaction in transfusion of blood from human to human. Shock, jaundice and hemoglobinuria accompanied these early blood transfusions. After Landsteiner’s classification of blood types into the well-known A, B, AB and O groups in 1909, the catastrophes of earlier blood transfusions were eliminated by transfusing blood only between individuals of the same blood group. Later, Landsteiner studied bleeding in newborns and contributed to the discovery of the Rh factor, which relates human blood to the blood of the rhesus monkey.

Another icon of modern blood banking is Charles Drew, MD (1914–1950), an African-American physician from Washington, DC. Early in 1940, the American Red Cross and the Blood Transfusion Betterment Association of New York began a project to collect blood for shipment to the British Isles. Eight New York City hospitals collected blood for what became known as the Plasma for Britain Project. During this project, Drew successfully used the laboratory experiments and blood research done by others to mass produce plasma. Drew heard that the British had successfully modified a cream separator to separate plasma from the red cells in blood, so he ordered two of the machines and constructed similar equipment to produce clear plasma on a large scale. Drew became a leading authority on mass transfusions and blood processing methods and was later asked by the American Red Cross and U.S. government to establish a similar program for the Plasma for Britain Project.

The quality movement

The 20th century marks the beginning of a quality movement in hospitals and laboratories that began with physicians and healthcare workers. As part of that movement, those who ran hospitals began to appreciate the skills that clinical chemists could bring to the hospital laboratory. In the early part of the century, many hospitals began reorganizing their laboratories so that they were headed by biochemists. Professional organizations emerged as self-regulating groups that helped ensure the skills and knowledge of laboratory professionals would pass the scrutiny of the hospitals that employed them. These professional organizations also served their members by lobbying in Washington for advantageous legislation.

The American College of Surgeons conducted the first inspections of hospitals in 1918. Initially, the inspections were based on a single page of standards, including a requirement for an adequately staffed and equipped laboratory. Surveyors inspected 671 hospitals of 100 beds or
1952 M.D. Poulik invents immunoelectrophoresis.

1954 Kuby develops the clinical laboratory method for serum creatine phosphokinase activity; A. Walsh develops the atomic absorption spectrometer.

1955 Wroblewski and LaDue develop the clinical laboratory method for serum lactate dehydrogenase; Karmen develops the clinical laboratory method for aspartate aminotransferase; Leonard Skeggles develops the concept of “continuous flow dialysis” in connection with treatment of renal disease; Severo Ochoa synthesizes RNA.

1956 Wroblewski and LaDue develop the method for serum alanine aminotransferase activity called “serum glutamic-pyruvic transaminase” and recognize its greater specificity for liver disease compared with that of aspartate aminotransferase; J. Edwards proposes prenatal screening for genetic disease.

1957 Van Handel and Zilversmit develop a direct chemical method for the determination of triglycerides.

1959 The first clinical laboratory chemical analyzer, the single-pyruvic transaminase and “serum glutam-alanine aminotransferase develop a direct chemical method for the determination of triglycerides.

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Certification of lab professionals

Physicians in the clinical lab have always played a large role in the status of other lab professionals. Until the last 20 to 30 years, physicians have managed to resist corporate domination throughout the history of medicine. Doctors were motivated not only to preserve their autonomy, but also to prevent third parties from making a profit that might otherwise go to the doctor. In 1934, the AMA stated in a section of its code of ethics that profit from medical work “is beneath the dignity of professional practice, is unfair competition with the profession at large, is harmful alike to the profession of medicine and the welfare of the people, and is against sound public policy.” This is not to say that the AMA did not want physicians to make profits for themselves; only that they should not become a part of a larger organization whose function it was to make money. Whether the motivation for this policy was capitalistic or humanitarian is still the subject of debate. This policy helped physicians establish a medical infrastructure that allowed them to delegate to other healthcare professionals work that was repetitive and time-consuming.

To maintain their autonomy, physicians needed technical assistants to help them use hospitals and laboratories without being employees of these facilities. The allied health professional began to emerge in the first 30 years of the century with the encouragement of the doctors who needed them. Doctors needed technical assistants who were competent enough to work in their absence yet not threaten their authority. These professionals were developed by physicians in two ways: (1) the encouragement of a kind of responsible professionalism among the higher ranks of subordinate healthcare workers, and (2) the employment of women in these auxiliary roles who could be professionally trained but would not challenge the authority or economic position of the doctor.

Because clinical pathologists were striving for professional recognition among other physicians, the American Society for Clinical Pathology (ASCP) was founded in 1922. Among the Society’s objectives were the goals of maintaining the status of clinical pathologists, as well as “encouraging a closer
channel “Auto-Analyzer,” is introduced by Technicon Corp.; Technicon first applies flame photometry to automated methods. **1960** Methods for serum creatine phosphokinase isoenzymes are developed; the first method for gamma-glutamyl transferase in serum is developed; Perkin-Elmer Corp. introduces atomic absorption spectrometry for the determination of calcium and magnesium; the laser is developed; Feichtmeier invents the mechanical pipetor (Auto Dilator).

**1961** Becton Dickinson Co. introduces disposable hypodermic syringe and needle.

**1962** Siegelman develops a method for glutamic dehydrogenase; IBM introduces disk storage for computers; International Society for Clinical Laboratory Technology is founded.

**1965** Scanning electron microscope is developed; the U.S. enacts Medicare and Medicaid (Titles 18 and 19 of the Social Security Amendments).

**1966** Medicare/Medicaid officially goes into effect.

**1967** G.I. Abelev shows that alpha-fetoprotein is elevated in serum of patients with testicular teratocarcinoma; MetPath Laboratories is founded; U.S. enacts the Clinical Laboratory Improvement Act (CLIA ’67).

**1968** The first random-access analyzer is introduced by DuPont (the ACA); the 1% Medicare allowance for unidentified costs is reduced to zero; Canada enacts the Federal Medical Care Act, creating a single-payer national health program.

Source: CLMA and Garrison. Portions of this time line are reprinted with permission from CLMA.

cooperation between the practitioner and the clinical pathologist.” By 1928, when the ASCP established its Board of Registry (BOR), 80% of the initial group of 350 applicants for ASCP medical technologist (MT) certification were women. The code of ethics for technicians and technologists was and continues to be that these professionals agree to work under the supervision of a physician, refrain from making written or oral diagnoses, and refrain from advising physicians on treatment options without the supervision of a physician or pathologist.

Meanwhile, other groups of nonphysician clinical laboratory scientists were striving for professional recognition of their own. The American Society of Medical Technologists (ASMT), now known as the American Society for Clinical Laboratory Science, was originally formed as a subgroup of the ASCP. Through the ASCP, pathologists prevented nonphysician MTs from becoming an autonomous profession. ASMT established committees to serve the needs of its members and implemented a process to certify MTs who had acquired specialized laboratory expertise. Before 1940, the ASCP’s BOR was restricted to pathologists who were ASCP members, but by 1949, the ASCP had amended its bylaws to allow three ASMT members on the Board with full voting rights. Ten years later, a fourth ASMT member was added, but ASCP maintained control with six of its own members on the Board. The ASMT continued its pursuit of independence with its own mission and objectives, and in 1947 held its first annual meeting independent of the ASCP. The ASMT changed its own bylaws to permit individuals with master’s and doctoral degrees to join the ASMT without ASCP BOR certification. Between the end of World War II and 1962, the ASMT began to reassess its views on personal licensure and regarded it as a positive step toward professional recognition. In the late 1950s, MTs sought governmental recognition of their educational qualifications through personnel licensure laws and position reclassification in the Civil Service and armed forces.

**Editor’s note:**

By the end of the first half of the 20th century, laboratory medicine had earned professional legitimacy through contributions to diagnosing disease and discovering drugs to treat formerly life-threatening illnesses. Professional societies emerged to develop professional identity and to provide educational support. In part 3 of this series, we will cover professional associations by reviewing the establishment of the American Medical Technologists and look at the history of U.S. national healthcare coverage, Medicare and Medicaid, and the myriad of regulations faced by modern laboratories.

**Bibliography**