A Century of Growth: A Century of Progress

Chemistry in the service of medical practice was relegated to the periphery of medical science until well into the nineteenth century. Biochemistry took shape near the close of the nineteenth century, when emphasis on living systems shifted from physiology to chemistry. The subsequent emergence of clinical chemistry in the opening years of the twentieth century, as the medical application of analytical biochemistry, was inevitable. During the latter part of the eighteenth and the early part of the nineteenth century, the study of chemistry in Great Britain at the university or hospital medical school was considered a branch of medicine, and the professor of medicine frequently held both chairs. Chemistry was becoming increasingly important in the education of the medical profession. At Guy’s Hospital Medical School in London, chemistry had been the first subject to be given up to a specialist by the clinicians. The crucial separation of chemistry from medicine—in spirit and doctrine—occurred when chemistry moved from the medical faculty to the philosophical faculty as an independent discipline (1).

The discoveries of new substances in the healthy and diseased body and the development of organic and physiological chemistry spawned a wave of interest in clinical chemistry in the late 1830s and 1840s. There followed a systematic search for pathologic changes in the chemical composition of body fluids to guide medical diagnosis, follow the course of the disease, and control therapy. A search for chemical explanations for biological phenomena became a major preoccupation of leading scientists during the nineteenth century (1).

Noel G. Coley (2) in this issue describes the development of clinical chemistry in Britain and work on the chemical composition of urine, urinary deposits, and calculi by the leading medical investigators there in the last half of the eighteenth century and the first half of the nineteenth century. During the mid-nineteenth century, tests were developed for many constituents in urine, and volumetric methods replaced the laborious gravimetric techniques. These and other tests and associated methods and techniques became the tools of research in the development of biochemistry. However, the many isolated pieces of chemical information in health and disease did not fit together and failed to produce any significant benefits for the clinician. This first phase of clinical chemistry as an independent science was brief.

In the training of professional chemists, England trailed both Germany and France. The amateur tradition of the Royal Society and the emphasis in Oxford and Cambridge on liberal, rather than professional, education were factors in the slow growth of British chemistry during the first half of the nineteenth century. Although chemistry was well established at British universities by the end of the century, it was mainly the microscope and bacteriologic examinations, not chemistry, that led to the setting up of clinical laboratories in England, beginning about 1880 (1).

Except for private laboratories in the homes of some doctors, there were no clinical laboratories anywhere in England, not even in the teaching hospitals of London, and few of the largest hospitals provided any facilities for clinical pathology. Despite individual achievements, England lagged behind the Continent in the laboratory investigation of disease. England trailed because all of the great teaching hospitals in the country were established as charities for the relief of the sick poor, and it was considered inappropriate to spend this money on laboratories or on research workers. Furthermore, the senior physicians in academic medicine were engaged in private practice, teaching, and clinical work in the wards—a professional routine not suited for purely scientific investigation. Not until the end of the century did the charity hospitals realize the service potential of research and clinical laboratories to the poor.

In Germany the academic profession enjoyed a favored status during a period of unprecedented economic growth during the middle of the nineteenth century. Latecomers to the industrial revolution, the Germans, more than their wealthier English and French competitors, had to rely on scientific methods for the improvement of technology. As a result, physics and chemistry found a more favorable environment for development under the patronage of the feudal German states than in the progressive and prosperous manufacturing centers in England and France (3).

The William Pepper Laboratory of the University of Pennsylvania, opened in December 1895, was the first laboratory of its kind in the United States equipped for both routine work and research. Although increasing numbers of physicians were relying on laboratory tests, these “diagnostic” procedures provided essentially qualitative (yes/no) results. Attempts to bring the practical application of methods developed in the clinical research laboratories to the bedside in the hospital were resisted by some authorities, who claimed that such laboratories were scientific luxuries because they required space, were expensive, and imposed on the busy schedules of the interns. Hospital laboratories, always a low priority, were assigned to small cramped quarters in the basement or the top floor of an annex not far from the autopsy room.

On the eve of World War I, blood chemistry in England was in a very elementary state and yielded little information of clinical value. Urine examinations showed no advance over the previous 50 years. Following the initial interest and activity in laboratory diagnosis and bedside teaching that accompanied the opening of clinical laboratories in the 1880s and 1890s, practitioners began to delegate the laboratory work to an auxiliary staff of technicians (3).

The ability of German universities to develop new disciplines was bound up with the system of German society, i.e., the uniform and high-quality secondary school system; the importance of education in the German
national identity; the firm hold of bureaucratic, paternalistic governments over university budgets and planning; and the structured character of German society, with its weak entrepreneur middle class and strong university-trained elites.

Physiological chemistry in the United States developed along different lines because of distinctly American cultural values and national character. American colleges and medical schools evolved in a society without a national system of high schools and where higher education was not the goal of its diverse, democratic, business-oriented middle class. In America the federal government was constantly under challenge by states’ rights, politics, and dislike of the bureaucratic professional civil service. The distinctive features of American universities, e.g., graduate school, professional school, organization of university research, and professionalization of research, were created when German standards were introduced into a utilitarian and egalitarian cultural system and when German elitist practices were adapted to a democratic mass society (4).

The depth-balancing comparator, originally designed and manufactured in 1854 by Jules Duboscq, made its debut as a basic scientific tool for clinical chemistry in 1904, in Otto Folin’s classic paper on the measurement of creatinine and creatine in urine by the Jaffe reaction with alkaline picrate solution (5). Folin subsequently developed a whole system of urine (and later blood) analysis based primarily on colorimetry methods.

The pattern of the future growth and development of clinical chemistry took shape during the first decades of the nineteenth century. Until then the United States had played no role in the growth or development of chemical pathology. Afterward, the nation quickly achieved leadership. Three names dominated this period—Otto Folin, Stanley Rossiter Benedict, and Donald Dexter Van Slyke. Their systematic explorations on blood and urine set the pattern for clinical chemistry during the remainder of the century as they developed practical and clinically applicable methods of analysis. On the basis of a new approach to methodology—analysis of small volumes of biological fluids—they determined reference values and related variations to pathologic conditions. None of the three held medical degrees, but their research in clinical chemistry demonstrated that chemists could make great contributions to advances in medical diagnosis.

A valuable assist in the development of clinical chemistry came from the “Flexner Report”, a study of American medical schools, published in 1910 (6,7). The report exposed the disgraceful practices of the American and Canadian medical school systems and made specific recommendations for correcting the deficiencies. The report had a far-reaching effect on the practice of science in the laboratories of medical schools and hospitals and on the research and teaching of biochemistry. Flexner made specific references to “clinical chemist” and “clinical chemistry”. Concerning university hospital laboratories, he wrote: “...experimental pathology and physiology have already won recognition; the next step in progress seems to lie in the field of clinical chemistry, thus far quite undeveloped in America”. His emphasis on the use of laboratory sciences in the training of medical students contributed to the favorable environment for the rapid growth of clinical chemistry.

In the 1930s, academic biochemistry and applied clinical biochemistry began to separate. The new American biochemists opted for a biochemistry of general principles relevant to all of the biological sciences that was situated in the graduate division, not the medical school. As departments of biochemistry began to abandon its analytical interests, clinical chemistry was left to fend for itself as an applied science adapted to the needs of hospital diagnostic laboratories and distinct from academic biochemistry. Progress in clinical chemistry in the United States during the first few decades of the twentieth century was the result of a close working partnership between biochemistry and clinical medicine. Now clinical chemistry was on its own. Medical school biochemists gravitated to newer, more academically prestigious lines of research. In the early years of medical reform, biochemistry in America had been nurtured by its service role in clinical chemistry, but by 1940 it could survive on its own. Development of clinical methods was abandoned to the clinical chemists, who found themselves no longer at the center of the biochemical sphere (8). The golden age of clinical chemistry, however, still lay ahead. But that is another story (9).

References

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