Carl Ludwig and the Leipzig Physiological Institute: ‘a factory of new knowledge’

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ONE OF THE MOST productive biomedical research departments in the history of mankind was Carl Ludwig’s physiologic institute at the University of Leipzig during the final third of the 19th century.1 The pioneering pharmacologist T. Lauder Brunton claimed nearly a century ago, “More than to anyone else since the time of Harvey, do we owe our present knowledge of the circulation to Carl Ludwig.”2 Although he was an outstanding physiologist who made several significant discoveries, Ludwig’s most important contribution was his role in training two generations of physiologists in his Leipzig institute.

It was from the German university system that much of the current structure and philosophy of American academic medicine evolved over the past century. In 1892, the eminent British biologist and educational reformer Thomas H. Huxley declared that the “modern” university is a “a factory of new knowledge: its professors have to be at the top of the wave of progress. Research and criticism must be the breath of their nostrils; laboratory work the main business of the scientific student; books his main helpers.”3 Carl Ludwig’s institute was the embodiment of Huxley’s ideal for higher education.

During the second half of the 19th century, unprecedented advances in knowledge about the structure and function of living organisms were made in the laboratories of the German universities. Government sponsorship of academic posts and research programs provided opportunities for individuals to devote themselves to careers in biomedical research and teaching. Although the emphasis in the physiology laboratories of the German universities was on pure research, many discoveries had important implications for clinical medicine. Scientifically oriented physicians in the United States were impressed with the flood of new knowledge coming from the German clinics and laboratories and began to encourage reforms in American medical education. Their goal was to make American medicine more scientific. By the early 20th century, most leading American medical schools had adopted two fundamental characteristics of the German universities: the full-time faculty system for their basic science teachers and the research ethic — the conviction that faculty members have an obligation to expand knowledge in their field.4, 5 Americans who studied with Ludwig were instrumental in this reform movement to reorganize American medical education and make medicine more scientific.

Why was Ludwig so influential and why was his physiologic institute so productive? William H. Welch, a pioneering American pathologist and medical educator, argued at the turn of the century that Ludwig’s institute “exerted the greatest and most fruitful influence” on the field of physiology because of “the general plan of its organization, its admirable equipment, the number and importance of the discoveries there made, its development of exact methods of experimentation, the personal character and genius of its director, and the number of experimenters trained from all parts of the civilized world.”6 Each of these aspects of Ludwig and his institute will be explored in this essay.

Carl Frederick Wilhelm Ludwig was born in the village of Witzenhausen in the electorate of Hesse, Germany, on December 29, 1816. Ludwig’s father was a former officer in the Napoleonic wars who held a municipal position in the city of Hanau, where young Ludwig attended preparatory school. Carl Ludwig was a political activist and a rather argumentative pupil; his studies at the Universities of Marburg, Erlangen, and Bamberg were marred by conflicts with institutional officials. Eventually, the spirited Ludwig received his

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doctorate, and in 1839 he was appointed prosector in anatomy under Franz Ludwig Fick at the University of Marburg. There, he came under the influence of the great chemist Robert Bunsen, whose devotion to research and talent for the invention of laboratory apparatus served to further stimulate Ludwig’s interest in experimental medicine. While working in Bunsen’s laboratory, young Ludwig met several pupils interested in the new experimental chemistry and physics. Ludwig received little encouragement from Marburg’s physiology professor, Hermann Nasse, however. He and Ludwig had a strained relationship and the physiology laboratory at Marburg was poorly equipped.

An event with great significance for Ludwig’s career and for the future of experimental physiology occurred in 1847. In that year Ludwig visited Berlin, where he met three students of Johannes Müller, the professor of anatomy and physiology at the University of Berlin. With François Magendie of France, Müller had redefined physiology as an experimental science and had contributed to the overthrow of the stifling “Naturphilosophie” that had characterized all aspects of German culture for several decades. With Müller’s pupils Emil Du Bois-Reymond, Hermann von Helmholtz, and Ernst von Brücke, Ludwig would extend this revolution in the philosophy of science. They recast physiology as an experimental science based on physics and chemistry rather than an empirical field preoccupied with speculation and untested theorizing. These four young scientists had a specific (and ambitious) goal. According to Ludwig, they “imagined that we should constitute physiology on a chemico-physical foundation, and give it equal rank with physics.”

Ludwig’s scientific career began during a period of great political and social instability in Europe. Then, as now, science and medicine were affected by larger issues in society. The “Revolution of 1848” influenced all aspects of German culture, and Ludwig and his new friend Du Bois-Reymond shared their frustrations in frequent correspondence during this turbulent era. In the spring of 1848, the pioneering electrophysiologist informed Ludwig of events of the revolution and complained, “You can well imagine that there is little talk of science here now. . . . I am trying to [remain] as aloof from political participation as I can without seeming to lack principles. But one is nonetheless greatly distracted from sustained serious activity.” Several months later, Du Bois-Reymond protested, “All public funds are taken up to such an extent that there can be no thought of throwing money about for scientific purposes.”

Although Ludwig became involved in the political upheaval, he was able to continue his scientific work at Marburg. Ludwig became impatient, however, and sought a more promising institutional setting for his growing interest in physiology. In 1849 he accepted the chair of anatomy and physiology at the University of Zurich. The university constructed a modest laboratory for Ludwig and, with the help of an assistant, he inaugurated a program of experimentation and physiology teaching. Ludwig also continued to work on a textbook of physiology he had begun at Marburg, and in 1852 the first volume appeared. In the opinion of Ludwig’s long-time friend and colleague Wilhelm His, this new textbook “appeared like a meteor on the scientific horizon.” In this classic work, Ludwig challenged traditional scientific theories, suggested new concepts, and proposed what he believed were the best experimental approaches for expanding man’s knowledge of living organisms. Ludwig explicitly outlined his formulation of physiology as a science based on the principles of physics and chemistry.

While writing his physiology textbook, Ludwig explained to Du Bois-Reymond, “To begin with, I shall deal with the complex chemical atoms of which the human body is composed, at the same time disclosing everything referring to their chemical constitution, conversion products, and physical characteristics. This prepares the way for the explanation of many physiological processes.” It was this emphasis on the physical and chemical basis of physiology that set Ludwig and his intellectual colleagues Du Bois-Reymond, Brücke, and Helmholtz apart from other contemporary physiologists. Although the French physiologists François Magendie and Claude Bernard had pioneered the use of vivisection and made many important discoveries, Du Bois-Reymond objected to their tendency toward vitalism. Writing from Paris in 1850, he informed Ludwig, “The ignorance and limited view of even the best men [physiologists] here is incredible. . . . Your textbook will be a couple of generations ahead of the French conceptions.”

During the early stages of their scientific careers, Ludwig and Du Bois-Reymond struggled with conflicts that affect individuals in academic medicine today. Ludwig’s career moves were made to improve his salary and opportunities for research. While at Zurich, he expressed frustration about the intense teaching demands that limited his time for research. Although they both recognized the importance of using Ludwig’s textbook as the signal that a new physiology was evolving, Du Bois-Reymond observed that for someone used to pursuing original research, working on a textbook “must be demoralizing.”
Cultural nationalism and the political instability of the age resulted in the relative isolation of Germans like Ludwig from the Swiss professors and staff at the University of Zurich. Ludwig found this unpleasant and welcomed an opportunity to go to Austria in 1855, when he was appointed professor of anatomy and physiology at the Josephinum in Vienna, a newly organized academy for military physicians. Ludwig’s facilities at Vienna consisted of small chemical and physiologic laboratories, a lecture room, a mechanical room for the construction and repair of equipment, and a room for experimental animals. The laboratory was well supplied with physiologic apparatus, and Ludwig’s staff included a laboratory assistant, a mechanic, and an orderly.18

Specialization in science and medicine is not a new phenomenon. This trend began more than a century ago, and Ludwig was able to devote himself to physiology for this reason. During the middle of the 19th century, physiology gradually gained independence from its traditional sister discipline of anatomy in the European universities. A separate chair of physiology was established at the University of Leipzig in 1865, where Ernst Heinrich Weber had held the combined chair of anatomy and physiology for a quarter of a century. Weber continued to teach anatomy at Leipzig and served as a role model for Ludwig, who joined the Leipzig faculty as professor of physiology in 1865. Among Weber’s important contributions was a series of valuable studies on hemodynamics, a subject of great interest to Ludwig.19 With his brother Wilhelm, Ernst Weber demonstrated the importance of capillary resistance and blood volume on circulatory dynamics and the distribution of the blood in the vascular system. Adapting the methods of the British physicist Michael Faraday to physiology, the Webers constructed an electric generator to stimulate the tissues of living organisms. In the course of these experiments, they described the phenomenon of vagal inhibition and demonstrated that electrical stimulation of the vagus nerve caused the heartbeat to slow dramatically or even stop.20

One of Ludwig’s first responsibilities at Leipzig was to design a building devoted to teaching and research in physiology. And this was not to be a modest facility. Ludwig had an unprecedented opportunity to develop his institute because the government of Saxony, led by the scholarly King Johann, was determined, according to Wilhelm His, to raise the University of Leipzig “to new importance and splendor with all the means at their disposal.” The Leipzig anatomist recalled, “The physiological laboratory was planned as the first of a series of new constructions, the final object of which was to be a complete revolution of the entire system of scientific instruction.”12

Ludwig conceived of physiology as a discipline based on physics and chemistry rather than on comparative anatomy. Nevertheless, he had great respect for careful morphologic studies, and he emphasized the complementary role that physiologic and morphologic investigations played in elucidating the functions of living organisms. He designed his institute to reflect these interrelationships. The building was in the shape of the capital letter E, with wings devoted to histology and chemistry in addition to experimental physiology, where emphasis was placed on vivisection. Writing from Leipzig shortly after it was opened in 1869, the recent Harvard medical graduate Henry P. Bowditch characterized Ludwig’s institute as “universally acknowledged to be the most complete establishment of its kind in Europe.”21 Indeed, when it opened, the Leipzig Physiological Institute had no equal in the world.

In 1870, a writer in Nature explained that state-sponsored institutions had a significant advantage over private ones: “This contrast cannot be illustrated in a more striking manner than by comparing the palace which the Saxon government has built in Leipzig for instruction in physiology, with the one or two rooms which the University College, London, is able to devote to the same purpose.”22 At that time, University College, London, had the most extensive program in physiology of any British institution. A sense of competition among the German universities contributed to the movement to build large research institutes during the second half of the 19th century. At the same time, French scientists such as Claude Bernard were forced to endure hardships due to inadequate funding for space, equipment, and staff. In an 1896 article on scientific laboratories, William H. Welch remarked, “Bernard, that prince of experimenters, worked in a damp, small cellar, one of those wretched Parisian substitutes for a laboratory which he has called ‘the tombs of scientific investigators.’”23

In contrast to that in France, German higher education was decentralized and there was intense competition among the regional universities for highly talented faculty members and students. This stimulated local government support of higher education to an unprecedented degree. Because of the belief that scientific research would ultimately benefit mankind, funding for programs in the life and physical sciences was especially generous in Germany in this era.23 Extraordinary opportunities for laboratory work and
original research attracted scientifically oriented medical graduates to the German universities. Among Ludwig’s European pupils were several individuals who made major contributions to our understanding of the structure and function of the heart and cardiovascular system. They included Robert Tigerstedt, Hugo Kronecker, Luigi Luciani, Angelo Mosso, Willy Kühne, Karl Ewald Hering, Samuel von Basch, Julius Cohnheim, Adolf Fick, Otto Frank, Heinrich Quincke, and Werner Spalteholz. His British pupils included Walter Gaskell, T. Lauder Brunton, E. Ray Lankester, William Rutherford, William Stirling, Augustus D. Waller, and Edward A. Schäfer.

One might wonder how such an international group of pupils could work together effectively in the laboratory of the Leipzig institute. During the 1870s, Ludwig’s assistant Hugo Kronecker facilitated communication among the international group of workers in Ludwig’s laboratory. Kronecker, who had studied under Du Bois-Reymond, von Helmholtz, and Willy Kühne, spoke fluent French, Italian, and English, as well as German. The experience of a Scottish pupil sheds light on the atmosphere of the laboratory and the enthusiasm of Ludwig for foreign graduate students. Joseph Coats, a recent medical graduate of Glasgow University, arrived in Leipzig in 1869. He recalled his five months with Ludwig: “I turned up there one day, in the month of May, a raw young graduate, who had learnt some German and had read Virchow’s *Cellularpathologie*, but who could scarcely speak the language, and found it still more difficult to understand it. I had no [letter of] introduction, but... Ludwig received me most kindly, immediately sent for a young Scotsman [T. Lauder Brunton] who was then working in the laboratory. ... With my new friend as an interpreter, I was made welcome to the laboratory; and without any ceremony, without any credentials except that I was a graduate of Glasgow University, I was set down to do a piece of work which, I am glad to say, opened up my way in the paths of exact science.” In Scotland, a few months after his brief period of study with Ludwig, Coats wrote in his diary, “I received on Friday last 25 reprints of a paper which Professor Ludwig has written of my work in Leipzig on the action of the vagus in the frog’s heart. It is marvelously kind of Ludwig to write these things... and get them printed in the name of the men who are merely his instruments.”

Without question, Carl Ludwig’s scientific ability and personality were major factors in the success of the Leipzig Physiological Institute for the three decades that he headed it. American physiologist Warren Lombard recalled, “Why was Ludwig’s laboratory always full when the other German physiological laboratories...
had only one or two workers? The instant one entered it, he felt that it was a place where things worth doing were being done. Ludwig’s enthusiasm pervaded it, and it was an intense pleasure to work in the stimulating atmosphere. Ludg’s private office was in a room attached to the main physiologic laboratory and his door was rarely closed. Indeed, Ludwig’s pupils had to go through his office to reach the departmental library, which was open to anyone working in the institute.

Ludwig’s intellectual generosity and unselfishness in order to further the careers of his pupils is legendary. Virtually all of his pupils who wrote obituary notices or biographical sketches of Ludwig noted this unusual character trait that contributed to the spectacular success of his research program. Although Ludwig would usually outline the hypothesis, design the experiments to test the theory, assist in the preparation and performance of the experiments, collaborate in the interpretation of the results, and revise the final report, he would rarely append his name to the published paper that would result from this process. Lombard’s experience illustrates this point. The young American medical graduate gave Ludwig an English draft of a paper based on experiments he had performed under the master’s direction. Lombard recalled that Ludwig translated the paper into German, “practically rewriting it. I shall never forget my feeling of embarrassment, as I said to him that I felt that I had no right to let the paper appear under my name [alone], for I had been only his hands; that it was really his work and not mine. ‘It is all right,’ he said, ‘it has been your work.’ Then he added, ‘But if you never do anything else, it will be thought that you did not do this.’” Lombard remarked that Ludwig “had so many ideas that he could well afford to be generous; he loved his science and rejoiced in the scientific achievements of his pupils.”

Ludwig’s productivity, and that of the students who worked in his laboratory, was remarkable. Not only were the papers numerous, a very high percentage were significant contributions to medical and scientific knowledge. For half a century, Ludwig and his pupils maintained a level of productivity and quality that was the envy of the biomedical world. Ludwig believed in division of labor and used his knowledge of his science and his understanding of those who worked with him to assign them to tasks to which they were well suited. Ludwig’s daily routine has been carefully detailed by his pupils. Each morning he stopped at every student’s work table to discuss the status of their project, deal with any problems, and give encouragement or advice as needed. If necessary, Ludwig would schedule time to participate in the performance of an experiment to ensure its success. He held frequent conferences with his pupils to facilitate their work. At the end of the day, Ludwig carried experimental protocols, preliminary data, and tracings to his apartment on the second floor of the institute, where he reviewed the accomplishments of his associates and pupils.

The comments of Max von Frey, one of Ludwig’s most successful pupils, provide insight into the atmosphere of the laboratory. Although Frey acknowledged that Ludwig’s intense involvement in all aspects of the work in his laboratory might lead to the conclusion that it had an atmosphere of military discipline, he claimed this was not the case. Nevertheless, Frey acknowledged that this comparison was of value in understanding the extraordinary success of Ludwig and his pupils in the institute: “Among other qualities, Ludwig possessed those which could be described as marked military virtues: boldness of design, tenacious perseverance in execution, presence of mind and high personal courage, an unusual talent for organization bound up with a knowledge of men, which knew how to put every force in its right place, strict discipline, frankness and heartiness in personal relations, indefatigableness in work, together with exemplary orderliness and punctuality.” Ludwig’s pupils shared a sense of devotion and loyalty to their master, and their common experience in his laboratory led to the formation of a special bond between his international pupils. Two “Festschriften” published in 1874 and 1886 contained dozens of papers by Ludwig’s former pupils and attest to their devotion to him and their success as biomedical scientists.

Why was Ludwig so successful in attracting capable students and shaping them into skilled experimental physiologists? Ludwig had unparalleled resources for his enterprise. Nevertheless, his pupils attributed the success of the Leipzig Physiological Institute to the man more than any other thing. Lombard recalled that Ludwig’s “intense interest in the problems that he was studying was infectious; his enthusiasm imparted itself to his pupils, and aroused all of their ingenuity and their best powers of observations and thought.” A perfectionist who refused to acknowledge defeat, Ludwig would pursue a research theme for years if necessary to prove a point or elucidate a problem. Although he encouraged his pupils to work independently to solve their problems, Ludwig was always ready to assist them if necessary. Ludwig’s interest in his pupils was sincere and persisted long after they left his laboratory to assume positions in medical schools and universities throughout the world.
Carl Ludwig and his pupils made numerous major contributions to our understanding of the structure and function of the living organism. Although he is correctly viewed as a physiologist, Ludwig used a wide variety of techniques and approaches in his investigations. His thorough training in anatomy provided him with an appreciation of the important information that can be derived from purely morphologic studies. Comparative anatomists and morphologists had long argued that function could be deduced from structure. Ludwig acknowledged that an organ’s form bore some relationship to its function, but he believed that the actual function was determined by physical principles that could only be discovered by experimentation. Ludwig’s 1842 dissertation in which he developed the filtration theory of urine formation reflected his early interest in applying physical principles to the functions of living organisms. With the publication of this thesis, Ludwig was widely acknowledged as an expert on renal physiology. These early experiments on urine formation were followed by a long series of studies on the diffusion of fluids through membranes.

Ludwig’s interest in the structure and function of the heart and circulatory system can be traced to 1843, when he was a junior faculty member at the University of Marburg. Throughout his long career, circulatory physiology remained a dominant area of research for Ludwig and his pupils. A year before Ludwig died, Brunton claimed, “It is to Ludwig and his scholars... that we owe the greater part of our knowledge of the mechanism of the circulation and of the varying distribution of the blood in various parts of the body.” Ludwig’s interest in the circulatory system led him to develop an instrument capable of accurately recording hemodynamic variables. In 1846 he invented the kymograph, an instrument that combined a stylus connected to a mercury manometer with a rotating smoke drum in order to graphically record physiologic events over time. In constructing this fundamental piece of laboratory apparatus, Ludwig adapted principles and designs previously developed to graphically record physical and vital phenomena by Stephen Hales, Thomas Young, Jean L. M. Poiseuille, Claude Pouillet, Charles Wheatstone, and M. G. Wertheim, among others.  

Several physiologic variables such as blood pressure, pulse rate, and respiratory frequency could be recorded over time with Ludwig’s kymograph. The objectivity provided by such recordings allowed Ludwig and his colleagues to identify previously unrecognized physiologic relationships. For example, by simultaneously recording the pulse wave and respiratory pattern, Ludwig first described sinus arrhythmia in 1847. He recognized the significance of his invention and later presented his Italian pupil Angelo Mosso with one of the first tracings made from the original kymograph. On the back of the tracing Ludwig wrote, “I give to my friend Mosso for his collection, this first stammering of the heart and of the chest.” One of Ludwig’s contemporaries, Salomon Stricker, a pioneering experimental pathologist, claimed that Ludwig’s invention of the kymograph was as important for biological research as was the development of an alphabet for human culture. The hemodynamic monitoring equipment currently used clinically as well as in research can be traced to Ludwig’s kymograph.

Ludwig’s brilliant work in cardiovascular physiology was the result of a sustained effort aimed at understanding the physical principles of the circulation. These studies were facilitated by the delicate instruments of precision he devised for this purpose. With his pupil Adolf Beutner, Ludwig used his kymograph and other apparatus to measure for the first time the pulmonary artery pressure by inserting a cannula into the left pulmonary artery. With Johannes von Kries, Ludwig first measured capillary pressure. Ludwig and his pupil Johann von Dogiel measured regional blood flow for the first time in 1867 using a “stromuhr,” or flowmeter, developed for this purpose by Ludwig. Adolph Fick, one of Ludwig’s earliest pupils, extended the principles of measuring blood flow pioneered by Ludwig to elaborate his theory of measuring cardiac output. The principles of graphic registration pioneered in the physiologic laboratory by Ludwig were soon applied to man when Alfred Volkmann in Germany and Étienne Jules Marey in France developed and refined techniques to record the pulse and apical impulse in the human.

Cardiovascular innervation was an area of special interest to Ludwig. He extended the studies of the Webers on the influence of the nervous system on the heart rate and, with his pupil Oswald Schmiedeberg, discovered the “accelerator nerve” of the heart. With his American pupil, Henry Bowditch, Ludwig discovered two fundamental laws of cardiac physiology: the “all-or-none” law of cardiac muscle and the “treppé” or staircase phenomenon. Shortly after Bernard demonstrated the existence of vasodilator and vasoconstrictor nerves, Ludwig undertook a series of experiments that demonstrated the importance of vascular tone in maintaining blood pressure.

With his Russian pupil, Elie de Cyon, Ludwig discovered the vasomotor reflexes in 1866. Their discovery of the “depressor nerve” represented the first pro-
posal that there was reflex regulation of the cardiovascular system through afferent nerve endings in the heart. Although later studies proved that the afferent nerves were actually located in the great arteries, the concept of autoregulation of the circulation can be traced to Ludwig’s observations. Five years later, Ludwig’s Russian pupil Philipp Owsjannikow reported that he and Ludwig had located a “vasomotor center” in the medulla. Ludwig was the first to describe ganglion cells in the interatrial septum. The physiology of the peripheral circulation also interested Ludwig. With his American pupil Franklin P. Mall, he showed in 1890 that the portal vein also responds to nervous control. In the words of a recent historian of the peripheral circulation, Ludwig’s studies “proved fundamental to our modern ideas of a tonic vasoconstrictor activity exerted by sympathetic fibers influencing nearly all the regional peripheral circuits.”32

Among Ludwig’s most important contributions were his discoveries in the area of respiratory physiology. While still at Vienna, Ludwig and his Russian pupil Ivan Sechenov invented a mercury blood pump that allowed them to separate the respiratory gasses in blood in vivo. In an extensive series of experiments, Ludwig and his pupils elucidated the physiology of tissue oxygenation and respiratory gas exchange. In the course of this work Ludwig first measured the oxygen tension in blood. His technique made it possible to measure the saturation of oxygen and carbon dioxide in the blood stream. The results of these experiments led Ludwig to conclude that the oxygen uptake of an organ was related to the work performed by that organ.

To evaluate various bodily functions, Ludwig developed or refined techniques to perfuse isolated organs. This made it possible to study the function of denervated organs that were perfused with blood or solutions containing various compounds. One particularly useful experimental model was an isolated frog heart preparation that could be kept beating for days by perfusing it with defibrinated blood. Many of Ludwig’s important discoveries in cardiac physiology were made with the isolated frog heart preparation. Eventually, other workers, most notably H. Newell Martin of the Johns Hopkins University, extended Ludwig’s technique and developed an isolated mammalian heart preparation that was used by Ernest Starling and others to elucidate fundamental principles of myocardial function.33

Despite his focus on physiology, Ludwig also made important contributions to anatomy. When it was necessary or desirable to have a better understanding of the morphologic aspects of a problem he was studying, Ludwig would not hesitate to turn to the microscope or to the dissecting room to explore the structure of an organ. Among his important contributions to anatomy were studies of the structure of the myocardium, the kidney, and the vasculature of the eye and inner ear. In the course of investigations to evaluate the vascular supply of various organs, Ludwig refined older techniques of injecting the vascular and lymphatic systems with substances that made it easier to study their minute anatomy. This skillful correlation of anatomy and physiology greatly facilitated Ludwig’s research and led him to discover many new facts regarding the function of various organs.

Reflecting the physicochemical philosophy he had articulated in his textbook, Ludwig had great respect for chemistry, and his institute staff included a chemist who could aid in the design and performance of chemical investigations. With his pupils, Ludwig made significant observations on the absorption and metabolism of sugars, fats, and proteins. Several important studies in pharmacology and physiologic chemistry were carried out under his supervision. Among his pupils were John J. Abel, a pioneering pharmacologist, and Willy Kühne, a leading physiologic chemist. Thus Ludwig’s physiologic institute was not narrow in focus: it was a dynamic association in which different scientific disciplines were represented and a wide variety of approaches used to advance man’s understanding of the functions of living organisms.

One reason that Ludwig’s institute became recognized as a leading center for biomedical research was the steady stream of publications that appeared from his laboratory. Beginning in 1866, Ludwig’s publications appeared in his own journal, Arbeiten aus der physiologischen Anstalt zu Leipzig. This periodical was issued for 11 years and included dozens of classic papers based on research performed in Ludwig’s institute. When Du Bois-Reymond assumed the editorship of the prestigious Archiv für Anatomie, Physiologie und wissenschaftlichen Medizin, Ludwig published the papers from his laboratory in that journal and the institute’s journal ceased publication.

Many factors contributed to the success of Carl Ludwig and his physiologic institute in Leipzig. Although Ludwig’s innate ability and intelligence were major factors, other individual, institutional, and larger social circumstances also contributed to the unprecedented productivity and prosperity of his institute at the University of Leipzig. Contemporary observers from other countries offered their opinions about Ludwig’s success a century ago. Americans were envious of the
financial support for salaries and apparatus that Germany’s basic scientists received. In 1879 Horatio C. Wood, Jr., a pioneering American pharmacologist, informed Army surgeon and educational reformer John Shaw Billings, “Ludwig is certainly a most skilled physiologist — I have never seen anything like his apparatus. But no one has impressed me as being far superior to our best American men in natural gifts.” Wood concluded that the extraordinary number of important discoveries made in the Leipzig laboratory were “chiefly the result of the system.” A writer in the American agreed, and claimed in 1881 that in the small university city of Leipzig more research in the biomedical sciences was performed in a year than was undertaken in the entire United States in half a decade. And this, he argued, was not because of the superior intellect of the Germans, “but because there is at present no encouragement to the medical scientist in this country; indeed, because a medical scientific career is practically impossible to any one who is not willing to exist as a pauper or has not been born to wealth.”

Some Americans did more than simply admire the scientific achievements of Ludwig and his pupils. They sought to reform American medical education so that research and advanced scientific training were encouraged in some medical schools in the United States. Nowhere was this effort more successful than at the Johns Hopkins School of Medicine, which opened in 1893. It is no coincidence that of the four original basic science professors, three had been pupils of Ludwig. William H. Welch in pathology, Franklin P. Mall in anatomy, and John J. Abel in pharmacology had great admiration for Ludwig and firmly believed in the system that existed in the German universities that provided salaries for full-time faculty positions and that generously supported research. Other American pupils of Ludwig encouraged reforms at the Harvard Medical School and the University of Michigan as well.

Welch told members of the Harvard Medical School Association in 1892, “It would do much to advance medical education and to encourage original research in medicine in this country, if the way were more freely open for academic careers in the sense in which it is in the German universities; that is, if young men who do good scientific work, who publish valuable results of original investigation, and who acquire reputation among those who are competent to judge them, could look forward with some reasonable assurance to securing positions in our leading medical schools. The incentive of this reward acts as a powerful stimulus to original investigation in Germany.”

Around the turn of the century, several of Ludwig’s American pupils worked to form a coalition of basic medical scientists, scientifically oriented practitioners, medical editors, university presidents, and influential laymen. In the American Medical Association’s council on medical education and the Carnegie Foundation for the Advancement of Teaching, the reformers gained powerful allies in their fight to introduce the critical elements of the German system into American medical schools. Decades of rhetoric were transformed into reality when the reforms advocated by Ludwig’s American pupils and their supporters were made possible at several leading medical schools through unprecedented grants from the General Education Board of the Rockefeller Foundation. Now, there were medical schools in the United States where full-time careers in biomedical science were possible and where research was liberally supported. As the scientific reformers had long claimed, the financial support of biomedical research in America resulted in a dramatic increase in scientific discoveries. The model developed in Germany during the second half of the 19th century and perfected in Ludwig’s institute at Leipzig had been successfully transferred to America’s elite medical schools.

As illustrated in this review of the life of Carl Ludwig and the impact of his physiologic institute in Leipzig, successful programs of research and advanced scientific training depend on a special set of circumstances. Factors at the individual, institutional, national, and international level contribute to the direction a scientific program may take. During the closing decades of the 19th century, favorable circumstances at several levels led to the development of a remarkably productive program of biomedical research at the University of Leipzig. Individuals concerned with the current state of, and future prospects for, biomedical research in America would do well to consider the factors that contributed to Ludwig’s success and that of his pupils. To him we owe much of the structure and philosophy of modern academic medicine as well as many important scientific discoveries that ultimately led to significant advances in clinical medicine.

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