The French connection

In the 19th century, Claude Bernard put physiology and medicinal chemistry on the road to experimental science.

BY RICHARD A. PIZZI

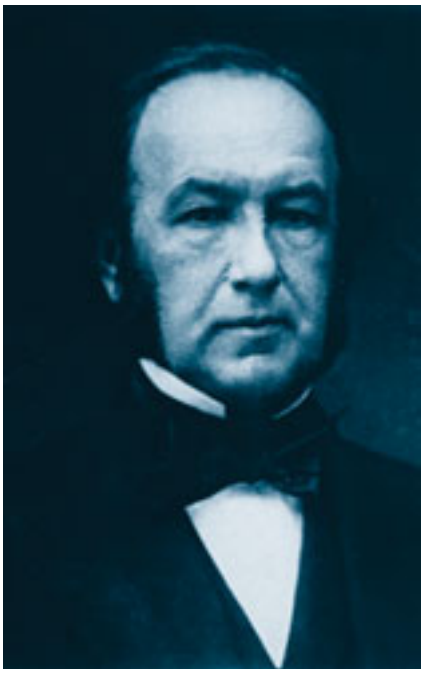
Medical research in mid-19th century Europe was centered in Germany. In contrast to the relatively weak state of laboratory-based research in Britain and France, experimental science flourished in German university laboratories. Things would improve for Britain as the 20th century approached, but in the increasingly important field of physiology, it was France, not Germany, that would produce one of the greatest medical scientists of the era. His name was Claude Bernard.

European traditions

Unlike Germany, France had few strongholds of laboratory medical research in the 19th century. Medical research in France was closely linked with the observation of hospital patients. Critics of this practice claimed that instead of the hospital, the laboratory was the ideal place for experimentation. Laboratory medicine dated back to the 17th century, but the new laboratory researchers of the 19th century created a unique culture of medical research in which microscopy, vivisection, and chemical investigation were used in a controlled environment conducive to experimentation.

New research traditions emerged from the European laboratories of the mid-19th century. Physiology, histology, cytology, pharmacology, and other fields grew to maturity on German university campuses. French medicine did not take to laboratory research as quickly. The French national universities emphasized teaching and accreditation of doctors and did not incorporate German ideas readily. Medicine in France was bureaucratic and was centralized in Paris. The long-standing French tradition of hospital-based observation led to an almost uniform rejection of the new university-centered laboratories.

Yet there were brilliant French physiological researchers in those years. François Magendie, a surgeon and anatomist, was professor at the Collège de France and was somewhat notorious for his willingness to perform vivisections. Yet even more famous would be his protégé, the physiologist Claude Bernard.



Claude Bernard (1813–1878).

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The theater's loss

Born on July 12, 1813, in Saint-Julien, Claude Bernard's earliest interests were literature and drama, not science. After high school, he worked as a pharmacist's assistant in a suburb of Lyon but intended to become a playwright. In fact, one of his plays was staged in Lyon when he was in his early 20s, and he moved to Paris in the mid-1830s with the hope of making a living as a dramatist.

In what turned out to be a fortuitous moment for medical science, a Parisian literary critic read one of Bernard's completed plays and convinced the young man that his future was not in the theater. The critic encouraged Bernard to take up a profession in order to make a living, and in 1835, he enrolled in the University of Paris to study medicine.

Unlike many great scientists, Bernard was not a particularly good student in medical school. He had difficulty completing his exams for an internship, finishing 26th out of a total of 29 students. After the exams, he took a post as assistant physician at Hotel Dieu, where he worked under the direction of François Magendie. Although Magendie was known primarily as a researcher and teacher at the Collège de France, he also worked as a physician at Hotel Dieu, where he supervised the young Bernard. Impressed by Bernard's skill at dissection, Magendie invited him to serve as his research assistant at the Collège de France.

Ironically, had Magendie first encountered Bernard in the classroom, he might not have been impressed, for it was Bernard's practical skills that drew his attention. While working with Magendie, Bernard discovered his vocation. He assisted in experiments on the "recurrent sensitivity" of spinal nerves and the physiology of digestion. His first publication dealt with a branch of the facial nerve, the chorda tympani, and his medical dissertation focused on the function of gastric juice in nutrition. Both topics anticipated Bernard's later career, much of which dealt with neurology and metabolism.

Magendie taught Bernard to use animal vivisection as a primary means of medical research, a technique that offended many physicians at the time but would become a cornerstone of Bernard's research methodology. Both Magendie and Bernard thought that vivisection was essential to advance experimental medicine, and Bernard would later elucidate its importance in his theoretical writings.

While working in Magendie's laboratory, Bernard's academic deficiencies haunted him once again. He failed the qualifying examination that would have allowed him to teach in the medical school, and he

resigned his position as Magendie's research assistant. At the point of financial ruin, Bernard agreed to a "marriage of convenience", arranged by a friend, with the daughter of a Parisian doctor. His wedding to Marie-Françoise Martin brought him a 60,000 franc dowry, enough to fund his research career. The marriage would prove to be unhappy, however, and the couple separated years later.

Physiology's gain

With the financial resources now available to live in relative comfort, Bernard embarked on a tremendously successful period of research and discovery. He continued his digestive research and began a collaborative examination of the South American poison curare. Bernard's studies of curare led him to reject long-standing ideas that all drugs have a generalized bodily influence. Instead, he claimed that certain drugs act at localized sites. For example, curare causes paralysis by preventing a nerve impulse from making a muscle contract at a specific location. These precise locations were later determined for other drugs, and the concept of drug "receptors" became crucial to the development of pharmacology.

In 1847, Bernard returned to the Collège de France, this time as Magendie's academic deputy, not his lowly assistant. Many of Bernard's major discoveries were made in his first decade at the College.

Some of his main achievements began with the use of rabbits as a model system. Bernard learned through autopsies of the animals that secretions of the pancreas break down fat molecules into fatty acids and glycerin, and that the principal processes of digestion take place in the small intestine rather than the stomach. This work on the pancreas led to his important discovery of the liver's glycogenic function.

Glucose gleanings

Bernard discovered that if animals were fed a sugar diet, glucose could be recovered from the hepatic veins carrying blood from the liver. Thus, sugar passed as expected through the liver. But even when the animals were fed sugarless diets, blood in the hepatic veins still contained high concentrations of glucose. He also discovered glycogen, a white starchy substance, in the liver. It was apparent that the liver was producing sugar independently. Other experiments also uncovered the presence of sugar in amniotic and cerebrospinal fluid. Bernard concluded that the body not only broke down complex molecules in digestion but made its own chemicals in normal functioning. He asserted that the body created sugar as a storage reserve of carbohydrates.

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The sugar levels produced in this way were not pathological, as they would be in a diabetic. Transitory increases in blood sugar were thus not indicative of a disease state but were part of normal metabolism—as long as the sugar level was regulated. Bernard called the glycogenic process "internal secretion", a term which would become fundamental to endocrinology.

In 1848, Bernard became the first vice president of the French Biological Society, and a year later he was named a chevalier of the Legion of Honor. He was moving quickly from obscurity to the highest levels of French science.

The next great achievement of Bernard's increasingly prominent physiological career was his explanation of the regulation of the blood supply by the vasomotor nerves. He discovered that the vasomotor nerves control the dilation and constriction of blood vessels in response to environmental temperature changes. For example, in cold weather the blood vessels of the skin constrict to conserve heat, and in hot weather they expand to dissipate excess heat.

The discovery of this control mechanism, combined with his knowledge of the glycogenic function of the liver, led Bernard to theorize about how an organism maintains its "internal environment" amid changing external conditions. "The stability of the internal environment is the prime requirement for free, independent existence," Bernard wrote. The regulatory measures and control systems that Bernard described were later termed "homeostasis", a concept critical to modern physiology and one taught at the beginning of university courses in the subject.

From art to science

As important as Bernard's discovery of homeostatic processes, however, was his advocacy of experimental scientific medicine. In 1865, he published his premier theoretical work, *An Introduction to the Study of Experimental Medicine*. In it, Bernard claimed that progress in medicine was possible only if medical research was founded on experimental physiology. He asserted that the medical researcher needs a guiding hypothesis that is put to the test in the laboratory and either confirmed or refuted by the results.

As he had throughout his career, Bernard argued that hospital medicine was limited because it was essentially a passive, observational science. Medical advancement depended on active experimentation in controlled environments. Pathology without physiology was helpless, he said. He also rejected the ancient notion that a "vital force" was necessary to explain life, and instead put his faith in the principles of scientific determinism. Finally, he reasserted the importance of vivisection for physiological research.

A senior professor at the Sorbonne and a member of the French Academy, Claude Bernard spent less time in the laboratory as his health declined in later years. He was named an imperial senator for life and was showered with honors unusual for a man of science. He died in February 1878 and was honored with a national funeral, the first ever granted to a scientist in France.

Further reading

Porter, R. *The Greatest Benefit to Mankind: A Medical History of Humanity*; W. W. Norton: New York, 1997.

Serafini, A. *The Epic History of Biology;* Plenum Press: New York, 1993.

The Claude Bernard Museum; www.fond-merieux.org/eng/musee.

Richard A. Pizzi is a freelance writer with an M.A. in history, currently working on a Ph.D. at Indiana University. Send your comments or questions about this article to mdd@acs.org or to the Editorial Office address on page 3. ■