CLAUDE BERNARD, 1813-1878

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A PIONEER IN THE STUDY OF CARBOHYDRATE METABOLISM

The old farmhouse where Claude Bernard first saw the light of day in 1813 stands on the brow of the hill overlooking the little village of St. Julien, some twenty kilometers from the busy industrial city of Lyons, France. The house today is surrounded by row upon row of grapevines, as it was at the time of his birth, but there has been affixed to it a plaque showing that it is now a national shrine in which are preserved the relics of the country boy who became the most illustrious physiologist that France, if not the world, has produced.

After attending nearby schools, Bernard was apprenticed in his late teens to an apothecary in Lyons; an occupation which brought him into contact with one aspect of medical science, the compounding of drugs. However, attending the theatre proved a more enjoyable occupation, so, caught up in the rising tide of the romantic movement, he tried his own hand at writing a play. The local success of this first effort spurred him on to write a second, which he thought was so good that it should bring him recognition in the capital. Once in Paris, however, his literary hopes were dashed and he was persuaded to enter medicine; a field not too unrelated to his previous training. Toward the end of his medical course, his skill at dissection attracted the notice of François Magendie, the pioneer exponent of experimental physiology, and, being taken on as this professor's laboratory assistant at the Collège de France, in 1841 his life's course was fixed.

Bernard never practiced medicine but devoted his whole time and energy to physiological investigations. Although he was employed in Magendie's laboratory, for his own original investigations he had to maintain and operate on his animals for several years in various out of the way corners in the maze of the Latin Quarter. His skill in dissection influenced these experiments, and certain of his earliest published papers, although directed toward the general question of digestion and the transformation of the products of digestion into the substance of the living body, actually dealt with the anatomical relations of the tiny chorda tympani nerve in the ear, and the spinal accessory nerve. He really got into his stride when he showed, in 1846, that the pancreas, in addition to secreting digestive agents which act on proteins and carbohydrates, also secretes a fat-splitting enzyme. It was in the course of these experiments that he attempted to depancreatize dogs, and produced in several animals symptoms which today would be recognized as indicative of the diabetic condition; namely, extreme emaciation in spite of a voracious appetite, and death by wasting away. Had he followed up this lead, it is not impossible that he might have anticipated the discovery of insulin by three quarters of a century.

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FUNCTIONS OF THE LIVER

His next discovery, however, did lay the foundations for our understanding of the physiological mechanisms which are disturbed in the diabetic condition, and most medical historians would say that Bernard's discovery of the glycogenic functions of the liver is the greatest of all his achievements.

The prevailing theory at that time was that only plants were capable of synthesizing materials; it was thought that animal metabolism consisted merely in breaking down substances originally supplied by plants. Bernard demonstrated that in the liver of a dog which had been fed exclusively on lean meat (and therefore on food from an animal source), he had discovered a starch-like substance, which although itself not a true sugar, could readily be transformed into glucose and appeared in the blood as such. To this compound he gave the name gycogen; that is, sugar-forming. He then found that in the normal animal, blood leaving the liver is richer in sugar than blood entering it. He argued that must mean that the liver could release its product directly into the blood stream ("internal secretion" as he termed it), in contrast to the well-known action of glands which release their products to the exterior through a duct. This idea was the origin of our present day endocrinology. Furthermore, he showed by his now famous piqûre experiment that the nervous system was involved in these reactions. This experiment consisted in wounding a small area in the floor of the fourth ventricle of the brain—even a pinprick would suffice—with the result that so great an amount of glucose was released into the blood stream that it appeared almost at once in the urine in considerable quantity. This condition, he described as "artificial diabetes."

CONSTANT EXPERIMENTATION

It must not be imagined that the story, told here in merest outline, of the discovery of these basic concepts of normal carbohydrate metabolism, a knowledge of which seems to us so necessary for an understanding of what may go wrong in the diseased state, was worked out in a short period of time. It took Bernard some fourteen years of constant experimentation before he arrived, in 1857, at the point of isolating the chemical compound in the liver which he had predicated long before. He read no foreign language and consequently did not know that a German investigator, Hensen, had anticipated him by nearly a year in reporting the successful isolation of glycogen. To this writer, this does not detract from the admiration due Claude Bernard for his steadiness of purpose, his gradual unfolding of one essential physiological fact after another until the essentials of an account of the glycogenic function of the liver were rounded out, and it only remained for future investigators to fill in the details. The completeness of this series of discoveries is unique in the history of physiology.

From 1843 to the end of his life (he died in 1878 at the age of 65) he retained an ardent interest in the subject of diabetes. He had succeeded Magendie as Professor of Medicine at the Collège de France in 1855, and in the very year before his death, Bernard published a series of lectures which he had delivered there entitled, "Lectures on diabetes and animal glycogenesis." In this volume of his late maturity, we find a clear statement of his attitude toward what in his most famous book, written twelve years earlier, he had called "experimental medicine," for he considered that so-called "morbid symptoms" are in reality "physiological phenomena, more or less exaggerated," and are therefore suitable material for experimentation. He shows the relation of sugar in the urine to sugar in the blood, traces the sugar back in the deposit of glycogen in the liver, and comments on the relation of different kinds of foods to the symptoms of diabetes. These lectures afford an excellent picture of the ideas about this disease current in the 1870's, and show, as well, Bernard's methods in attacking medical problems.

VASOMOTOR NERVES

His third great discovery was the action of vasomotor nerves. He was able to demonstrate that certain nerves when stimulated cause vasoconstriction; others, vasodilation. The caliber of our blood vessels is therefore under nervous control, and is not merely an expression of the amount of blood forced through them. This means that blood flow through a given part of the body is dependent on, and related to, functions in other parts, and is an illustration of his celebrated doctrine of the constancy of the "internal environment," that is, that state of dynamic equilibrium which is life itself. Although changes are constantly going on in the living body, these changes can proceed only so far before counteracting reactions set in; otherwise, death ensues.

A reflection of Bernard's early occupation as a pharmacist's apprentice may be seen early in his career as a physiologist, though it is much more probable that the immediate stimulus to his investigation of the action of certain drugs and poisons was the work which his master, Magendie, had done on strychnine quite early in the century. This drug, and samples of plants containing it, had been brought from Java to France by explorers, and Magendie was so fascinated by the violent death following its administration, that he began a long series of investigations to show how it was absorbed into the body, and its site of action. Bernard, in 1844, was presented with some South American arrows whose tips were coated with curare. To him, the astonishing feature about curare poisoning was the quietness with which the animals died, a striking contrast to the effects of Magendie's strychnine. Bernard was able to show that the curarized animal dies of asphyxiation; and because of the paralysis of all skeletal muscles, including those used in respiration, the death is a quiet one. His location of the site of the action of the drug is a classic example of the syllogistic reasoning followed by all experimenters when planning their experiments. He argued that the curare might attack the motor nerve; the muscle itself; or possibly the junction between nerve and muscle. By a simple, ingenious experiment he showed that in a curarized frog, motor nerves can still conduct and skeletal muscles still contract if stimulated directly, therefore the drug must exert its paralysing effect at the myoneural junction. No one would have guessed that a century after Bernard had satisfied his curiosity in solving this apparently academic question, his answer would prove to be of direct service to the clinician.

This brief summary of Bernard's contributions to physiology far from exhausts the list of his discoveries. It has been given to few experimenters to enrich their chosen science with so many important discoveries and fruitful ideas as he did. Although Bernard's work stopped three quarters of a century ago, a present day scientist, no matter what his field, can read with profit "The Introduction to Experimental Medicine." This is Bernard's own analysis of how his mind worked in making his discoveries, and won for him a seat among the Forty Immortals of the French Academy.

BOOK REVIEW

CLAUDE BERNARD AND THE EXPERIMENTAL METHOD IN MEDICINE, by J. M. D. Olmsted and E. Harris Olmsted, $4.00, Pp. 277, New York, Henry Schuman. 1952

Doctor and Mrs. Olmsted have collaborated in the production of this fascinating life story of the man they consider to be one of the founders of experimental medicine. It furnishes adequate evidence to justify the esteem and reverence of the authors in giving him this title.

"Why is the name of Claude Bernard associated with the experimental method as applied to medicine? The method is as old as science itself, and its application to medicine, although long delayed, was made through physiology two centuries before Bernard's time by William Harvey in England. In France, the experimental method was reinstated for medicine at the beginning of the nineteenth century by François Magendie, under whom Bernard was proud to have served his apprenticeship as a physiologist. Many of Bernard's contemporaries, especially in Germany, were using the experimental procedure with increasing success.

"In the first place, the sum of Bernard's achievements finally silenced skepticism about the power of experiment to draw from nature the secrets of the living organism. His work closed a period in the history of medicine. Considered singly, none of these discoveries was of the sort which transforms the whole scene overnight. Yet each brought to light some fundamental truth of organic function; and the whole of his accomplishment in the twenty years of his greatest activity, 1839 to 1859, did transform the scene and make him the foremost physiologist of his time.

"In the second place, after his most intensive period of work, Bernard paused to harvest his experience in another way. He composed a description of the experimental method as applied to physiology, and illustrated it by his own researches . . . ." This reference to his famous book: "Introduction to the Study of Experimental Medicine" gives an indication of its great influence, which has continued to recent times.

The article on Claude Bernard in this issue of DIABETES gives brief information regarding his life and points out specifically his achievements in relation to diabetes and associated physiological problems. The book gives interesting details concerning his early days as a French country boy and as a medical student in Paris; it describes his distinguished scientific career throughout his long adult life.

The authors are well qualified to write this book both from the standpoint of an understanding of physiology and interpretative biography. Doctor Olmsted was educated at Middlebury College and Harvard University and went to Oxford as a Rhodes scholar. He taught physiology at Harvard, Johns Hopkins, and the University of Toronto, and at present is Professor of Physiology at the University of California. Mrs. Olmsted holds degrees from Oxford University in England and the University of Toronto. She has been lecturer of classics at University College, University of Toronto. The book can be recommended not only to physicians and students of the biological sciences, but also to the general reader.