

AN INTRODUCTION
TO THE STUDY OF
EXPERIMENTAL
MEDICINE

CLAUDE BERNARD

NOTES FROM THE EDITORS

INTRODUCTION

From the immense body of literature that reflects the development of scientific thought in the western world, only a score or so volumes share the unique distinction of being recognized as landmarks by our two most widely respected modern bibliographic sources, England's *Printing and the Mind of Man*,¹ and the New York Grolier Club's *One Hundred Books Famous in Science*.² Claude Bernard's *An Introduction to the Study of Experimental Medicine* is of course one of these epochal works.

After its initial publication in 1865 came this assessment of the *Introduction* by no less a figure than Bernard's contemporary, Louis Pasteur, "Never has anything clearer, more complete, more profound been written about the true principles of the difficult art of experiment. The book is as yet little known because it stands at a level which is so far attainable by only a few."

The volume hardly remained little known for long. It immediately gained popularity throughout Europe, appearing in a number of French editions, and rapidly gained wide readership in the United States after the appearance of the first English translation of 1927, which we here reproduce in facsimile for our library edition.

Following upon his landmark contributions to physiology, including the role of the pancreas in digestion, the vasomotor innervation, the effect of curare on neuromuscular transmission, the glycogenic function of the liver; and his similarly influential theoretical formulations, particularly that of the *milieu intérieur*, or internal environment, the *Introduction* stands as the crowning literary achievement of a lifetime of inspired laboratory investigation and voluminous literary output. (Bernard's bibliography lists 221 separate journal articles and books!)

¹Carter and Muir, *Printing and the Mind of Man—The Impact of Print on Five Centuries of Western Civilization*: London, Cassell and Company, 1967.

²Harrison Horbitt, *One Hundred Books Famous in Science*: New York, The Grolier Club, 1964.

As Paul Bert remarks in his sketch of Bernard which is included in the English edition, the book "struck cultivated minds with admiration and astonishment. Here physiologists were happy to find, reduced to precise formulae, set in order with marvellous art, and lighted by examples which themselves were like so many intellectual experiments—here they were happy to find the rules of the experimental method, watching, seizing and, in spite of its struggles, mastering that organic Proteus of the deceitful metamorphoses."

In examining this first English edition of Bernard's magnum opus, we urge you not to overlook all of the appreciation by Bernard's favorite pupil and successor at the Sorbonne, Paul Bert, written two days after the death of the master, from which we have briefly quoted above; as well as the sensitive Introduction to the volume by Lawrence Henderson, the American physiologist who was instrumental in having the *Introduction* translated into English.

The illuminating remarks on Bernard by Professors Grande and Tosteson which appear in the accompanying "Notes from the Editors" are from an excellent modern retrospective on Bernard³ (which we regret to advise is now out of print), reprinted courtesy of its Publisher.

"It is the fate of medical books to age quickly, but there are exceptions. If in contemporary Paris we examine the booksellers' windows in the neighbourhood of the École de Médecine we shall find exposed for sale a work whose first edition was published in the year 1865. This is Claude Bernard's *Introduction à l'étude de la médecine expérimentale*. 'Never,' wrote Pasteur a year after it was issued, 'has anything clearer, more complete, more profound been written about the true principles of the difficult art of experiment. The book is as yet little known because it stands at a level which is so far attainable only by a few.' " (From Henry E. Siegerist, *The Great Doctors*, New York: W.W. Norton & Company, Inc., 1933).

³Claude Bernard and Experimental Medicine—Collected Papers from a Symposium Commemorating the Publication of An Introduction to the Study of Experimental Medicine, Cambridge: Schenkman Publishing Company, Inc., 1967.

INTRODUCTORY REMARKS AT THE 1965 CLAUDE BERNARD SYMPOSIUM⁴

By Francisco Grande, M.D.

Scientific knowledge is accumulating at such an increasing speed that the modern scientist is unable to keep abreast with the flow of information even in his narrow field of specialization. It is therefore understandable that today's research worker, being unable to follow the current developments, does not find the time to become acquainted with the work of his predecessors.

This is unfortunate, because science grows by the addition of new knowledge to that contributed by earlier workers. In the words of the famous physicist Rutherford, "Science proceeds step by step, each man depending on the work of his predecessors." Some knowledge of the evolution of science is indispensable for the scientist, and no good understanding of the nature of science is possible without an understanding of its historical development. The scientist to be successful must be a sort of Janus, looking at the same time to the future and to the past.

This characteristic of scientific knowledge has been described by many authors who have stressed the need for an awareness of the historical development of science. The medical historian P. Lain thus emphasizes this importance of historical knowledge: "Without historical education no truly original work is possible, nor is it possible to understand the present."

In a more pragmatic way, Santayana reminds us that "He who feels prepared to ignore history is doomed to repeat it." The frequency with which past discoveries are "rediscovered" is a good proof of the value his advice

⁴Reprinted from *Claude Bernard and Experimental Medicine—Collected Papers from a Symposium Commemorating the Publication of An Introduction to the Study of Experimental Medicine*. Cambridge: Schenkman Publishing Company, Inc., 1967. Reprinted through the courtesy of the Publisher.

has for the scientist. A similar view is expressed by Wilson in his well known book on the principles of scientific research: "An individual completely ignorant of what was known before has little chance of making a worthwhile contribution."

These and similar reasons, repeatedly expressed, are the main justification for our Symposium commemorating the centenary of the publication of Claude Bernard's *Introduction to the Study of Experimental Medicine*. It is our hope that by discussing Bernard's contributions and by analyzing their significance for contemporary medical research we can contribute to restimulate interest, not only on his remarkable work, but also in the historical development of medical knowledge in a broader sense.

The Work of Claude Bernard

Claude Bernard is universally considered one of the great scientists of all time and one of the men most influential in the development of scientific Medicine. Many of his scientific contributions have been incorporated in our store of knowledge as established physiological facts; many of his ideas are so commonplace today that we take them for granted without inquiring as to how they developed. It might be appropriate at this time to summarize his most important contributions; they can be considered under three main headings:

1. Physiological discoveries.
2. Theoretical concepts.
3. Philosophy of scientific research as applied to Physiology and Medicine.

Physiological Discoveries

Although Bernard contributed a large series of important discoveries to physiological knowledge, his name is usually associated with the following four major contributions:

- a. The role of the pancreas in digestion.
- b. The vasomotor innervation.
- c. The effect of curare on neuromuscular transmission.
- d. The glycogenic function of the liver.

The studies on the role of the pancreas in digestion originated from the observation that in meat-fed rabbits the lacteals appeared filled with chyle some 30 cm. below the pylorus in contrast with the dog, in which chyle-filled lacteals appear very close to the pylorus. Having found that in the rabbit the pancreatic duct enters the intestine lower down than in the dog, Bernard deduced that pancreatic juice must be responsible for making the fat absorbable. By incubating at body temperature neutral fat with crushed pancreatic tissue he demonstrated the breakdown of the fat in fatty acids and glycerine, showing also that the same effect was obtained by using pancreatic juice collected by means of a pancreatic fistula. He corroborated also the effect of pancreatic juice transforming starch into sugar and obtained some evidence of its proteolytic effect.

The studies on the vasomotor innervation originated from the observation, reported in 1851, that the section of the sympathetic nerve in the neck of the rabbit caused an increase in the temperature of the ear and an increase in the size of its blood vessels in the side of the section. This was followed later by the confirmation of the vasoconstrictor effect of the stimulation of the cut end of the nerve and by the discovery of the vasodilator effect of the stimulation of the chorda tympani on the blood vessels of the submaxillary gland.

The work on the effects of curare was begun by Bernard in 1844 and he returned to it several times over a period of more than 20 years. After studying the effects of different ways of administration of the drug Bernard showed that the electrical stimulation of the motor nerve did not produce contraction but that the muscle contracted if directly stimulated, thus giving experimental proof of the independent excitability of muscle tissue. He showed also that the sensory nerves were unaffected by the drug and that the effect of curare consisted in preventing the normal stimulus to reach the muscle. Bernard concluded (1867) that curare attacked the motor fiber at the peripheral end and that it did not act upon the nervous system as a whole. The experiments with curare developed Bernard's interest

in the use of drugs in physiological analysis and started an important series of studies on experimental toxicology.

The discovery of the glycogenic function of the liver began as a search for the origin of the sugar present in the blood of normal animals; first it was shown that this sugar was present also in starving animals and in animals fed with diets devoid of carbohydrates. In 1848, Bernard communicated evidence for the presence of sugar in the liver of a dog fed exclusively with meat; in 1855 he reported that the sugar content of the liver increased on standing; livers perfused with water until no more sugar was demonstrable, were shown to be rich in sugar after being kept for some time at mild temperatures. This work was completed with the isolation of glycogen from the liver, reported in 1857, and is one of the more important of Bernard's contributions; it is related to other important discoveries, such as the discovery of the so called "piqûre diabétique" (the production of hyperglycemia and glycosuria by wounding the floor of the fourth ventricle). The production of sugar by the liver was also the base of the concept of internal secretion that we shall mention later on.

Besides these four main discoveries Bernard contributed many other important observations. We remember in particular his studies on the effect of carbon monoxide and on the gases of the blood. The studies on animal heat, which led to the demonstration that oxidation of foodstuffs does not take place in the lung as believed by Lavoisier, should also be mentioned.

Theoretical Concepts

Although Bernard often expressed a dislike for generalization, he maintained the view that science is not a simple accumulation of facts. We are indebted to him for the introduction of some theoretical concepts which have had a marked influence in the development of scientific Medicine. His most important contributions in this respect may be summarized by saying that he introduced the following concepts:

1. The concept of General Physiology as the science

studying the physiological properties common to all living beings, as well as studying the immediate causes of these properties.

2. The concept of the constancy of the "milieu intérieur" or internal environment.
3. The concept of "internal secretion."
4. The concept of "organic unity."
5. The concept of "selective vivisection."
6. The concept of "directive idea."

The concept of "milieu intérieur" is undoubtedly the most famous of these theoretical concepts. It has been praised as being one of the most fruitful generalizations ever introduced in biological thinking; it has been the driving force behind much of the physiological research of the last decades; and it still influences the work of contemporary physiologists. The work of physiologists like Haldane and Barcroft in England and of Lawrence Henderson and Cannon in this country is directly related to this concept. The author of the concept of "homeostasis" proclaimed his debt to Bernard by writing in the Preface of the French Edition of his *The Wisdom of the Body*: "The central idea of this book, the stability of the inner medium of the organism in higher vertebrates, is directly inspired by the precise views and deep understanding of the eminent French physiologist Claude Bernard. This book can be even considered a tribute to his memory."

While the idea of organic regulations can be traced back many years before Bernard (Adolph, 1961), there is no doubt that he was the first to realize the importance of the constancy of the internal environment. His biographer Olmsted has summarized the significance of this concept as follows: "Bernard, without any grandiose intentions seems, in proposing his general conception of the internal environment, to have succeeded in providing a groundwork for some of the most productive investigation of a later generation and for an interpretation of the ultimate characteristics of the phenomena of life."

Philosophy of Scientific Research

It has been said (Olmsted and Olmsted, 1952) that the

climax of Bernard's career was reached when he presented to the Academy of Sciences in August 1865 his newly published *Introduction to the Study of Experimental Medicine*. Bernard had planned since 1858 to write such a treatise and by 1862 he had written a long introduction for that work. The treatise was never completed but the *Introduction* became, after extensive and careful revision, the "Introduction à l'étude de la médecine expérimentale," published in Paris in 1865.

The book was an immediate success. It had a profound influence not only on workers in the fields of physiology and Medicine but also on philosophers and writers. Bergson compared the influence of the *Introduction* with that of Descartes' *Discourse on Method* for the scientific thinking of the seventeenth and eighteenth centuries. Medical historians are unanimous in considering the *Introduction* as a landmark in the evolution of medical thought (Shryock), and it is still recommended today as valuable and stimulating reading for those about to embark on a career in the bio-medical sciences (Rothschuh).

Various reasons can be given to explain the singular position of the book in the scientific literature. In the first place, it was the first attempt to formulate a philosophy of scientific research as applied to Physiology and Medicine. It is obvious that the experimental method had been applied to medical problems before Bernard, but he deserves unqualified credit as the first biologist to undertake the task of analyzing the philosophical basis of the scientific method and to discuss its application to experimentation in living beings. The fact that many of the ideas expressed in the *Introduction* are today taken for granted is a good proof of Bernard's foresight. A large number of books dealing with the philosophical basis of scientific research have appeared in the last years, but most of these books deal exclusively with Physics and Mathematics. The *Introduction* continues to be almost the only contribution to the philosophy of science written by a biologist with the peculiarities of biological research in mind.

Other characteristics of the *Introduction* consist in the

fact that Bernard documented practically all of his reasoning with examples taken from his own researches. This gives the book an unusual freshness as well as impressive authority. This aspect of the *Introduction* has been characterized by Cohen as follows: "Reading the book one is tempted to make the generalization that sound philosophical analysis of science can be made only by a practicing scientist and the greater the scientist the better." In the same vein Lawrence Henderson wrote in his Preface to the English translation of the *Introduction*: "It is, therefore, not the least of the merits of Claude Bernard's *Introduction to the Study of Experimental Medicine* that we have here an honest and successful analysis of himself at work by one of the most intelligent of modern scientists, a man of genius and a great physiologist." It is this almost "autobiographical" character of the *Introduction* that makes its reading an unforgettable experience and a source of inspiration.

There is a third aspect of the *Introduction* that I must refer to before ending, and this refers to Bernard's endeavour to show over and over again how fact and idea must work together in experimental research. This endeavour has been particularly extolled by Bergson who considered it as Bernard's greatest contribution to the philosophy of science.

Bernard entered his scientific career when the intellectual climate in France was dominated by positivism. His teacher Magendie described himself as "Chiffonier des faits" or as "a scavenger of facts." Bernard considered Magendie's extreme empiricism as too exclusive and insisted in the importance of ideas and reasoning in scientific research. For Bernard science is built with well observed facts, but reasoning is needed for the interpretation of these facts and for the deduction of laws. His position is well summarized in the following quotation: "L'empirisme peut servir à accumuler les faits, mais il ne saurait jamais édifier la science. L'expérimentateur qui ne sait point ce qu'il cherche ne comprend pas ce qu'il trouve." ("Empiricism may serve to accumulate facts, but it will never build science. The experimenter who does not know what he is looking for will not under-

stand what he finds.")

This advice is as relevant for us today as it was when first formulated. With the increasing power that modern instrumentation has given us, we are apt to forget that the human mind, human reason, is the most important tool in scientific research.

"Claude Bernard held and clearly explained that it is the task of general physiology to study the phenomena of life which are common to animals and plants. These phenomena are physical and chemical phenomena; they are to be investigated by physical and chemical methods; they are conditioned by the same physical and chemical forces that may be discovered among inorganic phenomena. But in the living being they are also always harmoniously organized and integrated, and this is their most striking characteristic. It gives rise to the central problem of general physiology. Especially with the help of his theory of the milieu interieur, Claude Bernard was able to treat many facts, including his own discoveries, from this point of view and thus to embody in durable form ideas which were in advance both of the spirit of his contemporaries and of his own physico-chemical knowledge." (From Lawrence J. Henderson, *Blood*, 1928).

THE SIGNIFICANCE OF CLAUDE BERNARD'S PHILOSOPHY OF SCIENCE FOR MODERN MEDICAL RESEARCH AND EDUCATION⁵

By D. C. Tosteson, M.D.

"The ideas which we shall here set forth are certainly by no means new; the experimental method and experimentation were long ago introduced into the physico-chemical sciences, which owe them all their brilliancy. . . . We shall therefore make no claim to philosophy. Our single aim is, and has always been, to help make the well-known principles of the experimental method pervade medical science." This quotation taken from *An Introduction to the Study of Experimental Medicine*⁶ reveals several things about its author, Claude Bernard, and also about my intentions in this paper.

First, it expresses clearly, though somewhat protestingly, Bernard's fascination with the philosophy of science. It also brings out his suspicion (indeed one sometimes suspects his contempt) for the more nebulous aspects of philosophic thought. He was a practicing scientist and as such had little use for reflections which lacked relevance to his own work. On the other hand, his agile and energetic mind was both interested in a fantastic range of subjects and also strongly inclined toward systematics. He had a deep belief in the unity of science and indeed existence. He was not content to allow one domain of his awareness and activity to remain isolated from the rest of his concerns. It was, it seems to me, from some such inclinations that his treatise which we celebrate in this symposium emerged. As the passage quoted indicates, Claude Bernard would deny my allegation that *An Introduction to the Study of*

⁵*Ibid.*

⁶This and all other quotations from *An Introduction to the Study of Experimental Medicine* are from the translation by Henry Copley Green (Schuman, 1927). All quotations are from this source unless otherwise specified.

Experimental Medicine embodies a philosophy of science. He says that he "makes no claim to philosophy." I think that he is falsely modest. Perhaps I only reveal my own lack of philosophic sophistication in reaching this conclusion, but I do so on the basis of personal experience.

I first read this remarkable book fifteen years ago when I was an intern in medicine at Columbia University. I read the book during a period when I was quite captivated by the thought of that group of modern philosophers who refer to their point of view as logical positivism. I found that Bernard's treatise came through to me with an immediacy and relevance which the works of the philosophers lacked. Since that time I have returned to the book many times. Always it has provided me with a renewed sense of the purpose and plan of my own scientific work as well as a real feeling of community with one who may properly be called the first great colleague of all modern physiologists. The purpose of my lecture then is to share with you some of the reflections which Bernard's book has stimulated in my own mind. I hope that these reflections will reveal to you the relevance of his thought to at least one physiologist working today one hundred years after the publication of his book.

I would like to begin by considering three aspects of Bernard's thought which are relevant to modern medical research. First, I would note his concern with the relation between fact and theory in science, secondly, his attitude toward specialization, and thirdly his thoughts with regard to the physico-chemical basis of physiological processes. After discussing these aspects of research, I would like to discuss the relevance of Bernard's thought to modern medical education. In particular I will emphasize his delineation of the relationship between physiology and clinical medicine. Finally, I will describe what I take to be Bernard's view with regard to the proper goals of medical education.

A casual examination of modern medical research would surely lead to the conclusion that Bernard and his disciples have succeeded in "making the well-known principles of the experimental method pervade medical

science." The past century has produced a completely unprecedented increase in medical scientific knowledge. At the present time the rate of accumulation of information in this domain of intellectual activity is increasing according to some power function. One is tempted to conclude that we have learned the teachings of Bernard so well that there is little point in reiterating what has become part of our scientific intellectual fiber. I think that such a conclusion can be retained only if we restrict our view to the surface of modern medical science. What is the nature of the information that we are accumulating at a steadily increasing rate? In far too many cases, it seems to me that we are accumulating what, in Bernard's lexicon, would be called fact. Bernard expresses in many passages in his book his scorn for unadorned fact. For example, "Experimenters must doubt their intuition, i.e., the a priori idea or the theory which serves as their starting point; this is why it is an absolute principle always to submit one's idea to the experimental criterion so as to test its value. But just what is the foundation of this experimental criterion? This question may seem superfluous, after having repeatedly said that facts judge the idea and give us experience. Facts alone are real, it is said; and we must leave the matter to them, wholly and exclusively. Again, it is a fact, a sheer fact, men often repeat; there is no use in discussing, we must accept it. Of course, I admit that facts are the only realities that can give form to the experimental idea and at the same time serve as its control; but this is on condition that reason accepts them. I think that blind belief in fact, which dares to silence reason, is as dangerous to the experimental sciences as the beliefs of feeling . . . As in everything else, the only real criterion is reason.

"A fact is nothing in itself, it has value only through the idea connected with it or through the proof it supplies. We have said elsewhere that, when one calls a new fact a discovery, the fact itself is not the discovery, but rather the new idea derived from it; in the same way, when a fact proves anything, the fact does not itself give the proof, but only the rational relation which it estab-

lishes between the phenomenon and its cause. This relation is the scientific truth which we now must discuss further."

This recognition of the unity of the experimental method and in particular the worthlessness of not only the undocumented hypothesis but also the unrelated fact is a recurring characteristic of Bernard's thought. He illustrates his point with regard to the scientific valuelessness of unrelated irrational facts with a charming account of one of his experiences in the laboratory. "A few years ago, I experimented on the influence of ether on intestinal secretions. Now *a propos* of this, I happened to observe that injecting ether into the intestinal canal of a dog kept without food even for several days gave rise to splendid white lymphatics, absolutely like those in an animal actively digesting mixed food in which there is fat. After frequent repetitions, the fact was unquestionable. But what meaning could be ascribed to it? What reasoning was possible about its cause? Should we say: ether causes secretion of chyme? This is a fact. But that would be absurd, since there was no food in the intestine. As we see, reason rejected this causation as irrational and absurd in our present state of knowledge. I therefore tried to find the reason for this incomprehensible fact, and I finally saw that there was a source of error, because the ether dissolved the oil lubricating the piston of the syringe with which it was injected into the stomach; when the ether was injected with a glass pipette, instead of a syringe, it no longer produced the phenomenon. The irrationality of the fact, therefore, led me to see a priori that it must be false, and that it could not be used as a basis for scientific reasoning. Otherwise I should not have found the curious source of error located in the piston of a syringe. But when the source of error was once recognized, everything was explained, and the fact became rational in this sense, that the chyle was produced there, as everywhere else, by the absorption of fat. . . ." This vignette illustrates not only Bernard's insistence on establishing relations between his observations and a reasonable hypothesis but also his awareness of the im-

portance of experimental detail. It seems to me that this somewhat neglected aspect of Bernard's views, i.e. his rejection of unrelated or irrational facts, is particularly relevant in our time. In biology it is all too easy to make a new observation. It is merely necessary to make the same old measurement on a new organ, organism, cell, organelle or enzyme. The present and increasing deluge of biological and medical literature gives ample evidence of this fact. I venture to suspect that frequent repetition of Bernard's catechism with regard to the valuelessness of one more fact that is unrelated to some ordering idea might both reduce the quantity and increase the quality of our contemporary medical literature. Bernard makes many other comments with regard to the origins of scientific busyness. One of them cannot help but strike resonance. In speaking of the need for laboratories in hospitals and other places where experimental medicine is practiced, Bernard considers the importance of the scientific instruments. He says, "But as vital phenomena, whether in the normal or in the pathological state, are analyzed mainly by means of tools borrowed from physico-chemical science, instruments must necessarily be somewhat liberally provided. The solution of certain scientific questions often imperatively demands costly and complicated instruments, so that we may then say that scientific questions are secondary to the question of money. However, I do not approve the luxury as to instruments to which certain physiologists have yielded. In my opinion, we should seek to simplify instruments as much as possible, not only for pecuniary, but also for scientific reasons; for we need to learn that the more complicated the instrument, the more sources of error does it create. Experimenters do not grow great by the number and complexity of instruments; it is really the other way. The great experimenters, Berzelius and Spallanzani, made great discoveries by means of simple instruments. In the course of this work, our principle, then, will be to seek, as far as possible, to simplify means of study; for instruments must be allies, not sources of error because of their complications."

It is already evident from this discussion that Bernard was intensely concerned with the unity of science. He believed that this unity was based much more on process than on product. He was not optimistic about our capacity to evolve a grand theory of the universe which would include all biology. Indeed, despite his vigorous practical scientific determinism he sharply distinguished between the delineation of the necessary conditions for and the "true nature" of a phenomenon. He believed that "man would never know either the primary cause or the essence of things." However, if he was pessimistic with regard to ultimate scientific theories, he was optimistic about the generality of the experimental method. He believed that it is this consensus on approach which unites the sciences. In the mid-19th century he was already concerned about the threat of specialization to this consensus. He recognized that differentiation was inevitable but at the same time insisted that the separate aspects of the experimental method make sense only in relation to one another. His attitude is well expressed in the following passage: "But it more often happens in the evolution of science, that different parts of experimental reasoning are shared by several men. Some of these, both in medicine and in natural history, merely gather and assemble observations; others manage to formulate more or less ingenious and more or less probable hypotheses based on these observations; then others come in to create conditions favoring the birth of an experiment to control these hypotheses; finally others apply themselves more especially to generalizing and systematizing the results obtained by the different observers and experimenters. This parceling out of the experimental domain is useful, because each one of its various parts is all the better cultivated. In fact we can easily conceive that, in certain sciences, the means of observation and experimentation are such specialized instruments that their management and use require a certain manual dexterity or the sharpening of certain senses. But while I accept specialization in the practice, I reject it utterly in the theory of science. I believe, indeed, that making generalization

one's specialty is anti-philosophic and anti-scientific, . . .

"Experimental science, however, cannot advance on a single side of the method taken separately; it goes ahead only by the union of all parts of the method converging toward a common goal. Men who gather observations are useful only because their observations are afterward introduced into experimental reasoning; in other words, endless accumulation of observations leads nowhere. Men, who formulate hypotheses a propos of observations gathered by others, are useful only in so far as men seek to verify these hypotheses by experimenting; else these hypotheses, unverified or unverifiable by experiment, would engender nothing but systems and would bring us back to scholasticism. Men who experiment, despite all their dexterity, cannot solve problems unless they are inspired by a fortunate hypothesis based on accurate and well-made observations. Finally men who generalize can make lasting theories only in so far as they themselves learn all the scientific details that these theories are intended to represent. Scientific generalization must proceed from particular facts to principles; and principles are the more stable as they rest on deeper details just as a stake is the firmer, the farther it is driven into the ground." Truly this passage is as relevant to the science of the mid-sixties as it was in 1865.

I would not like to leave this brief consideration of the relevance of some of Bernard's philosophic thought to modern medical research without some more specific reference to his attitudes about the relation between biology and the physical sciences. He was, of course, an indefatigable and successful opponent of vitalism in all its forms. Indeed, modern physiology with its emphasis on the physico-chemical basis of biological processes may be said to have begun with his researches on such widely varying subjects as the mechanism of action of curare to the production of animal sugar. His attitude on this matter is expressed well in this statement, "Life is nothing but a word which means ignorance, and when we characterize a phenomenon as vital, it amounts to saying that we do not know its immediate cause or its

conditions. Science should always explain obscurity and complexity by clearer and simpler ideas. Now since nothing is more obscure, life can never explain anything. I emphasize this point, because I have seen even chemists at times appeal to life to explain certain physico-chemical phenomena peculiar to living beings. Thus the ferment in yeast is an organic, living material which has the property of converting sugar into alcohol, carbonic acid and several other products. I have sometimes heard it said that the property of decomposing sugar was due to the life inherent in a globule of yeast. This vitalistic explanation means nothing and explains nothing about the action of yeast. We do not know the nature of this property, but it must necessarily belong to the physico-chemical order and be as precisely defined as, for instance, the property of platinum sponge which produces a more or less analogous action that cannot be attributed to vital force." Despite his conviction that advancement of the physiological sciences depends intimately on the extent to which the conditions responsible for biological phenomena can be defined in physico-chemical terms, he well-recognized that living organisms display certain characteristics which are very difficult to formulate in such terms. For example, "Admitting that vital phenomena rest upon physico-chemical activities, which is the truth, the essence of the problem is not thereby cleared up; for it is no chance encounter of physico-chemical phenomena which constructs each being according to a pre-existing plan, and produces the admirable subordination and the harmonious concert of organic activity.

"There is an arrangement in the living being, a kind of regulated activity, which must never be neglected, because it is in truth the most striking characteristic of living beings . . .

"Vital phenomena possess indeed their rigorously determined physico-chemical conditions, but, at the same time, they subordinate themselves and succeed one another in a pattern and according to a law which pre-exist; they repeat themselves with order, regularity, constancy, and they harmonize in such manner as to

bring about the organization and growth of the individual, animal or plant.

"It is as if there existed a pre-established design of each organism and of each organ such that, though considered separately, each physiological process is dependent upon the general forces of nature, yet taken in relation with the other physiological processes, it reveals a special bond and seems directed by some invisible guide in the path which it follows and toward the position which it occupies.

"The simplest reflection reveals a primary quality, a quid proprium of the living being, in this pre-established organic harmony."* It is my impression that the validity of the point of view expressed in this passage is better recognized today than it was in 1945. It is no longer particularly estimable to isolate one more compound or one more enzyme from a biological source. It has been done, either in fact or principle. Rather, the attempt to understand the relation of such isolated molecules to one another in actual functioning cells increasingly draws the attention of biochemists and molecular biologists. The exquisite complexity of these relations has made even the most physico-chemically inclined biologists increasingly aware of the fantastic plasticity and sensitivity of even the simplest components of living systems such as individual proteins not to mention rather more organized structures such as membranes, organelles, etc. The recent successes in understanding the genetic coding of proteins, enzyme induction, repression, and feed back inhibition have only served to indicate more and more vividly the subtlety of the interactions which comprise a living thing.

I would like to turn now to the relevance of Bernard's thought for modern medical education. In my introductory lecture to the medical students at Duke each year, I usually read the following passage which defines clearly and concisely the relevance of physiology to medicine. "In the empirical period of medicine, which must doubtless still be greatly prolonged, physiology and therapeutics could advance separately; for as

*From Bernard's lectures on general physiology published in Paris, 1878.

neither of them was well established, they were not called upon mutually to support each other in medical practice. But this cannot be so when medicine becomes scientific; it must then be founded on physiology. Since science can be established only by the comparative method, knowledge of pathological or abnormal conditions cannot be gained without previous knowledge of normal states, just as the therapeutic action of abnormal agents, or medicines, on the organism cannot be scientifically understood without first studying the physiological action of the normal agents which maintain the phenomena of life."

There is little doubt that Bernard would continue to advocate a firm grounding in the so-called basic sciences for all students of medicine. Moreover, he was very sensitive about the views of many of his contemporaries with regard to the alleged conflict between experimental medicine and medical practice. For example, he says "For a long time, men have said and repeated that the physicians most learned in physiology are the worst physicians, and that they are the most awkward when action is necessary at the patient's bedside. Does this mean that physiological science is harmful to practice?" He answers this question in the negative in several spirited pages of discussion. He points out that experimental medicine is a direct outgrowth of the empirical approach used by followers of Hippocrates since antiquity. "I said above that compassion and blind empiricism are the prime movers of medicine; later came reflection bringing doubt, then scientific verification. This medical evolution can still be verified around us every day, for every man goes on learning, as does all humankind." He concludes that every physician whether in the laboratory or at the bedside should be an experimenter. He summarizes his views with the statement "—experimental medicine, as we conceive it, includes the problem of medicine as a whole and comprises both the theory and the practice of medicine. But when I said that every physician should be an experimenter, I did not mean to suggest that each one should cultivate the whole extent of experimental medicine. Of necessity,

there will always be physicians especially devoting themselves to physiological experiments, others to investigation of normal and pathological anatomy, others to surgical or medical practice, etc. This splitting up is not bad for the progress of science; on the contrary, practical specialties are an excellent thing for science, properly speaking, but on the condition that men devoting themselves to the investigation of a special part of medicine be so educated as to be conversant with experimental medicine as a whole, and to know the place which the special science they cultivate should occupy in that whole. By specializing in this way, they will direct their studies so as to contribute to the progress of scientific or experimental medicine. Practical studies and theoretic studies will thus work toward the same object; that is all that we can ask in a science, like medicine, which is forced to be ceaselessly in action before it is fully established."

Again note Bernard's recognition of the inevitability and indeed practical desirability of specialization. It seems to me that this aspect of his analysis of medicine is something which is of particular importance to those of us who are involved in the education of medical students. As the volume of information which is relevant to medicine continues to increase, we are under increasing temptation to enlarge the amount of material which we expect all medical students to "learn." This solution to the problem obviously neglects the fact that there are still only 24 hours in the day and a limited number of neurons in the brain. Clearly much of what is learned is soon forgotten. Bernard recognized this problem and the inevitable specialization which it produces. He did not fret about this development but rather welcomed it as a sign of progress. He was free to do this because he recognized that the bond of unity in science is in process. What all physicians and medical scientists share is not information but a method of approach, the experimental method. He insisted that the goal of medical education should be to teach this method as it is applied to any and all of the realms of medicine. He said "It has often been said that, to make discoveries, one must be ignorant. This opinion, mistaken in itself, nevertheless

conceals a truth. It means that it is better to know nothing than to keep in mind fixed ideas based on theories whose confirmation we constantly seek, neglecting meanwhile everything that fails to agree with them. Nothing could be worse than this state of mind; it is the very opposite of inventiveness. Indeed a discovery is generally an unforeseen relation not included in theory, for otherwise it would be foreseen. In this respect, indeed, an uneducated man, knowing nothing of theory, would be in a better attitude of mind; theory would not embarrass him and would not prevent him from seeing new facts unperceived by a man preoccupied with an exclusive theory. But let us hasten to say that we certainly do not mean to raise ignorance into a principle. The better educated we are and the more acquired information we have, the better prepared shall we find our minds for making great and fruitful discoveries. Only we must keep our freedom of mind, as we said above, and must believe that in nature what is absurd, according to our theories, is not always impossible."

Or again, "I have quoted examples of investigation, but have been very careful not to give needless explanations or to formulate a single or absolute rule; because I think a teacher's role should be limited to clearly showing his pupil the goal that a science sets itself and to pointing out all possible means at his disposal for reaching it. But a teacher should then leave his pupil free to move about in his own way and, according to his own nature, to reach his goal, only coming to his aid if he sees that he is going astray. I believe, in a word, that the true scientific method confines the mind without suffocating it, leaves it as far as possible face to face with itself, and guides it, while respecting the creative originality and the spontaneity which are its most precious qualities. Science goes forward only through new ideas and through creative or original power of thought. In education we must, therefore, take care that knowledge which should arm the mind does not overwhelm it by its weight, and that rules, intended to support weak parts of the mind, do not atrophy the strong and fertile parts.

I need not enter into further explanations here; I have had to limit myself by forewarning biological science and experimental medicine against exaggerating the importance of erudition and against invasion and domination by systems; because sciences submitting to these would lose their fertility and would abandon the independence and freedom of mind essential to the progress of humanity."

I believe that Claude Bernard would have been unhappy about the degree to which "erudition" is emphasized in medical education in the United States. He would also have been sympathetic with the difficulty of the problem of how to deal with the deluge of information. I would be most interested to discuss with him the experiment in medical education which we are undertaking at Duke. To learn process, to learn the "experimental method" requires some depth of involvement in a subject. Such involvement requires time. We propose to free that time by devoting the first two years of medical school to a survey which will expose the student to the surface of all of the disciplines, both so-called basic and clinical, represented in the School of Medicine. The last two years will be structured so that the student may choose to study in depth those aspects of what he has seen which seem to him most relevant to his own needs and interests. For example, a future neurosurgeon could spend most of the third year in neurophysiology while also taking courses in neuroanatomy and neurophysiology. He might devote most of his last year to medicine and psychiatry deferring his surgical experience until internship. The last two years are, in short, a serious attempt to leave the student "... as far as possible face to face with itself ..."

I have been unable in this paper to resist the temptation to quote extensively from some of the many eloquent passages in his book. To me Claude Bernard emerges from these pages as a highly intelligent, articulate, practical, clear-headed, tough-minded scientist who is not about to be stampeded by anyone. Above all, his ideas seem to me to be intensely alive, as relevant to us as they were to his contemporaries.

"One would like to believe that this master of experimental medicine passed the winter of his life in happy comfort amidst his devoted family. But if you had knocked at No. 40 Rue des Ecoles, you would have found that Claude Bernard lived alone with an old housekeeper who never let her duties to God interfere with her services to the physiologist. Claude Bernard sacrificed his home on the altar of his laboratory. Early in his career, this investigator made a bitter discovery—his wife was not interested in the experimental method. Hearing from his companions that he was clever, she demanded that he employ his talents to build up a large practice. That he should lock himself up in his laboratory, and after a long period of hard work emerge with nothing but the discovery of the vasomotor system, filled her with undisguised indignation. Claude Bernard knitted his ample brow, and realized he must choose between his spouse and science. But the rough call of Magendie, "I say, you there, I take you as my *préparateur* at the Collège de France," rang in his ears as a sacred passport to the temple of the experimental method, and Claude Bernard remained forever within its portals. The outraged Madame gathered together her belongings, took her daughters with her, and left the scientist homeless. His daughters grew up to hate their father, and one of them, who regarded him as a sinful vivisector, devoted her spare money to founding hospitals for cats and dogs." (From Victor Robinson, *Pathfinders in Medicine*, New York: Medical Life Press, 1929).

CHRONOLOGY OF CLAUDE BERNARD

1813-1878

- 1813 July 12, born at Saint-Julien, canton de Villefranche (Rhône), France, the son of a winegrower and schoolmaster.
- 1821 Age 8. Began schooling with instruction in Latin at house of Curé Bourgaud. Later entered the Jesuit College of Villefranche.
- 1830 Age 17. Attended the college of Thoissey (Ain) for one year.
- 1832 Age 19. Because his family could no longer afford to keep him in school, Bernard went to work for a pharmacist, M. Millet, in the Faubourg de Vaise of Lyons. In his time from work, he attended the local theatre, wrote a vaudeville, "La Rose Du Rhône," and a five act drama.
- 1833 Age 20. Discharged from the pharmacy shop because he was a dreamer.
- 1834 Age 21. Took his drama to Paris to M. Saint-Marc Girardin, professor of literature at the Sorbonne, who advised him to study medicine. Entered the Medical School of Paris where he studied anatomy diligently and showed skill in dissecting.
- 1836 Age 23. Became *externe* and taught natural history in a girls' school.
- 1839 Age 26. In competitive examination for *interne*, Bernard passed but ranked twenty-sixth out of twenty-nine.
- 1840 Age 27. Studied under Falret, Velpeau, Maison-neuve and Magendie.
- 1841 Age 28. Became Magendie's *préparateur* at the Collège de France.
- 1843 Age 30. Obtained his medical degree, writing a thesis on the gastric juice and its rôle in nutrition. He never practiced medicine but at once became a laboratory and research worker.

- 1844 Age 31. Sought position as assistant professor of anatomy and physiology on the Faculty of Medicine but failed in the competition.
- 1845 Age 32. Married Marie Françoise Martin whose father was Henri Martin, a physician in Paris; 2 daughters survived Bernard but 2 sons died in infancy. Sought to augment his income by preparing anatomical dissections, helping M. Ch. Huette prepare a book on surgery and seeking, with Dr. Lasèque, to establish a private laboratory.
- 1847 Age 34. Appointed substitute lecturer to Magendie at the Collège de France. Elected to his first scientific society, The Société philomathique de Paris.
- 1848 Age 35. Aided in founding the Société de Biologie, was one of its two vice-presidents and took a very active part in the meetings.
- 1849 Age 36. Awarded the red ribbon of the Legion of Honor in recognition of his work in the rôle of the pancreas in digestion, which had also won for him for the second time the prize in experimental physiology of the Academy of Sciences. Also announced his discovery of diabetes following a wound in the floor of the fourth ventricle.
- 1851 Age 38. Awarded, for the third time, the prize in experimental physiology, this time for his work on the glycogenic function of the liver.
- 1852 Age 39. Discovered the vasomotor system of nerves.
- 1853 Age 40. Given degree of Doctor of Natural Sciences. Awarded, for the fourth time, the prize in experimental physiology, now for work on the sympathetic nerves. Shortly afterward he became the chairman of the committee awarding the prize and thus never received it again.
- 1854 Age 41. Elected to membership in the Academy of Sciences. A chair of physiology on the Faculty of Sciences at the Sorbonne was created for Bernard.
- 1855 Age 42. On death of Magendie, Bernard suc-

- ceeded him as Professor of Medicine at the Collège de France.
- 1857 Age 44. Isolated glycogen.
- 1860 Age 47. Received the Order of the Polar Star from Sweden and Norway.
- 1861 Age 48. Elected to the Académie de Médecine. Illness prevented work.
- 1862 Age 49. Appointed by the Emperor to a consulting committee on Hygiene and Medical Service in the hospitals. Promoted to the rank of Officer of the Legion of Honor.
- 1864 Age 51. Became foreign member of the Royal Society of London, Academy of Sciences of Berlin and of St. Petersburg.
- 1866 Age 53. Forced to cancel his winter course at the Collège de France because of poor health which had incapacitated him frequently after 1861. Retired to his country home at Saint-Julien.
- 1867 Age 54. Returned to Paris but his health allowed him only to continue his writings and not to return to his lecture room or laboratory. Elected perpetual president of the Société de Biologie. Became Commander in the Legion of Honor.
- 1868 Age 55. Transferred his course in General Physiology from the Sorbonne to the Museum of Natural History. Elected a member of the French Academy.
- 1869 Age 56. His health being improved, he again began to lecture. Elected president of the Academy of Sciences. Became a senator by Imperial decree.
- 1872 Age 59. Elected first president of the French Association for the Advancement of Science.
- 1876 Age 63. Awarded the Copley Medal of the Royal Society.
- 1878 Age 65. Died February 16 of pyelonephritis. Buried in the cemetery of Père Lachaise after a funeral at public expense, the first scientist to be thus honored.