Traveling Around Physiology

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You may be reading this column in the fall, but I'm writing it in July, and right now, my number one problem is that it doesn't look like we're going to have much of a vacation this summer. I'm teaching summer school, and we *have* to do a major overhaul of the dining room. Last weekend, we stayed at a nice bed and breakfast house in Waterbury, Connecticut, after attending the opening night of the St. Mary's Elementary School production of "The Wizard of Oz." While it *really* was great, with my niece and nephew stealing the show, a night in Waterbury, no matter how star-studded, hardly counts as a vacation.

But I can't feel too sorry for myself, because I do have one nice alternative to travel: I can tour the world of biology. It is such a vast world, and my knowledge of it is so limited, that there are always new vistas to be explored or interesting areas to be revisited. While many biologists, like many tourists, tend to return again and again to the same areas, others, like myself, flit from region to region, now looking at ecology, then exploring microbiology.

This summer, I've decided to take a closer look at physiology. It's an area that I have some familiarity with, since I spent a great deal of time there when I started teaching. But lately, I've been visiting the worlds of ecology and zoology, so it's high time that I revisit physiology and gain a new perspective on this field. One way to do this is to take a historical perspective. And a nice thing about travel in the world of biology is that I can go back in time and explore such physiological landmarks as the *milieu intérieur* of Claude Bernard and the homeostasis of Walter Cannon. These are two of my favorite concepts in biology, and it's fun to revisit them.

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The Milieu Intérieur

To me, the *milieu intérieur*, the body's internal environment, is a very suggestive phrase. It signifies that the cells of the body are surrounded by an environment, an ambience, just as the body as a whole is. For Bernard, the term also signifies both the balance and tension which must exist between these two environments as the body struggles to maintain the constancy of its internal environment in the face of fluctuations in temperature, humidity and other aspects of the external environment to which it is exposed.

From my latest trip to the territory of the *milieu intérieur*, I discovered that Claude Bernard's idea of what the term signified changed over the course of his career. He first used the term to refer to the blood plasma as the environment in which an individual lives, and then extended it to include both the plasma and the interstitial fluid. This is hardly surprising. The meanings of many, if not most, scientific terms change over time. Bernard himself was aware of this. In *An Introduction to the Study of Experimental Medicine* (1957), the book in which he gives his thoughts on the processes of science, he wrote:

> *When we create a word to characterize a phenomenon, we then agree in general on the idea that we wish it to express and the precise meaning we are giving to it; but with the later progress of science the meaning of the word changes for some people, while for others the word remains in the language with its original meaning. The result is often such discord that men using the same word express very different ideas.*

The meaning of any word can change over time, that is a basic characteristic of language. But change in meaning is particularly common among scientific terms because it is fostered by new knowledge. As Bernard pursued his studies of physiology, he came to realize that there was interchange between the blood and the interstitial fluids, that one could not be considered without reference to the other, thus his concept of the *milieu intérieur* broadened.

But as Bernard notes, such change can lead to controversy if not everyone accepts or is aware of the altered definition. I had a slight "discord" with another biologist over the word homeostasis and what it signifies. Walter Cannon (1932), who coined the term, defined it as the coordinated physiological processes which maintain a steady state within an organism. My colleague and I were at a meeting to discuss what is essential in a biology curriculum (a question that biology teachers debate *ad infinitum*). I thought that homeostasis was a key concept which students should appreciate, and I went on about the power of this concept and its relevance to so many areas of biology. My colleague disagreed. He is a botanist, and to him this physiological concept didn't seem very vital. My enthusiasm in the face of his lack of interest bothered him. If I was so excited about it, maybe there was something he was missing. The next day he announced that he had checked in one of his textbooks and that homeostasis was mentioned—

even in a botany book! So he was then ready to concede that it might just be something worth discussing with students.

Part of the reason we were having trouble was that we were using the word homeostasis differently. The definition he was assuming was close to that of Cannon: homeostasis as a set of processes to maintain a steady state in the *milieu intérieur* of an animal. I, on the other hand, was using the more extended definition of the term which has evolved over the years. Many biologists speak of homeostatic mechanisms in the maintenance of ecosystems, of ant colonies and of a physiological steady state in plants. It is this broadened definition of homeostasis which, to me, makes this term so powerful and exciting. Throughout the living world there are mechanisms to create and maintain balance, from the molecular to the ecological level. I use the word, as many biologists do, to refer to all these mechanisms which tend toward balance, but my discussions with my colleagues reminded me that not only biologists have agreed upon this use of the term. It is a classic case of what Bernard described and a good example of the instability of word meanings.

The "Scientific Method"

Bernard's *An Introduction to the Study of Experimental Medicine* is a classic in the philosophy of science. Bernard is responsible for the formula for the "scientific method" with which we are so familiar. He states that in "experimental practice," the first step is to "note a fact" (or as we would say, make an observation), then "apropos of this fact, an idea is born" (a hypothesis). "In the light of this idea, he [the scientist] reasons, devises an experiment, imagines and brings to pass its material conditions." From this experiment, new phenomena result which must then be reconciled with the scientist's original idea, and so on. "The mind of the scientist is placed between two observations. One is the starting point for reasoning and the other serves as its conclusion."

This is very much like the standard rendition of the scientific method found in many introductory science texts today. But what this rendition lacks is all of the explanations and qualifications Bernard gives after he has outlined the method. For example, while he states that an idea is often triggered by a fact or hypothesis, he also writes that ideas may indeed come first, that "intuition or feeling begets the experimental." Reading Bernard is a good reminder of how difficult it is even for a brilliant scientist to put into words exactly what is involved in doing science. It is such a rich and varied experience that words can only relate the simpler and more straightforward parts.

If you are really interested in the ins and outs of how Bernard actually worked, you might want to read Frederic Lawrence Holmes's (1974) *Claude Bernard and Animal Chemistry: The Emergence of a Scientist*. This is a weighty tome which deals with only six years of Bernard's career, the early years when he was studying the digestive system. This book is long and rather difficult, but it's intriguing to see how Holmes reconstructs Bernard's sequence of experiments in the context of the other work being done at the time. It is a nice example of how a historian of science can recreate the intellectual atmosphere in which a great scientist worked.

The Wisdom of the Body

In my tour of Walter Cannon's work, I read *The Wisdom of the Body* (1932) which he wrote toward the end of his career as an overview of what homeostasis had come to mean to him. He begins by stressing that the human body is made of very unstable material, and it maintains stability through rapid physiological response to stimuli which blunt destabilizing effects. He reviews how the body adjusts to temperature extremes, water deprivation, emotional stress, etc. and ends by discussing how the principle of homeostasis would be valuable in the development of more stable political systems. This might seem a long way from Cannon's physiological research, but he is writing in 1932 at a time of great economic and political instability. It was tempting for him to apply the "wisdom" of bodily processes to the political situation. This was particularly apropos for Cannon because throughout his career, while actively doing research, he was also involved in the administrative and political end of science.

The multiple facets of his career come through in a biography of Cannon by Benison, Barger and Wolfe (1987). It covers the first half of his life and is to be followed by a second volume which hasn't appeared yet. Though they do discuss his research, his biographers cover all aspects of his life, from the family farm where he relaxed with his children to the work he did in building the physiology department at Harvard Medical School. They go into the background of the school and all its leading figures of the time. They also discuss in detail the antivivisection movement and Cannon's effort to combat it. This type of book reminds us that a scientist is usually more than just a scientist. He or she is a human being with interests beyond research, some involving family and others more closely related to research work in the case of administrative obligations, political commitments or social causes.

Oxford & Cambridge

In my tour of physiology, I did some geographical traveling to Great Britain which has a long history of great work in physiology. The early part of this history is recounted in Robert Frank's (1980) *Harvey and the Oxford Physiologists*, which covers the origins of Harvey's work on circulation and then goes on to discuss the group of younger physiologists who clustered in Oxford and whose work grew out of Harvey's. Frank has done a great deal of research on this period, when the Royal Society was founded and when modern science bloomed in England. He discusses the work of the members of this group, how they influenced each other and how their research developed over the years. They experimented on the chemical composition of the air, tried to figure out the function of the lungs and even attempted blood transfusions.

At the time, the later demarcations among the sciences were unknown. Robert Hooke, for example, examined biological material with a microscope, participated in dissections and also helped Robert Boyle with his air pump experiments. It was an exciting time; these men were interested in all kinds of explorations of the world around them. Frank does a very good job of describing their work and the times in which they lived. His book is a good example of how a historian of science can put the research of a time in context so it is seen to make sense in terms of the knowledge and culture of the time, rather than seen only in the light of later work.

After this book, I jumped to the 19th century and to Cambridge University with Gerald Geison's (1978) *Michael Foster and the Cambridge School of Physiology*. Here again is a study not just of individual research, but of the intellectual climate in which it was done.

Geison argues convincingly that, while Foster himself did not do much original work beyond his early studies on the vertebrate heartbeat, he was nonetheless responsible for a revitalization of physiological research in Great Britain. Geison describes the sorry state of such research before Foster's time and compares it to the flourishing work in physiology going on in France with Bernard and in Germany with Hermann Helmholtz, Carl Ludwig and others.

Foster was able to change this picture because of the generous support he received from Cambridge University and because of his skill in publicizing the work of his department. This was done first through a journal he established (in 1873) and edited called *Studies from the Physiological Laboratory in the University of Cambridge*. This was followed in 1878 by the *Journal of Physiology* which he also founded and edited. Indirectly, he promoted his department through his famous *Textbook of Physiology* which first appeared in 1877 and went through six editions. His writing skills were also evident in his biography of Claude Bernard and his book of lectures on the history of physiology.

Foster aided the development of physiology in Britain as an active member of a number of science organizations. He was biological secretary of the Royal Society for 22 years. He played an important role in the International Physiological Congresses, was instrumental in the founding of the British Physiological Society in 1876 and was president of the British Association for the Advancement of Science in 1899. He also furthered the cause of science as a member of Parliament for six years. Geison's biography makes it clear that a man can make an important contribution to the advancement of a science in other ways besides original research. Science requires not only brilliant minds but those with an organizational bent, and Foster is a preeminent example of the latter.

In 1976, the British Physiological Society celebrated its centenary with a volume titled *The Pursuit of Nature: Informal Essays on the History of Physiology* (Hodgkin et al. 1977). The research described here indicates that Foster's work in the development of British physiological research was still bearing fruit a hundred years later. Though these essays are labeled "informal," they do contain quite a bit of technical information about such work as that of Alan Hodgkin on the nerve impulse, Andrew Huxley on the neuromuscular junction and W.A.H. Rushton on the physiology of vision. The papers are, however, more informal than most journal articles in that the authors describe some of the difficulties they encountered and give their thoughts on the process of research.

Rushton writes of being "seduced" by the problem of color vision, and he makes the observation about communication in science that:

> *Whenever an investigator studies complex records for a long time, bumps and other features begin to declare themselves first as distinct personalities, and later as old friends. So he will recognize them like his friends in a crowd but cannot say enough about them for* me *to recognize them without more intercourse with them than I am generally disposed to give.*

Andrew Huxley warns "against the invincible attraction of theories which simplify and unify seductively." And at the beginning of his essay, Hodgkin argues for the importance of this kind of informal review because "the record of published papers conveys an impression of directness and planning which does not at all coincide with the actual sequence of events." All the essays in this book provide insights which wouldn't be found in the usual scientific literature. They make a nice contribution to the historical record about physiological research.

Aspects of Physiology

When I took a graduate course in physiology, I was struck by the way physiological control mechanisms develop both pre- and postnatally. I've just revisited this aspect of physiology in reading E.F. Adolph's (1968) *Origins of Physiological Regulation*. Adolph sees two levels of regulation: intrinsic, meaning imposed and controlled by mechanisms within the body itself, and extrinsic, meaning affected by external conditions. Usually, the intrinsic controls develop before the system in question is sensitive to extrinsic factors. For example, heart rate is controlled by pacemakers within the heart tissue. Left to themselves, they would stimulate the heart to beat at a certain rate, but as the heart tissue matures, it becomes sensitive to nerve messages which, in turn, are influenced by such extrinsic factors as the oxygen content of the air and the body's rate of activity.

An interesting book on physiology that I remember from my student days is Knut Schmidt-Nielsen's (1972) *How Animals Work*. This little volume examines physiological adaptations to extreme environmental conditions: how a kangaroo rat lives in the desert without ever drinking water; how a whale swims around in cold water without losing a lot of heat through its flippers; how birds inhale sufficient oxygen to provide energy for flight muscles. Schmidt-Nielsen also explains why panting helps keep dogs cool and why you have to be careful how much LSD you give an elephant (remember, this book was written in 1972). I recall that this book was very useful to me in graduate school because it contains such good explanations of countercurrent exchangers and countercurrent multipliers. I find both these mechanisms fascinating, but hardly easy to grasp. Schmidt-Nielsen explains them in a patient, but interesting way—something you rarely see in textbook explanations.

A book that wasn't around when I was in school, but one I could have used is N. Mrosovsky's (1990) *Rheostasis*. He begins by noting that while Bernard focused on the constancy of the *milieu intérieur*, Cannon saw that constancy as the result of the dynamic processes of homeostasis. It is Mrosovsky's contention that while homeostatic mechanisms are indeed important in maintaining the body's internal environment, they are hardly the only mechanisms involved, and the concept of how the body maintains its stable environment has to be extended beyond the negative feedback aspect of homeostasis. He gives this extended concept the name rheostasis and defines it as "the condition or state in which homeostatic defenses are present, but over time there is a change in the regulated level." For example, there are homeostatic controls over the calcium level in the bone, so it is maintained within narrow limits. But when a deer is growing antlers, or a hen is laying eggs, the "set point" for the calcium level is higher, so the bone can serve more effectively as a calcium reservoir. These are cases of what Mrosovsky calls programmed rheostasis, with other examples being body weight cycles in hibernators and sex hormone levels in seasonal breeders. Examples of reactive rheostasis, on the other hand, would include fever and the shut down of the reproductive system with weight loss.

Rheostasis points to the flexibility of the body in dealing with changing

conditions. While homeostasis emphasizes constancy, rheostasis points to the fact that constancy is not always desirable or possible, and that the body has ways to deal with these situations too. Rather than weakening the idea that the body is a beautifully stable system, rheostasis actually strengthens that idea by emphasizing the variety of stresses that the body can respond to and withstand.

Visiting the Kidney

One pleasant side tour I took on my travels in physiology was to the kidney. This might not seem like a great place to spend time, but Homer Smith (1953) manages to make it a fascinating place in *From Fish to Philosopher*. This is, quite simply, an evolutionary history of the vertebrate kidney. Smith starts at the very beginning, with the development of the solar system and of the planet Earth. Some of the material in this and later chapters is a little dated, but still very worthwhile reading because Smith has the gift of making his story both interesting and understandable.

After presenting the history of the Earth, Smith introduces the principles of evolution and of kidney function. In the remainder of the book, he traces the evolution of vertebrates, and how, at each step of that evolution, the structures and functions of the kidney changed in response to new demands. After reading this book, I have a new appreciation for the problems of waste disposal and water balance which the kidney deals with not only in land mammals, but in fresh and saltwater fish, amphibians and reptiles. The kidney has never been one of my favorite organs, but between Schmidt-Nielsen's explanation of its countercurrent exchange system and Smith's description of its evolution, I have developed a new respect for, and interest in, this organ. In fact, my tour of physiology has given me a new appreciation for this whole area of biology. It makes me a little sorry that I hadn't revisited it sooner.

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