Basic medical physiology: the whole is more than the sum of its parts

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Rosenberg, Edith, Henry Brown, Donald Jackson, and Keith Cooper. Basic medical physiology: the whole is more than the sum of its parts. Am. J. Physiol. 261 (Adv. Physiol. Educ. 6): S30-S33, 1991.—In this article we examine the role of basic medical physiology in medical school education. We discuss the historical background, courses in this subject, and methods of teaching it. We conclude that the teaching of medical physiology should emphasize the study of organ systems and of the intact body. The techniques should emphasize meticulous observation, the posing of hypotheses, and the subsequent testing of the hypotheses, i.e., the use of the method used successfully in research. Students should learn the power of the experimental approach and to appreciate the immense variability possible in responses in complex organisms. They should also learn that principles of statistical probability applied logically can detect important differences in data that may be obscured by this variability. They should learn that there are no rigid answers when studying an individual and that they must continue to learn throughout their lives.

The practice of medicine depends on the assessment of bodily function, and medical students must learn how to determine to what extent a patient's function differs from normal physiology. Physiology, the study of normal function, is built on structural, biophysical, and biochemical principles that can be examined at the cellular, subcellular, and organ systems level. How these principles at lower levels of organization interact to affect the intact body can, however, only be determined by studying the whole organism. Classical physiologists such as William Harvey in the seventeenth century, Claude Bernard in the nineteenth century, and Walter Cannon in the twentieth century did just this. They tested their hypotheses by experimentation on live animals as well as on people. The success of this experimental approach led to the establishment of separate departments of physiology in US medical schools late in the nineteenth century and became part of the training of physicians. Students so trained went on to apply their understanding to clinical situations, e.g., the management of acid-base problems in diabetics, electrolyte problems in renal failure, and the use of hypothermia in surgery. Some of them continued the experimental approach both in the laboratory and in the clinics and enormously advanced our understanding of the cardiovascular, renal, and pulmonary systems. All learned that despite considerable variability in biological responses between individuals, disciplined experimentation led to a better understanding of any one individual's reactions.

Society's demand that health maintenance and disease prevention be emphasized in the practice of medicine increases the need for every physician to determine whether a patient coming for treatment is healthy. The physician must decide by examining the whole person whether bodily function is normal, or if not, how and to what extent it differs from normal. Hence it is necessary to teach how normal bodily function can be assessed in the whole complex organism.

While there has been considerable growth in the last 40 years in the number of working physiologists, the increase in the number of investigators who study physiological mechanisms at the cellular and subcellular level has been exponential. This has led to the staffing of many basic science departments with faculty knowledgeable about physiology primarily at those levels. Physiological principles are now taught in most medical schools in anatomy (particularly histology), microbiology, biochemistry, and pharmacology departments among others. This is all to the good. However, most of the processes examined in depth are those that faculty members understand best because they do research on them, i.e., phenomena at cellular and subcellular levels. Each human body contains 100,000 billion cells (J. Engelberg, personal communication), each with a life of its own, and extrapolation of findings at the cellular level to the intact body are not always meaningful because the whole is more than the sum of its parts. Moreover, advances in genetics and biochemistry will make the manipulation of living organisms more and more common. Because a single gene change may profoundly alter function at every level of organization, it is imperative that the physicians we train are equipped to evaluate function in the whole intact organism. Some physicians will be among the scientists evaluating individual attempts at genetic engineering, but all must be aware of the kind of problem that can arise so that serious medical and social problems can be minimized. Our concern about these
matters led to a symposium held at the Federation of American Societies for Experimental Biology meeting in 1990. This paper is the result of the presentations and discussions at that symposium.

Basic medical physiology courses must emphasize the application of knowledge of physiological principles to the study of the whole body and to the determination of whether the intact organism is "normal." The healthy body maintains a relatively constant environment for the billions of cells within it so that they can produce energy and carry out their specialized functions. It does so by balancing the intake of what it requires from its surroundings (Fig. 1) and excreting waste products, i.e., it produces a dynamic equilibrium called the steady state. A few variables such as osmotic pressure and the plasma concentrations of certain simple ions are maintained within a narrow range of values throughout life. Other parameters are controlled at values that depend on activity. For example, blood glucose concentration varies in relation to food intake, blood pressure stabilizes at a higher value during steady-state exercise than at rest, and blood oxygen pressure is lower during sleep than in the waking state. Any substance that enters or leaves the body in the lungs has a concentration that fluctuates in arterial blood with each breath as well as with each heart beat (Fig. 2). It is the mean of these values over a period of several minutes that is maintained constant. Observations to determine whether a steady state is established must, therefore, extend over periods of at least several minutes. Many controlled variables have circadian rhythms that vary throughout the day, e.g., various hormone levels. Cortisol rises throughout the night and falls continuously throughout the day. On the other hand, growth hormone levels reach a peak after only a few hours of darkness and fall to a relatively stable value for the entire period of daylight. The time of day will also affect the response of the body to stimuli or interventions. To cite just one well-known example, the response to a standard dose of insulin (when glucose level is controlled) is significantly greater at 8 A.M. than at 5 P.M. A physician must be aware of the possibility that the time of day as well as calendar time affects every steady-state measurement examined. Improved technology has made it possible to measure and record many physiological variables repeatedly over long periods of time and to document many more examples of chronobiological patterns. In major cities there are now laboratories that study sleep disorders, and we expect them to become a rich source of data. It may be possible for some medical schools to collaborate with such laboratories and arrange that medical students can observe how data are generated and how mean steady-state values are calculated. However, because the acquisition of chronobiological data is a slow process, the physicians we train now must be able to critically evaluate the significance of new data obtained on appropriate populations throughout their lives.

Because the time available for teaching the basics of medical physiology in medical school is limited, it is important to concentrate on our primary instructional objective. This is to enable our graduates to apply what they have learned to evaluate the state of patients they see, i.e., to determine to what extent a patient's bodily function differs from that "predicted" for that patient. The scientific approach to diagnosis begins with very extensive meticulous observations of the individual studied and the environmental conditions of the examination. Measurements of various parameters are then compared with the normal values for the individual under the conditions of the study. An intervention follows, and the individual's response is compared with predictions made on the basis of established physiological principles. This technique, called experimental medicine by Claude Bernard, was used on other mammals as well as on humans to establish the fundamental principles of normal function of the organ systems and the whole body. The greater the use of this technique in teaching established principles, the more likely are our students to apply it later in life. It has been shown that medical students taught physiology in this manner performed better on their qualifying examinations than a comparable group of students whose studies had been directed primarily to the memorization required to pass standard multiple-
choice exams (3). The method has the added advantage of being enjoyed by the students because it permits them to discover information on their own.

The past 40 years have seen rapid growth in the number of investigations of physiological mechanisms in mammals and other organisms. The evidence that essentially the same fundamental processes occur in many very different organisms is now overwhelming, and this supports the use of lower vertebrates in physiology laboratories for students. Hands-on experimental learning of fundamental physiological processes is ideally taught in undergraduate courses so that students arrive at medical school with a conceptual framework of generic fundamental processes. However, it is our impression that the contemporary trend in undergraduate education is not in the direction of organ system level courses. For this reason, hands-on experiments on lower vertebrates are probably essential in a basic medical physiology course. The classic experiments on the frog nerve-muscle preparation (2) and on frog and turtle hearts (4) are invaluable. When studying complex systems, it is helpful to push them to their limits so as to provide dramatic clear-cut responses. This is an additional use of student laboratories. However, the time and money that can be spent on such laboratories is limited. For this reason, the use of lecture examples from comparative physiology to illustrate dramatic clear-cut responses of physiological systems under extreme stresses is helpful. For example, desert rodents have kidneys with concentrating mechanisms that produce a urine of extremely high osmotic pressure that enables them to conserve water. Giraffes have a central blood pressure higher than that of most mammals that enables them to overcome the hydrostatic pressure of blood in their necks. When they lower their heads to drink, cerebral circulation is protected from an excessively high hydrostatic pressure by the opening of a shunt at the base of the brain. The presentation of such examples dramatically reinforces important concepts while, at the same time, stressing biological diversity.

Despite the enormous increase in research and the resultant understanding of physiological processes in recent years, our understanding of function at the organizational level of the organ systems and the whole body is still based on a few physical and chemical laws established 100 years ago. It may be helpful to point out to students that the number of scientific concepts they learn in a basic physiology course is really very small. The understanding of the function of various organ systems depends on the repeated application of these concepts using varying vocabulary according to the system studied. Three general themes with broad applicability in physiology are as follows.

Conservation of mass and energy. Living organisms, including the human body, obey the laws of conservation of mass and energy, and these are applied when we consider how the body maintains constant weight, temperature, blood volume, etc. The law of conservation of mass, differently stated, is used to measure cardiac output by Fick's principle or by the dilution method. In another form (the clearance equation) it is used for the indirect measurement of kidney function.

Transport or flow relationships. The transport that is most relevant at the level of the organ systems and the whole body is macroscopic transport over relatively long time intervals. A simple formula can be used to describe the mass movement of substances, e.g., air, blood, lymph, or urine as well as the movement of molecules (diffusion)

\[ \dot{V} = \frac{E_1 - E_2}{R} \]

where \( \dot{V} \) is volume per minute; \( E_1 - E_2 \) equals the difference in potential energy, \( E \), between the place where flow begins and where it ends; and \( R \) is the resistance to flow. This simple relation between three interrelated variables is probably familiar to most students as Ohm's law. It can be repeatedly applied to physiological problems to calculate the third variable when two are measured. In the intact body, transport frequently occurs across membranes from one compartment to another. Under these conditions the solubility of the substance transported as well as the osmolarity of the fluids in adjoining compartments must be considered in addition to the simple Ohm's law relation. Students should be introduced to simple compartmental analysis either on paper or on a computer and become accustomed to calculating the quantities of substances transported.

Control and regulation of variables. To understand how the regulating systems produce a steady state in the intact body, physiologists study isolated systems under controlled conditions. The more rigidly controlled the boundaries of the system studied, the more precise the predictions about it. We borrow the concept of feedback loops from the engineers. In the simplest systems a quantity is maintained at a controlled value, \( C \), by a detector that both senses a deviation from this value and activates an effector to return the system to the controlled value. This is called a negative feedback loop. There are many in the body, e.g., the body's maintenance of normal blood pressure at different postures depends on the baroreceptors in the carotid sinus and aortic arch (1). However, the body also contains positive feedback systems. In positive feedback an increase in the controlled variable is sensed, and this causes the effector to further increase \( C \), an unstable situation. In the body an increase in a controlled quantity can stimulate other feedback loops. In fact, every controlled variable we observe in the intact body is probably regulated by a complex series of positive and negative feedback loops. The interactions between various feedback loops are not completely known for any system in the body nor do we, in general, know all the feedback loops that may affect a given measurable variable. For this reason it is essential that all predictions based on what is learned in controlled experiments on isolated systems be validated by experiments on the whole body. However, the use of the same simple models, as illustrated in the example above, to different systems in the body should facilitate the understanding of organ system function and decrease the need to memorize facts.

The study of complex biological systems and especially of the whole body can be done by using the students themselves or experimental animals. Simulated case his-
Physiologists must teach study of whole organism

Stories are useful in reinforcing this portion of basic medical physiology courses, but they do not provide the training in meticulous observation that laboratory experience provides. By using experimentation, students will discover that there is considerable variability between individuals. The variability is due to the fact that our knowledge of how physiological mechanisms in the intact body produce the controlled variables that can be measured is still very rudimentary and constantly evolving. This problem may be overcome, in part, by teaching the students to use basic statistical principles along with logic. They will then learn to combine good judgment with statistical analysis to decide what part of the variable data is important.

Perhaps the most important lesson that can be taught in medical physiology is this: there are no rigid answers when studying an individual. A good understanding of established principles, however, enables one to ask the right questions to obtain the best possible understanding of the functioning of one’s subject. This approach to the study of a complex system, the asking of a series of questions, each dependent on meticulous observation and the response of the system to the previous question, has been used in research with great success for centuries. Ideally, students will come to appreciate its power when studying the whole individual’s normal function and will later apply it to make their diagnoses. At the very least, they should learn to keep an open mind and continue learning throughout their lives.

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