Ernest Henry Starling as an officer during World War I. Attributed to Dr. Ralph Colp, Jr. Originally published in the *Annals of Internal Medicine*, 57, Supplement 2, 1962.

Ernest Henry Starling
medical educator

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Medical education in North America changed dramatically during the late nineteenth and early twentieth centuries. Although American medical schools had begun to establish ties with major universities in the 1870s,[1] few physicians in this country had any meaningful exposure to high quality basic science. According to William G. Rothstein,[2] there were 65 medical schools in 1860, 75 in 1870, 100 in 1880, and 160 in 1900; in fact, 457 medical schools actually opened during the nineteenth century, but many were short-lived and about 50 were fraudulent.[3] Admission standards shortly after the Civil War were often nonexistent[1] and most medical schools did not require a high school diploma.[2] The standard course of instruction consisted of two identical four-month series of lectures, the second term repeating the first,[1] and examinations were usually brief, casual and perfunctory. The Johns Hopkins Medical School, which opened in 1893, "became the single most potent influence ever for the dissemination of scientific medical education in America."[4p75] and provided a model for the modern academic health center. With its solid link to the parent university, Johns Hopkins exerted a strong influence on Abraham Flexner, who was commissioned by the Carnegie Foundation for the Advancement of Teaching to review the state of medical education in the United States and Canada. During 1909 and 1910, Flexner visited all of the 155 medical schools then open in the two countries and wrote a scathing report that exposed the uneven standards of American medical education. Described as "a highly explosive document,"[3p980] the Flexner report detailed the sorry state of most American medical schools, which had "multiplied without restraint, now by fission, now by sheer spontaneous generation."[5] The Flexner report forced the closure of many weaker schools and emphasized the role of the university in medical education. An important corollary to its recommendations was strengthening of the ties between clinical training and the basic sciences that were begining to flower at the turn of the twentieth century.

The alliance between medical schools and universities begun in the nineteenth and early twentieth centuries exposed American medical students to the high quality basic science that contributed to a century of discovery that has armed the modern physician with a solid understanding of disease. Today, as medicine enters the twenty-first century, we are witnessing a new revolution: the increasing impact of molecular biology on clinical practice. In seeking how best to familiarize students with a rapidly changing basic science in preparation for a career in medicine, it is useful to look back to the turmoil in medical education a century ago. This article reviews the contributions of Ernest Henry Starling, a leading British physiologist during the first decades of the twentieth century, who was a powerful advocate for strengthening the ties between medical education and university-based science.

English medical schools in 1900— good clinical training, poor science

British medical schools at the beginning of the twentieth century experienced tensions similar to those in America, although medical education in the two countries had developed differently. Proprietary medical schools, which before 1910 had dominated medical education in the United States, had lost their importance in nineteenth-century Britain, where hospital-based bedside teaching gained momentum.[6] In contrast to the situation in the United States and Canada, British medical schools were effectively regulated; in 1910 the London correspondent for *JAMA* wrote:

> British medical education is conducted by a large number of diverse bodies—17 universities, 7 Royal corporations and 2 other diploma-granting bodies [that] are controlled by a coordinating authority, the General Council of Medical Education and Registration . . . although the standard of examination varies a good deal among the different educational bodies, there is none which is not respectable or which is comparable with those bodies in the United States and Canada which have been censured in Mr. Flexner's recent report.[7]

Although effective in clinical training, few British medical schools at that time provided excellent education in the basic sciences. Outside lecturers were generally hired to teach subjects like botany and chemistry, often without careful vetting by the clinical faculty. Furthermore, the teaching of basic science was generally regarded as a distraction from patient care, the central task of the hospitals. Medical students served as unpaid workers who dressed wounds, did minor surgery, and gave anesthetics.[6] It is easy to understand how the increasing demands on student time imposed by such growing sciences as anatomy, pathology, bacteriology, and physiology began to unravel the accommodation between hospitals and medical schools. The high cost of maintaining laboratories for basic science research and teaching further increased tensions between clinical practice and medical education.

Battles among medical practitioners, medical schools, and universities in Britain at the end of the nineteenth century are exemplified in the failed efforts of a Royal Commission that, in 1888, examined the granting of medical degrees by the University of London. A petition seeking to place representatives from the Royal College of Physicians of London and the Royal College of Surgeons of England on the governing body of the University of London medical school was rejected "almost unceremonially."[8] A compromise was then drawn up to develop a university-based program for medical education. Although initially accepted by the Royal Colleges, the University of London, and London's major medical schools, this compromise was "finally and utterly damned"[8] when a convocation of the University of London voted overwhelmingly to reject the plan. The resulting fiasco led to the appointment of a new Royal Commission on University Education, chaired by Viscount Haldane, which first met in 1911.

Starling, who appeared before the Haldane Commission, gave lucid and forceful testimony that established his credentials as a leading advocate for including university-based science in the medical curriculum. Best known today for his description of the opposing forces exerted by hydrostatic and oncotic pressure in controlling fluid movements across the capillary,[9] the "Law of the Heart" that bears his name,[10] and the discovery that chemical messengers circulate in the blood,[11] Starling also had a keen appreciation of the importance of basic science in physician training.

Ernest Henry Starling, the clinician's physiologist

Starling was born in London in 1866,[12] when the focus of British education was on the classics. He did not begin to study the natural sciences until 1882, after he entered Guy's Hospital Medical School. In the summer of 1885, because of his outstanding scholarship, he was offered a chance to study in Germany, which then had surpassed Britain in providing opportunities to learn basic science. After examining the chemistry of digestion in Heidelberg, Starling returned to London where, in 1887, while still a student, he became a demonstrator in physiology at Guy's. He received his qualifying degree (M.B., Lond.) in 1889, and began a lifelong collaboration with W. M. Bayliss of University College, one of Britain's leading physiologists. Starling became Jodrell Professor of Physiology at University College in 1899, where, between 1910 and 1914, he carried out his seminal research on the regulation of the work of the heart.

Starling's research was interrupted by World War I. He tried to enlist as a foot soldier, but was made a captain and assigned to head research on antigas warfare.[12] Partly because of his prickly personality and habit of speaking what was on his mind—a poor fit with military culture—Starling was promoted and transferred to a functionless position in Greece. Quickly tiring of this, he retired from the Army. On his return to London, he became chairman of the Special Investigation Committee on Surgical Shock and Allied Conditions of the Medical Research Committee, which later evolved into the Medical Research Council.[12] After the war ended, Starling published several papers describing the food crises in Europe, along with analyses of renal function and the cardiovascular response to exercise.

Starling's success as a scientist reflected both the creativity of his research and his ability to communicate the practical significance of his findings to his clinical colleagues. As noted by Carleton B. Chapman, Starling was the "clinician's physiologist."[12] Starling's understanding of the clinical relevance of his scientific discoveries probably accounts for the credit he received for describing the role of ventricular volume in regulating the work of the heart. Although he was not the first to describe this relationship,[13] his influence explains why it is generally referred to as "Starling's Law of the Heart." The rapid acceptance of Starling's work by the medical establishment in Britain also reflected the impact of World War I, when British physiology and medicine were cut off from the stronger science of Germany. World War I also enhanced clinical interest in therapeutics at a time when the British pharmaceutical industry was bolstered by the medical demands of the war and weakening of international trade agreements.[14]

During the nineteenth and early twentieth centuries, students who sought to learn scientific aspects of medicine generally studied in continental Europe. Most, like Starling, worked in one of the first-class German academic departments. In Britain, medical science was usually taught in financially strapped facilities. Although Sir Michael Foster at Cambridge, Sir John Burdon-Sanderson at Oxford, and T. H. Huxley at University College in London established excellent physiology departments, few British medical students had contact with highly trained scientists.[15] The British system did develop outstanding clinical investigators, including Sir James Mackenzie and Sir Thomas Lewis, but few British medical students and physicians at the beginning of the twentieth century were encouraged to participate in clinical research and there were no university-based academic clinical departments.[14] Contrasting British and German medicine immediately before World War I, Flexner wrote:

> German medicine has taken up the physiological point of view. The German clinician is a trained, often a productive physiologist. English physiology has not yet conquered English medicine. With a few brilliant exceptions . . . the English surgeon and clinician have done little to apply physiological method and technique to clinical or surgical procedures.[16]

Changing English medical schools from trade schools to science based—a challenge

Starling noted the poor scientific background of British leadership in 1914 when he described "The astounding and disastrous ignorance of the most elementary scientific facts displayed by members of the Government and administration alike in the early days of [World War I]," adding: "The Government adopted the traditional method of poulticing the sore place in public opinion by the appointment of two committees."[17p365] In his testimony to the Royal Commission on University Education in London, chaired by Viscount Haldane, Starling noted that London's medical schools, having originated from an apprenticeship and pupilage system, had no effective relationships with the universities.[18] Although the medical schools had established informal connections with London hospitals in the mid-nineteenth century to provide instruction in such sciences as chemistry and physics, these and other preclinical subjects were initially taught by junior members of the medical staff. Starling characterized the London medical schools of that time as "trade schools." He observed:

> The teachers of science with whom [the medical student] first comes in immediate contact, in many cases not of marked ability, are in all cases in a position of inferiority to the clinical staff, whose servants they are. The work of these scientific teachers is to get the students under them as quickly as possible through the various Preliminary and Intermediate examinations, so that they may be passed on to the clinical work of the wards. The scientific teacher is, in fact, only useful in so far as he passes his students. The whole idea of the first three years, the most impressionable time of the student's career, is not educational but professional.[18p195]

Noting that basic science teaching in these schools was intended mainly to enable students to pass their examinations, Starling observed: "The student's interest must therefore be continually restricted to such facts as can be reproduced in an examination, so that teaching is stereotyped and originality suppressed."[18p195]

Starling recommended that universities be given "direct control of the first two and a half years or three years of the medical curriculum," which, he said, would expose students to the "University spirit," which he described as

> not simply diagnosing the patient and deciding what we can do for him in order to earn our fee, but what we can get out of this case in order to do better next time; how we can get some knowledge out of this patient in order to have more power when we have another man in the same condition. This is the University spirit, and that is what I think you may improve and increase by having a University Professor holding one of the wards and having the clinical laboratories under his charge in a big general hospital.[18p207]

Starling recognized the value of teachers who were trained in both the basic sciences and clinical medicine, noting:

> The men who should be now in a position to be University Professors of Medicine have not had the training; they have had to get down into the rut of practice at once, and they have not served their apprenticeship in laboratories and in research. You will find many good clinical men say, "If we had two excellently trained scientific men with us in the wards we could do much for the advancement of Medicine. These men, being trained, would know all the ordinary

laboratory methods, and we can suggest themes for them to work on." This is not the case. Until a man has actually done research he does not know what will get through the door of the laboratory. Clinical men will come to the laboratory men and will say, "I want you to tell me this or that," and they do not understand that the question is not yet answerable. A man must have been brought up in working out problems in order to know what problem is soluble and what is insoluble at the present time.[18p207]

Starling's views had a major impact on the report of the Haldane Commission, which in its final recommendations cited large sections of his testimony, including the following:

> in order to raise the study of clinical medicine to the level of university education, co-operation is necessary between the men who are working at the science of medicine and those who are more especially engaged in the pursuit of the ancillary sciences . . . The real end is to raise the teaching and the study of all subjects which bear upon medical science to a university level, and to provide for them in the Faculty of Medicine in as close proximity to each other as possible, so that there may be not only natural and easy communication between the professors of science and those of clinical medicine, but also reciprocal assistance in the investigation of problems which occur to either.[19p125]

The last sentence in this recommendation echoes Starling's earlier testimony that

> the younger physicians and surgeons should be making some use of the enormous mass of material for investigation which in the wards of the London hospitals is at the present time almost wasted. . . . The more immediate relation of the scientific work of the laboratories to the problems of the wards would tend to diffuse the scientific spirit among the staff and students to a much greater extent than can be effected when, as at the present time, the scientific men attached to the School are occupied in the solution of questions which seem to have, for the practical man, little or no bearing on the problems with which he is confronted.[18p199–200]

Although the work of the Haldane Commission was shelved during World War I, many of its recommendations were implemented over the following decade.[20]

Starling's commitment to improving medical education continued after the war when, in 1918, he criticized what he called the "incubus of the examination system."[21] His concerns were stimulated in part by a system that in the late nineteenth century "made it impossible for the average medical student with average ability and average diligence to attain the degree of M.D. in London [because] teachers of the highest rank [were required] to instruct their students according to schedules drawn up by others, often much less acquainted with the needs of the student."[7] Starling observed:

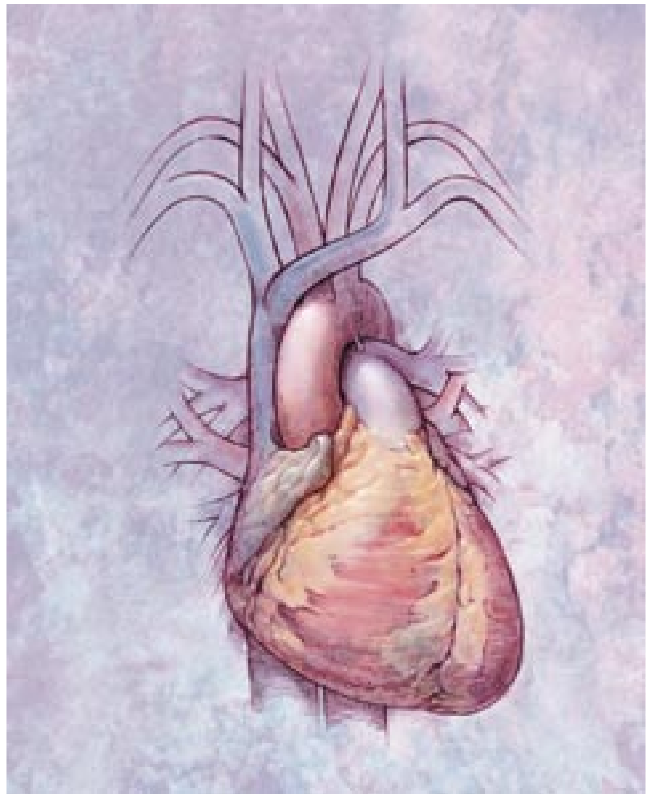
> The whole examination system is at variance with the spirit of university teaching; the latter has as its object the enlargement of the mental content of the individual, the broadening of his point of view, the training of his power to deal with new situations, and his familiarization with the avenues of new knowledge. An examination tests merely the student's power of acquisition; it determines whether he can retain for a few weeks or months a certain number of facts.[21p258]

Starling viewed cramming for tests as stifling the students' "spirit of curiosity in order to confine their whole attention to such facts that can be . . . presented in an examination." As a result, according to Starling, the curriculum becomes "overloaded and yet not full enough"[21p258] to impart to the student the "spirit of the subject and to lay a foundation for the student's future work."[21p259] Summarizing this dichotomy, Starling wrote:

> We do not want the medical man or student entering the wards to have at the tip of his tongue the properties and atomic weights of all of the elements, or to be prepared to give a historical account of the views concerning the origin of the heart beat. We do want, however, that the student shall have dipped so deeply into the sciences of chemistry and physiology that he has become imbued with the scientific spirit, and that he knows where to turn to refresh his knowledge on any matter germane to the problems which concern him in the wards.[21p259]

Overcoming tensions between clinical medicine and basic science

Today's explosive growth of basic science knowledge, which far exceeds anything imaginable during Starling's lifetime, is sometimes viewed as having increased the gap between basic research and clinical medicine. It is undeniable that the flood of information now coming from molecular biology makes it increasingly difficult to present the basic sciences to medical students. Much as inflating a balloon separates points on its surface, the current expansion of both basic and clinical knowledge tends to draw preclinical and bedside teaching away from one another. Consequences include difficulties in identifying teachers competent in both basic and clinical medicine, and the common complaint that medical students are taught basic science by professors who know little about the clinical problems relevant to their laboratory research, and clinical medicine by professors who know little about the basic science that can explain what is wrong with their patients. It can be argued, however, that although this expansion has made teaching more difficult, it has brought basic science closer to patient care. Support for this view is provided by examination of the interplay between scientific discovery and the management of heart failure.



Health, for the ancient Greeks and Romans, was generally viewed as a balance between opposing principles (the four humors); because blood was thought to contain the hot humor generated by the heart, bleeding was used to treat fevers. According to Hippocrates, pleural effusions occurred when phlegm (the cold humor) descended from the brain to the chest. Harvey's 1628 description of the circulation undermined Galen's views on the heart and led Vieussens to postulate that fluid accumulates in the chests of patients with mitral stenosis because blood flow through the lungs is slowed. However, knowledge of hemodynamics was to have little impact on patient care until the development of cardiac surgery more than three centuries later.

In the early nineteenth century, Claude Bernard challenged the then-prevalent view that health and disease are controlled by mysterious, unquantifiable "vitalistic" forces, suggesting instead that living organisms obey physical and chemical laws.[22] Thermodynamics, one set of these laws, provided a foundation for studies on the energetics of muscle contraction that dominated the work of cardiac physiologists during the late nineteenth and early twentieth centuries.[13] However physical chemistry made few contributions to patient care aside from reinforcing the view that heart failure should be treated with bed rest, a recommendation now recognized as often causing more harm than good. Starling's description of the "Law of the Heart," which related ventricular end-diastolic volume to the work of the heart,[10] returned the focus of cardiac research to hemodynamic physiology, which, following the introduction of cardiac catheterization in the 1940s, was to play a key role in the development of cardiac surgery.

The gap between bench and bedside closed further when biochemical changes in the myocardium were recognized to impair the pumping of the failing heart. For almost 50 years, most medical students had been taught erroneously that operation of the ventricle on the descending limb of the Starling Curve was a major cause of heart failure.[23] It was not until the 1950s that description of "families of Starling curves," which demonstrated the role of changing myocardial contractility, made it possible to show that contractility is depressed in acute heart failure. This quickly led to the use of β-adrenergic agonists, whose inotropic actions had also just been discovered, to treat cardiogenic shock.

Heart failure—more than a misshapen Starling curve

Subsequent efforts to understand the mechanisms that depress contractility in the failing heart, which took advantage of new understanding of the role of calcium in regulating cardiac contraction and relaxation, stimulated development of powerful inotropic drugs. As expected, these drugs caused an immediate improvement in hemodynamics. However, the view that heart failure is largely a hemodynamic disorder began to unravel in the 1990s, when several clinical trials had to be stopped because inotropic drugs, even though they improve symptoms, shortened survival.[24] Further challenges to the view that abnormal hemodynamics represent the central problem in heart failure came from trials that demonstrated that many vasodilators, which because of their energy-sparing effects had been introduced to "unload" the failing left ventricle, failed to improve prognosis; in fact, many vasodilators had adverse effects so serious as to require the premature termination of clinical trials.[24]

Explanations for these and other unexpected findings became possible when the focus of heart failure research returned to the deleterious effects of cardiac hypertrophy that had been recognized by the great clinician-pathologists of the

Ernest Henry Starling in the laboratory about 1925. Courtesy of Dr. Maurice Visscher. Originally published in the *Annals of Internal Medicine*, 57, Supplement 2, 1962.

nineteenth century.[25] By the late 1980s, of course, this research could draw on the emerging fields of molecular biology. A key observation, that among the vasodilators only converting enzyme (ACE) inhibitors, which block angiotensin II production, prolong survival, suggested that the ability of angiotensin II to stimulate proliferative (transcriptional) signaling might explain why this class of vasodilators slows progression. This and other evidence that the hypertrophic response to overload contributes to the poor prognosis in heart failure[24] promoted an interplay between clinical cardiology and molecular biology that has revolutionized treatment of this syndrome. Today, studies of transgenic mice showing that the same signal transduction pathways that mediate cardiac myocyte growth can also contribute to progression in heart failure[26] have virtually obliterated the gap between bench and bedside in heart failure research.

Although both basic research and clinical practice are becoming so complex that it is increasingly difficult for clinicians to understand molecular biologists and molecular biologists to understand clinicians, today's basic science is more relevant than ever to human disease. The science of the ancient Greeks and Romans, who viewed the heart as the source of the body's heat, neither explained heart failure nor aided in its treatment. Hemodynamics, while helping to understand pathophysiology and providing an indispensable foundation for cardiac surgery, contributed little to medical therapy for chronic heart failure. Understanding of myocardial contractility, along with appreciation of the biochemical basis of cardiac contraction, led to the introduction of the inotropic drugs that have become standard therapy for acute heart failure. However, in spite of short-term hemodynamic benefits, neither inotropes nor direct-acting vasodilators improve the poor long-term prognosis that has emerged as a major problem in chronic heart failure. Instead, the focus of therapy has shifted to efforts to ameliorate the maladaptive features of cardiac hypertrophy and, more recently, to attempts to stimulate cardiac myocyte proliferation. New knowledge of the signal transduction pathways that accelerate progression in heart failure can be expected to narrow further the gap between basic science and clinical medicine. Starling, although he could not have predicted how modern biology is helping to tailor therapy to pathophysiology, would not be surprised by the growing impact of basic science on clinical practice. This progress, after all, is an elegant example of the value of what he called the "University spirit."

Ernest Henry Starling's recognition of the importance of basic science as a foundation for understanding human disease is apparent when we examine the impact of his physiological

Starling, the educational idealist, of which there have been too few

research on clinical medicine: modern endocrinology is based on his discovery of circulating hormones, edema is understood in terms of his discovery of the opposing forces exerted by hydrostatic and oncotic pressure that control fluid movements across the capillary, and ventricular dilatation in acute pulmonary edema is among the manifestations of "Starling's Law of the Heart." In addition to his accomplishments as a scientist, Starling was an outspoken advocate for linking university science to medical education. By emphasizing the relevance of basic research to clinical practice and the importance of a solid grounding in university-based biomedical science—which Starling called the "University spirit"—he helped to lay the foundations for modern medicine. As summarized by Chapman:

> Starling on education is a grand, overwhelming phenomenon, vitally expressed and carrying great conviction; and as a working scientist he is considerably more convincing than many a platitudinous educator. . . . He wrote as an educational idealist of whom there have always been too few in the field.[12p34]

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