Acute coronary occlusion always results in death — or does it?

The observations of William T. Porter

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FREDRICK WILLIUS, a physician and historian of cardiology, claimed in 1945, "The achievement of scientific progress is irrevocably based on past experiences, not alone on the experience of one generation of scientists but rather on the numerous generations which have been predecessors." The recent introduction of thrombolytic therapy with intracoronary streptokinase for acute coronary occlusion has stimulated renewed interest in the consequences of acute obstruction of the coronary arteries.2-4 Although Pierre Chirac observed the effects of experimental ligation of the coronary arteries in a dog in 1698, there was little interest in this subject until the closing years of the 19th century.5 In 1893, William T. Porter, a young American physiologist, reported that experimental coronary occlusion in the dog was not always fatal. This observation contradicted the results of other investigators who claimed that ligation of the coronary arteries was followed by cardiac arrest in virtually all instances. The scope and sophistication of Porter's experiments on acute coronary occlusion, performed nearly a century ago, will surely surprise present day clinicians and investigators in the field. His thorough studies of the effects of acute coronary obstruction in experimental animals ultimately had a significant impact on clinical medicine. James B. Herrick's recognition of the clinical syndrome of acute myocardial infarction with survival in man can be traced, in part, to Porter's observations.

Porter was born in Plymouth, Ohio, in 1862.6,7 The son of a physician, he entered St. Louis Medical College in 1882. The year Porter matriculated the curriculum was extended from two to three years and laboratory demonstrations and experiments in physiology were introduced.8 Correspondence that has recently become available provides valuable insight into the genesis of Porter's interest in experimental physiology as well as the origin of his experiments on ligation of the coronary arteries.9 Porter's interest in physiology can be traced to Gustav Baumgarten, who had become professor of physiology at St. Louis Medical College in 1873. Baumgarten was born in Germany in 1837 and emigrated to St. Louis as an adolescent, where he graduated from high school and St. Louis Medical College. After graduation, Baumgarten returned to his native land for three years of postgraduate training. Although Germany would rapidly eclipse France as the world center of scientific medicine, Baumgarten was one of the first American medical graduates to study in Germany.10 As was the case with virtually all American medical professors in the 1870s, Baumgarten was primarily a medical practitioner who taught physiology part time. His reputation extended beyond St. Louis, however, and he was invited to be an original member of the Association of American Physicians when it was founded in 1886 by William Osler and other leading American physicians. Baumgarten attended the first meeting of the Association in June 1886. Other members present included the Philadelphia physician-scientists S. Weir Mitchell, William Pepper, Horatio C. Wood, and James Tyson, all from the University of Pennsylvania. Mitchell was a pioneering experimental physiologist and a trustee of the University of Pennsylvania.11 It is likely that Baumgarten arranged for his pupil Porter to work in the physiology laboratory of the University of Pennsylvania. The head of the laboratory at this time was Edward T. Reichert, a recent graduate of the University of Pennsylvania, who studied physiology in Berlin, Leipzig, and Geneva from 1882 to 1885.12

In 1887, at the age of twenty-four, Porter embarked on a career as a physiologist. Writing to Baumgarten from Philadelphia, he exclaimed that he was "begin-
ning to feel like a physiologist. . . . Fortunately I have full permission to work on my own lines and shall lean on others as little as possible. Experimental physiology is, it appears to me, very like many other things in this world, no amount of seeing other people work will make you competent to do the work yourself. So my plan is to have Dr. Kemp or Dr. Reichert do the experiment once, and after that to be at hand when I get into hot water, which will probably be rather often."13 At the University of Pennsylvania, Porter came into contact with several individuals who were familiar with modern techniques of experimental physiology. George Kemp had received a Ph.D. in biology at Johns Hopkins under H. Newell Martin, America’s leading physiologist. Porter also received encouragement from the University’s professor of chemistry, John Marshall, who advised him "to begin some original research immediately upon . . . return to St. L(ouis)."14

Baumgarten was obviously a major supporter of Porter’s interests in the scientific side of medicine. At the 1888 meeting of the Association of American Physicians, Baumgarten presented the results of his clinical observations in patients with cardiac arrhythmias.15 At this meeting Baumgarten heard William H. Draper, a New York physician-scientist, deliver his presidential address, "On the Relations of Scientific to Practical Medicine," in which the increasingly common theme of the need for specialization in science and in practice was put forth. Only a handful of Americans had devoted themselves to full-time careers in the basic medical sciences when Baumgarten heard Draper proclaim the value of, "... the independent cultivation of the science and the art (of medicine)."16 Baumgarten’s pupil Porter, while in Philadelphia, declared to his mentor, "I shall return home with a determination to devote my life, as far as possible, to scientific work."17 Porter recognized the obstacles to a scientific career and appealed to Baumgarten,

Will you let me take you into my confidence in respect to a ‘scheme’ which is very near to my heart? It is nothing more than the acquisition of a private laboratory, wherein I can carry on some original investigations. Now, surely, you will not condemn me as visionary until you hear all. There are two obstacles, 1. Lack of money. 2. Lack of time. . . . Such is my castle in Spain. I decline to believe it visionary. I am determined that this disembodied spirit shall eternally be a thing of flesh and blood, and very much alive. How, indeed, am I to do original work without a laboratory? While there are those who do not consider research to be the chief end of man, I trust that you will concede it to be a very prominent end.17

Porter was appointed assistant professor of physiology upon his return to St. Louis in the fall of 1887; the following year he succeeded his teacher Baumgarten as professor of physiology at St. Louis Medical College.

In the spring of 1889 Porter traveled abroad for a "studienreise" that would take him to a number of the leading medical and scientific institutions in Europe. This period of formal training in experimental physiology and related sciences was undoubtedly encouraged by Baumgarten and Porter’s Philadelphia teachers. Writing on Christmas day, 1889, from the Physiological Institute in Berlin, Porter informed Baumgarten he was writing a letter to the president of St. Louis Medical College "containing proposals for an extension of the physiological work. . . . The object to be gained is the establishment of a laboratory for advanced work in physiology, a laboratory in which research work shall be systemically pursued and encouraged. The plan is entirely practicable and I am sure it can be made to pay. Such an aim is as dear to you as to me and I do not fear that you will refuse your active support."18 Porter viewed the establishment of a program of original research at the medical school as a significant component of the larger movement to elevate the standard of medical education in America. As he witnessed firsthand the dramatic advances in medicine facilitated by the structure of the German university system with its emphasis on original research and specialization, Porter’s commitment to a career as a professional physiologist deepened. At the beginning of his second year abroad he wrote to Baumgarten

There can be no question that I can be more useful in St. Louis as a physiologist than as a practitioner. The making of a physiological institute in our community is worth living for. It is not possible to succeed in such an undertaking and to succeed in practice at the same time. To practice medicine and experimental physiology is to be an amateur in two things. I must make a choice. . . . Physiology means absolute poverty for some years, comparative poverty during life. Practice means giving up the best thing in sight for the sake of material comforts. These are the horns of the dilemma. I believe that I have chosen wisely.19

Porter returned to Europe in the summer of 1891. He went to the Physiological Institute at the University of Breslau to investigate the circulation of the brain under the supervision of Karl Hürthle, who had recently perfected a more sensitive manometer for recording intravascular pressures. Hürthle encouraged Porter to initiate a series of experiments in which the newly designed manometers were used to record intracardiac and intravascular pressures in experimental animals. In these sophisticated experiments Porter simultaneously recorded aortic and left ventricular pressures using a double-lumen catheter that had been passed retrograde into the left ventricle from the carotid artery. Porter, clearly proud of his research,
to Baumgarten, “I am quite happy over my Herzarbeit, for it is timely, and I think interesting. At all events it is a positive result and is altogether my own work. I am glad to be able to show our people something tangible to prove that the policy of allowing me to work here during the summer-semester is a good one. They would perhaps believe that I had learned something even if I had nothing to show for it, but it is just as well to have documentary evidence.”

The results of Porter’s hemodynamic experiments were published in the Journal of Physiology in 1892.21 Porter returned to Europe in the spring of 1892 and went to Berlin to resume his studies under Johannes Gad, with whom he had worked during his first year abroad. Gad had been a pupil and associate of many of the leaders of German physiology and one of his major interests was the circulatory system. The origin of Porter’s classic experiments on ligation of the coronary arteries can be traced directly to Gad. Porter explained to Baumgarten, “The morning after my arrival in Berlin, I went to the Physiological Institute where I had a very pleasant welcome. Prof. Gad talked a long time about various lines of investigation, and we finally selected the influence of ligature of the coronary artery upon the contractions of the heart.”22 Porter outlined the specific goals of his proposed experiments and revealed his expectation that this theme would serve as a focus for continued investigation upon his return to St. Louis.

The British physician and physiologist Marshall Hall had claimed in 1842 that sudden death was the usual result after interruption of the coronary circulation. This led John Erichsen, a medical graduate of University College in London and pupil of the innovative surgeon Robert Liston, to undertake a series of experiments in dogs and rabbits in which the coronary arteries were ligated. Erichsen demonstrated that ligation of all of the coronary arteries led to irregularities of the heart action and cardiac arrest within thirty minutes.23 Additional experiments on the effects of coronary ligation were reported in 1862 by Panum, a pupil of the great German pathologist Rudolph Virchow, and von Bezold in 1867, among others. Julius Cohnheim, another pupil of Virchow, initiated a series of experiments on the effects of coronary ligation in the late 1870s. He reported that ligation of any branch of the left or right coronary artery in the dog led to sudden cardiac standstill, usually within two minutes after occlusion.24 On the basis of his experiments, Cohnheim concluded that the coronary arteries were end arteries without functional anastomoses. Cohnheim’s observations and conclusions were controversial and this contributed to Gad’s suggestion that Porter pursue this line of investigation. Referring to the published work on experimental coronary occlusion, Porter exclaimed, “Seldom have the results of physiological studies been more at variance. The attentive reader finds no statement that is not denied, no fact not in dispute. These controversies would alone compel a new examination of the interesting phenomena in question, and the necessity of further research is increased by the knowledge that changes in intracardiac pressure following closure of the coronary arteries have been inferred rather than determined, and have never been studied with the improved methods of the present day.”

Porter’s experiments on ligation of the coronary arteries were begun in May 1892 at the University of Berlin and continued in St. Louis the following year. St. Louis Medical College had become the Medical Department of Washington University in 1891, and a year later a major new building was erected that contained “laboratories fully equipped with every modern apparatus adapted for demonstration and for original research work.”25 Porter published the results of his coronary artery ligation experiments in 1893. This paper began with a comprehensive review of the literature, which revealed Porter’s thorough knowledge of the earlier work on this subject. In his experiments, Porter ligated the right, left anterior descending, circumflex, or septal artery in dogs. The most important results related to the effect of ligation on left ventricular function and the incidence of fatal cardiac arrhythmias. Among Porter’s conclusions were that cardiac standstill frequently occurred with ligation of the left anterior descending or circumflex coronary arteries but was unusual with ligation of the right coronary artery. Unlike Cohnheim, Porter found that both ventricles stopped beating at essentially the same time in all instances. The arrhythmia Porter observed and described was ventricular fibrillation and he found it was irreversible. He also noted the relationship of the frequency of extrasystoles to the likelihood of cardiac arrest.

Using the sophisticated physiologic apparatus he had brought from Europe, Porter made the first accurate measurements of the effects of coronary ligation on intracardiac and intra-aortic pressure. He observed that ligation was followed almost immediately by a gradual but continuous decrease in peak intraventricular pressure. In addition to noting a decline in systolic pressure, Porter observed an increase in left ventricular diastolic pressure after the onset of ventricular fibrillation. A major conclusion Porter reached was that ligation of the coronary arteries was not uniformly fatal. This claim contradicted most other observations and
served as a stimulus for continued investigation by Porter and others into the effects of sudden coronary occlusion. Although there was increasing clinical interest in the relationship of coronary artery disease to sudden death, it would be more than a decade before these observations were used by a clinician (James B. Herrick) to explain certain phenomena observed in medical practice.\textsuperscript{27}

In separate experiments performed early in 1893, Porter investigated the pathology of myocardial infarctions produced by ligation of the left anterior descending coronary artery in the dog. These experiments, performed in St. Louis and subsequently presented before the Physiological Society of Berlin, were undertaken to confirm or refute the existence of a coordinating center for ventricular contraction, which had been proposed by the German physiologist Hugo Kronecker. Porter concluded that such a coordinating center did not exist, and in the course of his experiments he described the pathologic changes of the myocardium supplied by ligated coronary arteries. His were among the earliest pathologic and histologic descriptions of myocardial infarction, which had first been reported by Weigert in 1880.\textsuperscript{28, 29}

By the time Porter was thirty he had made several important career decisions. He was determined to become a professional physiologist, although the opportunities for this in America were severely limited. Although he pursued a number of research themes, including anthropometry and respiratory physiology, Porter’s dominant interest was circulatory physiology, especially the effects of coronary occlusion. It was becoming increasingly clear to Porter that it would be impossible for him to devote himself exclusively to physiology if he remained in St. Louis. Writing to Baumgarten on May 29, 1893, he claimed, “After nearly a year’s careful consideration I have decided that it would be inadvisable for me to accept any work in the university which would take me away from Physiology, in the traditional sense. The money has been a great temptation, but I am convinced that I must not take on any more responsibilities. I wish, you know, to be an investigator, not merely a teacher.”\textsuperscript{30}

The forced resignation due to alcoholism of H. Newell Martin from the chair of physiology at Johns Hopkins in April 1893 had major implications for Porter’s career.\textsuperscript{31} William Howell, a former pupil and associate of Martin, was called from Harvard to Baltimore to succeed Martin. This created an opening in Henry Bowditch’s physiology department at Harvard. It is not surprising that Porter was selected to fill this position; he shared Bowditch’s interests in circulatory physiology and anthropometry, had sophisticated postgraduate training in modern experimental physiology in Germany, and had demonstrated productivity in original research.\textsuperscript{32} Few Americans could claim the expertise in experimental physiology that Porter possessed by 1893. Bowditch and other physiologists had heard the results of Porter’s research on ligation of the coronary arteries at the fifth annual meeting of the American Physiological Society in December 1892. Porter was elected assistant professor of physiology at Harvard Medical School on October 30, 1893, and moved to Boston before Christmas.

Porter’s appointment at the Harvard Medical School allowed him to devote himself exclusively to physiology. Moreover, several members of the Harvard faculty shared his interest in the pathophysiology of the circulatory system. Henry Bowditch had a sound knowledge of cardiovascular physiology, which dated from his studies with Carl Ludwig at the Leipzig Psychological Institute two decades earlier. George Stewart, an assistant in Bowditch’s laboratory during the first year of Porter’s Harvard appointment, received his education at Edinburgh University and studied physiology at the University of Berlin in 1886. From 1889 to 1893 Stewart worked in Michael Foster’s physiology laboratory at the University of Cambridge, where he investigated the cardiac nerves and the velocity of blood flow.\textsuperscript{33} Porter undoubtedly received encouragement for continuing his investigations into the physiology of the coronary circulation from the newly elected professor of pathologic anatomy, William Councilman, who had been a pupil of H. Newell Martin in Baltimore, and subsequently studied pathology with Cohnheim and Weigert when those German pathologists were actively investigating the effects of coronary occlusion.\textsuperscript{27, 34}

The coronary artery experiments initiated in Germany and continued in St. Louis were resumed in Boston. By 1895 Porter was also studying the effect of acute anemia on left ventricular function.\textsuperscript{35} In addition to ligating the coronary arteries, Porter occluded these vessels by embolization with lycopodium spores and developed an innovative technique for obstructing them with a solid glass rod inserted through a small incision in the innominate artery. The tip of the rod was tapered and curved to facilitate its introduction into a coronary ostium. The tip of the sound was advanced to the sinuses of Valsalva until resistance was met from an aortic valve leaflet. Porter would then withdraw the sound slightly and by rotating the tip would locate the coronary ostium. This remarkable technique, performed before the discovery of x-rays,

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preceded clinical catheterization techniques by several decades. In other experiments Porter inserted a hollow glass tube into a coronary artery through which he infused warm, defibrinated, oxygenated ox blood to perfuse the myocardium. Using techniques he had learned in Germany and state of the art equipment, Porter studied the effects of coronary ligation on cardiac output in dogs. He noted the association of decreased cardiac output and the likelihood of fatal arrhythmias after ligation of the coronary arteries and implied that the extent of myocardial ischemia was a major factor in determining these consequences of acute obstruction of the coronary arteries.

Rudolf Kolster, a Scandinavian pathologist, had published his experiments on ligation of the coronary arteries in 1892. In 1896 Porter claimed, “The experimental production of infarcts in the heart has been attempted, so far as I am aware, only by Kolster and myself, in each case with complete success.” Porter was familiar with Kolster’s paper before the publication of his own 1893 article on ligature of the coronary arteries; a reference to Kolster appeared in the text and bibliography of Porter’s manuscript, but these were deleted in the published version. It seems likely that Porter suppressed this reference to Kolster’s work in his publication in part to make his own experiments appear more innovative and significant. Walter Baumgarten, the son of Porter’s mentor Gustav Baumgarten, received his undergraduate degree at Johns Hopkins, where he worked with H. Newell Martin, and his medical degree from Washington University in 1896. He then entered Bowditch’s department at Harvard and collaborated with Porter in several experiments. In 1898 young Baumgarten complained to his father that in his publications, “Dr. P. employs a personal style in which the ego appears very frequently.”

Porter’s 1896 paper included a thorough description of his operative technique. He reported that several of the dogs survived for various periods of time after ligation of the left anterior descending coronary artery. One dog survived four days and another fourteen and a half days. Postmortem examinations of these animals revealed “characteristic anemic infarcts . . . occupying the anterior part of the septum and that part of the anterior wall of the left ventricle which adjoins the interventricular furrow.” Porter concluded from his experiments that “the rapid closure of a coronary artery is followed by the death of the part which it supplies.” Addressing the controversial issue of the existence of anastomoses in the coronary circulation, Porter claimed that although anatomic anastomoses existed, they were not functionally significant in the context of acute occlusion of a major coronary artery. He proposed

The idea of terminal arteries is physiological, not anatomical. Terminal arteries differ from other arteries in that the peripheral resistance in the Anastomosing vessels is too high to be overcome by the normal blood pressure in any of the arteries of which the communicating vessels are branches. Hence the rapid closure of any terminal artery cuts off the nutrition of its own capillary area because sufficient blood for the life of the area can not be sent through the communicating vessels on account of the high resistance in them. The resistance in the communicating vessels, and not their size, is the factor of first importance. . . . I conclude, then, that the rapid closure of a coronary artery puts an end to the nutrition of the area which it supplied.

Porter’s experiments at Harvard were facilitated not only by enthusiastic and knowledgeable colleagues but also by access to assistants and apparatus that had been unavailable to him in St. Louis. Writing in January 1896, he enthusiastically informed Baumgarten that the staff of the department of physiology would increase ten the following year with the addition of four new assistants who would receive masters degrees after a year of advanced instruction and original laboratory work. Porter claimed, “The idea is chiefly pedagogical, — to train men in physiological science; to give them habits of thought which will be useful in whatever line of work they may take up.” There were implications for the department’s research output, however, and Porter predicted, “I am confident that a great deal can be done with good men in a year’s time.” He boasted, “The laboratory is now provided with every modern means of increasing production, including stenographer, typewriter, mechanic, phonograph, storage batteries, x ray apparatus, photographic department, etc. . . .” Porter and his junior colleagues published important papers on hemodynamics, cardiac innervation, and the origin of the heart beat in the late 1890s. In 1898 he published a significant paper on coronary blood flow in dogs in which simultaneous pressures were measured in the carotid and coronary arteries.

Cardiac arrhythmias attracted the attention of physiologists in the closing years of the 19th century. Stimulated by the work of MacWilliam and the earlier observations of Kronecker, Porter undertook a series of experiments on ventricular fibrillation, which he reported in 1898. Porter’s interest in this subject was in part due to his curiosity regarding “the cause of failure in many previous attempts to resuscitate the heart. . . .” Porter revealed that he was able to reverse ventricular fibrillation that had been induced in a variety of ways, most notably by ligation of a coronary artery, “by cooling the ventricles until all trace of
fibrillation has disappeared, and then bringing the heart back to a normal temperature by circulating warm defibrinated blood through the coronary vessels. Thus, before 1900, Porter had studied many of the major physiologic and pathologic consequences of acute obstruction of the coronary arteries. Using advanced techniques and sophisticated physiologic apparatus, he had investigated the effects of acute coronary obstruction on myocardial function, the induction of arrhythmias, and the histology of the left ventricle.

Porter collaborated with Walter Baumgarten in research that led to the publication of the most comprehensive and most insightful article on myocardial infarction written by an American in the 19th century. Baumgarten, under Porter’s supervision, studied the pathologic extent of myocardial infarctions in cats and dogs after coronary artery ligations. Within several months of the discovery of x-rays, they performed experiments in which roentgenograms were made after the injection of radiopaque substances into the coronary arteries of hearts excised from experimental animals. They were interested in the relationship of ischemia and myocardial contractility and raised issues that are currently of great clinical interest with the introduction of streptokinase therapy for acute coronary thrombosis. Baumgarten declared, “The discovery that portions of the mammalian ventricle will resume their contractions if fed with defibrinated blood enables us to determine how long an ischaemic area in the heart remains contractile.”

Porter and Baumgarten observed that loss of contractility after experimentally induced ischemia was reversible. They found that contractility persists for a time after acute coronary occlusion, but even if it ceased, the potential for the return of contractility after reperfusion of the coronary circulation existed for several hours. They also observed that contractility was most impaired in the central zone of an infarction and least impaired at the periphery. The clinical relevance of these important physiologic and pathologic observations is obvious in the 1980s.

Porter’s experiments, and those of his assistants, were of significance in the slow but steady recognition of the clinical syndromes of ischemic heart disease by contemporary clinicians. A direct link between Porter’s laboratory work and James B. Herrick’s classic description of the syndrome of acute myocardial infarction with survival in man was provided by two physicians working in the laboratory of experimental therapeutics at the University of Chicago early in the 20th century. In 1908 Joseph L. Miller and Samuel A. Matthews extended Porter’s experiments on ligation of the coronary arteries and cited his 1896 paper as the single most important contribution to the subject after Cohnheim’s observations published in 1881. Miller and Matthews had studied physiology under Warren P. Lombard while they were students at the University of Michigan. Lombard had graduated from Harvard Medical School, where he worked in Bowditch’s physiology laboratory, and subsequently studied with Carl Ludwig in Leipzig. Matthews began these experiments when he was assistant professor of experimental therapeutics at Rush Medical College. Miller had received his medical degree from Northwestern University. Both had recently been elected members of the American Physiological Society, of which Lombard was a founding member.

In the first of two papers presenting the results of their experiments, the authors explained that their studies were “undertaken with the view of determining the effect of drugs on animals after ligation of the coronary arteries, believing that information gained in this way may be directly utilized in the treatment of angina pectoris.” James B. Herrick was present during Miller’s presentation of their results before the Association of American Physicians in 1908. Herrick, a prominent Chicago physician and teacher at Rush Medical College, would present his classic paper on myocardial infarction before this same society four years later. Joseph Miller was present at that 1912 meeting and heard Herrick claim, “There are reasons for believing that even large branches of the coronary arteries may be occluded, at times acutely occluded, without resulting death, at least without death in the immediate future.” The critical concept that led to Herrick’s classic contribution to clinical medicine was the recognition that sudden obstruction of the coronary arteries was “not necessarily fatal.” Among the evidence Herrick cited for this conclusion were the experiments of Porter and Miller and Matthews. Just as Porter had found, unlike Cohnheim and others, that some dogs survived acute ligation of the coronary arteries, Herrick proposed that the analogous situation in man, acute thrombotic obstruction of a coronary artery, need not always result in death.

Porter made numerous important contributions to physiology in the 20th century. His most important discoveries, however, were those made in the 1890s relating to the physiology of the coronary circulation. Porter was instrumental in founding the American Journal of Physiology and was a strong advocate for meaningful student participation in sophisticated physiologic experiments as part of the physiology curriculum in American medical schools. Porter proclaimed, “The student shall perform for himself the
classical experiments which are the essence of the science. . . . The student should be trained rather than informed. The trained observer can and must be trusted to inform himself." In an effort to make high-quality physiologic apparatus more readily available and at a reasonable cost, Porter established the Harvard Apparatus Company, which was "organized for the advancement of laboratory teaching in physiology and allied sciences." Political and personality issues contributed to the selection of Walter B. Cannon as Bowditch's successor, and Porter was made professor of comparative physiology at Harvard, a position he held until his retirement in 1928.

By the time of his death in 1949, the experiments Porter had performed more than half a century earlier had been extended by many workers and a sophisticated understanding of the relationship of coronary artery disease, angina pectoris, and acute myocardial infarction was evolving. The critical role Porter's experiments played in the growing understanding of the pathophysiology of coronary artery disease is an ideal demonstration of the ultimate significance of basic science observations to clinical medicine.

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