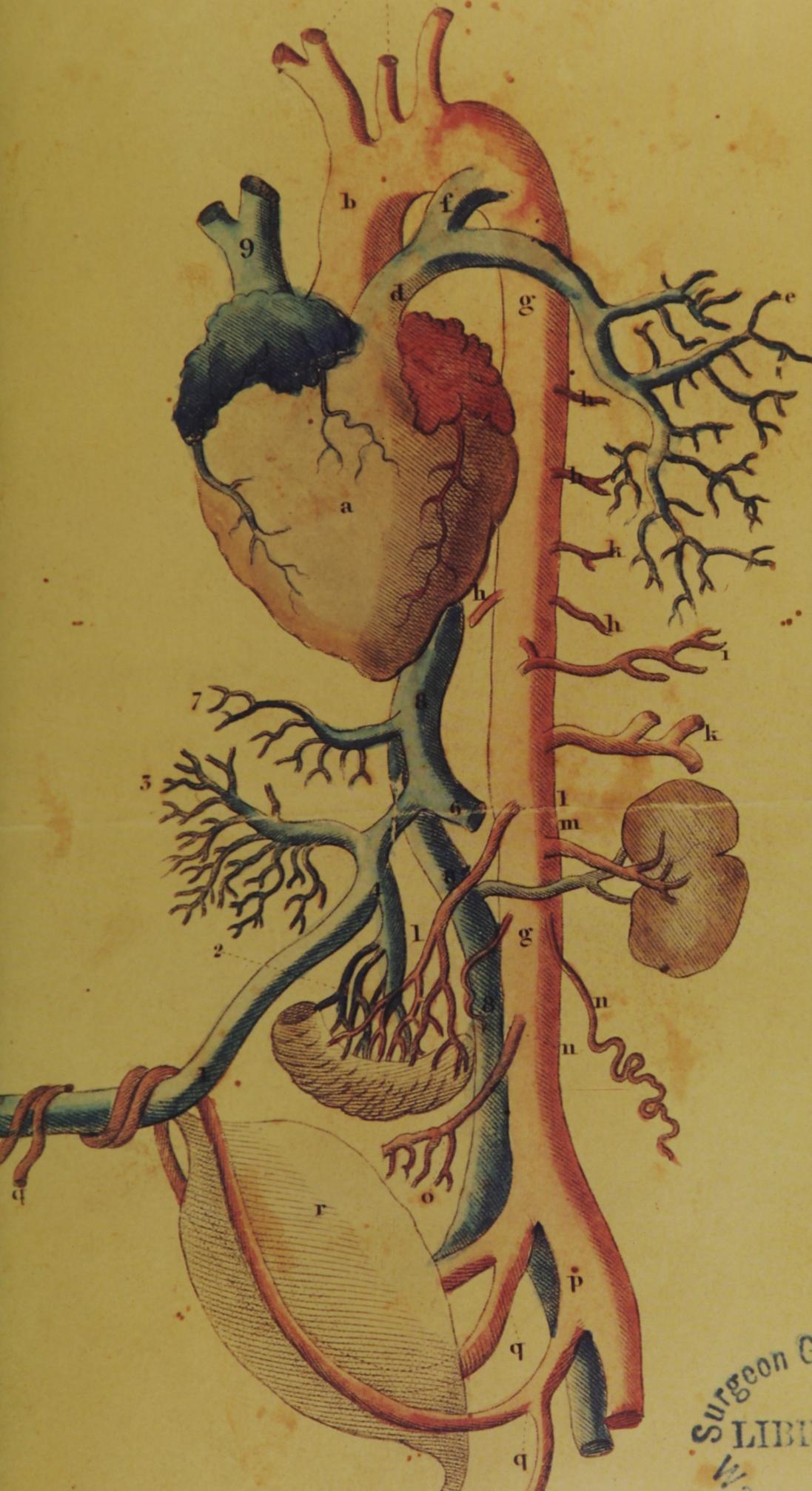


*AMERICAN  
CONTRIBUTIONS  
TO  
CARDIOVASCULAR  
MEDICINE  
AND  
SURGERY*



U.S. DEPARTMENT OF  
HEALTH AND HUMAN SERVICES  
Public Health Service  
National Institutes of Health

Surgeon General  
LIBRARY

*This booklet was issued in conjunction with an exhibit on "American Contributions to Cardiovascular Medicine and Surgery" at the National Library of Medicine, September-December 1986. The exhibit was prepared by the Library's History of Medicine Division with the National Heart, Lung, and Blood Institute as a companion activity to the X World Congress on Cardiology, held in Washington, D.C., in September 1986. The assistance of W. Bruce Fye, M.D., and of the American College of Cardiology in preparing the exhibit is gratefully acknowledged.*

Cover

*From "Plan of the Foetal Circulation of the Blood," a broadside published in Philadelphia in 1818.*

*Single copies of this booklet are available without charge by writing:*

Chief, History of  
Medicine Division  
National Library of Medicine  
8600 Rockville Pike  
Bethesda, Maryland 20894

About the Exhibit

*The National Library of Medicine exhibit "American Contributions to Cardiovascular Medicine and Surgery" was developed as a companion activity to the X World Congress on Cardiology, held in Washington, D.C., from September 14 to September 19, 1986.*

*All photos are courtesy of the National Library of Medicine, unless otherwise noted.*







## FOREWORD

The National Heart, Lung, and Blood Institute and the National Library of Medicine are pleased to pay tribute to the hundreds of scientists who have contributed through the years to cardiovascular research.

Their efforts in basic scientific study, applied research, and clinical investigation have led to the medical advances that are saving lives today. Thus, the scientific contributions highlighted in the exhibit and this booklet are more than historical artifacts. They are valuable steps in the process that has improved the diagnosis and treatment of disease.

Claude Lenfant, M.D.

*Director*

*National Heart, Lung, and  
Blood Institute*

Donald Lindberg, M.D.

*Director*

*National Library of Medicine*



## *PREFACE*

It has been necessary in this short booklet to select a handful of representative contributions from the tens of thousands of publications of Americans dealing with the cardiovascular system. Inevitably, some well-known names are missing, and some lesser known individuals are included. In many instances, the physicians and scientists whose contributions are mentioned spent several years—occasionally several decades—pursuing the research that ultimately resulted in a significant advance in cardiovascular medicine or surgery. The people responsible for many of these preliminary efforts, as well as the names of their predecessors and coworkers, are generally not noted in this brief essay, although the collaboration of several individuals or groups over many years often made possible the development which is described.

Space constraints have also necessitated the exclusion of certain topics of interest to many investigators and physicians who concern themselves with the circulatory system. In this booklet, however, the emphasis is on the heart itself, rather than on the cardiovascular system as a whole. For this reason, several broad (and important) areas of cardiovascular medicine and surgery are not discussed. For example, extracoronary atherosclerosis, hyperlipidemias, hypertension, preventive cardiology, cardiac rehabilitation, and noncardiac vascular surgery are not included. The decision to include or exclude a specific contribution



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was often difficult. In undertaking this difficult task, I relied upon the valuable publications of Comroe and Dripps<sup>1</sup> and Garrison and Morton<sup>2</sup> to help decide which advances should be included.

By definition, this essay describes American contributions to cardiology and cardiovascular surgery. Many of the advances described owe a great deal to discoveries and developments pioneered by workers around the world. Obvious examples of this are the development of electrocardiography by Einthoven, Waller, and many other Europeans and the discovery of x-rays by Röntgen. Americans subsequently applied these and other new techniques to the evaluation of patients with known or suspected cardiac disease and have used them to advance our understanding of the pathophysiology of the heart and circulatory system.

W. Bruce Fye, M.A., M.D.





## INTRODUCTION

Modern cardiology and cardiovascular surgery have been made possible by the cumulative efforts of several generations of clinicians and biomedical scientists around the world. The purpose of this booklet is to highlight some of the important contributions Americans have made to our knowledge of the heart in health and disease and to the treatment of congenital and acquired cardiac disorders. The preparation of this booklet was a most challenging undertaking. As Julius Comroe and Robert Dripps have demonstrated so persuasively, virtually all “break-throughs” in cardiovascular medicine and surgery have been the result of “previous work by scores or hundreds of competent scientists” whose efforts were “essential to provide the basic knowledge necessary for the widely known clinical advance, usually attributed to one man.”<sup>1</sup>

Americans made few substantive additions to medical knowledge prior to the 20th century. William Welch, a pioneering American pathologist and medical educator, complained to his pupil Franklin Mall in 1886, “it is a great misfortune of our country that the opportunities are so few for a man’s engaging in scientific medical work.”<sup>3</sup> As increasing numbers of American physicians were exposed to the European universities and clinics in the closing decades of the 19th century, a network of research-oriented physicians, educators, and scientists formed a coalition to encourage the development of full-time academic positions and the adoption of the research ethic by America’s medical schools. This transition occurred slowly, but by the early 20th century, Americans began making important contributions to knowledge in many areas of medicine.





## ANATOMY AND PHYSIOLOGY

The gross anatomy of the heart and many aspects of its microscopic structure were delineated by European workers prior to the 20th century. By the time Americans became involved in serious and sustained biomedical research, there were few fundamental discoveries in the gross anatomy of the heart that had not already been made. Franklin Mall and his Canadian pupil John MacCallum made important observations at the turn of the century on the embryology and morphology of the myocardium. The New York pathologist Louis Gross, reflecting a growing interest in the coronary circulation, published a valuable monograph on the anatomy of the coronary arteries in 1921.

Inspired by their experience in German physiology laboratories, some early American biomedical scientists made significant discoveries in cardiac physiology. Henry P. Bowditch, working under Carl Ludwig's direction at the Leipzig Physiological Institute, described two fundamental laws of cardiac physiology in 1871: the "all or none law" of cardiac contraction, and the "treppe" phenomenon.

Another important development that owed much to earlier efforts of German and British physiologists was the development, in the 1880's, of an isolated mammalian heart preparation by Newell Martin at the Johns Hopkins University. The critical contribution made by Martin was his recognition of the necessity of perfusing the coronary arteries in order to sustain the viability of the isolated mammalian heart. A century ago, Martin's pupils William Howell and Frank Donaldson used the isolated mammalian heart preparation to investigate ventricular function. In his classic studies on ventricular function published a generation later, Ernest Starling paid tribute to the Baltimore group's pioneering work in this area.

During a career that lasted nearly half a century and culminated in the receipt of the Nobel Prize, Joseph Erlanger made numerous important discoveries in circulatory physiology. In addition to classic observations on the cardiac conduction system, he made significant contributions to the recording of blood pressure and to the physiology and treatment of shock. Carl Wiggers, whose career in physiology also spanned half a century, made several notable discoveries in cardiac physiology through his application of instruments of precision to the study of the circulation. His pioneering studies of hemodynamics and his early efforts at resuscitation were especially significant.

Methods to measure the circulation time were developed by George Stewart, who used indicator-dilution techniques for this purpose in the late 19th century, and Herman Blumgart, who first employed radioisotopes to quantitate the circulation time in 1927. Stewart's approach was also used to estimate cardiac output. Once it was demonstrated by Werner



*Carl Wiggers (1883-1963)*



Forssmann and others that cardiac catheterization was safe in man, approaches previously used to investigate hemodynamic parameters in laboratory animals were extended to humans. Among the early American investigators who used catheterization techniques to measure cardiac output in man were Eugene Stead and James Warren. In the 1950's, Stanley Sarnoff and his associates in New York initiated a long series of studies that shed much light on myocardial contractility.



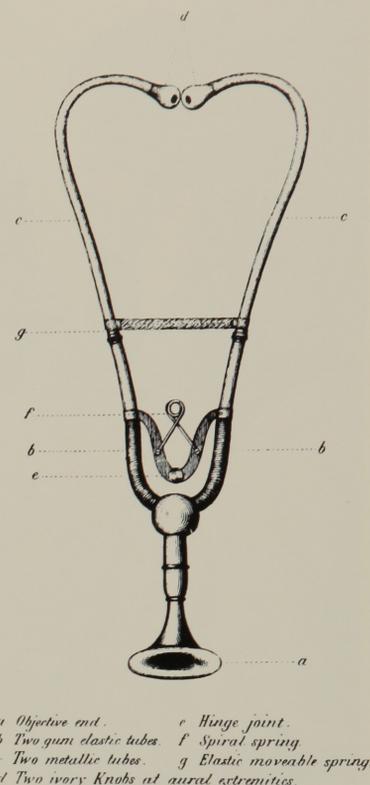
### Physical Diagnosis

Americans cannot claim many significant discoveries in cardiac physical diagnosis. During the first half of the 19th century, French and British physicians described many of the physical findings characteristic of various valvular lesions. Austin Flint, sometimes referred to by his contemporaries as the "American Laënnec," was a great popularizer of auscultation and other techniques of physical diagnosis applied to the heart, however. He is remembered eponymically for his description of the murmur of aortic insufficiency that mimics mitral stenosis. The binaural stethoscope with flexible tubes was introduced in 1852 by the New York physician George Cammann. This stethoscope represented a significant improvement over earlier models and eventually became the instrument of choice. A Massachusetts engineer, R.C.M. Bowles, patented a diaphragm for use with the stethoscope in 1894. Approximately 30 years later, Howard Sprague developed the combination bell and diaphragm stethoscope that became the most popular model.



### DIAGNOSTIC TECHNIQUES: Electrocardiography

Early in the 20th century, European and British workers used the newly developed electrocardiograph to investigate disorders of cardiac impulse formation and conduction. Stimulated by James Herrick's observations on coronary thrombosis, American workers made a number of important observations on the electrocardiographic manifestations of ischemic heart disease. In 1918, Fred Smith, encouraged by his associate Herrick, reported the electrocardiographic features of experimental ligation of the coronary arteries in dogs. The following year, Herrick published an electrocardiographic tracing of a man who suffered a myocardial infarction that demonstrated inverted T waves in leads 2 and 3. Harold Pardee, a New York pioneer of electrocardiography, extended these observations in the early 1920's. In 1928, Harold Feil and Mortimer Siegel published electrocardiograms before, during, and after attacks of angina pectoris in



*Stethoscope developed by George Cammann. From the New York Medical Times, Volume 4, January 1855.*

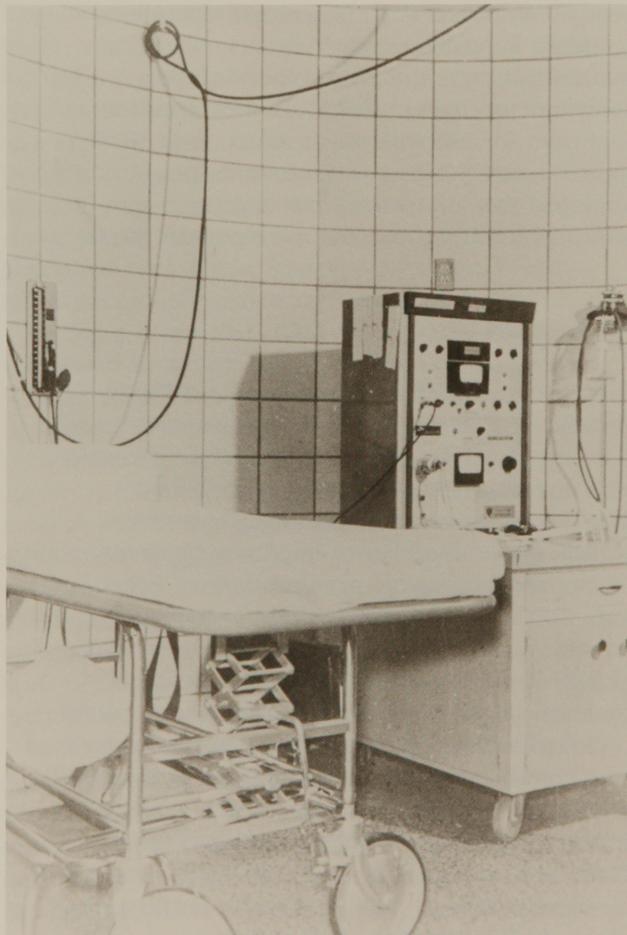


which ST segment depression was present during the episodes of pain. Paul Dudley White, together with Louis Wolff and John Parkinson, described the syndrome for which they are remembered eponymically in 1930. This is only one example of numerous collaborative efforts of American and foreign workers to advance our knowledge of the heart in health and disease.

Frank Wilson of the University of Michigan was an American pioneer of electrocardiography who made several important theoretical and practical observations regarding this useful diagnostic technique. One of his many contributions was the development of unipolar electrocardiographic leads. Chest leads were introduced by the Philadelphia physicians Charles Wolfarth and Francis Wood in 1932. These authors demonstrated the value of this new lead configuration in diagnosing myocardial infarction. By the 1940's, the electrocardiograph was considered an invaluable aid to the diagnosis of myocardial infarction. Indeed, for more than a quarter of a century, it provided the only objective means of distinguishing chest discomfort due to myocardial infarction from other causes of precordial pain.



*Austin Flint (1812-1886)*



*Cardiac Arrest Room,  
Mt. Carmel Mercy Hospital,  
Detroit, Michigan, 1966.*



*Paul Dudley White with  
Howard Sprague and T. Duckett  
Jones examining a young  
rheumatic fever patient, about  
1925.*



*Other Noninvasive  
Diagnostic Techniques*

Americans have contributed to the refinement and acceptance of several diagnostic procedures that were originally developed by workers in other countries. Within 6 months of Wilhelm Röntgen's discovery of x-rays, Francis Williams of Boston demonstrated the feasibility and utility of cardiac fluoroscopy. Echocardiography, pioneered in Sweden in the 1950's, received little attention in the United States until John Reid and Claude Joyner of Philadelphia emphasized the value of the technique in patients with mitral stenosis. Harvey Feigenbaum, who demonstrated the efficacy of echocardiography in detecting pericardial effusion and in evaluating left ventricular function, catalyzed interest in this noninvasive method through his extensive writings and lectures on the technique.

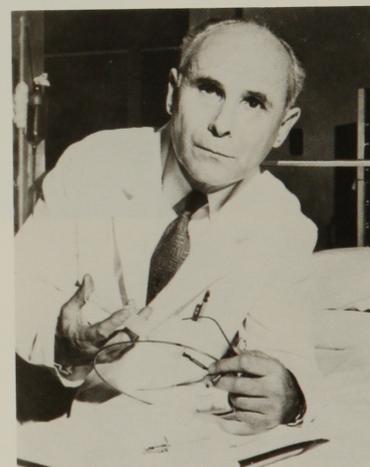
Radionuclide techniques have been applied in cardiology for decades. These procedures grew in popularity as several groups demonstrated the possibility of evaluating myocardial function, detecting shunts, and assessing coronary blood flow using radioisotopes. The development of these techniques depended upon many discoveries in physics and technological improvements made by workers around the world.

*Use of electrocardiograph at  
United States School of Aviation  
Medicine, Randolph Field, Texas,  
1932.*

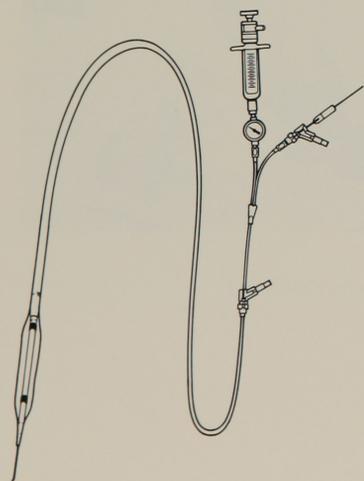
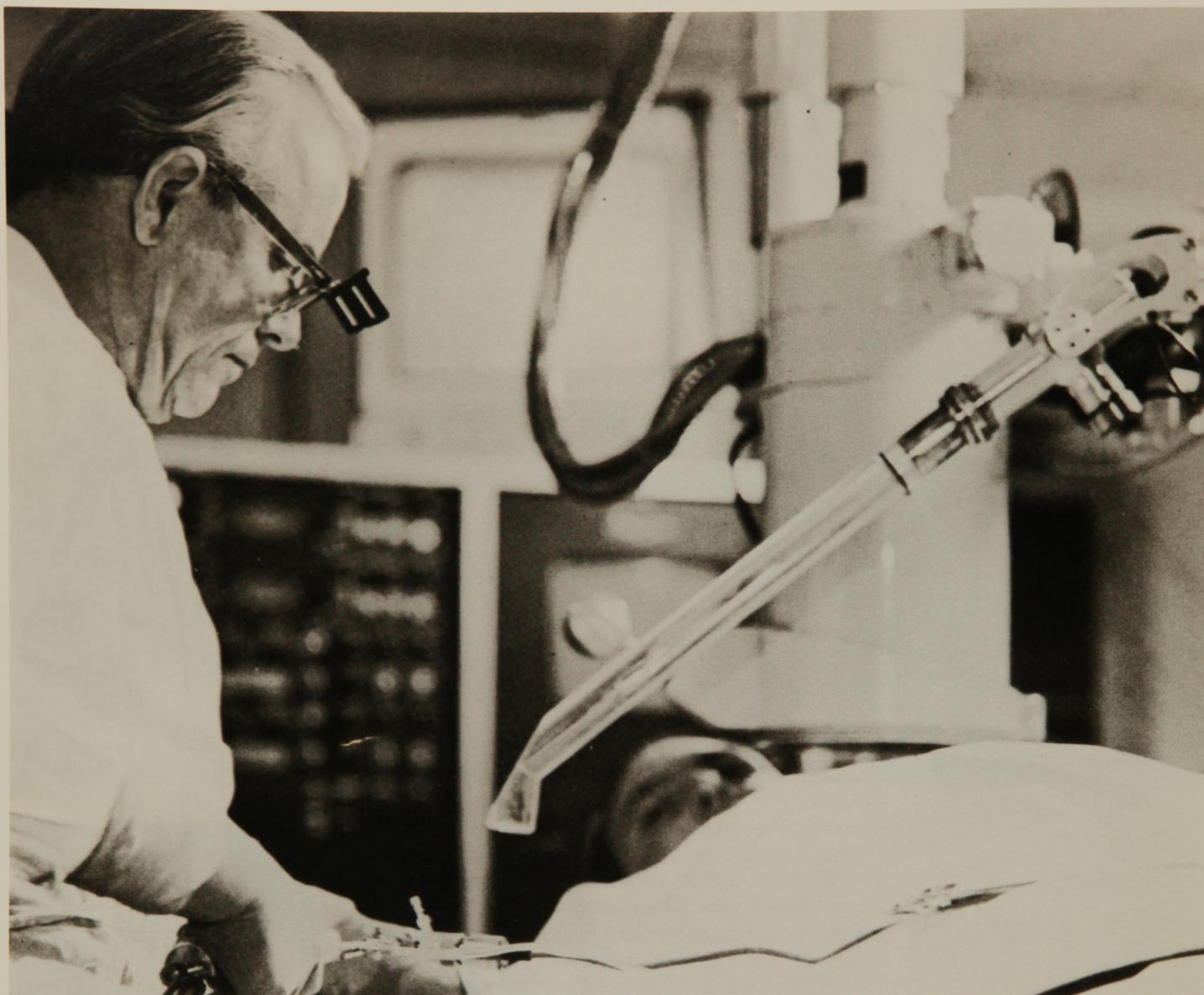
More than a century ago, French physiologists developed techniques for catheterizing the cardiac chambers of experimental animals. The daring German physician Werner Forssmann demonstrated the feasibility of using this technique in man when he catheterized his own right heart in 1929. Workers in Europe and Latin America extended Forssmann's technique to evaluate cardiac physiology in the mid-1930's. Soon, André Cournand, Dickinson Richards, and Hilmert Ranges, working in New York, performed catheterizations of the right heart in man to evaluate cardiac and pulmonary physiology. In 1941, they reported their technique for catheterization of the right atrium in man. During the 1940's, techniques were developed and refined to record intracardiac pressures, cardiac output, and other physiologic parameters.

While Cournand and his group were seeking physiological information, other innovative investigators used the new catheterization techniques to explore the anatomy of the heart. Israel Steinberg and George Robb, also working in New York, perfected the technique of visualizing the cardiac chambers radiographically by the injection of contrast material into the venous circulation. A number of workers, including Richard Bing and Lewis Dexter, applied this procedure to the diagnosis of congenital heart disease shortly after the Second World War. Henry Zimmerman described the technique of retrograde left ventricular catheterization in 1950 that facilitated the angiographic evaluation of left ventricular function.

Several Americans, including Carleton Chapman, Harold Dodge, and Richard Gorlin, have contributed to the development of angiographic techniques for the evaluation of left ventricular function and semiquantitative assessment of valvular heart disease. Many early pioneers of cardiac catheterization and angiography were encouraged in their efforts by surgeons who were anxious to have more precise anatomical and physiological data as they planned surgical approaches for the treatment of congenital and acquired heart lesions. Surgeons in Cleveland had been interested in the operative treatment of coronary artery disease for more than two decades when Mason Sones of the Cleveland Clinic developed the technique of selective coronary arteriography in 1958. Although several European and American groups had already demonstrated the feasibility of visualizing the coronary arteries by injecting contrast material into the proximal aortic root, this nonselective approach to coronary arteriography was unreliable and, in most instances, provided incomplete information on the coronary anatomy. The selective technique developed by Sones was shown to be safe and provided high quality images of the coronary circulation in man. This



*André Cournand*



*USCI PTCA Steerable Dilatation System for coronary angioplasty.*

development was fundamental for the subsequent widespread application and ultimate acceptance of aortocoronary bypass surgery.

In 1970, Henry Swan, William Ganz, and their coworkers demonstrated the feasibility of using a flow-directed balloon-tipped catheter for bedside hemodynamic monitoring in man. This technique placed the hemodynamic management of critically ill patients on a more sound physiological basis. The recent development of transluminal coronary angioplasty represents an extension to the coronary vessels of a balloon dilatation technique for stenotic systemic vessels developed two decades ago by Charles Dotter. In Germany, Andreas Gruntzig adapted this technique to the coronary circulation and, after emigrating to the United States, played a major role in popularizing this procedure.

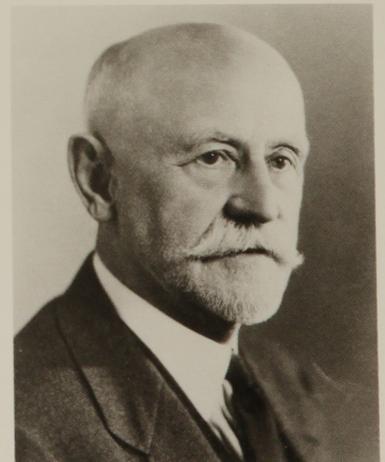
*F. Mason Sones (1918-1985).  
From the cover of Modern Medicine,  
May 18, 1970.*

The most significant American contributions to ischemic heart disease have related to the pathophysiology, diagnosis, and management of acute myocardial infarction and its complications. Although Adam Hammer of St. Louis reported the first case of coronary thrombosis recognized during life in 1878, his patient did not have atherosclerotic cardiovascular disease. The coronary artery was occluded by a thrombus attached to an aortic valve vegetation, and Hammer did not reveal any insight into the relationship of acute coronary occlusion to myocardial necrosis. During the last quarter of the 19th century, Cohnheim, Weigert, Huber, and others working in Europe advanced our understanding of the pathophysiology of ischemic heart disease. Trained and inspired by European workers, the American physiologist William Porter began investigating the effects of ligation of the coronary arteries in the early 1890's. Porter's experiments demonstrated that acute obstruction of a coronary artery was not invariably fatal, a widely held belief in this era. Porter's pupil Walter Baumgarten extended these animal experiments and, in 1899, published a sophisticated description of the pathophysiology of coronary occlusion and resulting myocardial infarction.

Basing his conclusions on the scientific observations of Porter and others and on the clinical observations of George Dock and several European authors, James Herrick presented a comprehensive description of the clinical syndrome of acute myocardial infarction in 1912. Earlier observers came close to recognizing this event, but it remained for Herrick to synthesize the clinical observations and experimental results of more than half a century and delineate the clinical manifestations of acute myocardial infarction. Nevertheless, until the electrocardiograph became recognized as a valuable tool for objectively identifying evidence of myocardial ischemia or necrosis, Herrick's observations had little effect on clinical practice.

During the 1920's and 1930's, physicians made the diagnosis of coronary thrombosis with increasing frequency. Through Herrick's efforts, they were more aware of the clinical features of this event, and the growing availability of the electrocardiograph allowed them to confirm the diagnosis. In an attempt to identify individuals at risk for myocardial infarction, Arthur Master of New York, beginning in 1929, used exercise tests to evaluate circulatory and myocardial efficiency. This approach ultimately resulted in the development of the standard exercise tolerance test as a means to evaluate the adequacy of myocardial blood supply and exercise tolerance.

The syndrome of angina at rest associated with ST segment elevation was described in the 1950's by Myron Prinzmetal and his colleagues. Although



*James Herrick (1861-1954)*



coronary artery spasm was proposed more than a century ago as a mechanism of angina pectoris, objective proof of this mechanism of myocardial ischemia has become available only recently. Over the past three decades, Americans have contributed to the enzymatic diagnosis of myocardial necrosis. John LaDue reported the association of elevated serum glutamic oxaloacetic transaminase levels in the setting of acute myocardial infarction in 1955. More recently, several groups have demonstrated the value of measuring other serum enzymes and isoenzymes in assessing the extent of myocardial necrosis.



### *Arrhythmias*

Palpation of the pulse has played an important role in the evaluation of patients since antiquity, but insight into the relationship of cardiac arrhythmias to syncope did not develop until the 19th century. Resuscitation was attempted for generations before there was any understanding of the pathophysiology of cardiac arrhythmias. Although Prevost and Battelli of the University of Geneva demonstrated in 1899 that it was possible both to induce and terminate ventricular fibrillation by passing strong electrical currents through the heart, these observations did not lead to any practical developments in the management of patients for nearly half a century. Concern about accidental electrocution grew during the early 20th century and was responsible for the establishment of a committee of scientists whose mission was to investigate the mechanisms and possible treatment of this dramatic event. Donald Hooker and William Kouwenhoven and their associates at Johns Hopkins repeated and extended the observations of Prevost and Battelli on electrical defibrillation of the ventricle and published their results on this subject in 1933.

Over the next two decades, these studies were extended by the pioneering American physiologist Carl Wiggers at Case Western Reserve University. Wiggers advocated the combination of direct cardiac massage, used by others for several years in the context of attempted resuscitation; intravenous injection of Adrenalin and other drugs; and electric countershock to resuscitate the fibrillating heart. His surgical colleague Claude Beck began using this approach in the operating room in 1941 and, 6 years later, successfully resuscitated a patient who suffered intraoperative ventricular fibrillation. Beck's report of the successful resuscitation of a patient with ventricular fibrillation attracted widespread attention. His group organized a series of courses on cardiac resuscitation attended by more than 3,000 individuals in the late 1940's and early 1950's.



Paul Zoll and his Boston colleagues extended to man the earlier observations of Hooker and Kouwenhoven that it was possible to defibrillate the animal heart by a transthoracic shock. In 1956, Zoll reported the successful defibrillation of the human heart by a countershock delivered through the chest wall. Kouwenhoven resumed his studies of resuscitation in this context and, with James Jude, proposed a comprehensive approach to cardiopulmonary resuscitation in man in 1960. Their method, with some modifications, remains the standard method of attempting to resuscitate patients. Other approaches have been introduced more recently, including the implantable defibrillator developed by Mieczyslaw Mirowski and his Baltimore colleagues.

In recent years, there have been many discoveries and developments that have led to a significant reduction in the mortality of patients who have suffered an acute myocardial infarction. One of the most significant advances was the introduction of the coronary care unit, where trained personnel respond immediately to life-threatening cardiac arrhythmias detected by continuous electrocardiographic monitoring. The prompt administration of antiarrhythmic drugs and rapid initiation of cardiopulmonary resuscitation were fundamental components of the coronary care unit concept. Hughes Day of Kansas City was the leading proponent of this approach to managing patients with known or suspected acute myocardial infarction. Following his demonstration of the efficacy of the coronary care unit in 1962, special areas for patients with acute myocardial infarction have become standard in even the smallest acute care hospitals.

A more sophisticated understanding of the mechanism of cardiac arrhythmias and a more rational approach to their management have been made possible by the recent development of invasive electrophysiological techniques by many workers throughout the world. Among the early American pioneers of invasive electrophysiology were Benjamin Scherlag, Anthony Damato, and Richard Helfant, who developed the technique of His bundle recording in the 1960's. More recently, several groups have extended these techniques to the evaluation of patients with supraventricular and ventricular arrhythmias.



Americans played a prominent role in the development and progressive refinement of artificial pacemakers. Hugo von Ziemssen, a German physician, demonstrated in 1879 that it was possible to alter the heart rate and rhythm not only by applying electricity directly to the heart but by passing direct current through the chest wall as well. In the early 20th century, Joseph Erlanger studied the physiology of heart block in dogs and demonstrated that it was possible to excite the sinus node by electrical stimulation with a transthoracic electrode. Other workers extended these observations, and in 1932 Albert Hyman of New York demonstrated the feasibility of pacing the heart in man by using an “artificial pacemaker.” Hyman’s technique consisted of administering a pulse of electricity to the right atrium through a transthoracic needle electrode. This approach was impractical, and interest in the possibility of artificially stimulating the heartbeat was not actively pursued for nearly two decades. In 1952, Paul Zoll reported experiments in which he successfully stimulated the heart with an external pacemaker. Five years later, William Weirich, Vincent Gott, and Walton Lillehei of the University of Minnesota successfully paced the human heart with a myocardial electrode attached to an external power source. In 1959, Seymour Furman demonstrated the efficacy of using endocardial electrodes for temporary and permanent pacing. During the past quarter century, numerous technical advances that have greatly expanded the capabilities of the electrical control of cardiac rhythm have resulted from the collaboration of clinical scientists, engineers, and physicians, many of whom have been Americans.



*Joseph Erlanger (1874-1965)*



### *Congenital Heart Disease*

Until surgical techniques for the palliation or total correction of congenital heart defects were developed beginning in the 1940’s, there was relatively little interest in this class of heart disease. In the 1930’s, Helen Taussig of Johns Hopkins devoted herself to the study of congenital heart disease and demonstrated that accurate diagnosis was often possible through careful cardiac examination, electrocardiography, and fluoroscopy. Her role in encouraging Alfred Blalock to develop the shunt operation for tetralogy of Fallot has become better appreciated in recent years. The field of pediatric cardiology owes much to this pioneering woman physician.

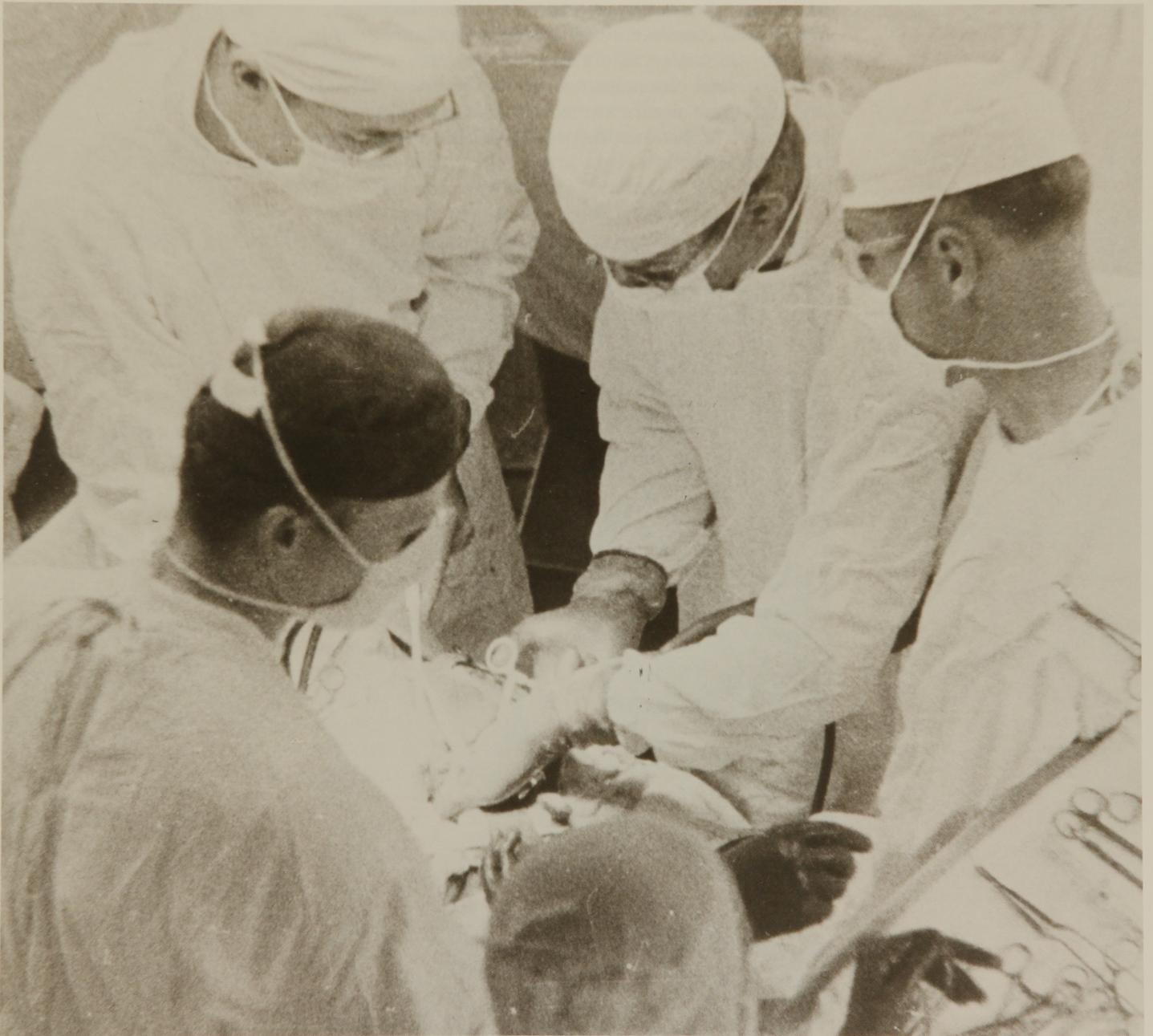


Congenital heart disease provided fertile ground for surgeons in the middle of the 20th century. In 1939, Robert Gross demonstrated the feasibility of ligating the patent ductus arteriosus. Great interest in the surgical treatment of congenital heart disease resulted from the report of Alfred Blalock and Helen Taussig in 1945 of an operative approach for the palliation of tetralogy of Fallot. Robert Gross reported the successful surgical correction of coarctation of the aorta the same year. Other shunt operations for the treatment of congenital and acquired heart disease were reported by Willis Potts, Edward Bland, and Richard Sweet shortly thereafter.



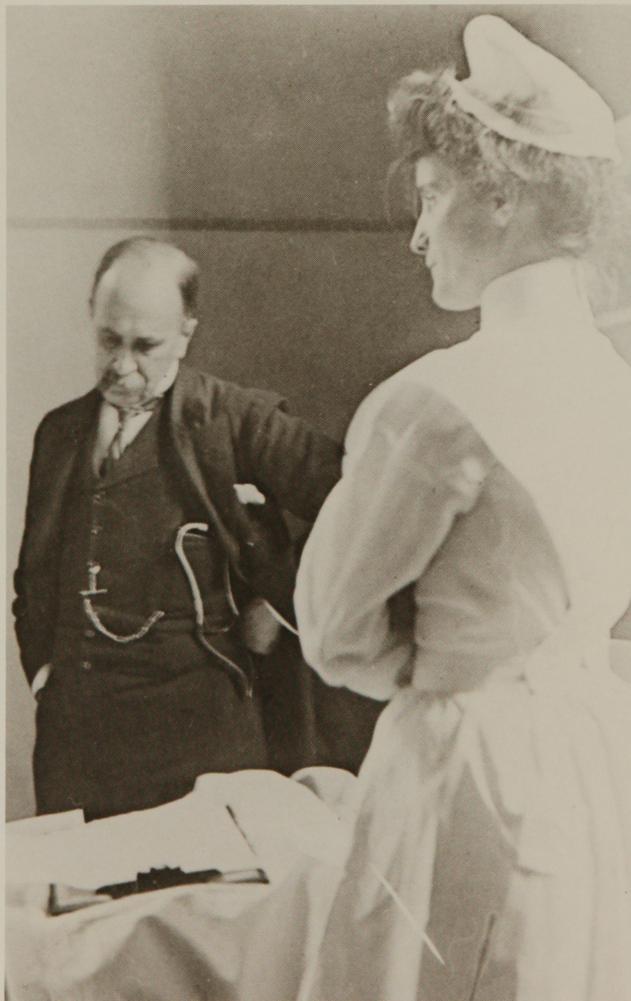
*Helen Taussig (1898-1986)*

*Operation for correction of defective aorta at Johns Hopkins Hospital, 1955. Surgeon Alfred Blalock (1899-1964) is second from the right.*



### *Miscellaneous Conditions*

Although he spent only two decades in the United States, William Osler is widely thought of as an American physician since many of his most widely known contributions occurred during his years in Philadelphia and Baltimore. The cardiovascular system was of special interest to Osler, and he made important additions to our understanding of many heart and circulatory diseases. His most significant observations related to the pathophysiology and natural history of infective endocarditis. In the early 20th century, Emanuel Libman of New York described atypical verrucous endocarditis with Benjamin Sacks and emphasized the value of blood cultures in the diagnosis of subacute bacterial endocarditis. The somewhat ephemeral syndrome of neurocirculatory asthenia was characterized by the Philadelphia physician Jacob Mendes DaCosta in 1871. More recently, several Americans have made valuable observations on two newly recognized syndromes, mitral valve prolapse and hypertrophic obstructive cardiomyopathy.



*William Osler (1849-1919) at the bedside of a patient, Johns Hopkins Hospital, about 1903.*



**TREATMENT:**  
*Pharmacologic Therapy*

One of the most widely used drugs in cardiology is nitroglycerin. This agent was first introduced into medical therapy by Constantine Hering, a pupil of Samuel Hahnemann and a founder of American homeopathy. Although Hering advocated in 1847 the use of nitroglycerin in a wide variety of ailments, neither he nor his fellow homeopaths prescribed it for angina pectoris. It remained for William Murrell of England to advocate nitroglycerin for this distressing complaint. Nevertheless, were it not for the peculiar doctrine of homeopathy and Hering's early work on this substance, it is unlikely that this explosive compound would have been introduced into the pharmacopoeia.

A discovery of fundamental significance for the subsequent development of beta-adrenergic blocking drugs was Raymond Ahlquist's 1948 proposal of the division of adrenergic sites of action into alpha and beta receptor groups. The antiarrhythmic property of procaine hydrochloride was first reported in 1936 by Frederick Mautz, a Cleveland surgeon. Fifteen years later, Mark and his associates synthesized procainamide hydrochloride and demonstrated its efficacy in the treatment of cardiac arrhythmias. J.L. Southworth and his colleagues first described the successful treatment of ventricular fibrillation with lidocaine in 1950. The American pharmaceutical industry has subsidized much research and development that has resulted in the introduction of efficacious remedies for a wide range of cardiovascular diseases.

Americans played an important role in the discovery of anticoagulants. William Howell studied various aspects of blood coagulation for more than half a century. His pupil Jay MacLean isolated heparin in 1916. Workers in Canada and Europe extended these early observations and introduced heparin into the management of patients with thromboembolic disease just prior to the Second World War. Heparin was a critical discovery for the eventual development of open heart surgery. A long-acting oral anticoagulant became available with the isolation of dicumerol in 1940 by Karl Paul Link of Wisconsin. An important advance in diuretic therapy occurred in 1958 with the recognition of the powerful diuretic effects of chlorothiazide by Karl Beyer.





*THERAPEUTICS:  
Cardiac Surgery*

One of the most important American contributions to medicine was the discovery of anesthesia in 1846. Nineteenth century American surgeons were noted for their aggressive and innovative approach to a variety of problems. For nearly two centuries, from Valentine Mott to Michael DeBakey, American surgeons have demonstrated the possibility of the operative approach to the treatment of arterial aneurysms. The development of cardiac surgery had to await numerous discoveries and technical innovations, however. Early in the 20th century, Alexis Carrel, a native of Lyons, France, left his native country at the age of 31 to continue his studies of vascular surgery and transplantation in the United States. As part of a long and extensive series of investigations on the surgery of the heart and blood vessels, he demonstrated the feasibility of coronary bypass surgery in experimental animals in 1910. Carrel experimented with nearly all of the present day techniques of vascular anastomosis in experimental animals more than half a century ago. It would be several decades, however, before these techniques would be applied to the human heart.

Surgeons sought to attack stenotic lesions of the cardiac valves early in the present century. In Boston, Elliott Cutler and Samuel Levine demonstrated that it was possible to surgically relieve mitral stenosis using a



*Alexis Carrel (1873-1944)*



cardiovalvulotome they devised in 1923. It would be a quarter of a century, however, before a sustained effort at developing surgical techniques for the palliation or correction of valvular heart disease developed. Working independently, shortly after the Second World War, Charles Bailey and Dwight Harken devised the procedure of closed mitral commissurotomy. In 1950, Bailey extended this approach to the treatment of aortic stenosis. Charles Hufnagel addressed the problem of aortic insufficiency in the early 1950's and developed a prosthetic aortic valve which he implanted in the descending aorta in an attempt to palliate this lesion. These innovative surgical approaches to the treatment of valvular heart disease were undertaken prior to the era of cardiopulmonary bypass, so direct visual correction of intracardiac lesions was still impossible.

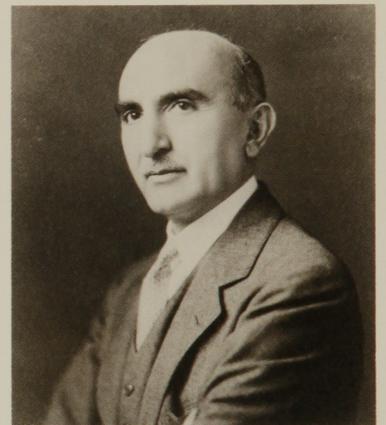
Definitive repair of congenital heart defects and acquired valvular disease was virtually impossible when the patient's heart was serving its normal function of circulating the blood through the body and lungs. Artificial respiration was used in experimental animals for centuries, and Newell Martin and others demonstrated the feasibility of sustaining myocardial function in the isolated mammalian heart several decades before these approaches were combined and refined to permit open heart surgery. John Gibbon, Jr., became interested in this problem in the 1930's when confronted with the high mortality rate of patients subjected to pulmonary embolectomy. He devised an oxygenator that was successfully used in 1939 as a heart-lung machine in animals. In 1952, Forest Dewey Dodrill of Detroit demonstrated the feasibility of partial heart bypass which did not include an oxygenator. Gibbon continued his work on the heart-lung machine and successfully used it in an operation to correct an atrial septal defect in 1953.

The following year, Walton Lillehei and his colleagues at the University of Minnesota used the technique of cross-circulation in which a human donor served as an oxygenator in order to make it possible to work in a dry intracardiac field through total inflow occlusion. Using this technique, Lillehei and his colleagues demonstrated that it was possible to perform total correction of intracardiac defects in man. In the early 1950's, workers in Canada, Europe, and other American institutions attempted to develop heart-lung machines. John Kirklin and his associates at the Mayo Clinic used a modified Gibbon heart-lung machine to perform total repair of congenital heart defects in humans.

The 1960's witnessed many bold and innovative developments in cardiac surgery. In 1961, Albert Starr and Lowell Edwards reported their experience with



*Elliott C. Cutler (1888-1947)*

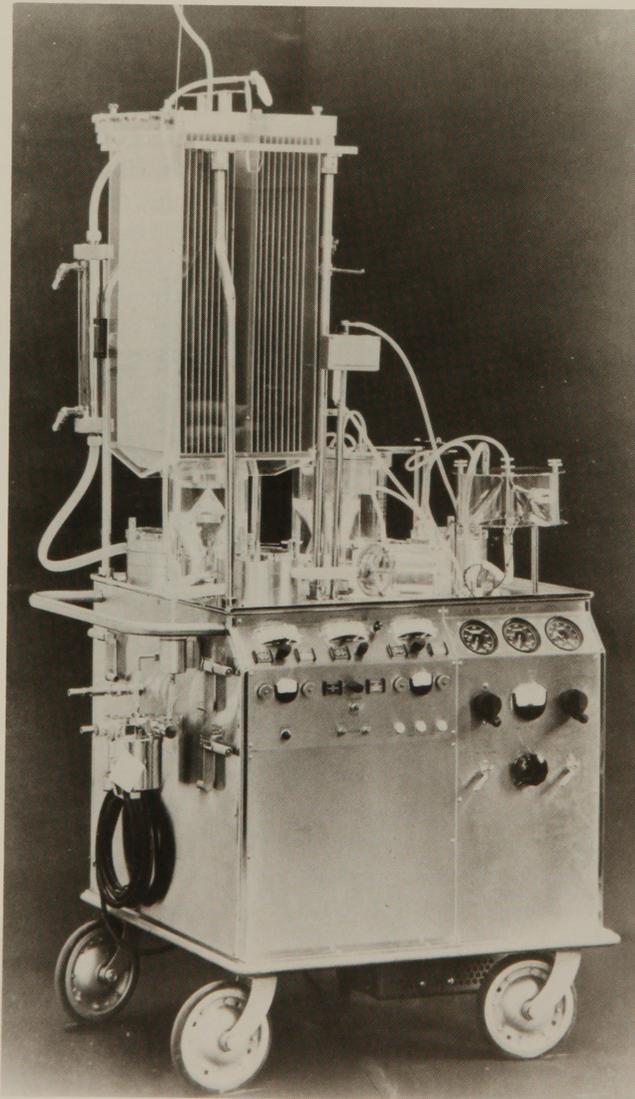


*Samuel A. Levine (1891-1966)*



replacing the mitral valve with a cage-ball prosthesis. In an example of international cooperation and the merger of clinical experience and basic science, Swedish surgeon Viking Bjork collaborated with American engineer Donald Shiley to develop their monostrut tilting disc valve in 1968.

Coronary artery disease became the focus of cardiac surgery in the late 1960's and early 1970's as various groups began using aortocoronary saphenous vein bypass grafts, a procedure pioneered by Rene Favaloro and Donald Effler at the Cleveland Clinic. Earlier surgical approaches designed to improve myocardial blood supply such as the Vineberg mammary direct myocardial implant procedure and coronary endarterectomy were soon abandoned in favor of the bypass operation as several workers confirmed the results reported by the Cleveland group. Congenital and acquired valvular heart diseases were successfully



*Gibbon-Mayo Pump-Oxygenator Model 10, 1957. Developed by Mayo Clinic engineers, based on heart-lung machine developed by John Gibbon, Jr. (1903-1973).*



treated with the new surgical approaches made possible by the efforts of scientists and clinicians around the globe.

Many patients, however, were dying from congestive heart failure due to loss of myocardium as a result of ischemic heart disease or cardiomyopathy. Several groups attempted to develop methods to temporarily assist the failing ventricle, and a few centers focused on the development of cardiac transplantation and the construction of an artificial heart. Dwight Harken and William Birtwell of Harvard developed the technique of intra-aortic counterpulsation in 1957. James Hardy reported the first human heart transplant in 1964 in which a chimpanzee heart was transplanted into a terminally ill man. The patient did not survive, however. Norman Shumway and his colleagues at Stanford University persisted when many other groups withdrew from the field of human cardiac transplantation following the early enthusiasm that resulted from the first successful human cardiac transplant by Christiaan Barnard in 1967. Shumway's group later led the effort to develop an operation for combined heart and lung transplantation. This procedure was successfully performed in 1980.

America's noted aviator Charles Lindbergh collaborated with Alexis Carrel in the 1930's in an effort to develop an artificial heart by refining the techniques of isolated organ perfusion that dated back to the 19th century. The development of the heart-lung machine by Gibbon and others in the 1950's gave new impetus to the quest for a true substitute for the heart. Willem Kolff, who constructed an effective apparatus for hemodialysis, emigrated to America and, in the 1950's, initiated a long series of experiments to develop an artificial heart. Other groups were developing artificial hearts as well. In 1969, Denton Cooley implanted a pneumatically driven artificial heart as a temporary assist device while awaiting a human donor heart. The patient was kept alive by this artificial heart for nearly 3 days, when a human donor heart was implanted. During the late 1970's, Kolff collaborated with Robert Jarvik, and they developed the Jarvik-7 artificial heart which was implanted in a patient in 1982 by William DeVries at the University of Utah.





## *Epilogue*

Most of the advances discussed in this booklet have been made within the past half century. This reflects the explosive growth of the scientific base of medical knowledge and the resultant clinical advances during this time period. The full-time faculty system and liberal support for basic and clinical investigation have greatly facilitated the research efforts of American biomedical scientists, physicians, and surgeons in recent decades. The National Heart Institute was established at the National Institutes of Health in 1948 and was the site of many important studies by a succession of talented basic and clinical scientists such as Eugene Braunwald, Andrew G. Morrow, and Donald Fredrickson. Grants from the National Heart, Lung, and Blood Institute have made it possible for thousands of individuals to investigate many aspects of the cardiovascular system in health and disease. Most would agree that the nation's investment in basic and clinical research has been worthwhile. Few would have predicted the dramatic advances in the diagnosis and management of patients with heart disease that have occurred during the past 50 years. New developments and directions in basic and applied science promise to further expand our understanding of the cardiovascular system in health and disease with ultimate benefit to mankind. Sustained support of basic and clinical research is critical, however, if this promise is to be fulfilled.





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## For Additional Information

Of necessity, this review of American contributions largely ignores the valuable advances made by workers outside of the United States. Readers of this essay can gain a more balanced view by a study of the international character of these disciplines. A classified list of references on the history of cardiology and cardiovascular surgery is available upon request. If you would like to receive this supplementary material, please write to the History of Medicine Division, National Library of Medicine, 8600 Rockville Pike, Bethesda, Maryland 20894 and request the "Bibliography of the History of Cardiovascular Medicine and Surgery," compiled by W. Bruce Fye, M.A., M.D.

### *The National Library of Medicine*

The National Library of Medicine was originally established in 1836 as the Library of the Office of the Surgeon General of the Army, and it consisted of a few shelves of medical books. The first major expansion of the collection was begun in 1865, when John Shaw Billings, a Civil War surgeon who had been given charge of the holdings, during the next 30 years assembled a substantial medical literature collection of international repute. The collection was later renamed twice—the Army Medical Library in 1922 and the Armed Forces Medical Library in 1952—and was designated the National Library of Medicine (NLM) in 1956. The NLM moved to its present modern building on the NIH campus in 1962 and became a component of the NIH in 1968. Today's NLM, which employs about 600 persons, is the world's largest library in a single scientific field, and it is the central resource for the nation's biomedical information system. Its holdings, which date back to the 11th century, number more than 3 million books, journals, microforms, pictures, audiovisuals, and other forms of recorded medical knowledge. In the History of Medicine collection alone, there are about 500,000 items, including over 500 incunabula (15th century books). An extensive computerized literature retrieval system provides rapid and convenient access to almost all the materials in the library's collection. The NLM appropriation for 1985 was \$55.9 million.

### *The National Heart, Lung, and Blood Institute*

The National Heart, Lung, and Blood Institute (NHLBI) was created within the U.S. Public Health Service by the United States Congress in 1948 as the National Heart Institute (NHI). In that same year, the NHI was made one of the Institutes of the National Institutes of Health. The NHI was renamed the National Heart and Lung Institute (NHLI) in 1969 to reflect an expansion of its mission. The National Heart, Blood Vessel, Lung, and Blood Act of 1972, which enlarged the authority of NHLI, provided for expanded, intensified, and coordinated Institute activities through a comprehensive National Heart, Blood Vessel, Lung, and Blood Disease Program. Four years later, the NHLI was redesignated the National Heart, Lung, and Blood Institute, and its mandate was further expanded to include research on the uses of blood and blood products and the management of blood resources. Today's NHLBI provides leadership for a national research program in diseases of the heart, blood vessels, lungs, and blood and in the uses of blood and the management of blood resources. It plans, fosters, and supports, through investigations in its own laboratories and through extramural contracts and grants, an integrated and coordinated research program that includes basic investigations, clinical trials, and demonstration and education projects relating to the causes, diagnosis, treatment, and prevention of heart, blood vessel, lung, and blood diseases. The program includes studies of the clinical uses of blood and all aspects of the management of blood resources. In addition, the Institute supports research training and career development in basic and clinical research relating to heart, blood vessel, lung, and blood diseases and transfusion medicine. The NHLBI employs more than 900 persons, and its appropriation for 1985 exceeded \$805 million.

### *The National Institutes of Health*

The origin of the National Institutes of Health (NIH) can be traced to the Laboratory of Hygiene, a one-room bacteriological laboratory established in 1887 at the Staten Island (New York) Marine Hospital for research on cholera and other infectious diseases. It was renamed the Hygienic Laboratory in 1891 and was moved to Washington, D.C. In 1930, it was designated the National Institute of Health. The Bethesda, Maryland, campus was made possible by a gift of land in 1935 for the NIH, and construction of Building 1 (now called the James A. Shannon Building) was begun the following year. The National Heart Institute was authorized in 1948, and the name of the National Institute of Health was pluralized to the National Institutes of Health. The NIH today consists of 20 Bureaus, Institutes, and Divisions and employs over 13,000 persons. Its campus consists of about 300 acres with over 40 buildings, which house offices, animal colonies, conference facilities, and hundreds of modern, highly sophisticated laboratories. The NIH campus also includes the Warren Grant Magnuson Clinical Center (Building 10), a 540-bed research hospital. The total appropriation for the NIH for 1985 was about \$5.2 billion.







