Two seminal events in cardiology

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Cardiac catheterization and interventional cardiology are foundational in contemporary medical practice. More than a half million coronary stents are implanted yearly, and percutaneous valve repair and replacement procedures are increasing. While there are many reviews on the history of invasive cardiology,[1-6] few have been written by primary observers.

Two young physicians, James V. Warren (AΩA, Harvard Medical School, 1951, Alumni), and Eugene Braunwald (AΩA, NYU Grossman School of Medicine, 1951) were present at the birth and dissemination of invasive cardiology at the Cardiopulmonary Laboratory at Bellevue Hospital and were trained by the then future Nobel Prize laureates, Drs. André Cournand (AΩA, Columbia University Vagelos College of Physicians and Surgeons, 1951), and Dickinson W. Richards, Jr. (AΩA, Columbia University Vagelos College of Physicians and Surgeons, 1922).[7,8] I witnessed Dr. Andreas Grüntzig's initial demonstration of coronary balloon angioplasty in patients at the 1977 American Heart Association meeting in Miami Beach and witnessed a mixed reception untold until now. Our stories fill in the missing pieces in the development of contemporary cardiac care.

The man who touched his heart

Self-experimentation has been critical to scientific progress.[9] The notion that one could safely place a catheter into the heart was heretical in Germany in 1929 when Dr. Werner Forssmann, intrigued by classic animal experiments of prior centuries, tricked an operating room nurse and self-inserted a urethral catheter into the antecubital vein of his left arm and threaded its tip into his right atrium, capturing it on a chest X-ray. Forssmann believed that this technique would allow administration of emergency intracardiac medication to avoid the trauma of percutaneous intracardiac injections. Forssmann also opined that such intracardiac catheterization might be useful in evaluating the heart's electrical system.[2]

Although others performed self-administered intravenous catheterizations before, and after Forssmann,[2] it was his paper that caught the eyes of Cournand and Richards who began a systemic study of cardiopulmonary physiology using intracardiac catheters. Their research accelerated when the exigencies of war led them to the study of shock.[10,11]

Unfortunately for Forssmann, as is the case for many medical innovators, his experiments led to his dismissal and a blemished career including imprisonment during WWII as a German army surgeon.[12] However, in contrast to others, he did live to be eventually recognized for his contribution to medical science.

The Bellevue Hospital Cardiopulmonary Laboratory

The 1956 Nobel Prize in Medicine or Physiology was awarded to Forssmann for demonstrating that right heart catheterization in humans was possible and to Cournand and Richards for their physiologic studies using right heart catheterization in humans in their laboratory at Bellevue Hospital.

Dickinson W. Richards Jr. graduated from Yale and served as an artillery officer in World War I. He obtained an MA degree in physiology in 1922 and his MD the next year, both from Columbia University's College of Physicians and Surgeons. In 1927, after residency training, he worked with the future Nobel laureate Sir Henry Dale, discoverer of acetylcholine and neurotransmission, at the National Institute for Medical Research in London.[13] Upon his return to the United States, Richards began research on circulatory and pulmonary physiology, mentored by Professor Lawrence Henderson of Harvard. Richards began his collaboration with Cournand in 1931 at the Columbia Division at Bellevue Hospital.[14]

Nobel Prize ceremony, highlighted left to right, André Cournand, Werner Forssmannn, and Dickinson W. Richards. Stockholm, December 1956.
Dickinson W. Richards Papers Open for Research I Archives & Special Collections

André Cournand's father was a dentist and scientist, and his mother was an intellectual. Cournand studied both science and humanities at the Sorbonne and graduated from the University of Paris with a Bachelor's degree in 1913 and a certificate in science in 1914. Cournand served in the French armed forces from 1915 to 1919 and was awarded the *Croix de Guerre* with bronze stars for heroism as a field surgeon. Returning to medical school and post-graduate training in Paris, Cournand was active in clinical investigation, co-authoring reports on a number of disorders.[14] After obtaining his MD degree in 1930, he obtained a residency position under Dr. James A. Miller on the world-renowned Chest and Tuberculosis service run by Columbia University at Bellevue Hospital. In 1932 Miller asked Cournand, his chief resident, to develop a pulmonary physiology laboratory at Bellevue, which Richards then joined.[14]

Cournand, Richards and their research group at the Columbia Division of Bellevue Hospital had taken Forssmann's self-experimentation as a starting point for the systematic evaluation of cardiopulmonary function using right heart catheterization.[15] Beginning in 1936 with animal experiments, then using human cadavers, they overcame technical challenges and by 1942 obtained right atrial oxygen samples and pressure measurements in healthy and ill men. The group continued to improve catheters and equipment as their journey progressed from the right atrium to the pulmonary artery.[16] In 1941, with U.S. entrance into WWII looming, the New York group began the study of shock.

The shock studies

James V. Warren joined the group in 1942 and wrote:

> ...but I believe the real impact of the catheter in clinical medicine came with the shock studies that were being conducted in New York during World War II by Cournand, Richards, and their group at Bellevue Hospital. They used the catheter as a device for physiologic observations. From blood samples, they calculated the cardiac output by the Fick principle and gradually explored the right side of the heart. The earlier reports, however, deal with blood sampled only from the right atrium.[7]
> This all took place during WWII. A major focus of medical research at that time related to the medical needs of the armed forces. An agency, the Office of Scientific Research and Development (OSRD), was set up in Washington as a funding mechanism for supporting this research. It was under an OSRD contract that the studies at Bellevue were undertaken. Lower Manhattan provided many casualties that simulated those on the battlefield. The program was based in the emergency room in

Bellevue Hospital. Although highly commendable, this program was not large enough and efforts were made to establish another focus of studies on shock. As a result of this, in 1942 Dr. Alfred Blalock (AΩA, The Johns Hopkins University School of Medicine, 1935, Alumni), Professor of Surgery at Johns Hopkins, and a group of distinguished physicians visited Dr. Eugene A. Stead, Jr. (AΩA, Emory University School of Medicine, 1943) at Emory University with offices at Grady Hospital in Atlanta. Their mission was simple. They wished to establish a shock unit at Grady because its emergency room had a considerable amount of trauma. If memory serves me correctly, at that time there were over 300 patients with hemopneumothorax admitted per year. I was particularly enthusiastic about the problem and volunteered to go to New York to see the Bellevue operation for myself.[7]

My visit added to my enthusiasm and within literally a few days Dr. Stead visited Bellevue and within a month I suddenly found myself listed as a special resident in pulmonary diseases at Bellevue Hospital so that I might be present for the shock studies day and night. After a period of training in the techniques there, I returned to Atlanta, assembled the necessary equipment and we were in business by mid-1943. We did indeed carry out studies on shock victims, but also found it wise to develop certain normal standards such as the cardiac output by the Fick principle, the effect of tilting, and the effect of anxiety. The British medical journal, *Lancet*, in an editorial at this time noted that that there were three major centers for this kind of clinical study, New York, London, and Atlanta.[7]

Funding the shock studies

Despite the limitations observed by Warren, the Chest Service at Bellevue was able to report data on circulatory shock. Their results acknowledged the contract the Committee on Medical Research (CMR) recommended between OSRD and Columbia and New York Universities and the additional funding by the Commonwealth Fund and the Josiah Macy Jr. Foundation.[10,11]

At the outset of our investigation, our hypothesis was that Henry L. Stimson, the Secretary of War, was personally involved in the funding of the Bellevue Cardiopulmonary Laboratory's shock studies. Beginning in 1939, Stimson's diaries document his recognition of the importance of science in the strategic planning for war.[17]

Although the United States was technically neutral at that time, there was a perceived threat that German

Dr. Alfred Blalock, Surgeon in Chief at Johns Hopkins Hospital, February 21, 1958. University of Southern California / Contributor

V1 and V2 intercontinental ballistic missiles could reach our east coast. The devastating bombings of European cities, with civilian crush injuries and battlefield casualties prompted the War Department to support research in trauma medicine. Did Secretary Stimson, a member of Yale's Skull and Bones secret society, use family and social connections to advance scientific research during WWII?

The "Old Boys" network

"The Colonel," as Henry L. Stimson was known,[18] (he served in WWI), was the son of Dr. Lewis Atterbury Stimson, who performed the first antiseptic operation in the U.S. Dr. Stimson was a founder and first Surgeon-in-Chief of the Cornell University Medical College (CUMC), and solo author of a popular surgical textbook, qualifying him as a trauma surgeon.[19] CUMC was funded by Dr. Stimson's Yale classmate and lifelong friend, Oliver Hazard Payne, one of John D. Rockefeller's partners in Standard Oil of Ohio.[20]

Moreover, Stimson's first cousin once removed, Dr. Lewis Atterbury Conner (AΩA, Weill Cornell Medical College, 1925), a Yale graduate, was second Chair of Medicine at CUMC and the first president of the New York and American Heart Associations.[21] Conner was friend and physician to Secretary and Mrs. Stimson. Was

Conner [my historical mentor] the cardiologist who suggested that Stimson fund the Bellevue lab?

There is ample documentation of Stimson's personal involvement in the development of radar and OSRD's "S-1" project, later called the Manhattan Project, both initiated by his cousin, Alfred Lee Loomis.[17]

Loomis was the son of Henry Patterson Loomis and Julia Josephine Stimson, Dr. Stimson's sister, and grandson of CUMC co-founder, Dr. Alfred Lebbeus Loomis, a friend and colleague of Dr. Stimson. Loomis was a Yale College and Harvard Law graduate and acolyte of cousin Henry L. Stimson. After leaving his cousin's firm, Loomis became a Wall Street tycoon. He anticipated the stock market crash of 1929 and created great wealth for many, including Henry Stimson. Loomis was also an amateur physicist and inventor, turning his home into a laboratory.

Loomis' work on radar and the Manhattan Project is documented in Jennet Conant's book, *Tuxedo Park*.[22] Ms. Conant's grandfather, James B. Conant, was a chemist who worked on poison gas during WWI and subsequently became the President of Harvard University. Conant was selected by President Franklin D. Roosevelt to run the National Defense Research Council (NDRC) during WWII.

Were Secretary Stimson and Dr. Conner behind the funding of the Bellevue Lab? Stimson had secretly acquired $2 billion from Congress for the creation of the atomic bomb.[23] Had Stimson secured Congressional funding for the shock studies as well? While Stimson's diaries mention meetings with Loomis,[17] there are no entries regarding support for the Bellevue shock studies. The trail went cold. If Secretary Stimson and Conner were not involved, who was?

Government support for military medicine

The National Academy of Sciences (NAS) was created by Congress in 1863 to recruit scientists and engineers for service to the government during the Civil War. Because of the growing importance of science, technology, engineering and mathematics, during WWI President Woodrow Wilson expanded the Academy's ability to aid the federal government by creating the National Research Council (NRC). By 1940, the NRC had 1,100 active consultants from whom the government could seek advice. Under that model, the Army and Navy departments would generate the ideas for equipment needed for war.

However, in the spring of 1940, with American involvement in the new world war looming, the Roosevelt administration saw that a federal agency was required to independently assess what scientific and technical resources the U.S. armed forces would need in such an engagement and develop them.

Previously, the armed services would ask civilian scientists for assistance in creating weapons. The Roosevelt administration believed that science and technology were advancing so quickly that the paradigm needed to be reversed: those at the cutting edge of knowledge should advise those about to engage in war what weaponry could be created for their use. Hence, the NDRC of the Council of National Defense was created. Dr. Vannevar Bush, President of the Carnegie Institution of Washington and former Dean of the Massachusetts Institute of Technology's School of Engineering, became Chairman.

It soon became apparent that while the NDRC excelled at research, a development apparatus was required. There was a need for inter-agency crosstalk and primary research in the field of military medicine. Therefore, in 1941 the OSRD was created by President Roosevelt's Executive Order. The CMR was a principal subdivision of OSRD, Tables 1 and 2.

Bush was made Chairman of OSRD and Conant became Chairman of NDRC. FDR appealed to Dr. Frank Jewett, President of the NAS, asking the NAS and NRC to support the OSRD in defense of the country. The close contacts that the NDRC developed with the NAS and the NRC extended to the OSRD. The Division of Medical Sciences of the NRC aided in the launching of the CMR.

In trying to find the "players" who were responsible for the initial funding of the Bellevue Laboratory, we had the archives of the OSRD and CMR examined. (Warren cited OSRD[7] and Richards the CMR.[11]) However, we found that the initial government grant to Richards was from the NRC in 1942 for $22,000.[25]

In 1941-1942, the officers of the Division of Science and Technology of the NRC were Lewis H. Weed and

Table 1: Office of Scientific Research and Development[22]
Vannevar Bush, Director, OSRD, Chairman
H.H. Bundy, Spec. Asst.to the Secretary of War
J.B. Conant, Chairman, National Defense Research Committee
Rear Admiral J.A. Furer, Coordinator of Research & Development
J.C. Hunsaker, Chairman, National Advisory Committee for Aviation
A.N. Richards, Chairman, Committee on Medical Research

Table 2: Committee on Medical Research 1941-1946
Division 1 (Medicine): E. Cowles Andrus, Chief (Internal Medicine, Johns Hopkins University)
Section I (Preventive Medicine): Colin M. MacLeod, Chief (Bacteriology, New York University) **Section 2** (Venereal Diseases): J. Earle Moore, Chief (Internal Medicine, Johns Hopkins University) **Section 3** (Tropical Diseases and Mycotic Infections) **Section 4** (Convalescence, Neuropsychiatry, and Clinical Investigations) Emmet B. Bay, Chief (University of Chicago)
Division 2 (Surgery): John S. Lockwood, Chief, (Yale University)
Section 1 (Wounds and Bums) **Section 2** (Neurosurgery): Cobb Pilcher, Chief (Surgery, Vanderbilt University)
Division 3 (Aviation Medicine): Detlev W. Bronk, Chief(Physiology, University of Pennsylvania)
Division 4 (Physiology): Joseph T. Wearn, Chief (Western Reserve University), C.N.H. Long, Deputy Chief(Physiology and Biochemistry,Yale University)
Section I (Blood Substitutes) **Section 2** (Shock): Dickinson W. Richards, Jr. Chief, (Medicine, Columbia University) Section 3 (Nutrition and Clinical Investigation)
Division 5 (Chemistry): Milton C. Winternitz, Chief (Pathology, Yale University), C. Chester Stock, Deputy Chief, (Biochemistry, Memorial Hospital, New York City)
Division 6 (Malaria): George A. Carden, Jr. Chief (Internal Medicine, Columbia University
Records Section: Kenneth B. Turner, Chief, (Internal Medicine, Columbia University)

Blalock. Weed was Chairman, Professor of Anatomy, and Director of the Johns Hopkins University School of Medicine, and Blalock was Vice-Chairman, Professor and Chairman of Surgery, Johns Hopkins University School of Medicine. They were responsible for approving the initial NRC grant to Richards.

As evidence of the close association of these government agencies, on March 19, 1942 Dr. Alfred Newton Richards, Chairman of the CMR, wrote to Richards (no relation) that:

> Dr. Frank C. Mann (AΩA, Indiana University School of Medicine, 1928, Alumni), of the Mayo Clinic has consented to undertake for the CMR, as well as for the Committee on Shock of the National Research Council, a survey of the present status of the contracts now in force with the OSRD in that field. He will doubtless wish to visit your laboratory and discuss your work with you...[25]

Mann was a world-renowned, wide-ranging experimental physiologist with interests in traumatic shock, hepatic physiology, gastrointestinal, renal, and vascular surgery and organ transplantation.

Alfred Richards graduated from Yale and obtained his MD at the University of Pennsylvania, where he served as the Chairman of the Pharmacology Department from 1910 to 1946. His technique for studying renal function was a landmark in animal physiology.

Alfred Richards' scientific career earned him eight honorary Doctor of Science degrees, two honorary Doctor of Laws degrees, fellowship in the Royal Society, and the Albert Lasker Clinical Research Award, among others. The Richards Medical Research Laboratories building at Penn, designed by architect Louis Kahn, was named in his honor.

How do we treat shock?

In a letter dated March 18, 1942, Richards asked Dr. John Mulholland (AΩA, NYU Grossman School of Medicine, 1924), Chief of Surgery at New York University, to ask Blalock's opinion regarding Dr. Robert Loeb's (AΩA, Harvard Medical School, 1918) query of whether a standardized treatment for shock was possible.[25]

On March 23rd Blalock responded:

> I am very anxious to be of aid to you and your group, but I am not certain that I can answer your questions. It seems to me that it is almost impossible to standardize the treatment of all instances of shock. I think one can have a definite routine as regards the treatment of burns with plasma, that one can have a routine as to the treatment of uncomplicated hemorrhage with whole blood; but I do not see how one can have a form of therapy that fits all cases...if you should care to send me your data I shall be glad to criticize it... I think you probably have the best rounded unit in the country for this study, and I am sure that you are going to have a lot of success.[25]

Richards' and Blalock's letters to Mulholland indicate another unique feature of the grants to the Bellevue shock studies: Bucking tradition, the project funded the faculty of several different departments at two medical schools, NYU and Columbia, who worked together at Bellevue

Hospital.[25] It was not until 1968 that NYU had sole control, once Columbia and Cornell had left Bellevue due to the reduction of beds from 2,000 to 1,000 in the plan for the new Bellevue Hospital building. Another demonstration of the "old boys" network was the appointment of Richards as Chief of the Shock Section of the CMR while he was a grant recipient. In a letter to Richards on July 13, 1944, Dr. Joseph T. Wearn (AΩA, Harvard Medical School, 1927), Chief, Division of Physiology of the CMR, wrote "Dear Dick: I am returning to you your application for contract. It has been discovered recently that individuals holding office on the CMR may not be responsible investigators on contracts. This is purely a technicality, but on talking it over with Chester Keefer he thinks it would be wise to have someone else designated as the responsible investigator on this contract. It could still be under your direction and it would not change the actual working conditions." Cournand was named.[25]

The critical role of Blalock in the shock studies

As demonstrated above, the medical scientist responsible for the initial NRC government funding of the shock studies at Bellevue and its academic support was Blalock who as Warren wrote also played a critical role in its replication at Grady Hospital. Providing subsequent support were Alfred Richards and Mann.

Blalock was repeatedly rejected by Dr. William Halsted for advancement in the Hopkins surgical residency program due to Blalock's average academic record. Hence, Blalock spent 16 years at Vanderbilt University, much of it in the surgical research laboratory, studying hemorrhagic and traumatic shock. He returned to Hopkins in 1941 as professor and Chief of Surgery. There he operated on over 1,000 children with congenital heart disease, employing the Blalock-Thomas-Taussig shunt. Among his honors was the Albert Lasker Clinical Research Award and the naming of the Hopkins Clinical Sciences building in his honor. Blalock was nominated for the Nobel Prize in Medicine or Physiology several times.

Government contracts for research in shock were not limited to Bellevue. Dr. Carl J. Wiggers (AΩA, Case Western Reserve University School of Medicine, 1923), and his group at Case Western Reserve University received funding as did several other prominent laboratories. The total wartime expenditure for shock research from the NRC and CMR-OSRD contracts was $820,333.[21] The Bellevue Lab received $93,440.[26]

Philanthropic support for the shock studies

The Commonwealth Fund began in 1918 with a $10 million endowment by Anna M. Harkness, widow of Stephen V. Harkness, the second largest shareholder in Standard Oil, "to do something for the welfare of mankind." From 1940 to 1949, the Commonwealth Fund awarded Columbia University over $158,000 for clinical studies in respiratory physiology and cardio-respiratory physiology. These funds resulted in thirty-five publications, including seven in the Journal of Clinical Investigation, six in the *Proceedings of the Society for Experimental Biology and Medicine*, and three in the *American Journal of Physiology*.[27]

The Josiah Macy Jr. Foundation was founded in 1930 by Kate Macy Ladd in honor of her father. Mr. Macy was a prominent philanthropist himself, whose wealth was also derived from investment in Standard Oil. The Macy Foundation initially focused on innovations in medical research, and currently is the only national foundation solely dedicated to continuing education of health professionals.

The major early goal of the Macy Foundation was to fund research on physical and mental shock. In a summary of their research support under the title, "The War Years," the Macy Foundation's Medical Committee wrote:

> In November, 1940, the directors, anticipating the inevitable involvement of the nation in a second world war, made a special appropriation for research on health problems affecting national defense. The Foundation promptly embarked upon vigorous support of studies on traumatic shock and war neuroses, problems closely related to the Foundation's earlier interest in surgical shock and in psychosomatic interrelations. A review of the literature of each of these topics was initiated, funds were made available to the National Research Council for meetings of committees and for conferences, and support was offered to research projects at a time when government funds were not yet available and the Office of Scientific Research and Development with its Committee on Medical Research, had not been established. [28]

Hence, the Macy Foundation may have provided the money for the initial $22,000 NRC grant to Richards:

> In the course of the next five years, the Macy Foundation expended more than $630,000.00 in support of the war effort without deviation from its established interest in medical research and education. During the war years,

> 1941-1945, more than sixty per cent of all funds appropriated were devoted to medical aspects of the national emergency.[28]

In the 1950s, the Macy Foundation continued funding research and yearly meetings on "shock and circulatory homeostasis" with Richards, one of the 15 Medical Committee members, and Cournand, a guest speaker, presenting an extensive review on "The Pulmonary Circulation."[29]

The Commonwealth Foundation, through its commitment to medical research at the Columbia Presbyterian Medical Center, and the Macy Foundation, through its fidelity to studies on shock, funded the majority of the research for the Bellevue Laboratory before, during and after WWII. Both foundations, begun by descendants of investors in Standard Oil of Ohio, promoted medical science that continues to have a major impact on contemporary clinical practice.

The shock studies: A post hoc assessment

Professor G. Liljestrand, Secretary of the Nobel Committee for Physiology or Medicine of the Royal Caroline Institute in Sweden, wrote in his 1956 Nobel Prize award ceremony speech:

> During WWII, as well as on earlier similar occasions, secondary wound shock constituted a serious problem. This is a state of circulatory failure which may appear several hours after a severe injury. Cournand, Richards, and co-workers showed that, although the causative mechanism varies, the essential feature is a considerable decrease in the minute volume, due to a diminished return of blood to the heart. This may, in turn, be a result of blood loss, or it may also be due to insufficient contraction of the smooth muscles in the blood vessel walls. A study of the improvement brought about by blood transfusion could be made by means of cardiac catheterization....The turn came to the acquired heart diseases.... Although congenital heart disease occupies a relatively modest place in the large complex of cardiac disorders, it is by no means a rarity....These results, of which brief mention has been made, have been the fruit of extensive investigations, implying the cooperation of a large number of highly skilled research workers. Cournand and Richards, have, however, consistently been the pioneers and the leaders. Moreover, the contributions made by the New York school have been a source of inspiration in other parts of the world and have, there as well, led to successful study of countless problems.[30]

Dr. Frank Glenn (ΑΩΑ, Washington University School of Medicine in St. Louis, 1953, Alumni), as the President of the New York Academy of Medicine, on presentation of the Academy Medal to Cournand and Richards, wrote about the Bellevue Cardiopulmonary Laboratory:

> This program was marked by the development of the technique of cardiac catheterization in 1940, by studies of traumatic shock in man, from 1941 to 1946, followed by investigations in the diagnosis of congenital heart diseases, the physiology of heart failure, analysis of various forms of dysfunction and chronic cardiopulmonary diseases and their responses to treatment.[31]

Richards wrote:

> The various investigations of traumatic shock in man carried out during WWII under the direction of the CMR can be considered under four general headings: the mechanism of shock; the effects of certain therapeutic agents, particularly blood substitutes; special inquiries into vasomotor behavior and possible chemical or toxic factors; and the particular problem of thermal burns.[32]

Richards acknowledged the failures of the shock studies:

> During the last two years of the war, attention was again directed to the possible effects of toxic factors in the cause or maintenance of peripheral circulatory failure... The clinical investigation that was conducted in this field did not go far enough to provide any conclusive proof of the importance or even existence of specific toxic factors.[33]
>
> Irreversible states in traumatic shock were also encountered, both in early hours after injury, when the latter was overwhelmingly severe, and on subsequent days, after initial resuscitation had been successful. In these cases restoration of blood volume to normal did not restore and maintain the circulation. Detailed studies were not, however, made on a sufficient number of such cases to provide a definitive description.[33]
>
> It was at this point-the investigation of massive and complex injuries-that the shock program broke down. As indicated above, a technique had been developed for comprehensive study of the mechanism of shock and the results of treatment. On the other hand, the severest and

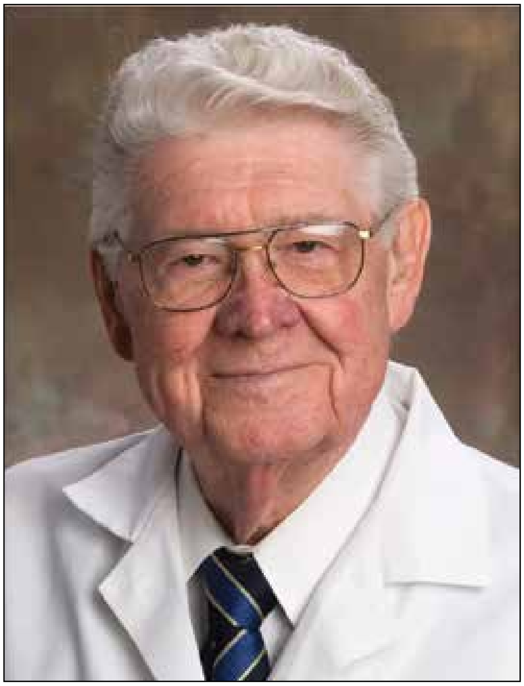
> most multiple forms of injury were being encountered only in the military theaters. The obvious solution was to have research teams, using the newer technics, study military casualties. When permission to do this was requested from the Surgeon General's office, however, it was refused...the whole question of irreversible shock in man, which some of the severest cases probably represented, went by default. So far as exact knowledge of what happens to the circulation in such cases is concerned, this vast amount of clinical material was lost.[33]

While research teams were not placed at the military front, beginning in 1943, medical-surgical teams ("Auxillary Surgical Groups") were located near combat zones to reduce the incidence of battlefield death. Colonel Michael DeBakey (AΩA, Tulane University School of Medicine, 1931), played a prominent role in creating the Mobile Auxiliary Surgical Hospitals ("MASH" units) which by employing systematic triage protocols and helicopters equipped with trained medical staff ("air ambulances") transporting the wounded to hospitals located at the rear, battlefield mortality was decreased from four percent during WWII to 2.5 percent during the Korean War.[34]

Nevertheless, regarding Cournand and Richards, "Many of their trainees and collaborators went on to different centers in the United States and elsewhere and adding their own original contributions to a rapidly growing field."[35] Dr. John R. West (AΩA, Columbia University Vagelos College of Physicians and Surgeons, 1943) opened the second Columbia Cardiopulmonary Laboratory at Presbyterian Hospital in 1951.[35]

The Bellevue shock studies initiated the birth of invasive cardiology and the explosion of physiologic research in the U.S. Table 3 lists the prominent positions obtained by the trainees of the Bellevue Cardiopulmonary Laboratory.[14] Missing from the list is James Warren, since he only spent weeks at Bellevue before starting the shock program at Grady (1942 to 1946). It was at Emory that Warren was on the cardiology faculty with Dr. J Willis Hurst (AΩA, Medical College at Augusta University, 1943), who included Warren's reminiscences in his review on the history of cardiac catheterization.[7] Warren went on to become Professor and Chairman of the Department of Medicine at Ohio State University and President of the American Heart Association.

One of the Bellevue Cardiopulmonary trainees, Braunwald, wrote in the abstract of his reminiscence, "Cournand's laboratory, his work habits, and his rigorous approach to science are described, as well as the stimulation the author received during the author's fellowship. As a result, the author went on to extend to the left side of the heart the observations that the Cournand group had conducted in the right heart."[8] Braunwald became a major clinical investigator, editor of an eponymous textbook, and educator. Braunwald's work and that of his trainees have brought science to the daily practice of cardiovascular medicine.



Dr. J. Willis Hurst, circa 1990. FlickreviewR 2, cc-by-sa-2.0.

The exigencies of war accelerate scientific investigation. It has been said that WWI was the chemist's war and that WWII was the physicist's war. The Committee on Medical Research's support for the study of shock made it also the physiologist's war.

Throughout history, scientific advances have often been double-edged swords demonstrating the dialectic of the good and evil that can come from invention. Alfred Nobel left the bulk of his fortune to reward innovation, largely to expiate his guilt for having forged such a sword, dynamite.

Hurst became Chairman of Medicine at Emory in 1955 and helped develop the medical center into a leader in cardiovascular medicine. Home to the second cardiac catheterization laboratory in the US, Emory produced leaders in invasive cardiology. In addition to editing an eponymous textbook, Hurst supported Dr. Spencer King, III in recruiting Grüntzig to Emory, establishing it as an international center of interventional cardiology.

Table 3: Collaborators/Fellows of Cournand and Richards

James K. Alexander became Chief, Cardiology, Baylor University School of Medicine, Houston, Texas

Robert Austrian became Chair, Department of Research Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Richard Bader and Morton Bader became Co-Directors, Pulmonary Function Laboratory, Mount Sinai Hospital, New York, New York

Eleanor deF. Baldwin was Director, Cardiopulmonary Laboratory, Columbia-Presbyterian Medical Center, New York, New York

Janet S. Baldwin became Chief, Pediatric Cardiology, Columbia-Presbyterian Medical Center, New York, New York

Norma Braun, currently Clinical Professor of Medicine, Mount Sinai School of Medicine, New York, New York

Eugene Braunwald became Chair, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts

William B. Briscoe became Chief, Pulmonary Medicine, Cornell University Medical College, New York, New York

Peter R. B. Caldwell succeeded R. M. Harvey as Chief, Pulmonary Medicine, Columbia-Presbyterian Medical Center, New York, New York

Robert C. Darling became Chair, Department of Rehabilitation Medicine, Columbia-Presbyterian Medical Center, New York, New York

Luigi Donato became Chief, First Medical Clinic, University of Pisa, Pisa, Italy

David Dresdale became Chief, Cardiology, Maimonides Hospital, Brooklyn, New York

Michael Dunnill became Consultant in Pathology, Radcliffe Infirmary, Oxford, United Kingdom

Jacques Durand became Professor of Physiology, University of Paris, Paris, France

Yale Enson succeeded M. I. Ferrer as Director Electrocardiographic Laboratory, and succeeded P. R. B. Caldwell as acting Chief, Pulmonary

Medicine, Columbia-Presbyterian Medical Center, New York, New York

M. Irene Ferrer was Director, Electrocardiographic Laboratory, Columbia-Presbyterian Medical Center, New York, New York

Alfred P. Fishman became Director, Cardiovascular Pulmonary Division, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Harry W. Fritts Jr. became Chair, Department of Medicine, State University of New York at Stony Brook, Stony Brook, New York

Carlo Giuntini became Chief, Second Medical Clinic and Director, Pulmonary Function Laboratory, University of Pisa, Pisa, Italy

Domingo M. Gomez became Professor of Experimental Medicine, New York University, New York, New York

Hans-Peter Gurtner became Chief, Cardiology, University of Bern, Bern, Switzerland

Peter Harris became Director, Institute of Cardiology, University of London, London, United Kingdom

R ´ejane M. Harvey became Chief, Pulmonary Medicine, Columbia-Presbyterian Medical Center, New York, New York

Alfred Hardewig became Chief, Cardiology, Marburg University, Marburg, Germany

Aaron Himmelstein was Chief, Cardiac Surgery, Columbia Presbyterian Medical Center, New York, New York

A. Gregory Jameson became Director, Medical Service, The Roosevelt Hospital, New York, New York

Thomas King, currently Professor Emeritus of Clinical Medicine, Weill Cornell Medical College, New York, New York

Milena L. Lewis became Chief, Pulmonary Medicine, Manhattan Veterans Administration Hospital, New York, New York

Alain Lockhart became Chair, Department of Physiology, Cochin Medical School, Paris, France

Attilio Maseri became Director, Cardiology, Hammersmith Hospital, London; Director, Cardiology, Catholic University, Rome, Italy

John H. McClement became Director, Chest Service, Bellevue Hospital, New York, New York

Hurley L. Motley became Chief, Pulmonary Medicine, Wayne State University School of Medicine, Detroit, Michigan

Attilio D. Renzetti became Chief, Pulmonary Medicine, University of Utah School of Medicine, Salt Lake City, Utah

Richard L. Riley became Chair, Department of Environmental Medicine, The Johns Hopkins University School of Hygiene and Public Health, Baltimore, Maryland

Dudley F. Rochester became Chief, Critical Care and Pulmonary Medicine, University of Virginia, Charlottesville, Virginia

Phillip Samet became Chief, Cardiology, University of Miami School of Medicine, Miami, Florida

Harry M. Thomas, III became Chief, Pulmonary Medicine and Director, Will Rogers Pulmonary Research Laboratory, Burke Rehabilitation

Institute, White Plains, New York

Ewald R. Weibel became Chair, Department of Anatomy, University of Zurich and, then, University of Bern; subsequently became Rector, University of Bern, Bern, Switzerland

Lars Werko became a member of the Karolinska Institutet, Stockholm, Sweden

Walter Wichern became Director, Surgical Service, The Roosevelt Hospital, New York, New York

Robert Wylie was Chief, Thoracic Surgery, First (Columbia) Surgical Service, Bellevue Hospital, New York, New York

Grüntzig and the birth of coronary balloon angioplasty

Andreas Roland Grüntzig was born in Dresden, Germany. His father was a polymath Ph.D chemist, writer, composer, and educator and his mother was a piano teacher. Grüntzig was a talented student who obtained his MD degree from Heidelberg University in 1964. He had extensive post-graduate training in angiology and radiology and became fascinated by mechanisms of dilatation of vascular stenoses. In 1974 Grüntzig performed the first balloon angioplasty of an iliac artery stenosis in a patient and a year later performed a coronary angioplasty in a canine model.[36]

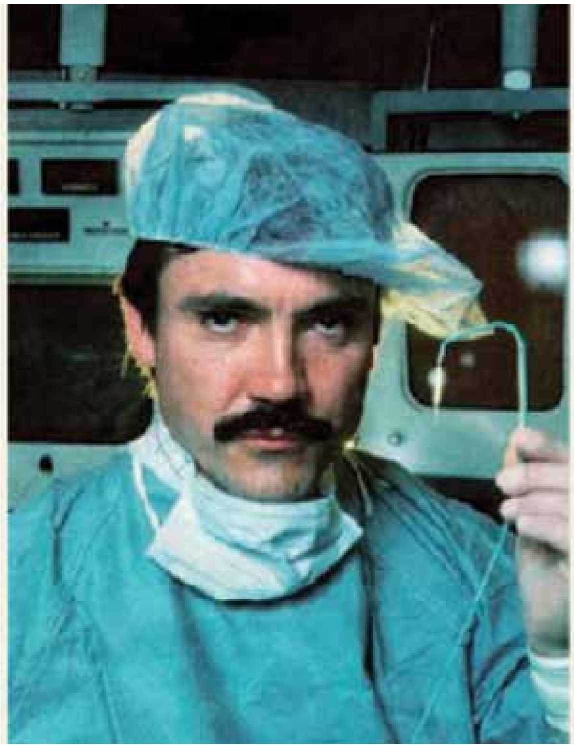
It is known that Grüntzig's poster presentation on canine coronary angioplasty at the American Heart Association (AHA) in 1976 was met with skepticism, with his poster being rejected by Cardiology and accepted by Radiology.[37]

However, accounts of the reception he received at his 1977 AHA demonstration of successful percutaneous coronary angioplasty in patients differ greatly from that which I observed sitting in the audience. I was a medical intern and presented research I had performed as a senior medical student at a different session.[38]

Grüntzig later recounted to Dr. King, III, "I also showed the slide of the fourth patient with the incredible success of mainstem dilatation and it was during this case that the audience started applauding in the midst of the lecture. I was so surprised that I almost could not proceed with my ten-minute presentation."[39] King wrote, "When he showed the films from those first four patients, he received a standing ovation. It was the most astonishing thing."[40]

The applause that Grüntzig and King heard during the former's demonstration did not emanate from near where I was seated. I recall that the immediate reaction at the conclusion of Grüntzig's presentation was mixed at best. I do not recall a standing ovation. Indeed, I heard many physicians express horror at the potential dangers of balloon explosion, embolization, iatrogenic infarction, arterial dissection and cardiac perforation. Grüntzig spoke with a German accent. In the audience were cardiologists who had served in WWII and many Jewish physicians. In my area during Grüntzig's talk, I heard boos, heckling and loud comments, including "this is human experimentation" and "he's another Nazi, like Forssmann."

The anger of many physicians in attendance was spurred by their skepticism of how Grüntzig had found a 38-year-old man with single vessel coronary artery disease on whom to perform the first successful angioplasty on a conscious human patient.[36] The audience was aware that multivessel disease was far more common than single vessel disease; the cardiologists present wanted to know how Grüntzig had found this young man with single vessel disease.



Dr. Andreas Grüntzig, circa 1980.

Grüntzig explained that the patient was referred to him because he had developed angina from a supra-normal positive stress test. The patient's symptoms occurred while skiing at high altitude in Switzerland. This explanation mollified a number of the skeptics and the mood in the room lightened. Yet, as I was leaving the auditorium, I heard many cardiologists express doubt about the veracity of Grüntzig's data. This is confirmed by Grüntzig himself, who stated that Dr. Mason Sones wanted to personally review the original cineangiography films.[39]

When I returned to the Albert Einstein College of Medicine in the Bronx, my cardiology attendings were uniformly unenthusiastic about the future of coronary balloon angioplasty. Dr. David Faxon, associate chief of cardiology at Brigham and Women's Hospital, said of the prevailing sentiment, "The idea of putting a balloon inside the coronary artery and blowing it up was almost considered blasphemy; it was forbidden."[40]

Dr. Peter Block opined:

> Nine months after the first procedure, only 50 or 60 cases had been performed around the world. In 30 percent to 40 percent of those, balloon angioplasty failed and some patients were sent for emergent CABG. With more than one-third of failures and up to 10 percent of patients being sent for emergency surgery we had to ask ourselves: Are we really doing something useful?[40]

This intellectual skepticism was quite different from what has previously been written: "Recognition of Grüntzig's triumph was immediate and widespread; unlike 1964 and 1976, the medical community was ready to embrace percutaneous revascularization.[2]

Despite "mainstream cardiology's" reluctance to embrace coronary balloon angioplasty, Grüntzig's genius was recognized by Drs. Richard K. Myler, Simon H. Stertzer, and Martin Kaltenbach, in addition to King and Hurst. As early as 1978, Dr. William Foley, a vascular medicine physician at Cornell, nominated Dr. Charles T. Dotter and Grüntzig for a Nobel Prize.[36] Foley interviewed both Dotter[41] and Grüntzig[42,43] and published their experience with percutaneous vascular intervention. By 1982 Grüntzig had performed 750 procedures with an 84 percent success rate, a 5 percent acute closure rate and zero mortality.[43]

Back in Europe, Grüntzig had difficulty establishing coronary angioplasty due to a hierarchical academic structure and technical challenges. He was recruited to Emory in 1980 where he had a brilliant but tragically short-lived career training hundreds of angiographers before he died in 1985 at age 46 in an airplane crash.

In 2011, King wrote after the death of his mentor, Hurst:

> He will be remembered for many things, but his role in clinical medical education and his embrace of the advances in cardiology, including coronary bypass surgery and subsequently percutaneous interventions have been most important for our specialty. Some are surprised because they think of Hurst as medically conservative, but when the benefits of surgery were demonstrated in his patients, he became a major proponent. And despite initial skeptism (sic) towards percutaneous transluminal coronary angioplasty, his enthusiastic involvement in the recruitment of Andreas Grüntzig to Emory was essential.[44]

Hurst gave Grüntzig one half of his personal office suite to use as his office.[45] Hurst's career at Emory, home of the second U.S. cardiac catheterization laboratory likely played a role in his support for Grüntzig and the advent of interventional cardiology.

There were many years of technical advances that improved upon Grüntzig's initial balloon dilatation system. Moreover, the problem of restenosis with balloon dilatation monotherapy was significant. Grüntzig's struggles to establish coronary balloon angioplasty were similar to those experienced by Sir James MacKenzie in gaining recognition for his work in non-invasive cardiology[46] and by Forssmann's quest to have his important contribution to cardiology acknowledged.[12] However, the latter two lived long enough to enjoy their success in later life. Grüntzig was fortunate to have his genius recognized fairly early in his career but doomed to live a very short life.

Contemporary interventional cardiology

Grüntzig's development of coronary balloon angioplasty gave birth to the new field of interventional cardiology and paved the way to create a device to keep arteries open that was named after a Victorian era English dentist, Dr. Charles Stent, and his denture mold cream. "Stents mass" evolved from use by plastic surgeons to deployment by interventional radiologists and cardiologists.[47] Coronary stents were initially bare metal, then drug-eluting, and are now bioresorbable. Moreover, today vascular interventionalists have new tools to employ in addition to stents: cutting, scoring, and drug-eluting balloons. Advantage, Grüntzig.

Advances in interventional cardiology have provided relief of angina for those refractory to medication, and has reduced the need for life-altering open heart surgery in patients with multivessel disease and chronic total occlusions. Percutaneous coronary intervention is the treatment of choice for acute ST segment elevation myocardial infarction and has been demonstrated to reduce myocardial necrosis and mechanical sequalae from coronary occlusion.

Percutaneous repair or replacement for congenital or acquired valvular disease is commonplace as is electrophysiologic ablation for atrial and ventricular tachyarrhythmias. Percutaneous closure of the left atrial appendage reduces the risk of stroke in patients with atrial fibrillation unable to tolerate anticoagulation.

While it is difficult to quantify the improved mortality and morbidity resulting from these procedures, they have clearly had a profound effect on improving and prolonging life.

Happily, medical science marches on. However, we do well to remember our history. Had Cournand and Richards not received funding for the shock studies, would the surge in cardiopulmonary scientific investigation have occurred so rapidly? Had Grüntzig lived, he too, would likely have been awarded a Nobel Prize as the father of interventional cardiology, thanks to the academic freedom provided by King and Hurst at Emory.

Hurst had seen the explosion of invasive cardiology begun at Bellevue in the 1940s by two subsequent Nobel laureates disseminated at Emory and he enthusiastically promoted the development of coronary balloon angioplasty in the 1980s which began the field of interventional cardiology.

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