NATIONAL ACADEMY OF SCIENCES

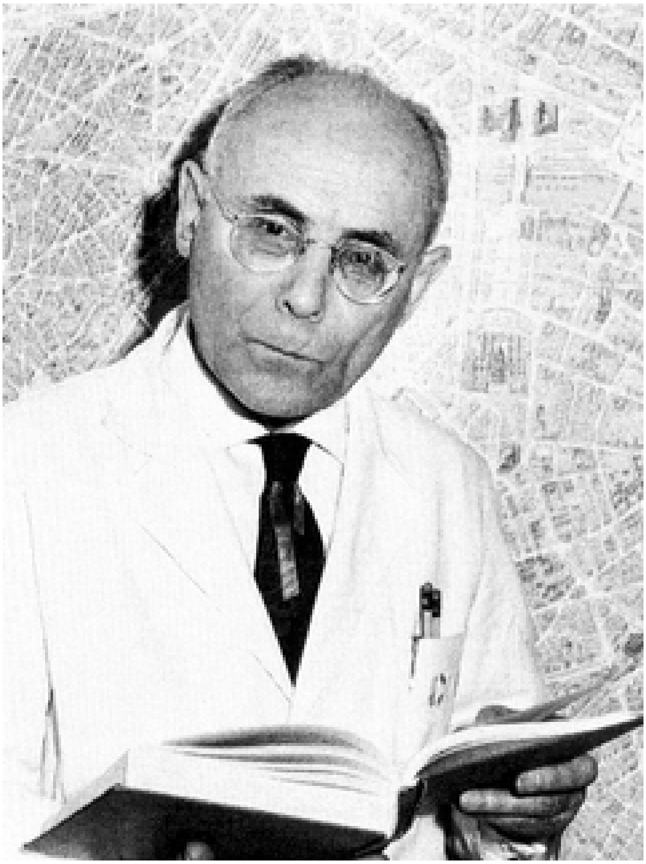
ANDRE FREDERIC COURNAND

1895—1988

A Biographical Memoir by
EWALD R. WEIBEL

Biographical Memoir

NATIONAL ACADEMIES PRESS
WASHINGTON D.C.



ANDRÉ FRÉDÉRIC COURNAND

September 24, 1895–February 19, 1988

BY EWALD R. WEIBEL

The subtitle of André Cournand's autobiography—*The Intellectual Adventures of a Medical Scientist*—conveys the essence of his life. As a basic scientist he was a medical man concerned about helping his patients through fundamental research. As a medical scientist he was adventurous, just as he had dared to climb high mountains in his younger years. His courage to introduce a catheter into a man's heart changed physiology, but only because of its intellectual backing by a rigorous analytical concept. André Cournand was an artist among scientists; he combined imagination with discipline and rigor in his analytical approach, a sense of drama with critical thinking about the course to take both in his research projects and, in later years, in his concerns about shaping the future.

André Frédéric Cournand was born in Paris, where he lived the first thirty-five years of his long life until his emigration to the United States. He felt very much French and European. His mother was the daughter of an Alsatian businessman, and his father descended from a Corsican author and poet who had participated in the French revolution of 1848. As Cournand writes in his autobiography, the influence of his mother was to give him a strong sense for the arts and an inclination toward adventure: "In my mother the adventurous spirit expressed itself primarily through imagination and sympathetic recognition of the impetus of adventure in others. This same eager readiness for the new and the unexpected was to make its influence felt in my own life." He was to receive a classical education, but at the age of sixteen he left the lycée to split his time between private tutoring in philosophy and work in a private laboratory to learn about scientific techniques. He nevertheless completed his undergraduate studies and enrolled in the Faculty of Sciences in order to be admitted to the Faculty of Medicine, a decision prompted chiefly by the influence of his father.

Cournand's father, Jules, was a dentist in private practice but of high renown academically, particularly because of his many innovations in dental technology for which he was awarded twenty-five patents. "My father inspired my interest in medicine and helped me to conceive it as neither an academic discipline nor a field of practical action alone; rather, he showed me by example how the interaction of theoretical and clinical interests could provide the basis for imaginative creations that contributed both to general knowledge and to solution of practical problems," writes Cournand, and this should, indeed, become the hallmark of his career in medical science. With his father he would not only explore the treasures of Paris but also begin his long career in mountain climbing.

In 1914 Cournand entered the Faculté de Médecine, just as World War I broke out. Even before his first year of medical school ended, he was enlisted in the army to serve as auxiliary battalion surgeon, for the most part in the trenches near the German enemy. For his distinguished services tending wounded soldiers at the front he was awarded the Croix de Guerre with three bronze stars. This experience in the battlefield lasted three and one-half years and left a deep impression on him: "It had been necessary to develop the attitudes of mind and feeling to face danger and take risks," and he believed that this was the undergirding of his emerging dual disposition to be open to the intellectually new and skeptical of received wisdom.

After returning from the war and recovering from some injury incurred at the end of his service, Cournand resumed his medical studies in 1919. During his internship he trained in pediatrics, chest diseases, internal medicine, and neurology in the Hôpitaux de Paris. He prepared his dissertation, required for the M.D. degree, on the topic of acute disseminated sclerosis ("La Sclérose en plaques aigue"), which involved experimental studies at the Institut Pasteur on isolating a virus from brain tissue. In his autobiography Cournand remains rather brief on his career as an intern in Paris, but he notes that his promotions came with difficulty. For one, his "conception of liberal thinking and action" did not help him in the still conservative French medical system marked by paternalism, but then also he spent much of his time and energy on a different type of activity.

During his service at the front he became friends with the young painter Jean Lurçat, who later became the famous designer of tapestries. This friendship brought Cournand into close contact with the so-called modern movement that determined the art life in Paris during the 1920s; he was introduced into the circle around Jeanne Bucher, whose gallery was an important meeting point for the modern artists. Here he met, among many other artists of renown, Jacques Lipschitz, one of the leading sculptors of the cubist period, with whom he maintained a lifelong close friendship. It was in this circle that he met his future wife, Sibylle, the younger daughter of Jeanne Bucher and her husband, the Swiss pianist Fritz Blumer. They married several years later and raised four children: three daughters, Muriel, Marie-Eve, and Claire, and Sibylle's son by a first marriage, Pierre Birel Rosset.

Around 1930 Cournand felt ready to go into private medical practice. But since he wanted to specialize in chest diseases he decided to enlarge his experience by working for one year in an American hospital. He felt fortunate to be admitted as resident to the well-known Chest Service at Bellevue Hospital in New York City. After a few months of service, partly in a sanatorium, Cournand was offered the possibility to participate in a long-range research project on pulmonary physiology by joining the group of Dickinson Woodruff Richards, a man of his own age but already quite advanced as an investigator. To accept this offer, however, meant not to return to France. Considering Cournand's exquisitely "French" or even "Parisian" life-style during the past decade this required a radical decision, but one taken by him and his wife with a positive mind. In his autobiography Cournand justifies this decision with several arguments. One was that the "free exchange of views in the United States had made a strong impression" on him and that here he would have "the prospect of an academic career where achievements count far more than nepotism." And he says that, in retrospect, the possibility to "leave behind a way of life whose disregard for the conventional bore little relationship to some values that constituted the treasure of my education" was an additional though unconscious element. Last, but not least, he felt excited "to participate in creating techniques to be applied to new protocols of clinical investigation and in rationalizing treatment." He returned to Paris briefly in 1932 to arrange his affairs after the accidental death of his father and then came back to New York to stay. But he always remained much attached to his home country. A large artistic map of Paris adorned one wall in his office at Bellevue, and he used to remark: "Je n'aime pas les départs . . . sauf pour Paris."

THE SHAPING OF AN INVESTIGATOR

Cournand's serious research activity began with what he called his "transplantation to the United States." In his bibliography he lists ten papers from his time in Paris, mostly case reports presented to French medical societies. When, in 1933, he published his first major paper he was already thirty-eight years old. It was a report on his work at the Bellevue Hospital Chest Service but was written in the European tradition, based purely on clinical evidence (1933,1); it makes no reference to pulmonary function tests that would be the main focus of Cournand's subsequent work, which, indeed, was already ongoing at the time of publication (1933,2).

Cournand became an experimental investigator through his association with Richards, with whom he remained closely associated throughout their lives and with whom he won the Nobel Prize in 1956.[1] Born in New Jersey the same year as Cournand, Richards also took up his medical studies in 1919 after some war service. Already during his residency he began with research projects that he extended during a fellowship in Sir Henry Dale's laboratory in London. Back in New York he directed his research to blood and circulation. One aspect of these studies was to improve on blood gas measurements, particularly of CO_2, because this was needed for the estimation of cardiac output. The so-called indirect Fick method then in use calculated cardiac output (or total blood flow) as the ratio of CO_2 output from the lung to the CO_2 concentration difference between the blood entering and leaving the lung. Whereas CO_2 concentration in arterial blood was easy to measure, CO_2 concentration in mixed venous blood had to be estimated indirectly from the CO_2 partial pressure in alveolar air.

When Cournand joined Richards in 1932 he became involved with this line of work. His first project was to test and improve a rebreathing method for estimating mixed venous CO_2 content and to apply it to some cases of pneumothorax (1933,2; 1935,1). The results remained only partially satisfactory, which led Cournand and Richards, some eight years later, to develop the method of right heart catheterization in order to obtain direct samples of mixed venous blood as it enters the lung.

In the meantime they directed their attention to some problems that had emerged when studying diseased lungs, namely that gases do not mix evenly in the lung, particularly in cases with pulmonary emphysema (1937,1,2). An important series of studies were undertaken in collaboration with Robert Darling, who developed a breath-by-breath analysis of intrapulmonary mixing of inspired air, introducing the simple method of washing out intrapulmonary nitrogen through the inhalation of pure O_2 (1940,1), a method that has been widely used and further improved by many other investigators. In the normal lung alveolar nitrogen is rapidly washed out, but in emphysematous lungs this is much slower because nitrogen is retained in the enlarged air spaces. In subjecting the closed-circuit method for estimating residual air volume mentioned above to a systematic critique (1940,2), they concluded that its failure was due to unequal distribution of gases *within* the lung. To overcome these shortcomings, a new open-circuit method with pure oxygen breathing was introduced (1940,3) that had theoretical advantages but still did not solve all the problems. At the time, these systematic studies of pulmonary ventilatory function, in which Cournand, Darling, and Richards themselves served as the normal subjects, made a very significant contribution to the advance of clinical respiratory physiology (1941,6).

With these methods in hand, Cournand and Richards proceeded to a systematic study of pulmonary insufficiency, which they classified according to the prevailing ventilatory, respiratory (i.e., gas exchange), or cardiocirculatory disturbances (1941,2). They developed the tests by which to differentiate between these functional disturbances. The efficiency of alveolar ventilation, studied at the time by several other groups, was combined with the measurement of arterial O_2 saturation as a test for adequate matching of alveolar ventilation with capillary perfusion. It is of historic interest that two papers of this series (1941,3,4) use these concepts and tests to estimate the effects on "pulmono-circulatory" function of various types of collapse therapy: in the late 1930s pulmonary tuberculosis was still a major disease, and collapse therapy was one of the major modes of treatment.

THE BREAKTHROUGH: CARDIAC CATHETERIZATION

In reflecting in his Nobel lecture on the state of their capabilities at that time, Richards concluded: "We were able to describe the ventilatory functions of the lung and . . . to define to some extent the mixing and the diffusional aspects of pulmonary alveolar or alveolar-capillary functions. But we still could not measure blood flow through the lungs and could not, therefore, move into those broader concepts of cardiopulmonary function which now began to be our goal." The problem still was how to obtain adequate samples of mixed venous blood to reliably apply the Fick principle. In 1936 Cournand and Richards decided that the only way of securing such samples was to introduce a catheter from a peripheral vein into the right atrium. They knew that this technique had been used in animals since the pioneering work of Claude Bernard in 1846 and that the young German surgeon Werner Forssmann had, in a heroic self-experiment in 1929, introduced a thin ureteral catheter into his own right atrium from an arm vein, but yet the procedure was not considered safe for human application. In order to assess the question of risk, Cournand went to Paris, where a former medical teacher of his, Dr. P. Ameuille, had introduced a catheter from an arm vein toward the right atrium in over 100 cases in view of introducing radio-opaque contrast medium for visualization of pulmonary vasculature. “I reviewed all the cases and returned to New York persuaded that cardiac catheterization could be used safely and would meet our needs,” Cournand writes in his autobiography. He then reports that for the next four years, in collaboration with Robert Darling, he carried out experiments in dogs and one chimpanzee and “adapted Bernard’s method” to their problem of obtaining samples of mixed venous blood for estimating O_2 and CO_2 concentrations. It is said that Cournand and Richards also tried the catheterization technique on human cadavers, but there is no mention of this in the published record.

Finally in 1941 Cournand and Hilmert Ranges published a note on “Catheterization of the Right Auricle in Man” (1941,1), detailing the technique already developed to near perfection and assessing the possible effects of the catheter on blood and heart function; the catheter was left in position fifteen to sixty minutes and no ill effects were found. They obtained mixed venous samples and could report the calculation of cardiac output by the Fick principle in one case. That was a breakthrough. Cournand did not invent cardiac catheterization, as is often said; his first paper on the method starts out as follows: “Forssmann first used catheterization of the right heart on himself” (1941,1). But he perfected the technique for safe and widespread use in humans, even in severely ill patients, and thus brought it to fruition; more importantly still, he pioneered the use of this method by obtaining the first significant measurements of cardiopulmonary function in health and disease. Cardiopulmonary physiology was different after that.

The paper of Cournand and Ranges is based on eight catheterizations in four cases of which the first one was catheterized on October 25, 1940. The third patient, considered normal with respect to the heart and lung, was catheterized three times in December, with the most comprehensive set of measurements performed on New Year's Eve 1940. In May 1941 Richards and Cournand presented their estimations of right atrial blood pressure, mostly based on the study of the same cases (1941,5), and on January 6, 1942, a paper (1942,1) was accepted by the *American Journal of Physiology* that reported in detail in these and some additional cases the direct measurement of the blood pressure in the right auricle and in peripheral veins, demonstrating the rise in atrial pressure in right heart failure. In this paper they also reported on some of the results of their preliminary animal studies. The first measurements were done with saline manometers; improved recordings of the actual pressure waves were obtained a few years later when the catheter was connected to a Hamilton manometer, a technique introduced by Stanley Bradley from the group of Homer Smith at New York University (1944,2).

On December 2, 1941, a paper by Cournand, Ranges, and Richard L. Riley was published in the *Journal of Clinical Investigation* (1942,2) that reported on twenty-one estimations of cardiac output by the direct Fick method. Using both O_2 uptake and CO_2 discharge, excellent agreement between the estimates was obtained in all cases. When on June 27, 1944, a much extended study was submitted for publication (1945,1), the group had reportedly performed some 260 catheterizations on humans, and they had introduced many improvements in their methods of analysis. The resulting estimates of cardiac output were very consistent and consequently appeared definitive.

With these studies the great value as well as the safety and feasibility of catheterization of the right heart were established. Some small but ingenious technical details contributed to the success: the catheter tip was given a curve to allow better positioning, and a double lumen catheter was constructed for simultaneous pressure recording or blood sampling from two serial points along the bloodstream (1945,2); a special needle for arterial blood sampling (the "Cournand needle") was designed. But, most importantly, a battery of physiological methods was set up to obtain the most reliable measurements of blood gases and of pressures. It is the whole concept of an analytical system that set the precedents just as much as the ingenuity of probing the heart with a fine catheter.

PHYSIOLOGICAL CONTRIBUTIONS WITH THE CARDIAC CATHETER

Cournand and Richards were now ready to approach questions of the pathophysiology of pulmonary circulation. The first condition that imposed itself was traumatic shock, a most pressing problem in those years of World War II with its many casualties in the U.S. armed forces that had just entered combat. The foremost problem of shock is hemodynamic deterioration due to severe blood loss. In the shock unit set up at Bellevue Hospital, cardiac catheterization was used to show that with about half the blood volume lost cardiac output became critically depressed, with the result that shock worsened; also, the importance of variable reduction in peripheral blood flow, particularly to the kidneys, was elucidated by Stanley E. Bradley. Most importantly, the new method was used to monitor therapy in these severe conditions.

With the end of the war a period of intense research began that established the basis for understanding the role of blood flow in pulmonary gas exchange, directed mainly to three topics: (1) pulmonary insufficiency, (2) maldistribution of ventilation and perfusion in chronic lung disease, and (3) congestive heart failure and cor pulmonale.

A most important set of by now classical studies approached the problem of alveolar ventilation-perfusion relationship as a determinant factor of pulmonary gas exchange (1949,6; 1951,7,8). Richard L. Riley, who had already been associated with the shock program, and Cournand (1949,6) applied a method for estimating "ideal" alveolar air composition and addressed the importance of variations in the ventilation-perfusion relationship for gas exchange, a concept that triggered innumerable subsequent studies by many investigators to the present day: ventilation-perfusion mismatch is considered one of the most important impairments of lung function. Complex four-quadrant graphs were used to interpret physiological measurements of the composition of gas and blood obtained simultaneously through a cardiac catheter and an indwelling arterial needle while the subject was breathing into a spirometer. The equipment and approach described in perfected form in 1951 (1951,8) is a masterpiece of strategy and rigor reflecting the highest laboratory standards, so the conclusion was certainly justified: "The method . . . makes possible the quantitative evaluation, for the lung as a whole, of all the major factors affecting the partial pressures of oxygen and carbon dioxide in the gas and the blood of the lungs." These papers should be mandatory reading for respiratory physiologists.

Cardiac catheterization also allowed pressures to be recorded from the right auricle, the right ventricle, and the pulmonary artery once the catheter tip could be positioned at will along the bloodstream. Cournand and his collaborators therefore directed their major research effort to studying the hemodynamics of the lesser circulation: if flow and pressures could be measured, the work of the heart could then be calculated. And since an indwelling needle was routinely placed in the brachial artery, systemic pressure recordings could also be obtained, which allowed an integrated assessment of the hemodynamics in the greater and lesser circulation. In exercise, they noted that the increase in cardiac output was accompanied by a slight fall in pulmonary artery pressure and hence in pulmonary vascular resistance; the lungs' small vessels open up, and this also improves the efficiency of gas exchange.

Cournand reviewed the new insights on pulmonary hemodynamics gained during the first few years in two major lectures. In the first review of 1946 (1947,2), he could base his report mostly on work done in his own laboratory, whereas four years later several groups from different places in the United States and Europe had already made significant contributions after they had adopted the technique of cardiac catheterization. In the Walter Wile Hamburger Memorial Lecture delivered in 1950 (1950,5)—which Cournand considered one of the first recognitions of his work—he reviewed the knowledge on the physiology of pulmonary circulation acquired during the few years since his first successful attempt at cardiac catheterization and then went on to discuss the value of "modern physiologic methods" for the study, understanding, and treatment of pulmonary diseases. He focused on pulmonary hypertension as related to left ventricular failure and on pulmonary emphysema where severe structural changes and functional disturbances add up to increase the load on the heart, thus setting the stage for right heart failure. Cournand concluded this lecture with the statement that "a better knowledge of the physiology of the pulmonary circulation in normal man has been of help in understanding some of the adaptive changes which occur in the course of diseases of the heart and lungs. In retracing the steps that lead to the breakdown of homeostasis . . . the cause of sound and effective treatment of these diseases has been well served."

In 1947 Cournand had confirmed in man the observation of the Swedish investigators U. S. von Euler and G. Liljestrand that hypoxia causes a rise in pulmonary arterial pressure (1947,4). This suggested that hypoxic vasoconstriction could regulate blood flow distribution to well-ventilated alveoli. With Alfred P. Fishman and Harry W. Fritts, a series of studies (1955,3; 1960,3,4) were undertaken to identify the mechanism and site of action of acute hypoxia on the pulmonary vasculature, but they failed to do so; indeed, even at the time of writing this memoir some three decades later the true cause of this effect remains elusive.

The potential to probe the cavities of the right heart and the pulmonary artery with a catheter found its use in yet another field: in the accurate diagnosis of congenital malformations of the heart and great vessels. Together with the pediatric cardiologist Janet Baldwin and the surgeon Aaron Himmelstein, Cournand set up a group devoted to the study of congenital malformations. Cardiac catheterization and angiocardiography were used to establish the functional disturbance of the anomaly in preparation for surgery (1947,5; 1949,1; 1952,2). In his Nobel lecture Richards noted that the advances in surgery of congenital heart disease were under way before cardiac catheterization and that it has moved ahead on its own but that the cardiac catheter has been a primary aid.

"A TIME FOR REWARDS"—PEER RECOGNITION

By the early 1950s André Cournand had published about 100 papers on the physiology and pathophysiology of the cardiopulmonary system, several of which have become true classics as they have brought significant innovations. He introduced the nitrogen washout method for studying the gas compartment of the lungs. He greatly advanced the study of the role of uneven ventilation-perfusion relationship for gas exchange. He pioneered cardiac catheterization in humans and was the first to measure cardiac output with the direct Fick method using mixed venous blood samples and the first to record blood pressure in the right heart and the pulmonary artery. By that he has most significantly contributed to the development and innovation of cardiopulmonary physiology. If one reads his early papers one is impressed by the scientific rigor of his approach as much as by the ingenuity of the meticulous techniques he had to develop. The artistic spirit of adventure inherited from his mother had blended with the imaginative inventiveness received from his father to bring about these advances.

Recognition of these achievements did not come his way easily. Cournand was made professor of medicine at the Columbia University College of Physicians and Surgeons only in 1951, at the age of fifty-six and after having served in various teaching positions at this university for eighteen years. In 1946 he was awarded the Andreas Retzius Silver Medal by the Swedish Society of Internal Medicine, and in 1950 he received the Lasker Award. Then in 1956 he was awarded the Nobel Prize for Physiology or Medicine together with his long-time partner, mentor, and friend Dickinson W. Richards, and the German surgeon Werner Forssmann, the heroic pioneer of heart catheterization. This prize emphasized cardiac catheterization as the most significant innovation in cardiopulmonary physiology. But by this emphasis it does not perhaps render true justice to the achievements of Cournand and Richards, for it is what they did using this technique in association with a whole battery of other methods that set a new standard of physiological research and thus fully justified this highest distinction.

Following the Nobel Prize, broad recognition flowed freely. Cournand was made a member of the National Academy of Sciences in 1958 together with Richards. He, the Frenchman, was admitted as a foreign associate to the French Academies of Sciences and of Medicine and in time became an honorary member of many learned societies around the world. He collected nine honorary doctorates, including one from Columbia University and three from France. His home country distinguished him by the highest honors it could give, naming him Commandeur de la Légion d'Honneur and Commandeur des Palmes Académiques. The years following the Nobel Prize were a true "time for rewards," as Cournand titles a chapter of his autobiography, and he thoroughly enjoyed it.

THE UNRELENTING SCIENTIST

I had the privilege of joining Cournand's group for two years as a research associate. I came into a newly refurbished laboratory that was sizzling with scientific activity. Cournand was full of energy and of a restlessness that bordered on impatience. It was still his time for rewards, and the part he enjoyed most was that he was in great demand as a lecturer. He was indeed a good speaker, who, with his French charm and accent, could elicit enthusiasm and sometimes irritation in his listeners; and furthermore he had a scientific message to deliver. For the Cardiopulmonary Laboratory at Bellevue Hospital this meant that he was in and out of the place. He would come to the laboratory, stir up the crew, discuss all the projects, collect information and slides, and take off for the next lectures.

Disputes on scientific and other issues were almost the order of the day in the laboratory when Cournand was around; he loved arguments. They were indeed an important part of what Richard Riley called "the Cournand magic" in his presentation of the Trudeau Medal to Cournand in 1971, and he went on to say that "one must be a little irreverent to convey a feeling of this magic. . . . He was outrageous at times but always exciting to be with. His moods changed from moment to moment, sometimes bringing about a graceful end to an argument with a sudden tension releasing: 'You are right' and sometimes a withering exclamation: 'That man is impossible.'" For all that he was certainly exciting to be with, particularly for all the young investigators who were in his laboratory at my time. And he was still eager to explore new scientific avenues.

In those years the research was chiefly directed towards two main topics: study of the ventilation-perfusion relationship and its disturbance, particularly in emphysema, directed by William A. Briscoe; and pulmonary blood flow and cor pulmonale, led by Réjane Harvey, Irène Ferrer, and Harry W. Fritts. In typical Cournand tradition these topics were approached with novel techniques. Radioactive tracer gases were introduced and used in various ways to estimate the degree of uneven ventilation and perfusion of airspaces and to find new ways of determining pulmonary hemodynamics.

Cournand and Richards had for a long time nurtured an interest in introducing structural studies into their program, as Richards noted even in his Nobel lecture. During my training as an anatomist I studied the structural relation between bronchial and pulmonary arteries; following a seminar I gave at Bellevue on this topic, they invited me to join their laboratory "to do anything on the structure of the lung that is of interest for physiology," an unusual offer that turned out to be a true challenge. Cournand gave me complete freedom and generous support to set up a histological laboratory. My great fortune was that, by the time I arrived, Cournand had given refuge to Domingo M. Gomez, who had fled his native Cuba to escape Fidel Castro's reign of terror. A cardiologist and biomathematician, Gomez had formerly worked with Homer Smith and had thus become involved with some of the early studies on estimating cardiac output. Now he was interested in theoretical aspects of pulmonary gas exchange that could establish a link between lung structure and function. Together we began to study the architecture of the human lung with new quantitative methods, and this led to what is now called morphometry. Cournand was not directly involved in these studies, but his way of asking questions and his keen interest in seeing this new line of work develop were most important. His laboratory provided the best environment to pursue this kind of new enterprise; it was traditionally a place to do new things.

In 1964 André Cournand retired as director of the Cardiopulmonary Laboratory at Bellevue Hospital, and a few years later the laboratory he had established thirty-two years earlier was closed. This ended a most productive period of research that can be divided into three main phases: the first ten years were devoted chiefly to developing new methods of investigation; the study of heart and circulation followed; and finally, exploration of the lung and pulmonary circulation along several tracks.

"LATE BUDDING": TURNING TO BROADER ISSUES

André Cournand freely admitted that "the idea of enforced termination of a scientific career that had provided great satisfaction . . . was in my case hardly welcome. . . .

How was I to escape idleness by starting new and satisfying activities?" In retrospect this was indeed an understandable concern considering that he would have over twenty years ahead of him, in full vitality and with a vivid intellect. He would, in time, have some difficulties with his eyes, ears, and knees but not with his mind, which remained sharp and lucid to his last weeks. His autobiography, published in 1986, shows no sign that its author had passed the ninetieth-year mark. During these twenty years Cournand directed his interest and still considerable work capacity to three fields: planning for the future, the ethics of science and social responsibility, and exploration of the historical roots of his life's work.

Cournand notes that the Nobel Prize had somehow transformed his life in that he felt a greater responsibility to step out and address broader issues. After his retirement he was able to devote himself fully to a concern that had captured his interest a few years earlier: study of the "Prospective Approach to the Future," a methodology formulated by the French philosopher Gaston Berger, which offered a creative way of planning the future by placing preferred futures as the driving force for planning, instead of merely allowing the present to project itself into the future. Cournand, who had met Berger during the fifties, translated some of his works into English; compiled them in a book, *Shaping the Future,* that was published in 1973; and organized meetings and seminars on the topic in an attempt to disseminate these ideas.

Concern about the role of responsible creativity led Cournand to reflections about the specific responsibilities of scientists. Clearly, he had an excellent background of a practical nature, and I should say that three features of his scientific career demonstrate his sense of responsibility in his own scientific work: the fact that he strived for investigative methods that would stand all tests and yield credible insights; his endeavor to address the important and pressing questions; and his willingness to employ his new methods for the benefit of his patients. But now he wanted to work out principles of an ethical code of the scientist. In that vein he joined the Frensham Pond group and developed a close relationship with the social scientists Robert K. Merton and Harriet Zuckerman. In 1976 he published in *Science* his views on "The Code of the Scientist and Its Relationship to Ethics," identifying seven principles: objectivity, tolerance, recognition of error, recognition of priorities, doubt of certitude, unselfish engagement, and sense of belonging to the scientific community.

His third line of interest concerned "looking back at the roots" with his remarkable autobiography, *From Roots . . . to Late Budding*, as the main result. He looked back at the development of cardiopulmonary physiology from Claude Bernard to his own time. And finally, he wrote a biographical memoir on Dickinson Woodruff Richards, a very personal portrait of his lifelong partner to whom he was bound, as he said, in "a friendship [of which] the essence is not to look into each other's eyes, but to look in the same direction."

André Cournand had a very long and productive life. He certainly knew that he had fulfilled his mission. This life full of work saw joy and hardship. During the Second World War he lost his only son in combat, and in 1959 his wife Sibylle died at the age of fifty-eight after long suffering. Four years later he married Ruth Fabian, his associate of many years; with her he would start his active post-retirement life that caused him to travel frequently to Europe. On one of these trips to London in 1973 Ruth died unexpectedly, leaving Cournand to "plunge [himself] into concentrated thinking and writing," as he says. In 1975 he invited Beatrice Bishop Berle, an old family friend and widow, herself a physician, to accompany him on a trip to Lindau, where Nobel laureates regularly meet, and a few months later they were married. They led a very happy life, full of rewards, splitting their time between their New York apartment and Beatrice's beautiful farm in Massachusetts, when they were not in Paris or traveling in Europe, attending meetings and visiting friends and former disciples. These years were marked by Cournand's active interest in the education and careers of his grandchildren, who were often at his side. Then, for the last months of his life he "retired" to the Berkshire farm; he put down his pen. His heart began to weaken and he felt he had come to the end of his long journey. Early in February of 1988 I visited him for the last time; our intercourse was wordless. On February 19, 1988, he passed away peacefully at the age of ninety-two. A long rich life had come to an end.

NOTE

1. Dickinson Woodruff Richards, by André Frédéric Cournand. In *Biographical Memoirs,* vol. 56, pp. 459-85. Washington, D.C.: National Academy Press, 1986.

BIOGRAPHICAL DATA

Education

1914	B.A., University of Paris, Faculties of Arts and of Sciences
1930	M.D., University of Paris, Faculty of Medicine

Professional Appointments

1926-30	Interne des Hôpitaux de Paris
1930-68	Resident, Attending Physician, Consultant, and Director of Cardiopulmonary Laboratory, Bellevue Hospital, New York
1935-88	Columbia University College of Physicians and Surgeons
1951-61	Professor of Medicine
1961-64	Professor of Clinical Physiology
1964-88	Professor Emeritus
1965-69	Member of the Institute for the Study of Science in Human Affairs

HONORS AND DISTINCTIONS

Croix de Guerre, France (1914-18)
Commandeur de la Légion d'Honneur (France)
Commandeur des Palmes Académiques (France)

1946	Andreas Retzius Silver Medal of the Swedish Society of Internal Medicine
1950	Lasker Award, U.S. Public Health Service
1956	Nobel Prize for Physiology or Medicine (with D. W. Richards and W. Forssmann)
	Associé Etranger, Académie des Sciences de l'Institut de France
	Associé Etranger, Académie Nationale de Médecine, Paris
1958	Gold Medal, Royal Academy of Medicine, Brussels
	Member, National Academy of Sciences
	Honorary Fellow, Royal Society of Medicine, London
1959	President, Harvey Society, New York
1962	John Phillips Memorial Award, American College of Physicians
1966	Academy Medal, New York Academy of Medicine
1969	Associé Etranger, Académie Royale de Médecine de Belgique
1970	Jimenez Diaz Prize, Madrid
1971	Trudeau Medal, American Thoracic Society
1975	Fellow, American Academy of Arts and Sciences
	Honorary Associate Member, Académie des Sciences, Belles-Lettres et Arts de Lyon

Doctor Honoris Causa

1957	University of Strasbourg
1958	University of Lyon
1959	University of Brussels
1961	University of Pisa
1961	University of Birmingham
1963	Gustavus Adolphus College
1965	Columbia University
	University of Brazil
1968	University of Nancy

SELECTED BIBLIOGRAPHY

1922

With Ch. Achard and L. Binet. Variation de la glycémie après injection de novarsénobenzol. *Soc. Biol.* April 1.

1924

With Lereboullet and Lelong. Un cas de réanimation du coeur par injection intracardiaque d'adrénaline chez un enfant en état de syncope au cours du tubage. *Soc. Pédiatr.* July 8.

1929

With Ch. Achard and Pichot. Transfusion du sang dans le coeur pour une enterorhagie typhoïdique. *Acad. Méd.* January 29.

1930

With Guillain and Rouques. Encéphalomyélite aigue disséminée du type de la sclérose en plaques avec syndrome de Parinaud et signe d'Argyll-Robertson transitoire. *Soc. Neurol.* January 9.

1933

With O. R. Jones. The shrunken pulmonary lobe with chronic bronchiectasis. *Am. Rev. Tbc.* 28:293.

With D. W. Richards and N. A. Bryan. Applicability of rebreathing method for determining mixed venous CO_2 in cases of chronic pulmonary disease. *J. Clin. Invest.* 14:173.

1935

With N. A. Bryan and D. W. Richards. Cardiac output in relation to unilateral pneumothorax in man. *J. Clin. Invest.* 14:181.

With D. W. Richards and I. Rappaport. Relation of the regulatory mechanism of respiration to clinical dyspnea. *Proc. Natl. Acad. Sci. USA* 21:498.

1936

With H. J. Brock, I. Rappaport, and D. W. Richards. Disturbance of action of respiratory muscles as a contributing cause of dyspnea. *Arch. Int. Med.* 57:1008.

1937

With H. C. A. Lassen and D. W. Richards. Distribution of respiratory gases in a closed breathing circuit. I. In normal subjects. *J. Clin. Invest.* 16:1.

With H. C. A. Lassen and D. W. Richards. Distribution of respiratory gases in a closed breathing circuit. II. Pulmonary fibrosis and emphysema. *J. Clin. Invest.* 16:9.

With D. W. Richards, J. L. Caughey, and F. L. Chamberlain. Intravenous saline infusion as a clinical test for right-heart and left-heart failure. *Trans. Assoc. Am. Physicians* 52:250.

1938

With A. Van S. Lambert, F. B. Berry, and D. W. Richards. Pulmonary and circulatory function before and after thoraco-plasty. *J. Thorac. Surg.* 7:302.

1939

With D. W. Richards and R. C. Darling. Graphic tracings of respiration in study of pulmonary disease. *Am. Rev. Tbc.* 40:487.

1940

With R. C. Darling, J. S. Mansfield, and D. W. Richards. Studies on the intrapulmonary mixture of gases. I. Nitrogen elimination from blood and body tissues during high oxygen breathing. *J. Clin. Invest.* 19:591.

With R. C. Darling, J. S. Mansfield, and D. W. Richards. Studies on the intrapulmonary mixture of gases. II. Analysis of the rebreathing method (closed circuit) for measuring residual air. *J. Clin. Invest.* 19:599.

With R. C. Darling and D. W. Richards. Studies on the intrapulmonary mixture of gases. III. An open circuit method for measuring residual air. *J. Clin. Invest.* 19:609.

1941

With H. A. Ranges. Catheterization of the right auricle in man. *Proc. Soc. Exp. Biol. Med.* 46:462.

With D. W. Richards. Pulmonary insufficiency. I. Discussion of a physiological classification and presentation of clinical tests. *Am. Rev. Tbc.* 44:26.

With D. W. Richards. Pulmonary insufficiency. II. The effects of various types of collapse therapy upon cardiopulmonary function. *Am. Rev. Tbc.* 44:123.

With D. W. Richards and H. C. Maier. Pulmonary insufficiency. III. Cases demonstrating advanced cardiopulmonary insufficiency following artificial pneumothorax and thoracoplasty. *Am. Rev. Tbc.* 44:272.

With D. W. Richards, R. C. Darling, and W. H. Gillespie. Pressure in the right auricle of man, in normal subjects and in patients with congestive heart failure. *Trans. Assoc. Am. Physicians* 56:218.

With E. deF. Baldwin, R. C. Darling, and D. W. Richards. Studies on intrapulmonary mixture of gases. IV. The significance of the pulmonary emptying rate and a simplified open circuit measurement of residual air. *J. Clin. Invest.* 20:681.

1942

With D. W. Richards, R. C. Darling, W. H. Gillespie, and E. deF. Baldwin. Pressure of blood in the right auricle, in animals and in man: Under normal conditions and in right heart failure. *Am. J. Physiol.* 136:115.

With H. A. Ranges and R. L. Riley. Comparison of results of the normal ballistocardiogram and a direct Fick method in measuring the cardiac output in man. *J. Clin. Invest.* 21:287.

With C. W. Lester and R. L. Riley. Pulmonary function after pneumonectomy in children. *J. Thorac. Surg.* 11:529.

With F. B. Berry. The effect of pneumonectomy upon cardiopulmonary function in adult patients. *Ann. Surg.* 116:532.

1943

With H. C. Maier. Studies of the arterial oxygen saturation in the postoperative period after pulmonary resection. *Surgery* 13:199.

With R. L. Riley, S. E. Bradley, E. S. Breed, R. P. Noble, H. D. Lauson, M. I. Gregersen, and D. W. Richards. Studies of the circulation in clinical shock. *Surgery* 13:964.

1944

With R. C. Darling and D. W. Richards. Studies on intrapulmonary mixture of gases. V. Forms of inadequate ventilation in normal and emphysematous lungs, analyzed by means of breathing pure oxygen. *J. Clin. Invest.* 23:55.

With H. D. Lauson, R. A. Bloomfield, E. S. Breed, and E. deF. Baldwin. Recording of right heart pressures in man. *Proc. Soc. Exp. Biol. Med.* 55:34.

With H. D. Lauson and S. E. Bradley. The renal circulation shock. *J. Clin. Invest.* 23:381.

With R. P. Noble, E. S. Breed, H. D. Lauson, E. deF. Baldwin, G. B. Pinchot, and D. W. Richards. Chemical, clinical, and immunological studies on the products of human plasma fractionation. VIII. Clinical use of concentrated human serum albumin in shock, and comparison with whole blood and with rapid saline infusion. *J. Clin. Invest.* 23:491.

1945

With R. L. Riley, E. S. Breed, E. deF. Baldwin, and D. W. Richards. Measurement of cardiac output in man using the technique of catheterization of the right auricle or ventricle. *J. Clin. Invest.* 24:106.

With R. A. Bloomfield and H. D. Lauson. Double lumen catheter for intravenous and intracardiac blood sampling and pressure recording. *Proc. Soc. Exp. Biol. Med.* 60:73.

1946

With R. A. Bloomfield, H. D. Lauson, E. S. Breed, and D. W. Richards. Recording of right heart pressures in normal subjects and in patients with chronic pulmonary disease and various types of cardiocirculatory disease. *J. Clin. Invest.* 25:639.

With H. D. Lauson and R. A. Bloomfield. The influence of the respiration on the circulation in man: With special reference to pressures in the right auricle, right ventricle, femoral artery and peripheral veins. *Am. J. Med.* 1:315.

With H. L. Motley, A. Himmelstein, D. Dresdale, and D. W. Richards. Latent period between electrical and pressure pulse waves corresponding to right auricular systole. *Proc. Soc. Exp. Biol. Med.* 63:148.

1947

With A. Lowell and D. W. Richards. Changes in plasma volume and mean arterial pressure after the intravenous injection of concentrated human serum albumin in 38 patients with oligemia and hypotension. *Surgery* 22:442.

Recent observations on the dynamics of the pulmonary circulation. *Bull. N.Y. Acad. Med.* 23:27.

With H. L. Motley, L. Werkö, D. Dresdale, A. Himmelstein, and D. W. Richards. Intravascular and intracardiac pressure recording in man: Electrical apparatus compared with the Hamilton manometer. *Proc. Soc. Exp. Biol. Med.* 64:241.

With H. L. Motley, L. Werkö, A. Himmelstein, and D. Dresdale. The influence of short periods of induced acute anoxia upon pulmonary artery pressures in man. *Am. J. Physiol.* 150:315.

With H. L. Motley, A. Himmelstein, D. Dresdale, and J. Baldwin. Recording of blood pressure from the left auricle and the pulmonary veins in human subjects with interauricular septal defect. *Am. J. Physiol.* 150:267.

With H. L. Motley, L. Werkö, and D. W. Richards. Observations on the clinical use of intermittent positive pressure. *J. Aviat. Med.* 18:417.

1948

With H. L. Motley, L. Werkö, and D. W. Richards. Physiological studies of the effects of intermittent positive pressure breathing on cardiac output in man. *Am. J. Physiol.* 152:162.

With R. L. Riley, A. Himmelstein, H. L. Motley, and H. M. Weiner. Studies of the pulmonary circulation at rest and during exercise in normal individuals and in patients with chronic pulmonary disease. *Am. J. Physiol.* 152:372.

With W. F. Hamilton, R. L. Riley, A. M. Attyah, D. M. Fowell, A. Himmelstein, R. P. Noble, J. W. Remington, D. W. Richards, N. C. Wheeler, and A. C. Witham. Comparison of the Fick and dye injection methods of measuring the cardiac output in man. *Am. J. Physiol.* 153:309.

With E. deF. Baldwin and D. W. Richards. Pulmonary insufficiency. I. Physiological classification, clinical methods of analysis, standard values in normal subjects. *Medicine* 27:243.

With M. I. Ferrer, R. M. Harvey, L. Werkö, D. T. Dresdale, and D. W. Richards. Some effects of quinidine sulfate on the heart and circulation in man. *Am. Heart J.* 36:816.

1949

With D. G. Green, E. deF. Baldwin, J. S. Baldwin, A. Himmelstein, and C. E. Roh. Pure congenital pulmonary stenosis and idiopathic congenital dilatation of the pulmonary artery. *Am. J. Med.* 6:24.

With B. Coblentz, R. M. Harvey, M. I. Ferrer, and D. W. Richards. The relationship between electrical and mechanical events in the cardiac cycle of man. *Br. Heart J.* 11:1.

With E. deF. Baldwin and D. W. Richards. Pulmonary insufficiency. II. A study of thirty-nine cases of pulmonary fibrosis. *Medicine* 28:1.

With M. I. Ferrer, R. M. Harvey, H. M. Weiner, and R. T. Cathcart. Hemodynamic studies in two cases of Wolff-Parkinson-White syndrome with paroxysmal AV nodal tachycardia. *Am. J. Med.* 6:725.

With E. deF. Baldwin and D. W. Richards. Pulmonary insufficiency. III. A study of 122 cases of chronic pulmonary emphysema. *Medicine* 28:201.

With R. L. Riley. "Ideal" alveolar air and the analysis of ventilation-perfusion relationships in the lungs. *J. Appl. Physiol.* 1:825.

With R. M. Harvey, M. I. Ferrer, R. T. Cathcart, and D. W. Richards. Some effects of digoxin upon the heart and circulation in man: Digoxin in left ventricular failure. *Am. J. Med.* 7:439.

With R. L. Riley, R. Austrian, K. W. Donald, and A. Himmelstein. Studies of pulmonary circulation and gas exchange in 3 cases following the resolution of various diffuse miliary infiltrations of the lungs. *Trans. Assoc. Am. Physicians* 62:134.

1950

With R. L. Riley, A. Himmelstein, and R. Austrian. Pulmonary circulation and alveolar ventilation-perfusion relationships after pneumonectomy. *J. Thorac. Surg.* 19:80.

With M. I. Ferrer, R. M. Harvey, R. T. Cathcart, C. A. Webster, and D. W. Richards. Some effects of digoxin upon the heart and circulation in man: Digoxin in chronic cor pulmonale. *Circulation* 1:161.

With J. B. Johnson, M. I. Ferrer, and J. R. West. The relation between electrocardiographic evidence of right ventricular hypertrophy and pulmonary arterial pressure in patients with chronic pulmonary disease. *Circulation* 1:536.

With R. E. Johnson, P. Wermer, and M. Kuschner. Intermittent reversal of flow in a case of patent ductus arteriosus: A physiologic study with autopsy findings. *Circulation* 1:1293.

The Fourth Walter Wile Hamburger Memorial Lecture, Institute of Medicine of Chicago: Some aspects of the pulmonary circulation in normal man and in chronic cardiopulmonary diseases. *Circulation* 2:641.

With E. deF. Baldwin, K. A. Harden, D. G. Greene, and D. W. Richards. Pulmonary insufficiency. IV. A study of 16 cases of large pulmonary cysts or bullae. *Medicine* 29:169.

1951

With D. Carroll, J. McClement, and A. Himmelstein. Pulmonary function following decortication of the lung. *Am. Rev. Tbc.* 63:231.

With J. R. West, J. H. McClement, D. Carroll, H. A. Bliss, M. Kuschner, and D. W. Richards. Effects of cortisone and ACTH in cases of chronic pulmonary disease with impairment of alveolar-capillary diffusion. *Am. J. Med.* 10:156.

With J. R. West, E. deF. Baldwin, and D. W. Richards. Physiopathologic aspects of chronic pulmonary emphysema. *Am. J. Med.* 10:481.

With J. K. Alexander. M. I. Ferrer, and R. M. Harvey. The Q-T interval in chronic cor pulmonale. *Circulation* 3:733.

With R. M. Harvey, M. I. Ferrer, and D. W. Richards. Influence of chronic pulmonary disease on the heart and circulation. *Am. J. Med.* 10:719.

With R. Austrian, J. H. McClement, A. D. Renzetti, K. W. Donald, R. L. Riley. Clinical and physiologic features of some types of pulmonary diseases with impairment of alveolar-capillary diffusion: The syndrome of "alveolar-capillary block." *Am. J. Med.* 11:667.

With R. L. Riley. Analysis of factors affecting partial pressures of oxygen and carbon dioxide in gas and blood of lungs: Theory. *J. Appl. Physiol.* 4:77.

With R. L. Riley and K. W. Donald. Analysis of factors affecting partial pressures of oxygen and carbon dioxide in gas and blood of lungs: Methods. *J. Appl. Physiol.* 4:102.

1952

With K. W. Donald, A. Renzetti, and R. L. Riley. Analysis of factors affecting concentration of oxygen and carbon dioxide in gas and blood of lungs: Results. *J. Appl. Physiol.* 4:497.

With A. Himmelstein. Cardiac catheterization in the study of congenital cardiovascular anomalies: An evaluation. *Am. J. Med.* 12:349.

With A. P. Fishman, J. McClement, and A. Himmelstein. Effects of acute anoxia on the circulation and respiration in patients with chronic pulmonary disease studied during the "steady state." *J. Clin. Invest.* 31:770.

With M. I. Ferrer, R. M. Harvey, R. T. Cathcart, and D. W. Richards. Hemodynamic studies in rheumatic heart disease. *Circulation* 6:688.

Cardiopulmonary function in chronic pulmonary disease. In *The Harvey Lecture Series* vol. 46. Springfield, Illinois: Charles C. Thomas.

1953

With M. I. Ferrer, R. M. Harvey, M. Kuschner, and D. W. Richards. Hemodynamic studies in tricuspid stenosis of rheumatic origin. *Circ. Res.* 1:49.

With J. H. McClement, A. D. Renzetti, and A. Himmelstein. Cardiopulmonary function in the pulmonary form of Boeck's sarcoid and its modification by cortisone therapy. *Am. Rev. Tbc.* 67:154.

With A. P. Fishman. Heart. *Ann. Rev. Physiol.* 15:247.

With R. M. Harvey and M. I. Ferrer. The treatment of chronic cor pulmonale. *Circulation* 7:932.

With R. M. Harvey, M. I. Ferrer, R. T. Cathcart, and D. W. Richards. Mechanical and myocardial factors in chronic constrictive pericarditis. *Circulation* 8:695.

1954

With R. A. Bader, M. E. Bader, and S. W. Kim. Comparative studies, in normotensive man, of the effectiveness, retention, and elimination of various plasma expanders. *Surgery* 35:366.

With D. W. Richards, R. A. Bader, M. E. Bader, and A. P. Fishman. The oxygen cost of breathing. *Trans. Assoc. Am. Physicians* 67:162.

1955

With A. M. Mitchell. The fate of circulating lactic acid in the human lung. *J. Clin. Invest.* 34:471.

With R. M. Harvey, M. I. Ferrer, P. Samet, R. A. Bader, M. E. Bader, and D. W. Richards. Mechanical and myocardial factors in rheumatic heart disease with mitral stenosis. *Circulation* 11:531.

With A. P. Fishman, A. Himmelstein, and H. W. Fritts. Blood flow through each lung in man during unilateral hypoxia. *J. Clin. Invest.* 34:637.

With M. I. Ferrer, R. M. Harvey, R. H. Wylie, A. Himmelstein, A. Lambert, M. Kuschner, and D. W. Richards. Circulatory effects of mitral commissurotomy with particular reference to selection of patients for surgery. *Circulation* 12:7.

With A. P. Fishman and P. Samet. Ventilatory drive in chronic pulmonary emphysema. *Am. J. Med.* 19:533.

The mysterious influence of unilateral pulmonary hypoxia upon the circulation in man. *Acta Cardiol.* 10:429.

1956

With O. L. Wade, P. Combes, A. W. Childs, H. O. Wheeler, and S. E. Bradley. The effect of exercise on the splanchnic blood flow and splanchnic blood volume in normal man. *Clin. Sci.* 15:457.

With E. Braunwald and A. P. Fishman. Time relationship of dynamic events in the cardiac chambers, pulmonary artery and aorta in man. *Circ. Res.* 4:100.

With P. Harris, H. W. Fritts, R. H. Clauss, and J. E. Odell. Influence of acetylcholine on human pulmonary circulation under normal and hypoxic conditions. *Proc. Soc. Exp. Biol. Med.* 93:77.

1957

With P. Samet, H. W. Fritts, and A. P. Fishman. The blood volume in heart disease. *Medicine* 36:211.

With H. W. Fritts, P. Harris, C. A. Chidsey III, and R. H. Clauss. Validation of a method for measuring the output of the right ventricle in man by inscription of dye-dilution curves from the pulmonary artery. *J. Appl. Physiol.* 11:362.

Pulmonary circulation. Its control in man, with some remarks on methodology. *Am. Heart J.* 54:172.

Pulmonary circulation: Its control in man, with some remarks on methodology. (Nobel lecture.) *Science* 125:1231.

Control of the pulmonary circulation in man with some remarks on methodology. In *Les Priz Nobel en 1956*, p. 196. Stockholm: Norstedt & Söner.

1958

With H. W. Fritts, P. Harris, R. H. Clauss, and J. E. Odell. The effect of acetylcholine on the human pulmonary circulation under normal and hypoxic conditions. *J. Clin. Invest.* 37:99

With A. Himmelstein, P. Harris, and H. W. Fritts. Effect of severe unilateral hypoxia on the partition of pulmonary blood flow in man. *J. Thorac. Surg.* 36:369.

With H. W. Fritts. The application of the Fick principle to the measurement of pulmonary blood flow. *Proc. Natl. Acad. Sci. USA* 44:1079.

With E. Braunwald and A. P. Fishman. Estimation of volume of a circulatory model by the Hamilton and the Bradley methods at varying flow/volume ratios. *J. Appl. Physiol.* 12:445.

1959

With C. A. Chidsey III, H. W. Fritts, A. Hardewig, and D. W. Richards. Fate of radioactive krypton (Kr^{85}) introduced intravenously in man. *J. Appl. Physiol.* 14:63.

With W. A. Briscoe. Uneven ventilation of normal and diseased lungs studied by an open-circuit method. *J. Appl. Physiol.* 14:284.

With H. W. Fritts, J. Filler, and A. P. Fishman. The efficiency of ventilation during voluntary hyperpnea: Studies in normal subjects and in dyspneic patients with either chronic pulmonary emphysema or obesity. *J. Clin. Invest.* 38:1339.

1960

With P. Harris and H. W. Fritts. Some circulatory effects of 5-hydroxytryptamine in man. *Circulation* 21:1134.

With H. P. Gurtner and W. A. Briscoe. Studies of the ventilation-perfusion relationships in the lungs of subjects with chronic pulmonary emphysema, following a single intravenous injection of radioactive krypton (Kr^{85}). I. Presentation and validation of a theoretical model. *J. Clin. Invest.* 39:1080.

With A. P. Fishman and H. W. Fritts. Effects of acute hypoxia and exercise on the pulmonary circulation. *Circulation* 22:204.

With A. P. Fishman and H. W. Fritts. Effects of breathing carbon dioxide upon the pulmonary circulation. *Circulation* 22:220.

With W. A. Briscoe, E. M. Cree, J. Filler, and H. E. J. Houssay. Lung volume, alveolar ventilation and perfusion interrelationships in chronic pulmonary emphysema. *J. Appl. Physiol.* 15:785.

With L. Donato, J. Durand, D. F. Rochester, J. O. Parker, R. M. Harvey, and M. L. Lewis. Separate performance of both ventricles in man during the early phase of exercise, as analyzed by the method of selective radiocardiography. *Trans. Assoc. Am. Physicians* 73:283.

With G. P. Zocche and H. W. Fritts. Fraction of maximum breathing capacity available for prolonged hyperventilation. *J. Appl. Physiol.* 15:1073.

With H. W. Fritts, A. Hardewig, D. F. Rochester, and J. Durand. Estimation of pulmonary arteriovenous shunt-flow using intravenous injections of T-1824 dye and Kr^{85}. *J. Clin. Invest.* 39:1841.

1961

With G. Emmanuel and W. A. Briscoe. A method for the determination of the volume of air in the lungs: Measurements in chronic pulmonary emphysema. *J. Clin. Invest.* 40:329.

With H. W. Fritts, P. Harris, C. A. Chidsey III, and R. H. Clauss. Estimation of flow through bronchial-pulmonary vascular anastomoses with use of T-1824 dye. *Circulation* 23:390.

With H. W. Fritts and D. W. Richards. Oxygen consumption of tissues in the human lung. *Science* 133:1070.

1962

With Y. Enson, W. A. Briscoe, and M. L. Polanyi. In vivo studies with an intravascular and intracardiac reflection oximeter. *J. Appl. Physiol.* 17:552.

With L. Donato, C. Giuntini, M. L. Lewis, J. Durand, D. F. Rochester, and R. M. Harvey. Quantitative radiocardiography. I. Theoretical considerations. *Circulation* 26:174.

With M. L. Lewis, C. Giuntini, L. Donato, and R. M. Harvey. Quantitative radiocardiography. III. Results and validation of theory and method. *Circulation* 26:189.

1963

With H. W. Fritts, B. Strauss, and W. Wichern. Utilization of oxygen in the lungs of patients with diffuse, non-obstructive pulmonary disease. *Trans. Assoc. Am. Physicians* 76:302.

1964

With Y. Enson and A. G. Jameson. Intracardiac oximetry in congenital heart disease. *Circulation* 29:499.

Air and blood. In *Circulation: Men and Ideas*, eds. A. Fishman and D. W. Richards, p. 3. New York: Oxford University Press.

1965

With P. R. B. Caldwell and H. W. Fritts. Oxyhemoglobin dissociation curve in liver disease. *J. Appl. Physiol.* 20:316.

With N. A. Lassen, H. W. Fritts, P. R. B. Caldwell, C. Giuntini, and W. Dansgaard. Intrapulmonary exchange of the stable isotope $^{18}O_2$ injected intravenously in man. *J. Appl. Physiol.* 20:809.

1970

With H. Zuckerman. The code of science: Analysis and some reflections on its future. *Stud. gen.* 23:941. Also in *Knowledge in Search of Understanding: The Frensham Pond Papers*, ed. P. A. Weiss, p. 126. New York: Futura Publishing Company, 1975.

1971

Prospective philosophy and methods: Some reflections on their preliminary application to medical education. *Futures* (December):372.

Applications of prospective thinking and method to medical education; The initial results of a practical experiment. *Stud. gen.* 24:1405.

1973

With M. Meyer. Overcrowding, a disease of social growth. *Futures* (June):287.

With M. Levy (eds.). *Shaping the Future: Gaston Berger and the Concept of Prospective.* London: Gordon & Breach.

Dickinson Woodruff Richards: 1895-1973. *Trans. Assoc. Am. Physicians* 86:33.

On the codes of science and scientists. In *Proceedings of the Third International Conference—From Theoretical Physics to Biology*, p. 436. Basel: S. Karger.

1975

Cardiac catheterization: Development of the technique, its contributions to experimental medicine, and its initial applications in man (edited and expanded version of the Jimenez Diaz Memorial Lecture, 1970). *Acta Med. Scand. (Suppl.)* 579:1.

1976

With M. Meyer. The scientist's role. *Minerva* 14:80.

1977

The code of the scientist and its relationship to ethics. *Science* 198:699.

1979

Claude Bernard's contributions to cardiac physiology. In *Claude Bernard and the Internal Environment, a Memorial Symposium,* ed. E. D. Robin, p. 97. New York: Marcel Dekker.

1980

Historical details of Claude Bernard's invention of a technique for measuring the temperature and the pressure of the blood within the cavities of the heart. In *Science and Social Structure: A Festschrift for Robert Merton. Trans. N.Y. Acad. Sci.*, p. 1.

1981

Science in service of society. *The Sciences* 21:7.

1985

Special lecture: Origin and historical development of clinical physiology in pulmonary disease. *Bull. Eur. Physiopathol. Respir.* 21:205.

1986

Dickinson Woodruff Richards, 1895-1973. *Biographical Memoirs,* vol. 57, p. 459. Washington, D.C.: National Academy Press.