DIALOGUES

Icons of Cardiology

André Frédéric Cournand: integration of pulmonary and cardiovascular pathophysiology

Arnold M. Katz, MD

Professor of Medicine Emeritus - University of Connecticut School of Medicine
Visiting Professor of Medicine and Physiology - Dartmouth Medical School - Dartmouth, Mass - USA
From the Cardiology Division - Department of Medicine - University of Connecticut Health Center - Farmington, Conn - USA

One of the major advances in cardiology began in the 1930s when André Cournand *(Figure 1),* a pulmonary physiologist, and Dickinson W. Richards *(Figure 2),* an expert on cardiovascular medicine, collaborated in a long-term effort to integrate the roles of the heart, the lungs, and the peripheral circulation in gas exchange. Among the initial clinical goals of this research was a clearer understanding of the pathophysiology of pulmonary disease that could answer such questions as the consequences of thoracoplasty and other means then used to collapse the lungs in patients with tuberculosis; it was only later that diagnosis of heart disease emerged as a major practical benefit of this work. Central to the success of this research was a means to quantify pulmonary blood flow using the three variables that make up the Fick equation: total body oxygen consumption and the oxygen contents of the blood entering and leaving the lungs. The first is readily determined by collecting and measuring the volume and oxygen content of expired air, while the third is easily measured using samples of arterial blood; the problem faced by Cournand and Richards was how to obtain mixed venous blood to determine the second variable. Because blood returning to the right heart from some organs, such as the kidneys, is rich in oxygen, whereas other organs, notably the heart, extract virtually all of the oxygen delivered in the arterial blood, the only precise way to quantify the oxygen content of the blood entering the lungs is to sample from the pulmonary artery, which lies downstream from the mixing chamber provided by the right ventricle. However, direct puncture of the thin-walled pulmonary artery by a needle passed through the chest wall is far too dangerous to be used clinically, and in the 1940s the idea of exposing the heart to mechanical stimulation of any kind was viewed by many as likely to cause the heart to fibrillate, which at that time was fatal.

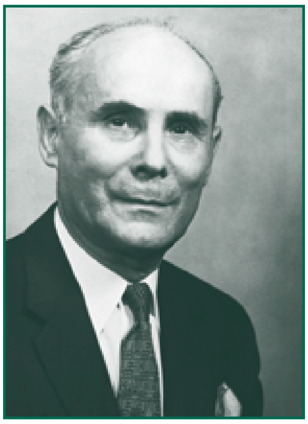

Figure 1. *André Frédéric Cournand (1956). © Bettmann/CORBIS.*

Figure 2. *Dickinson Woodruff Richards (1956). Courtesy of the author.*

A solution to this problem had been foreshadowed more than a decade earlier by Werner Forssmann *(Figure 3, next page),* who in 1929 described passing a catheter into his own right atrium without ill effects.[1] During the 1930s, several angiographers had introduced catheters into the right atrium of humans to perform pulmonary angiography, and Forssmann's technique had been used by a few clinical physiologists to obtain mixed venous blood. However, the potential physiological applications of these observations were not appreciated; as noted by Cournand, although "many possibilities were envisaged… no systemic plan, nor the proper scientific background and facilities for its wide-scale implementation, were then available."[2] There was, of course, a notable exception; this was the Cardiopulmonary Labora-

Address for correspondence:
Prof Arnold M. Katz, 1592 New Boston Road, PO Box 1048, Norwich VT, 05055-1048, USA (e-mail: arnold.m.katz@dartmouth.edu)

Dialogues Cardiovasc Med. 2006;11:231-235

***Figure 3.** Werner Forssmann in his laboratory in 1956. © Bettmann/CORBIS.*

tory at Bellevue hospital, led by Cournand and Richards (see below), where the effort to obtain mixed venous blood for determination of cardiac output was part of an ongoing long-term research effort. Cournand describes a planning session in the early 1930s at which Richards "produced an issue of the 1929 *Klinische Wochenschrift* describing Forssmann's self-experiment."[2] This conversation led Cournand, in 1936, to visit a former teacher in Paris who had performed pulmonary angiography in about 100 patients. Upon his return, Cournand, along with Richards and their colleagues in the Cardiopulmonary Laboratory, familiarized themselves with this method and placed catheters first in the right atrium of dogs and chimpanzees, then in cadavers, and in 1941 in living humans.[3] The observation that the tips of right atrial catheters could suddenly appear in the pulmonary artery led to catheterization of the right ventricle in 1941, and in 1944 of the pulmonary artery *(Figure 4)*.[4]

ANDRÉ FRÉDÉRIC COURNAND

Cournand[5-7] was born on September 24, 1895, in Paris, where his father was a prominent dentist who held several patents in dental technology. He studied both science and the humanities at the Sorbonne and after he received his BA in 1913 began medical school. These studies were interrupted by World War I, in which he served from 1915 to 1919 as an "auxiliary battle surgeon" (a rank established for medical students) and was both wounded and gassed. Among his tasks was to retrieve wounded soldiers from no-man's-land, which exposed him to the terrible prognosis of hemorrhagic and traumatic shock. After serving in the trenches for 3 years, for which he received the Croix de Guerre with 3 bronze stars, he returned to medical school and from 1924 to 1939 was a house officer at the Hôpitaux de Paris.

It was at this time that his interest in the physiological basis of medicine matured; he published papers on several subjects, including the excitability of the facial nerve, the effects of drugs on blood sugar, and the use of epinephrine in infants with pulmonary edema. His interest in pulmonary disease emerged in 1928 when he published papers on bronchiectasis, disseminated nodular tuberculosis, and surgical therapy for pulmonary tuberculosis. In 1930, he was awarded the MD degree for which he wrote a thesis on multiple sclerosis, after which he came to the United States for further training as a first year resident on the well-known Columbia Chest Service at Bellevue Hospital in New York. He

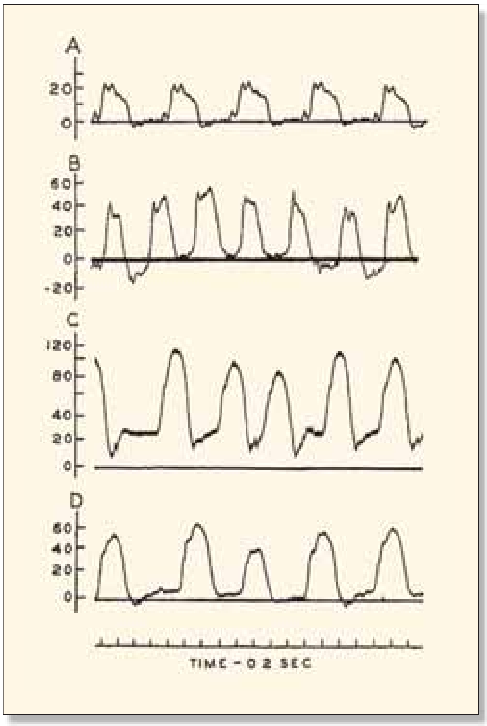

***Figure 4.** Recordings of right ventricular pressure in humans.*
***A:** Normal young female.*
***B:** Young male with extensive pulmonary fibrosis with normal sized heart showing elevated pressure and increased respiratory variations in pressure.*
***C:** Patient with mitral stenosis and insufficiency, aortic insufficiency, and atrial fibrillation showing elevation of both systolic and diastolic pressures.*
***D:** Same patient as C after treatment with digitalis and bed rest.*

***Reproduced from reference 4:** Cournand A, Lauson HD, Bloomfield RA, Breed ES, Baldwin E de F. Recording of right heart pressures in man.* Proc Soc Exp Biol Med. *1944;55:34-36. Copyright © 1944, Blackwell Science.*

subsequently learned that he had been recommended as "a nice young Frenchman who did not speak a word of English."[8]

Although Cournand was qualified to begin a private practice in France at the end of this training, he chose instead to pursue a full-time career that combined clinical practice, research, and teaching. In 1932, he became Chief Resident on the chest service and, in 1933, was asked to develop a laboratory for the study of pulmonary function in collaboration with Dickinson Richards who, after completing his residency in Medicine at Columbia 5 years before, had been a fellow in London with Sir Henry Dale, a Nobel Laureate. Although Richards was then uptown at Columbia Presbyterian Hospital, his interest in gas exchange by the peripheral circulation fit closely with that of Cournand, which was in gas exchange by the lungs.

THE CARDIOPULMONARY LABORATORY AT BELLEVUE HOSPITAL

Cournand and Richards together established the Cardiopulmonary Laboratory at Bellevue[5,7,9] where, during the 1930s, they worked to characterize the movements of oxygen from the lungs to peripheral tissues by way of the circulation *(Figure 5).* Their first projects included a study of the role of the respiratory muscles in causing dyspnea, the effects of the various forms of collapse therapy then used to treat pulmonary tuberculosis, and an effort to characterize the inhomogeneous distribution of inspired gases in the lungs that contributed to the arterial hypoxia seen in patients with chronic obstructive lung disease.[7] A major discovery during these early years was the demonstration that the hemodynamics in patients with chronic obstructive pulmonary disease differed from those in heart failure. The imminence of World War II, which recalled the terrible prognosis in soldiers with hemorrhagic and traumatic shock that Cournand had seen during World War I, led to efforts to define the effects of severe injury on hemodynamics, oxygen transport, and tissue metabolism; one practical benefit was the development of dextran to expand blood volume. These studies, along with the challenges posed by high altitude aviation, also stimulated work to develop mechanical respirators. Of course the most important scientific advance to come from this laboratory was the intro-

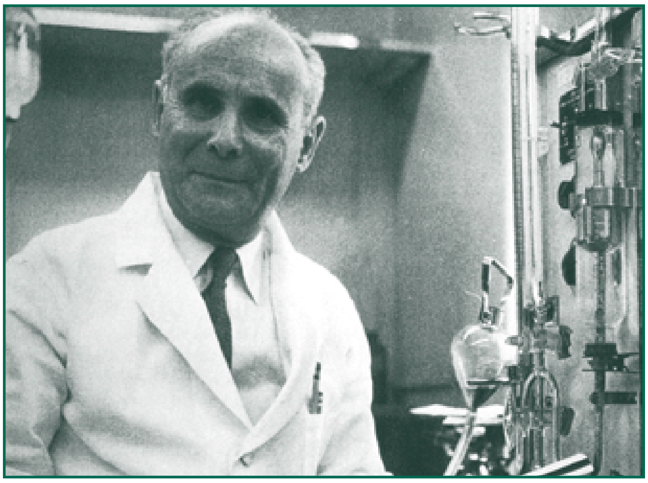

***Figure 5.** André Cournand in the Cardiopulmonary Laboratory at Bellevue. Next to Cournand's left shoulder is a Van Slyke apparatus; note the mercury-filled reservoir with a handle that was used to vary the pressure in the apparatus. In expert hands, this apparatus measured oxygen and carbon dioxide contents in blood with an accuracy of 1-2 parts per 1000.*

***Reproduced from reference 5:** Franch RH. Andre F. Cournand: father of clinical cardiopulmonary physiology.* Clin Cardiol. *1986;9:82-86.*

duction of cardiac catheterization described above. Although this technique was initially developed to calculate cardiac output, within a year a detailed description of the abnormal hemodynamics in patients with heart failure was published.[10] I vividly recall my father, Louis Katz, upon returning from the meeting at which these data were first presented, stating: "This is it!" by which he meant he foresaw that this new technique would bring to the bedside several decades of hemodynamic research that most clinicians had previously viewed as arcane basic science. Because of the need to learn more about shock, a major focus of medical research during World War II, cardiac catheterization was used in the Cardiopulmonary Laboratory to measure cardiac output, blood volume, intracardiac and intra-arterial pressures, blood gases, pH, respiratory gas exchanges, and even renal blood flow in patients with various forms of this syndrome.[2] At the same time, this technique continued to be used to define the hemodynamics of rheumatic heart disease, cor pulmonale, and hypertension.

Following the end of World War II, in 1945, Cournand's collaboration with Richards was facilitated when the latter moved to Bellevue to become director of the First (Columbia) Medical Service, which, by combining a high-quality academic program and a city hospital, established one of the top training programs in the US. Cournand continued to direct the Cardiopulmonary Laboratory, which became the international focal point for research into the pathophysiology of pulmonary diseases and so provided the foundation for modern pulmonary medicine. In addition to characterizing the hemodynamic and ventilatory abnormalities in patients with pulmonary fibrosis and emphysema, Cournand and his group discovered that hypoxia constricts the pulmonary arterioles, rather than elucidating the vasodilatory response seen in virtually every other tissue. At the same time, they continued to characterize the hemodynamic abnormalities in rheumatic and congenital heart disease, the circulatory effects of cardiac glycosides and antiarrhythmic drugs, and the hemodynamic consequences of chronic atrial arrhythmias. Many of those trained at the Cardiopulmonary Laboratory went on to leadership positions in academic medicine; the list includes 8 chiefs of pulmonary medicine, 7 chiefs of cardiology, 5 chiefs of medicine or experimental medicine, 3 chiefs of cardiac surgery, 2 professors of physiology, and 1 chief of pediatric cardiology.[7]

Figure 6. *Nobel Prize Winner's reception. The photograph shows 8 of the 9 recipients of the 1956 Nobel Prize, with Dickinson Richards (second from left), André Cournand (third from right), and Werner Forssmann (first from right), who shared the Nobel Prize in Physiology or Medicine for their discoveries concerning heart catheterization and pathological changes in the circulatory system. © Hulton-Deutsch Collection/CORBIS.*

Cournand at that time is described as physically vigorous, endowed with gravitas and unbounded scientific curiosity and kindness, but "enthusiastically volatile under appropriate stimulation."[7] Enson and Chamberlin tell of a junior fellow who told Cournand that his critique of a recently published paper seemed paranoid, which caused the latter to spring to his feet, confront the fellow nose-to-nose, and state: "Correct! And by the end of your fellowship, doctor, you will also have a yellow streak of paranoia down your back eighteen inches wide."[7] A similar portrait is provided by Riley,[11] who describes Cournand as "arguing violently with Israel Rappaport… trading insults with his beloved associate, Aaron Himmelstein… running to Dick Richards to settle particularly intractable controversies… He was outrageous at times and 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, if you were not right—and occasionally even if you were—a withering exclamation: 'That man is impossible!"

Although the work for which Cournand shared the Nobel Prize *(Figure 6)* centered on a physiological technique, he was a sensitive clinician who understood that the patient, not the test, is central in medicine; as noted by Lequime,[6] Cournand recognized that

> …the application of new methods requires not only a profound knowledge of the techniques used, but also that of the patient under examination: the value of precise physiological measurement is all the greater when the clinical study is more elaborated; before presenting his conclusions, the investigator must always ensure that he has explored in all its clinical aspects the problem which he proposes to resolve.

"RETIREMENT"

Cournand officially retired in 1964, but remained active until his death in 1988. During these later years his interests expanded to a consideration of the philosophy of scientific research, and in 1970 led to a remarkable article describing the importance of "the growing involvement of science in social life.[12] Writing with Harriet A. Zuckerman, then an Assistant Professor of Sociology at Columbia, Cournand emphasized 7 principles, which I have abridged slightly from ref. 12:

- *Intellectual Integrity and Objectivity:* Scientists are obliged to approach the natural world and their own investigations of it with as much objectivity and care as they can summon.
- *Tolerance:* …it is wise to be tolerant of [new ideas] and to see if their factual bases appear to fall within the boundaries of sound science. Tolerance is also expressed through dissent as long as mutual respect is maintained between dissenters.
- *Doubt of Certitude:* …[because] truth emerges from the confrontation of contraries, scientists must approach what is generally considered certain with an ever-questioning mind. The tension so created is one of the main-

springs in the pursuit of knowledge.

- *Recognition of Error:* The systematic application of doubt is apt to reveal errors that must be recognized and acknowledged publicly.
- *Unselfish Engagement:* Scientists should be motivated by the desire to extend knowledge and not by the wish for personal gain or by the desire to foster the primacy of one intellectual perspective.
- *Sense of Belonging:* Scientists should conceive of their work as being part of a larger enterprise, and of themselves as joined to their scientific colleagues through collective contributions to this enterprise.
- *Recognition of Priorities:* Scientists are required to recognize as scrupulously as possible other investigators' priorities in discovery.

This description of the qualities of the ideal scientist, which is as important today than when it was written 35 years ago, ranks with contributions to cardiopulmonary science and medicine that together represent André Cournand's magnificent legacy.

REFERENCES

1. Forssmann W.
Die Sondierung des rechten Herzens.
Klin Wochschr. 1929;8:2085-2090.

2. Cournand A.
Cardiac catheterization. Development of the technique, its contributions to experimental medicine, and its initial application in man.
Acta Med Scand Suppl. 1975;579:3-32.

3. Cournand A, Ranges HA.
Catheterization of the right auricle in man.
Proc Soc Exp Biol Med. 1944;46:462-466.

4. Cournand A, Lauson HD, Bloomfield RA, Breed ES, Baldwin E de F.
Recording of right heart pressures in man.
Proc Soc Exp Biol Med. 1944;55:34-36.

5. Franch RH.
André F. Cournand: father of clinical cardiopulmonary physiology.
Clin Cardiol. 1986;9:82-86.

6. Lequime J.
André Cournand (1895-1988). His role in the development of modern cardiology.
Acta Cardiol. 1988;43:437-442.

7. Enson Y, Chamberlin MD.
Cournand & Richards and the Bellevue Hospital Cardiopulmonary Laboratory.
Columbia Magazine. 2001;Fall:34-44.

8. Cournand A.
Acceptance of the Trudeau Medal for 1971.
Am Rev Resp Dis. 1971;104:616-617.

9. Cournand AF.
Dickinson Woodruff Richards: 1895-1973. A survey of his contributions to the physiology and physiopathology of respiration in man.
Am J Med. 1974;57:312-328.

10. Richards DW Jr, Cournand A, Darling RC, Gillespie WH, Baldwin E de F.
Pressure of blood in the right auricle in animals and man: Under normal conditions and in right heart failure.
Am J Physiol. 1942;136:115-123.

11. Riley RL.
Award of the Trudeau Medal for 1971.
Am Rev Resp Dis. 1971;104:615-616.

12. Cournand AF, Zuckerman H.
The code of science. Analysis and some reflections on its future. .
Stud Gen 5(Berl). 1970;23:941-962.