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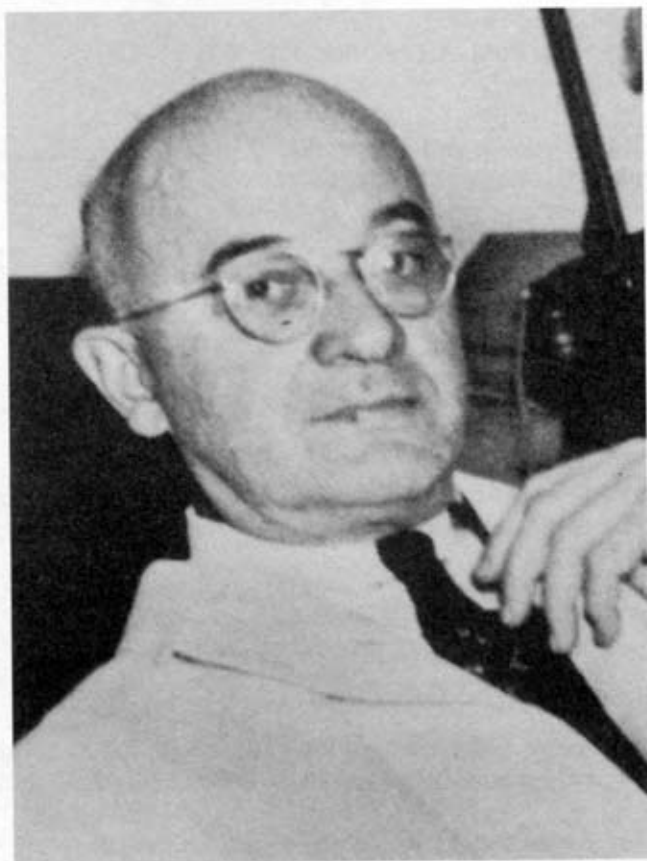
WILLIAM CHRISTOPHER STADIE
1886—1959

A Biographical Memoir by
ISAAC STARR

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Biographical Memoir

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Wm C Stadie

WILLIAM CHRISTOPHER STADIE

June 15, 1886–September 12, 1959

BY ISAAC STARR

FEW INVESTIGATORS have been so consistently productive as William Stadie. His life work can be most easily presented by dividing it into three parts. In the first, his attention was focused on the cyanosis so conspicuous in patients with influenza; he was the father of oxygen therapy. In the second—responding to the needs of World War II—he was chiefly concerned with oxygen toxicity. In the third, Stadie made major contributions to our knowledge of the abnormalities of carbohydrate metabolism and diabetes.

For many years, Bill Stadie and I had adjacent laboratories on the eighth floor of the Maloney Building of the University Hospital and we usually lunched together. He was one of my oldest medical friends.

Bill had an unusually difficult time completing his medical education. Believed to have pulmonary tuberculosis as an adolescent, he was taken out of school and sent to work on a farm for a year. When this episode was evaluated later by experts in the diagnosis of tuberculosis, using both his old and more recent chest X-rays, all agreed that Stadie had never, in all probability, had TB at all. But the episode cost him a year of his working life. In addition, he had to earn money by teaching school for several years before he was able to finish college at New York University, from which he took his degree in 1907.

Stadie liked to boast, with a twinkle in his eye, that he had put himself through medical school at the College of Physicians and Surgeons (which granted him the M.D. degree in 1916) by writing a textbook of pathology. If listeners expressed surprise at so major an accomplishment by so young a man, they soon learned that Bill had helped finance his education while a medical school undergraduate by typing the manuscript of McCallum's well-known pathology text.

After a stint in the Army Medical Corps during World War I, Stadie's successful internship at the Presbyterian Hospital won him a research job at the Hospital of the Rockefeller Institute, where a group was being organized to study the newer treatments of syphilis. But before this study could get off the ground, the great influenza epidemic paralyzed the country.

In many influenza cases, cyanosis of bronchial pneumonia was a conspicuous symptom. After learning the new techniques of blood-gas analysis from Van Slyke (who had just originated them), he worked to perfect techniques of arterial puncture—experimenting first with animals, then on himself and other volunteers, and finally on his patients—proving to the satisfaction of everyone that arterial puncture, long thought by clinicians to be a dangerous procedure, was harmless in skilled hands. Many give Stadie the credit for the first arterial puncture on a patient, but I often heard him deny, with characteristic modesty, that he had been first, insisting rather that Hurter, a German researcher, had preceded him.

Having introduced the arterial puncture in clinical medicine, Stadie was able to make pioneering studies of lung function in his patients by comparing the oxygen content of the air inhaled with that of arterial blood. This technique allowed him to demonstrate that the cyanosis was due to arterial anoxemia of a dangerous severity. Studies on the effectiveness of various methods of treating cyanosis followed,

and Stadie soon found that anoxemia could be overcome by breathing air enriched with oxygen. He then supervised the construction of a small, gas-tight room in the Rockefeller Hospital with controls for oxygen, carbon dioxide, moisture, and air temperature that permitted bed patients to breathe the desired concentrations over long periods without the discomfort of masks and nose-pieces. The principles of Stadie's chamber formed the basis for the oxygen chambers and tents that have since become routine hospital equipment.

After four productive years with the Rockefeller Hospital, Bill Stadie moved to Yale, where Francis Blake was putting new life into the Department of Medicine. He served on Yale's medical faculty from 1921 to 1924, then came to the University of Pennsylvania. He was appointed John Herr Musser Professor of Research Medicine in 1941. In 1944 he served with the Office of Scientific Research and Development of the United States Public Health Service. Though he had retired from teaching in 1956, Stadie continued as the Musser Professor Emeritus and was actively engaged in research at the time of his death, at the age of seventy-three, in 1959.

After his groundbreaking discoveries in oxygen therapy and his introduction of the arterial puncture into clinical medicine, Stadie moved on to investigate oxygen toxicity—a concern of the military during World War II. He extended his researches to the combination of oxygen and carbon monoxide with hemoglobin and assisted in clarifying the roles of the carbamino compounds and of carbonic anhydrase in accelerating the shifts of carbon dioxide to and from the blood. Stadie contributed refinements of methods for blood-gas analyses, determinations of hemoglobin, methemoglobin, fixed-base cations in blood, and an electron-tube potentiometer for blood pH measurements.

During his researches he discovered a discrepancy in the data then available on the supposedly well-understood pro-

cess of oxygen and CO_2 exchange in blood. According to his findings, much more CO_2 emerged from the blood during its passage through the lungs than the views of physical chemistry of blood then current could account for. To interpret this unexpected finding, new techniques were needed: those of enzyme chemistry to measure enzyme activity and those of radioactivity to locate the enzymes in tissues and identify the sources of their metabolic byproducts. Stadie not only mastered these new techniques, he added considerably to our knowledge of abnormalities in carbohydrate metabolism—work for which he was particularly suited by his unusual facility with mathematics.

He was the first to label insulin with radioactive tracers and to demonstrate that a high-affinity binding of the hormone to its target tissue was required for its biological effects. More than two decades later, quantitative studies of insulin-binding have fully confirmed Stadie's observation.

He further demonstrated that the hyperketonemia of animals with acute experimental diabetes results primarily from hepatic overproduction of ketone bodies rather than from a defect in their utilization. Stadie adduced an important part of the evidence on which presently accepted views regarding diabetes are based: that the liver splits fats almost quantitatively into acetoacetic and hydroxybutyric acid, which are circulated to the other tissues for combustion; that the muscles of a diabetic can burn acetoacetic acid at a normal rate; and that excretion of acetoacetic and hydroxybutyric acids occurs in diabetes—when carbohydrate is not available for combustion—because these acids are formed faster than the tissues can burn them.

Any tribute to Bill Stadie as a scientist would be incomplete without a tribute to him as a man. His talents were not limited to research. He ran a happy and successful laboratory—as his many associates, graduate students, and techni-

cians are glad to attest. Those of us made welcome in his home often paused to admire the beautiful mahogany furniture and were surprised to learn that he had made the pieces himself. He played both the cello and the clarinet—if not well, well enough to enjoy it—and great music always delighted him. Outside his house was his carefully tended garden, bordered by a row of beehives.

The quality of the man and his work have been recognized everywhere. He was an editor of the *Journal of Biological Chemistry* for many years and was editor-in-chief of the American Diabetes Association journal, *Diabetes*, for the last three years of his life.

Elected to the National Academy of Sciences in 1945, Stadie received the Alverenga Award of the Philadelphia College of Physicians in 1957, the Phillips Medal of the American College of Physicians in 1941, the Kober Medal of the Association of American Physicians in 1955, and the Banting Medal of the American Diabetes Association in 1956. He acted as a consultant to the National Institutes of Health's Division of Metabolic Diseases. He was a member of the American Philosophical Society, the American Society for Clinical Investigation, the American Society of Biological Chemists, and the Association of American Physicians and received the honorary degree of doctor of science from the University of Pennsylvania in 1959.

He married Amanda Brugger, who was working in the library at Yale while he was on the faculty there. Their daughter was a constant source of delight to them both. The death of his first wife from a brain tumor was so devastating to him that his friends feared he might not recover, but he eventually did, and his second marriage to Catherine Tyler was also a happy one.

Throughout his active years and even after his retirement he never showed signs of the mental rigidity that so often

comes with age. During his later years—despite considerable ill health—his mind remained as fertile for new ideas as in his younger days. He also took an interest in his fellow man and—poor himself in his youth—was greatly concerned with social problems of the poor.

Suffering from mild angina pectoris occasionally for several years, he died of a heart attack. His refined experiments, which so much advanced his fields of interest, will live long after him.

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