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YANDELL HENDERSON

1873—1944

A Biographical Memoir by

JOHN B. WEST

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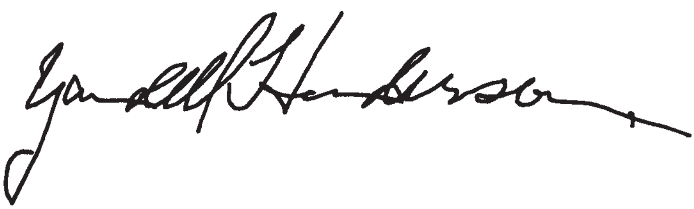

YANDELL HENDERSON

April 23, 1873–February 18, 1944

BY JOHN B. WEST

YANDELL HENDERSON MADE important contributions to cardiorespiratory physiology over a broad area with a particular emphasis on practical applications such as resuscitation, air pollution, mine safety, and aviation medicine. Although his initial training was in biochemistry, he early turned to cardiovascular physiology, including the output of the heart, venous return, and shock. His interest in high-altitude physiology was sparked when, with J. S. Haldane of Oxford University, he helped to organize the Anglo-American Pikes Peak Expedition of 1911. His involvement with high-altitude physiology remained throughout his life and he subsequently studied the blood changes with acclimatization, work capacity at extreme altitude, and problems in aviation medicine. Issues of mine safety prompted his interest in carbon monoxide poisoning, resuscitation, and ventilation standards for long vehicular tunnels. He made an early plea for recognition of clinical physiology as a discipline and contributed to the physiology of anesthesia and asphyxia in the newborn. Henderson's emphasis on applied physiology has gone out of fashion (which may partly explain why this memoir is fifty years late), but his philosophy that one of science's main responsibilities is to the human condition will find a resonance in many quarters.

EARLY LIFE AND EDUCATION

Yandell Henderson was born in Louisville, Kentucky, oldest son of Isham Henderson and Sally Nielson Henderson, née Yandell. His father was trained in law, but he disliked its practice and instead became owner and manager of the Louisville *Courier Journal* newspaper. In addition, he was a contractor and builder of canals and railroad, which made him a substantial fortune. Yandell's paternal grandfather Isham was an eminent judge in Kentucky. His maternal grandfather was Dr. Lundsford Pitts Yandell, the first dean of the first medical school west of the Allegheny Mountains. One of Dr. Yandell's sons practiced medicine in Louisville from an office above a drugstore in which the young Simon Flexner was apprenticed.

Yandell Henderson attended Chenault's school in Louisville and then entered Yale University in 1891, graduating with an A.B. in 1895. For the following four years he studied physiological chemistry at Yale under Russell Henry Chittenden, doyen of American biochemistry and one of the organizers of the American Physiological Society. Henderson received his Ph.D. in 1898. During his period as a student, Henderson spent most summer vacations traveling in Europe. An exception was in 1894, when with some friends from Yale he explored the region around Lake Louise in Alberta, Canada, surveying the lake and naming several of the peaks. It is interesting that the splendid Chateau Lake Louise, which was built by the Canadian Pacific Railroad, is now the site of international meetings on the physiology of hypoxia every two years; these would have been of great interest to Henderson. During these years, Henderson also joined the naval militia, and for one summer served as ensign in the U.S. Navy on the *U. S. S. Yale* in Cuban waters, with a later expedition to Puerto Rico.

Henderson's thesis work was published in 1899 in the new *American Journal of Physiology* (this was only the second volume) with Chittenden and Mendel under the title "A Chemico-Physiological Study of Certain Derivatives of the Proteids" (proteid was an early name for protein). By this time Henderson was at the University of Marburg with Albrecht Kossel, who was later awarded a Nobel Prize in physiology and medicine for his work on the biochemistry of proteins, especially nucleoproteins. A year later Henderson was in Munich with Carl Voit, whose main interests were nutrition and metabolism, especially in regard to proteins. Henderson returned to Yale in 1900.

PHYSIOLOGICAL LABORATORY, YALE MEDICAL SCHOOL

In 1900 Chittenden had become temporary head of the physiological laboratory in addition to his appointment in physiological chemistry. Chittenden turned the laboratory instruction and some of the lecturing over to Henderson, who was given an appointment as instructor. This marked the beginning of a remarkable career change for Henderson from biochemistry to physiology. Furthermore, he gradually abandoned research on isolated tissues and organs to work on the whole animal, including man. Henderson rose through the ranks to become professor of physiology in 1911, a position that he occupied until 1920.

It is not entirely clear what prompted Henderson to make the switch from the biochemistry of proteins to cardiorespiratory physiology. It may have been his conviction that the time was ripe for medical science to exploit the new advances in organ and clinical physiology. Certainly, he voiced that belief in his chairman's address to the Section of Pathology and Physiology at the annual meeting of the American Medical Association in 1911. For example, he stated, "Physiologists now and in the next few years will find their richest and most fruitful problems in the field of clinical, rather than in that of purely abstract, physiology . . . development of clinical physiology might well be the greatest event in the progress of medicine during the second decade of the twentieth century." In fact, Henderson's subsequent scientific career was dominated by problems posed by clinical and applied physiology, such as the physiology of shock, resuscitation, aviation medicine, carbon monoxide poisoning, atelectasis, and the effects of alcoholic beverages.

Henderson's first major investigation in cardiorespiratory physiology was a plethysmographic study of the filling of the ventricles of the heart, which was published in 1906. He noted that atrial systole played a minor role in the filling of the ventricles and argued that the atria should be "regarded as elastic reservoirs rather than as force pumps." This led him to become interested in the factors determining venous return to the heart and particularly the way positive pressure ventilation of the lungs interfered with venous return. This prompted a study of the effects of hyperventilation and the resulting reduction in the partial pressure of carbon dioxide on the heart and venous return; he concluded that a low P_{CO_2} (which he referred to as acapnia following the introduction of the term by Angelo Mosso) could be responsible for surgical shock. This proposal led to a spirited confrontation with Samuel J. Meltzer at one of the meetings of the American Physiological Society and brought out Henderson's combative propensity, which was to remain with him the rest of his career.

Henderson's interest in the filling pressures of the left ventricle has a modern ring to it because this remains a somewhat controversial area. An interesting sidelight to this work was that previous experiments on isolated cardiac muscle seemed to disagree with Henderson's results on the whole heart. This may have been a factor in directing his interest away from isolated tissue to whole animal preparations and eventually to human beings. At this time, Henderson also wrote one of the earliest papers on ballistocardiography, which he thought would be useful in studying the ejection of the left ventricle.

Henderson continued his interest in the output of the heart and wrote later articles on the topic. However, he was led astray by experiments that suggested that the stroke volume of the heart remained almost constant under a variety of physiological conditions when the heart rate was relatively slow, but at rapid heart rates the stroke volume was always substantially decreased. This result would be expected if venous return remained constant as in Henderson's preparation. However, his generalization to other situations brought him into conflict with German physiologists, such as Nathan Zuntz, who recognized that the large increase in cardiac output accompanying physical exercise was brought about both by an increase in heart rate and stroke volume. Because it was difficult to reconcile the known increase in oxygen consumption during exercise with the limited increase in cardiac output, Henderson concluded that there might be a change in "pulmonary oxidation during vigorous muscular work." Here he was apparently referring to the theory of oxygen secretion, which was championed by Christian Bohr and vigorously supported by Haldane.

It may have been Henderson's interest in the physiological effects of low levels of carbon dioxide that was responsible for his meeting with J. S. Haldane from Oxford, and Henderson's subsequent introduction to high-altitude physiology. Haldane had pioneered the role of carbon dioxide in the control of ventilation, but, as alluded to above, he also believed that the lungs secreted oxygen, and that the best place to investigate this was at high altitude. Henderson met Haldane and his colleague C. G. Douglas for the first time at a cafe in Vienna during the International Congress of Physiology held there in 1910. About half an hour into their conversation, Haldane remarked that he was planning an expedition to high altitude and that what he needed was “a nice comfortable mountain” for the expedition. Haldane and Douglas were familiar with the Capanna Margherita at an altitude of 4559 m on the Italian Monte Rosa, but to reach it required several hours of climbing over snow and ice, and the conditions in the hut were very Spartan. By contrast, Pikes Peak near Colorado Springs had a cog railway to the summit where there was a well-appointed “summit house” with several rooms. Henderson is reported to have said, “Come to America next summer and we will spend a month or two on the top of Pikes Peak.” Thus began the famous Anglo-American Pikes Peak Expedition of 1911 (referred to by Henderson as the Yale-Oxford expedition).

The participants were J. S. Haldane and C. G. Douglas from Oxford University, Yandell Henderson, and Edward C. Schneider, formerly at Yale but at the time professor of biology at Colorado College in Colorado Springs. Pikes Peak had many advantages for a study of high-altitude physiology. Although the summit at an altitude of 4300 m (14,110 ft) was not quite as high as that of the Capanna Margherita, the fact that it could be reached by railway and that four rooms of the summit house were made available to the expedition made Pikes Peak very attractive. One of the rooms was fitted out as a laboratory. The investigators initially stayed for about five days in Colorado Springs and then took the railway to the summit, where they spent five continuous weeks.

Initially the whole party had some symptoms of acute mountain sickness, but most of these disappeared after two or three days. A wealth of information was obtained on the acclimatization process including the changes in alveolar

P_{CO_2} and blood hemoglobin concentration. Periodic breathing was observed particularly at night, and this was abolished by breathing oxygen. The only finding that could not subsequently be confirmed was the evidence for oxygen secretion (that is, that the partial pressure of oxygen in the arterial blood exceeded that in the alveolar gas). The blood measurement was made by an indirect technique based on the color of the blood when carbon monoxide was breathed, but it is still not clear where the investigators went wrong. Haldane who was a great champion of oxygen secretion actually believed in it until his death in 1936. The Pikes Peak expedition was described in generous detail in a 134-page paper in the *Transactions of the Royal Society of London, Series B.*

Mabel FitzGerald was also connected with the expedition, but for reasons that are not clear she did not stay on the summit with the four men. Instead, she toured mining camps in Colorado measuring alveolar P_{CO_2} and hemoglobin concentration in residents at moderate altitudes. When she was a student at Oxford, women were not granted degrees, and she had the distinction of being given an honorary M.A. at the age of 100! Henderson remained interested in high-altitude physiology the rest of his life and one of his last papers was on the problem of reaching the summit of Mt. Everest without supplementary oxygen. Along with several other physiologists of his generation, he believed this would be impossible, but the successful ascent by Reinhold Messner and Peter Habeler in 1978 proved them wrong.

Henderson also carried out a well-known study of the volume of the respiratory dead space. This was prompted by his interest in the carbon dioxide content of alveolar gas and the factors leading to acapnia. He made the important observation that some alveolar gas exchange can occur with tidal volumes that are much smaller than the dead space because of the axial flow of inspired gas through the airways. He pointed out that the size of the dead space is increased by lung inflation because of radial traction by the lung tissue on the bronchi. However, he overestimated the amount of carbon dioxide exchange that can occur in the airways of the lung, arguing that under some conditions such as in hyperemia of the bronchi, as much as one half of the total amount of carbon dioxide exhaled may come from the dead space. This conclusion has not stood the test of time.

Henderson's strong links with Europe, particularly Germany, led him to oppose America's entry into World War I. However, when the United States did enter the war, he took an active role in problems associated with chemical warfare. He became chief of the medical section of the U.S. War Gas Investigations, which became the research department of the Chemical Warfare Service. He was responsible for improvements in the gas masks used by the Allied armies in France. In addition, he was chairman of the Medical Board, Aviation Section, Signal Corps of the U.S. Army, and worked on problems of aviation physiology. Henderson was apparently the first person to suggest that decompression sickness ("bends") could occur at high altitude, although he pointed out that the performance of aircraft at the time made this unlikely. When aircraft improved and particularly when cabins were pressurized, decompression sickness frequently occurred if there was a loss of pressure. Decompression sickness is currently a serious problem in space medicine.

After the war, Henderson was asked to study the problems of ventilation of vehicular tunnels including the Holland tunnel under the Hudson River. With H. W. Haggard he developed standards for appropriate ventilation based on levels of carbon monoxide and other toxic gases, and these were subsequently adopted all over the world and applied to tunnels in the United Kingdom, New Zealand, and Belgium. He worked extensively on carbon monoxide poisoning and the best methods of treatment, recommending that 8-10% of carbon dioxide be added to the inspired gas to stimulate ventilation. However, modern practice is to treat carbon monoxide poisoning with 100% oxygen, either at normal pressures or in a hyperbaric chamber. Henderson also advocated that the tail pipes of cars, buses, and trucks be placed at the tops of the vehicles and pointed vertically so that the hot exhaust gases would be vented upwards. He argued that this would reduce pollution by carbon monoxide and other toxic gases at street level.

PROFESSOR OF APPLIED PHYSIOLOGY, YALE UNIVERSITY

In 1920 there was a reorganization of Yale Medical School, and Henderson left with assignment to the graduate school, where he became professor and director of the laboratory of applied physiology. Over the next eighteen years or so, being free of teaching responsibilities, he worked in areas of research that interested him, and these were always characterized by some practical application. In 1922, together with Howard W. Haggard, he invented the H and H inhalator, which was used extensively by rescue crews, particularly for resuscitation of victims of carbon monoxide poisoning. He became very interested in the use of carbon dioxide after anesthesia to prevent collapse (atelectasis) of the lung. The effects of other industrial toxic gases, including hydrogen sulfide, were studied, and he wrote articles on appropriate forms of resuscitation.

Henderson maintained a lifelong interest in air pollution, particularly the effects of automobile exhaust gas on city streets, again being far ahead of his time. He continued his work on the physiology of anesthesia and chaired a commission that investigated anesthetic accidents caused by the explosion of anesthetic gases. Another interest was the maximal work capacity of elite athletes, and realizing that competitive rowing used a large proportion of the total skeletal muscle in the body, he studied the Yale University crew, which won the Olympic rowing championship in Paris in 1924. He took up the issue of neonatal mortality and, believing this was sometimes caused by inadequate expansion of the lungs, advocated inhalational therapy using carbon dioxide to stimulate ventilation.

Henderson became professor of physiology emeritus in 1938, but he continued his research interests. Some of these led him into more applied areas with political overtones. He became very concerned with the control of alcoholic beverages after the repeal of Prohibition and wrote a colorful paper on "Four Percent Beer and Its Place in Student Life" in the *Yale Alumni Weekly*. He worked on such diverse issues as the consumption of milk, fungus infection of the feet, and the use and abuse of barbiturates and other narcotics. He was particularly confrontational on the use of the inhalation machine known as the pulmotor, which was recommended as a resuscitator by some people rather than his own H and H inhalator. One of his last papers was a polemic in the journal *Science* with the title "The Return of the Pulmotor as a 'Resuscitator': A Backstep Toward the Death of Thousands." Henderson also had an interest in politics. He was a candidate for Congress on the Progressive ticket in 1912 and 1914, and was chairman of the Progressive party of New Haven.

In 1903 Henderson married Mary Gardner Colby of Newton Center, Mass. There was one son, Malcolm Colby Henderson, who was a professor of physics at Dartmouth College and later chairman of the department of physics at the Catholic University of America in Washington, and one daughter, Sylvia Yandell Henderson, who married G. McLean Harper, who became professor of Greek and Latin at Williams College. Henderson died in La Jolla, Calif., while visiting his son.

Henderson received many honors including election to the National Academy of Sciences in 1923. He was also a member of the American Philosophical Society. He was granted an honorary M.D. degree from the Connecticut Medical Society two years before his death. The charter of that society included this privilege and the only previous recipient was Russell Chittenden, Henderson's mentor. The M.D. degree gave Henderson a great deal of satisfaction, and in retrospect, with his strong interest in many aspects of clinical physiology, it may be that he regretted not having obtained an M.D. early in his career. In fact, in the lecture to the American Medical Association referred to earlier he stated, "I hold that in the future students who are being trained to be physiologists, whether in the field of physical and nervous or of chemical physiology, ought to have the M.D. degree . . . I do not regard the Ph.D. degree alone as ensuring a sufficiently broad training for a physiologist, either in the chemical or physical line."

As a man, Henderson apparently could be a very loyal friend, but equally a formidable enemy. Cecil K. Drinker, who knew him well and wrote Henderson's obituary in the *Journal of Industrial Hygiene and Toxicology*, stated, "By the death of Dr. Henderson many of us lost a warm friend. Many others lost an equally ardent enemy, for Dr. Henderson cherished both his friends and enemies and was so forthright a man, so impetuous in his regard or disdain, that all knew where they stood in his world . . . Friends and foes alike will miss Dr. Henderson. He was a valiant, yeasty man whose scientific life made for the growth of many subjects, of which industrial hygiene was one, and for the growth of many workers who followed his venturesome leadership."

SELECTED BIBLIOGRAPHY

1899

With R. H. Chittenden and L. B. Mendel. A chemico-physiological study of certain derivatives of the proteids. *Am. J. Physiol.* 2:142-81.

1906

The volume curve of the ventricles of the mammalian heart, and the significance of this curve in respect to the mechanics of the heart-beat and the filling of the ventricles. *Am. J. Physiol.* 16:325-67.

1909

With F. P. Chillingworth and J. R. Coffey. Acapnia and shock. II. A principle underlying the normal variations in the volume of the blood stream, and the deviation from this principle in shock. *Am. J. Physiol.* 23:345-73.

1910

Acapnia and shock. IV. Fatal apnœa after excessive respiration. *Am. J. Physiol.* 25:310-33.

1911

Clinical physiology—an opportunity and a duty. *J. Am. Med. Assoc.* 57:857-59.

1913

With others. Physiological observations made on Pikes Peak, Colorado, with special reference to adaptation to low barometric pressures. *Phil. Trans. R. Soc. Lond. B* 203:185-381.

With T. B. Barringer. The relation of venous pressure to cardiac efficiency. *Am. J. Physiol.* 31:352-69.

1915

With F. P. Chillingworth and J. L. Whitney. The respiratory dead space. *Am. J. Physiol.* 38:1-19.

1916

Carbon monoxid poisoning. *J. Am. Med. Assoc.* 67:580-83.

Resuscitation apparatus. *J. Am. Med. Assoc.* 67:1-5.

1917

With W. H. Morriss. Applications of gas analysis. I. The determination of CO_2 in alveolar air and blood, with the CO_2 combining power of plasma, and of whole blood. *J. Biol. Chem.* 31:217-27.

1919

The physiology of the aviator. *Science* 49:431-41.

1920

With H. W. Haggard. Hemato-respiratory functions. IV. How oxygen deficiency lowers the blood alkali. *J. Biol. Chem.* 43:15-27.

1921

With H. W. Haggard. The treatment of carbon monoxid poisoning. *J. Am. Med. Assoc.* 77:1065-67.

1923

With H. W. Haggard. Health hazard from automobile exhaust gas in city streets, garages and repair shops. *J. Am. Med. Assoc.* 81:385-91.

1925

With H. W. Haggard. The maximum of human power and its fuel. From observations on the Yale University crew, winner of the Olympic Championship, Paris, 1924. *Am. J. Physiol.* 72:264-82.

Physiological regulation of the acid-base balance of the blood and some related functions. *Physiol. Rev.* 5:131-60.

1926

With others. Ventilation of vehicular tunnels. *J. Am. Soc. Heat. Vent. Engr.* 32:658-78.

1927

With H. W. Haggard. The validity of the ethyl iodide method for measuring the circulation. *Am. J. Physiol.* 82:497-503.

1928

The initiation of respiration at birth. *Nature* 122:282-83.

The prevention and treatment of asphyxia in the new-born. *J. Am. Med. Assoc.* 90:583-86.

1929

With others. The treatment of pneumonia by inhalation of carbon dioxide. I. The relief of atelectasis. *Arch. Int. Med.* 45:72-91.

1930

The hazard of explosion of anesthetics. Report of the Committee on Anesthesia Accidents. *J. Am. Med. Assoc.* 94:1491-98.

1938

Adventures in Respiration. Modes of Asphyxiation and Methods of Resuscitation. Baltimore: Williams & Wilkins.

1939

The last thousand feet on Everest. Physiological aspects. *Nature* 143:921-23.