ESSAYS ON APS CLASSIC PAPERS

Eugene M. Landis and the physiology of the microcirculation

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This essay looks at the historical significance of two APS classic papers that are freely available online:


EUGENE MARKLEY LANDIS (Fig. 1) was born in New Hope, Pennsylvania, in 1901. He received MD and PhD degrees from the University of Pennsylvania in 1926 and 1927, respectively. While still a medical and graduate student, he undertook a research project that began a series of outstanding contributions to the physiology of the minute blood vessels. One of his professors suggested that he try microinjecting synthetic dyes of known molecular size and configuration into capillaries in living animals. Their intense colors might make it possible to evaluate their permeation through the capillary walls. Landis carried this project to a spectacularly successful and fruitful conclusion. The novel techniques he developed and the important information he obtained with them opened an entirely new approach to the study of the physiology of the minute blood vessels. They remain the basis for much of the research done on microcirculation today (for example, Refs. 1, 6, 8).

Two papers dating from this period stand out as landmark contributions (2, 3).

The first of these papers (2) describes a new method to measure blood pressures in microvessels of the frog mesentery and the novel results Landis obtained by this method. To inject dye solution into a vessel, pressure in the micropipette had to be greater than the pressure in the vessel. If the pressure was lower, the dye front moved back into the pipette tip as blood plasma flowed in. Landis realized that when pressure in the pipette was just equal to pressure in the micropunctured vessel, the dye front remained stationary in the pipette tip. Using this method, he demonstrated a continuous fall of blood pressure from arterioles to capillaries to venules. Pressures in true capillaries averaged 14.4 cmH2O and in venous capillaries 10.1 cmH2O. Microvascular pressures and blood flows were increased by arteriolar vasodilatation and decreased by vasoconstriction.

The second paper (3) has two parts. Part I is about the project initially suggested to Landis. It deals with his attempts to measure capillary and venular permeability to certain dyes in relation to their molecular weights and to capillary pressure. Dyes were microinjected into a vessel, and their first appearance outside was timed. The results of this part of the study were inconclusive because many of the dyes became bound to plasma proteins and were only partly free in plasma. Many years later, when dyes of known binding characteristics were available and photometric measurement techniques had been developed, a new generation of microcirculatory physiologists was able to exploit this approach to studying solute permeabilities.

The second part of this paper is about the influence of capillary blood pressure on transcapillary fluid movement. Again, Landis’ approach was novel and ingenious. He had observed that if a capillary was blocked by a blunt microrod, pressure rose toward arteriolar pressure on the upstream side of the block and fell toward venular pressure downstream of the block. Because there was no blood flow through the blocked capillary, any movement of the trapped red blood cells toward the block indicated outward fluid movement through the cap-

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illary wall ("filtration"), and any movement away from the block showed fluid movement into the capillary ("absorption"). A plot of individual measurements of filtration or absorption rates in many capillaries against the corresponding capillary pressures showed a narrow scattering of points about a straight line, with an intercept of zero flow at a capillary pressure of 11.5 cmH2O.

According to Starling’s hypothesis of transcapillary fluid balance by opposing actions of hydrostatic and colloid osmotic forces (9), the intercept of this line defines the effective osmotic pressure of the plasma proteins. The slope of the line is a measure of the permeability of the capillaries to ultrafiltered fluid (k, capillary filtration coefficient). Consistent with Starling’s hypothesis, the average zero-flow pressure observed by Landis was within the range of frog plasma colloid osmotic pressures measured by other investigators (10–12 cmH2O). The near equality of hydrostatic and colloid osmotic forces showed that normal capillary walls were nearly impermeable to plasma colloids. In capillaries injured by application of alcohol or mercuric chloride, the intercepts were at lower pressures and the slopes were greater, showing that permeabilities to plasma colloids and to filtered fluid were increased. The significance of these observations for future research was immense. They demonstrated how transcapillary fluid movement is related to capillary pressure and defined capillary permeabilities to filtered fluid and to plasma colloids in precise, measurable terms.

After he had obtained his MD and PhD, Landis continued to be a leader in research in the field of cardiovascular physiology. He remained at the University of Pennsylvania in research and faculty positions until 1939, with an interruption from 1929 to 1931 as a Guggenheim Fellow working with August Krogh in Copenhagen and Thomas Lewis in London. During this period, he made direct measurements of microvascular pressures in human skin in normal individuals and in patients with Raynaud’s disease and developed indirect methods of measuring capillary filtration coefficients in human subjects.

In 1939, Landis was appointed Chair of the Department of Medicine at the University of Virginia where he continued his cardiovascular research. In 1943, he moved to Harvard Medical School as George Higginson Professor and Chair of the Physiology Department, succeeding Walter B. Cannon. He conducted research on factors affecting capillary permeability and on the pathophysiology of hypertension. During World War II, he served on the Committee on Aviation Medicine in Washington, DC. After the war, he collaborated with colleagues on several important reviews of research in cardiovascular physiology. Landis played a leading role in the development and expansion of biomedical science after World War II. His scientific publications are numerous and include research reports, topical reviews, and book chapters, as well as lectures and essays. Landis also served on the editorial boards of important scientific journals. He was active in the affairs of the American Physiological Society (President, 1952–1953) and the American Society for Clinical Investigation (President, 1943), as well as other professional societies.

Professor Landis contributed to the education and career development of many young physiologists, including the writer of this essay. His 1964 essay “APS and Youth” (5) looks back to the excitement of his first oral presentation at a meeting of the American Physiological Society. Landis concluded his essay, “All of this is simply to say that in this Society of ours, youths of all ages are offered a whole span of graded challenges and opportunities to make an entire lifetime in physiology especially rewarding.”

Landis continued to work on the physiology of hypertension until his retirement from the Chair at Harvard in 1967. He then returned to the region where he grew up and until 1971 was an Adjunct Professor of Biology at Lehigh University in Bethlehem, Pennsylvania. It was at Lehigh that he completed his last research project, a study of the osmotic effects of permeating solutes in frog capillaries. He died in 1987.

Landis’ chapter on the capillary circulation in Richardson and Fishman’s book on the history of cardiovascular physiology (4) and C. C. Michel’s obituary of Prof. Landis, which includes his description, in a letter to Dr. Michel, of how he got started in research on capillaries (7), are recommended reading.

REFERENCES