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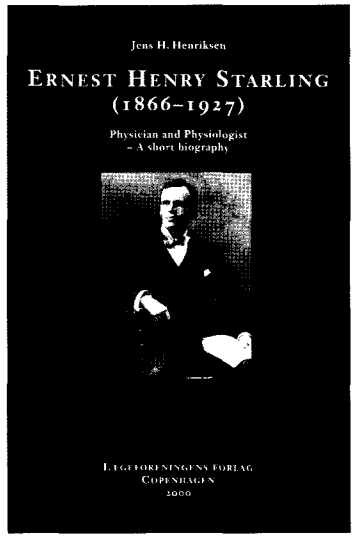
BOOK REVIEW



Ernest Henry Starling
(1866-1927)
by Jens H. Henriksen
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Whereas Assellius, Rudbeck, Pecquet, Bartholin, Mascagni, William and John Hunter and several others are usually credited with the basic discoveries of the lymphatic system, it was Ernest Starling through a series of epochal experiments in the late 19th century who set the stage for the modern understanding of the origin of lymph and the key microcirculatory forces regulating the partition of the extracellular fluid between plasma and the interstitial space. With Bayliss, Starling also introduced the concept of hormones with the discovery of secretin and promulgated the "law of the heart" regulating cardiac stroke volume. Despite these monumental contributions, surprisingly little has been written about Starling's life, and equally remarkable he never received the Nobel Prize or was knighted unlike some of his British colleagues and students. Stimulated by these omissions, Jens H. Henriksen, a renowned clinical physiologist at Hvidore Hospital and the University of Copenhagen, decided on the centennial anniversary of Starling's now classical investigations into lymph formation to write a "short biography" of this investigator's extraordinary career.

Raised in a family of 6 children with his British lawyer-diplomat father out of the country most of the time, Starling received a classical education including the German language. He initially qualified as a physician from Guy's Hospital but his major interest was in physiology. He soon joined forces with his brother-in-law, William Bayliss, to forge a professional collaboration which eventually led to global acclaim for both men. Early on, Starling studied with Rudolf Heidenhain in Breslau, and it was that celebrated investigator's misguided ideas that eventually led to Starling's epic discourses on the origin of lymph while he was working at the University College in London (UCL). Although, as mentioned, Starling later discovered hormonal secretions and the fundamental principle regulating the strength of myocardial contraction, it was the "filtration hypothesis" that is most meaningful to lymphologists.

Beginning in the early 1890's, Starling began his investigations into the dynamics of microvascular filtration and lymph formation. Ludwig of Leipzig had earlier proposed that lymph derived from plasma by filtration governed by arterial pressure. Two major stumbling blocks, however, seemed incompa-

tible with that hypothesis. Thus, when arterial pressure was artificially raised by intravenous crude pituitrin (vasopressin), arterial hypertension followed but thoracic duct lymph flow either was unchanged or decreased. Even more disconcerting was that when the inferior vena cava above the diaphragm or the portal vein was constricted, arterial hypotension was profound (as venous return and cardiac output decreased) but thoracic duct lymph flow sharply increased. Such discrepancies propelled Heidenhain into proposing that lymphagogues (i.e., vital forces) beyond physicochemical forces were responsible for lymph formation. But Starling ingeniously reinterpreted the dynamic responses of thoracic duct lymph flow including its changing protein composition to conclude that capillary pressure (in this instance selectively heightened either in the liver or extrahepatic portal bed), not arterial pressure, was the underlying mechanical force regulating blood capillary filtration and lymph formation. Starling further realized from these same experiments the importance of colloid osmotic pressure as a countervailing microvascular force–"although the osmotic pressure of the proteids of the plasma is so insignificant, it is of an order of magnitude comparable to that of the capillary pressures; and whereas capillary pressure determines transudation, the osmotic pressure of the proteid of serum determines absorption...so that, at any given time, there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids. With increased capillary pressure there must be increased transudation, until equilibrium is established at a somewhat higher point, where there is a more dilute fluid in the tissue-spaces and therefore a higher absorption force to balance increased capillary pressure" (1).

Starling also appreciated the varied permeability of the capillary membrane in different organs–"According to the permeability of the membrane, the amount and composition in proteids of the transudate fluid will vary...we can therefore arrange the capillaries of the body in a descending order of permeability, the liver capillaries being the most permeable and the limb capillaries the least permeable" (2).

Henriksen succinctly relates these brilliantly conceived and imaginatively interpreted experiments to the understanding of edemas and coelomic effusions while describing the resistance of many renowned physiologists to explanations that seemed too mechanical and too simple. A list of Starling's most important and famous lectures on these subjects is also provided including the Arris and Gale Lectures (1984, 1896, 1897) and the Croonian Lectures in 1904 and 1905. Although it took another 30 years for the detailed microcirculatory experiments by Pappenheimer, Soto-Rivera and Landis to verify the filtration hypothesis almost in its entirety, Starling certainly appreciated the clinical implications in almost every detail. As Cecil Drinker expressed it (3), "those who have reworked the field, though able to describe many things which would have been immensely interesting and gratifying to Starling, have added comparatively little to the fundamental principles which he formulated of lymph formation and the movement of fluid from and into blood capillaries. Starling's evidence though although technically crude, was nevertheless the product of an intelligence which had a habit of being right in the great essentials."

Using original diagrams to illustrate key findings and innovative equipment utilized in these animal experiments as well as seldom seen photographs of the laboratory and of Starling as a young investigator, Henriksen captures the excitement and significance of those halcyon days for clinical physiology and medical practice.

Several chapters are devoted to the discovery of secretin and investigations into the "law of the heart," which are also fascinating to read not only for the originality

of the experimental preparations but also for the inspiration galvanized for future investigations. Ironically, Starling's law of the heart is now thought to also govern propulsion of lymph. Thus, distention of the lymphangion stimulates a more potent thrust in lymphatic contraction and hence greater lymph transport (the law of the "cor lymphaticum").

Other chapters dwell on Starling's experience at Guy's Hospital, the constructive atmosphere for inquisitive learning, his time as Jodrell Professor at UCL, the struggles with antivivesectionists buttressed by cartoons of the day and old and new photographs (the latter taken by Henriksen) including Starling's office chair and laboratory (now a conference room and library).

Later chapters deal with Starling's frustrations as a medical officer in World War I. Despite his misgivings as an old (48 years) physiologist, Starling took a refresher course in medicine and went to work on strategic research to counteract the effect of poisonous gas. Like the renowned physician and contemporary William Osler, Starling expressed open hostility and disappointment at German aggression. Both men had had enormous respect for the German Universities and their progressive teaching policies and felt betrayed by the Kaiser and "Prussian power." Unlike Osler who lost his only son in that war, Starling had no children. Unfortunately, Starling found military politics overbearing, and became impatient and critical of personnel, which led to his promotion and "banishment" to the Greek Isles and ultimately to resignation from his commission. As Henriksen relates, Starling's blunt criticism of politicians, bureaucrats and the aristocracy probably accounts for why Starling was never granted a knighthood like other British physiologists of that era (Barcroft, Bayliss, Burdon-Sanderson, Dale, Evans, Hill, Lewis, Sharpey-Shäfer, Sherrington).

The last chapters deal with Starling's persona, his impact on others, the relationship with his students and colleagues, including a handwritten reproduction of correspondence with August Krogh and a compendium of official and unofficial Starling memorial lectures delivered between 1963-1999. Starling's final years were characterized by travel, declining health (? colon cancer), and his last journey to the West Indies where he died aboard ship and his burial site in Kingston, Jamaica.

For the author Henriksen, this book was clearly a labor of love, packed with pictures, vignettes, and even a color photograph of himself on the back cover sitting in Starling's original chair at UCL. All in all, Henriksen has done an incalculable service to the memory and contributions of Starling to clinical physiology and to lymphology by putting together this historical tribute to one of England's and the world's greatest physician-scientists. As Lovatt Evans eulogized Starling (4), "generalizations on the grand scale...as opposed to niggling details always had a great fascination for him and it was the noble and sweeping gesture of 19th century biology [Darwinism]...which impressed him more than the minutiae of contemporary biological teaching."

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