CC/NUMBER 6
FEBRUARY 10, 1992

This Week's Citation Classic®

Mellander S & Johansson B. Control of resistance, exchange, and capacitance functions in the peripheral circulation. *Pharmacol. Rev.* 20:117-96, 1968. [Inst. Physiology, University of Lund, and Dept. Physiology, University of Göteborg, Sweden]

The 1960s were characterized by unique progress in peripheral circulatory research. This article attempted to review new concepts of the functional organization and regulation of the peripheral circulation in hemodynamically meaningful terms. [The *SCI*® indicates that this paper has been cited in more than 600 publications.]

The Peripheral Circulation: Organization and Regulation

Stefan Mellander
Department of Physiology & Biophysics
University of Lund
S-223 62 Lund
Sweden

After completing my medical education in the late 1950s, I started PhD studies at the University of Göteoorg, where Björn Folkow introduced me to cardiovascular research. His elegant studies on the functional organization of the autonomic nervous system and its control of peripheral vascular resistance were already dassics in cardiovascular physiology. Although several other vascular functions in the peripheral circulation (in addition to overall vascular resistance) were recognized as important physiological variables at that time, no techniques were available for studying their integrated regulation. In attempts to approach this largely unknown field experimentally, it appeared that, if capillary pressure, fluid exchange, and the large blood reservoir in the veins were controlled variables via vascular smooth muscle adjustments, their regulatory responses would be reflected by changes in tissue volume. I therefore developed a sensitive ptethysmographic tech]nique for continuous recording of tissue volume changes in a cat skeletal muscle preparation under simultaneous observations of perfusion pressure and blood flow. From the very first experiment, in which the sympathetic nerves were excited in a graded manner, and from later detailed validation tests, it was evident that the new technique offered unique possibilities for simultaneous quantitative investigations of functionally important macro- and microvascular events and their integrated regulation by neural adrenergic mechanism.

The overall regional vascular resistance function was assessed fn n perfusion pi ire divided by flow, the venous capacitance function from a neurally induced rapid decrease in tissue volume coordinated in time with the resistance response, and the transcapillary fluid exchange function from a characteristically slower, but continuous, tissue volume decline in the steady state of sympathetic activation. The extent of the associated capillary pressure fail, evoked by increased pre- to postcapillary resistance ratio, was derived from the observed net transcapillary fluid absorption rate divided by the capillary filtration coefficient The latter variable also proved to be a reliable index of the size of the functional capillary surface area as controlled by the precapillary "sphincters." The results were presented in 1960 in my thesis[1] describing the sympathoadrenal regulation of the resistance, exchange, and capacitance functions in skeletal muscle and skin tissues.

This methodology opened the field to quantitative microvascular research on the whole-organ level. It was used, with various modifications, by our team of Swedish and foreign collaborators, and in other laboratories, in a long-term fruitful research program aimed at defining the control of the resistance, exchange, and capacitance functions by central and reflex nervous influences, by myogenic and metabolic regulatory mechanisms, and by endogenous and exogenous vasoactive agents in several tissues and species, including man.

In 1968, when I had moved to the University of Lund, I was invited to review this topic for *Pharmacological Reviews.* My good friend and colleague Börje Johansson agreed to be a coauthor. His expertise in vascular smooth muscle and circulatory physiology contributed greatly to the successful outcome of this article.

Circulatory research along this line continued intensely in the 1970s. It was then complemented by other important experimental approaches, in particular the vital microscopy technique, leading to further conceptual development of capillary physiology and microvascular regulation, as reviewed by C.C. Michel[2] and ELM. Renkin.[3] Further progress followed whole-organ method developments, permitting continuous recordings of capillary pressure in absolute terms and simultaneous registration of segmental resistances in morphologicalry strictly defined, and functionally differentiated, consecutive sections of the vascular bed.[4-5]

1. **MeUander** S. Comparative studies on the adrenergic neuro-honnonal control of resistance and capacitance blood vessels in the cat. *Acta Pysioi Scand.* 176(Suppl. 50): 1-86,1960. (Cited 225 times.)
2. **Michel** C C Fluid movements through capillary walls. (Renkin E M & Michel C C, eds.) *Handbook of physiology: the cardiovascular system.* Bethesda, MD: American Physiological Society, 1984. VoL IV. p. 375-409.
3. **Renkin** E **M.** Control of microcirculation and blood-tissue exchange. (Renkin E M & Michel C C, eds.) *Handbook of physiology. the cardiovascular system.* Bethesda, MD: American Physiological Society, 1984. Vol. IV. p. 627-87.
4. **Mellander** S. Myogenic mechanisms in local vascular control. *Acta PhysioL Scand* 133(Suppl. 571):25-42,1988.
5. . Functional aspects of myogenic vascular control. *J. Hypertension* 7(Suppl. 4): S21-S30, 1989.

Received November 12, 1990