

Strandgaard S, Olesen J, Skinhøj E & Lassen N A. Autoregulation of brain circulation in severe arterial hypertension. *Brit. Med. J.* 1:507-10, 1973.

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Cerebral blood flow is normally autoregulated; that is, within wide limits it is kept constant during perfusion pressure changes. This paper demonstrated that in chronic hypertension the lower blood-pressure limit of autoregulation of cerebral blood flow is shifted towards high blood pressure, impairing the tolerance to low blood pressure. Evidence was also found for the existence of an upper blood-pressure limit of autoregulation beyond which cerebral blood flow increased. (The SC¹® indicates that this paper has been cited in over 240 publications.)

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This paper and one published three years later¹ formed part of my MD thesis, which was supervised by two of my coauthors, N.A. Lassen and the late E. Skinhøj. The work was done at Bispebjerg Hospital in the early 1970s and was extended with animal studies at the Wellcome Surgical Institute at the University of Glasgow, under the guidance of A.M. Harper.

The idea for the work, which was to look for the functional equivalent of the well-known hypertensive structural changes of cerebral arterioles, was suggested by Lassen in 1959,² but until the early 1970s it was practically dormant. Thus, the study could have been undertaken at least 10 years earlier than it actually was.

Cerebral blood flow was studied with the arteriovenous oxygen difference method. Since global cerebral oxygen consumption is constant in conscious humans, the reciprocal

value of the cerebral arteriovenous oxygen difference can be used as a relative measure of cerebral blood flow. This method, which goes back to 1932, allows multiple measurements within a short span of time, and in this study such measurements were made while manipulating the blood pressure by drug infusion and head-up-tilt.

The finding of a shift of the lower end of the autoregulation curve towards higher pressure in hypertension corroborated the clinical impression that severely hypertensive patients will not, without risk, tolerate an immediate normalization of blood pressure. It should, however, not be interpreted as a general warning against antihypertensive treatment; after all, the brain is the organ that has benefited most from modern antihypertensive treatment. In the 1976 paper¹ it was shown that some patients probably readapt their autoregulation of cerebral blood flow towards normal during long-term antihypertensive treatment. This has been demonstrated in young rats with renal hypertension given antihypertensive treatment.³

The part of this work that dealt with the upper limit of autoregulation confirmed the results of an earlier Swedish paper.⁴ In a later study,⁵ it was shown that the "sausage-string" pattern of localized dilations and constrictions seen in severe hypertension in cerebral arterioles and small arteries is associated with a rise in cerebral blood flow. The "sausage-string" pattern consists of localized hypertensive vasodilation superimposed on autoregulatory constriction. The old concept of "hypertensive vasospasm" leading to cerebral ischemia is thus erroneous.

One reason this paper has been cited above the average may be because I have written a host of reviews on the subject and have quoted the work incessantly. Aside from this self-citation, it is my impression that these studies initially went rather unnoticed, but that they were rediscovered around 1980 when a wave of clinical papers was published on cerebral ischemia caused by overtreatment of severely hypertensive patients.

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3. Vorstrup S, Barry D I, Jarden J O, Svendsen U G, Braendstrup O & Strandgaard S. Chronic antihypertensive treatment reverses the hypertension-induced changes in cerebral blood flow autoregulation. *Stroke* 15:312-8, 1984.
4. Strandgaard S. The upper limit of cerebral blood flow autoregulation in experimental renovascular hypertension in the baboon. *Circ. Res.* 37:164-7, 1975. (Cited 55 times.)
5. Farrar J K, Jones J V, Graham D I, Strandgaard S & MacKenzie E T. Evidence against cerebral vasospasm during acutely induced hypertension. *Brain Res.* 104:176-80, 1976.