
In olden times, hypertension was a simple story. Dr. Goldblatt's clamps had pointed to the insidious humour which the kidneys were capable of generating, and when Page and Braun-Menendez captured the demon in a bottle, the problem appeared to be solved. Alas, the harder investigator's toiled to confirm this mechanism, the greater the confusion became. The periodic enclaves which these hypertension researchers held to dispute each other's findings were frequently invaded by a Belgian spy. After listening to the conversation for a bit, he would rise to his full noble stature and expostulate: "But Gentle-men, what of the baroreceptors and the neural regulators? Surely they must be somehow involved in hypertension!" This remark by Corneille Heymans was always followed by a period of deathly silence, after which the arguments over the best technique for assaying angiotensin would resume. Eventually James McCubbin, an associate of Page, provided us with the first unequivocal evidence that in the experimental hypertensive animal there is a resetting of the baroreceptors to operate at a new homeostatic level. What has become of this concept during the decade since the evidence was presented?

In an attempt to answer this question, Dr. Paul Kezdi organized an international symposium held in Dayton, Ohio, in 1965, attended by some 50 invited guests. This symposium is now available in published form, presenting the 37 formal papers, brief discussions, and summary statements. Neither space nor wisdom would justify reviewing all 37 reports; I shall confine my remarks to the barest substance of the reports and leave the reader to identify the authors and their detailed contributions by referral to the original volume.

The carotid sinus, situated at the transition between the elastic arterial reservoir and the distributing muscular arteries, remains the most important of the baroreceptor mechanisms, reinforced by subsidiary pressure sensitive regions on the common carotids, the aortic arch, the pulmonary arteries, and other major arterial conduits. Within the wall of the sinus are sensory terminations, some apparently ending in naked aborizations while others are associated with lamellar corpuscular structures. Some of these endings are intimately associated with the elastic elements within the wall, while others seem to be closely associated with the muscular elements. This anatomic differentiation offers ample support for the differential response mechanisms seen in the neurograms, although the definitive evidence to correlate anatomic arrangement with functional role is not yet forthcoming.

When the coded message being transmitted up the sinus nerve is examined, one is impressed that some elements appear to be signaling static pressure, while others are dynamically signaling the rate of change of that pressure. Testimony to the importance of the dynamic component, which has different sensitivities to rising and falling pressures, is seen in the fact that proper selection of the contour of artificial pulses can "fool" the system, and result in changes in mean systemic blood pressure in the "wrong" direction. The total response of the system to pulsatile pressure appears to be characterized by a logarithmic response of the systemic pressure as a function of the logarithm of the sinus pressure. Nonlinearity of the system seems to reside chiefly in the sensory input, reflecting the integration of static and dynamic components, the distribution of thresholds among the individual receptors, and the properties of the mechanical transducers themselves. This input traverses a polysynaptic pathway to reach the nucleus solitarius, from which arise diffuse relays to the reticular centers and the descending sympathetic and parasympathetic pathways. In traversing this complex polysynaptic pathway, sufficient phase dispersion occurs to erase the pulsatile synchronization of the normal sensory input, accounting for the failure to find much activity in the reticular network which can be identified with cardiovascular function on the basis of pulse synchrony.

The baroreceptor loop, from the carotid sinus to the effectors of the cardiovascular system, operates with a time constant of 15 seconds and a gain factor on the order of 2 to 4. In other words, a disturbance that would tend to displace blood pressure by 30 to 50 mm Hg is reduced to a deviation in arterial pressure of only 10 mm Hg. In its normal operation, however, it must be regarded as part of a larger complex of homeostatic regulators, including chemoreceptor elements, which can act synergistically in the normal
unanesthetized animal to achieve a gain factor more on the order of 20, as would be demanded of an effective homeostatic regulator.

The output of this control system not only regulates the resistive component on the arterial side of the circulation, but also controls the capacitative component on the venous side, reinforced by chronotropic and inotropic effects on the myocardium in which sympathetic and parasympathetic effects act reciprocally. It follows that alterations in cardiac output should be considered as a component of the normal baroreceptor response. However, since pressure rather than flow constitutes the control signal, anesthesia or other experimental interventions may suppress the cardiac output response without disrupting the operation of the baroreceptor control. In shock, for example, the cardiac output response to carotid occlusion may be reversed even though the pressor response is nearly normal.

One of the most interesting points which arose during this conference were numerous examples of the lability in blood pressure observed when the function of the homeostatic regulators is disturbed. That loss of baroreceptor function does not uniformly result in a sustained hypertension of significant magnitude has been appreciated for a long time. Much more conspicuous is the blood pressure lability observed in such animals, which will show wide swings with postural shifts, high peaks with exercise or feeding, and drastic falls during sleep even when buffer reflex loss is superimposed on renal hypertension. A somewhat comparable lability of blood pressure can be produced by continuous minimal infusions of angiotensin which apparently sensitize the system to catecholamines and produce gross exaggerations of neurogenic responses.

Having briefly sketched our knowledge of the baroreceptor reflexes which is documented in considerable detail in the published report of this conference, we now turn to what might be considered the real point of the conference: namely, what is their role in hypertension? Here the record is distressingly thin. There is confirmation of the earlier reports that “resetting” of the baroreceptors occurs in experimental hypertension. Direct evidence is presented that the same occurs in clinical hypertension: The hypertensive patient shows evidence of normal carotid sinus function except that it is operating about a higher “set” point. But what are the cause-and-effect relationships? Only a few scanty suggestions were forthcoming.

It is still agreed that alterations of the smooth muscle tone in the wall of the sinus can alter the sensitivity of the receptor mechanism, but no one has defined what role, if any, this plays in clinical hypertension. In animal experiments, a possible basis for resetting was reported in the fluid and electrolyte changes occurring in the wall of the sinus, which alter its mechanical properties and hence could alter its sensitivity. In the older chronic hypertensive patient, there appears to be definite evidence of degenerative changes in the wall of the carotid sinus, including a conspicuous loss of neural elements. The evidence suggests that this is more the result than the cause of the chronic disease process, but such findings could offer a plausible basis for explaining why hypotensive therapy may be somewhat more successful in the earlier hypertensive, whose resetting should be reversible, as contrasted with the older chronic hypertensive, in whom degenerative loss prevents regaining the original sensitivity of the reflex. Resetting, however, may not be exclusively a receptor phenomenon; central neural adjustments may also take place.

As a final postscript to the conference, a pair of reports are given of artificial stimulation of the carotid baroreceptors in the hypertensive patient as a means of lowering blood pressure. The fact that our theoretical knowledge can be converted to practical application is always a source of some satisfaction, and possibly this technique may prove of value in some types of cases. This can scarcely be hailed, however, as a solution to the problem of hypertension.

In summary, this volume presents an excellent “state-of-the-art” digest of our present understanding of the baroreceptor mechanism and its possible relation to hypertension. Perhaps its most valuable feature is that it brings under a single cover the contributions from the diverse disciplines which can be brought to bear on this problem. At best it remains a progress report which defines many more questions than it answers. For the research worker or the clinician, who wishes to gain some insight into the workings of this key regulator of the cardiovascular system, it is a unique reference source. It can scarcely claim to offer a satisfactory answer to Dr. Heymans’ query as to just what role the carotid sinus plays in clinical hypertension, but this volume makes it clear that this question is still relevant.

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