Blood pressure set point

The late ALBERTO C TAQUINI *, **

Chairman, Institute of Cardiovascular Research; Emeritus Professor, Medical School, University of Buenos Aires, Buenos Aires, Argentina

This paper has two main purposes: A) to emphasize the role of the kidney in setting peripheral resistance, thus arterial blood pressure and flow distribution since birth to full grown; and B) to bring attention to the role that changes in pulse pressure and pulse velocity may have in the genesis of aging hypertension.

A) According to the tonus regulation at basal steady conditions, the arterial system may be divided into three areas: I) the skin, in which the vascular tonus is regulated by heat; II) the kidney, whose vessels are regulated by glomerulo-tubular balance; and III) the rest of organs and tissues of the body, whose tonus is regulated according to the oxygen the cell needs to maintain its energetic equilibrium (ATP/ADP relationship). As area III has the higher flow and lowest equivalent resistance, the kidney is -hemodynamically- the organ that sets arterial blood pressure during life. Nevertheless, since birth to full grown, the kidney must progressively adjust the peripheral resistance of area III, in order to allow arterial blood pressure and renal distribution to match glomerular filtration with the increasing body metabolism. The tool that the kidney uses to adjust resistance of area III, thence arterial blood pressure and blood distribution, is the renin-angiotensin system.

B) Aging decreases vascular distensibility. Lower distensibility of the arterial tree results in a progressive increase in amplitude and velocity of the pulse wave, then in its potency. Small resistance vessels must increase Bayliss response in order to reduce pulse impact on the precapillarial arteries. Structural changes in the resistance vessels, as well as in preglomerular arteries, should establish a feed-back mechanism responsible for the evolution of arterial blood pressure.

Key terms: *arterial blood pressure, hypertension, kidney, peripheral resistance, set point, vascular tone*

The knowledge about the control of arterial blood pressure (BP) and the factors related to the maintenance and regulation of vascular tone –main variable involved in BP determination– have substantially increased in the last decades. However, an integrated explanation of the mechanisms that fix its level is still lacking. On the other hand, even though the participation of the kidneys in the genesis of the level of BP seems to be sustained by many facts (15, 16), their role and the mechanisms that

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** **Correspondence to:** Dr Nidia Basso, Instituto de Investigaciones Cardiológicas, Facultad de Medicina, Universidad de Buenos Aires, Marcelo T de Alvear 2270, 1122-Buenos Aires, Argentina. Fax: (54-1) 961-7569

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actually may be involved are still far from being explained. The aim of this paper is to present a hypothesis on this subject.

The circulation should be adjusted to the changing physiological requirements of the whole body. Then, cardiac output (C0) and total peripheral resistance (TPR) are continuously changing. Even though the autonomic nervous system and the hormonal system lessen these changes, different BP values could be obtained from one moment to the next, variations covering a wide and significant range (8). Notwithstanding, one should accept that each human being at basal steady state conditions must have a level of BP sufficient to provide all organs and tissues with the blood they need to fulfill their minimal normal function, which implies processes (utilization and synthesis) that yield heat, water and metabolites, that should be removed in order to maintain homeostasis (14).

Cardiac output must be distributed to satisfy three basic requirements: 1) to provide an adequate tissue flow, to supply cells with the materials and oxygen needed to preserve energetic reserve (ATP-ADP relationship); 2) to ensure a renal circulation that grants the kidney blood clearance performance; 3) to establish a cutaneous circulation that allows the skin to preserve body temperature.

At basal steady state, CO distribution –according to requirements– primary depends on myogenic tone of small vessels. Hemodynamically, the skin and kidneys are singular units, since they are the only ones with flows that do not respond to energetic demands and thus their basal tonus is not related to oxygen provision. Skin vessels tonus is regulated by heat and it is the highest in the organism (approximately 90%), condition which allows multiplication of flow without significant changes in BP. Renal vessels tonus is regulated in function of glomerular pressure (GP) and glomerular/tubular balance, being the lowest (around 10%) in basic conditions. Contrary to the skin, the kidneys maintain blood flow and GP constant along a large range of BP variations (renal autoregulation) (9).

The rest of the organism is integrated by organs and tissues, with own functions and requirements, and thus the tonus of their vessels differs in magnitude, as also in participating factors (3, 6, 9). In spite of this, under strict basic conditions, all territories integrating this sector may be conceived as a unit, because all of them adjust their flows and thus their tonus exclusively to match their own energetic wastes. Oxygen provision is the critical variable. Obviously, BP is the result of adding blood flow and peripheral resistance of the three mentioned sectors (CO x TPR). Notwithstanding, hemodynamically, its level is defined by the dependent energetic sector, which receives the major flow and thus puts the minor resistance. The energetic-dependent sector would settle the minimum BP necessary to assure oxygen provision.

As to accomplish their function, the kidneys require a high flow and a critical BP to maintain adequate filtration; in addition, this organ must operate on the vessels that control the resistance tonus of the energetic-dependent sector, to allow BP to reach its critical level. The renin-angiotensin system (RAS) –due to its vasoactive and trophic effects– appears as the primary operative mechanism the kidney make use of to adjust TPR and –as a consequence– arterial blood pressure.

The above mechanism is in function provided an unbalance exists between the demand of blood depuration and renal functional potential capacity. Such is the case during the period of corporal development. When the provision of metabolites by the organism, and renal flow and glomerular filtration are in equilibrium, the RAS should drop to a level that maintains the GP/TPR feed-back.

Compartmentalization of the arterial system and the roles displayed by the kidney and RAS would offer a basis to explain adjustment of BP during development (13).

Since the first year of life, glomerular filtration (GF) normalized by body weight remains constant, thus implying a sustained increase in GF to satisfy the progressive charge of metabolites, particularly the proteic ones. Simultaneously, TPR

increases, in spite of a sustained decrease in cardiac index (17). Coincidentally, although values of plasma renin activity (PRA) progressively drop from birth to complete development, they still remain at high levels until full development (2, 4).

In view of the above, it may be postulated that the kidney modulates TPR, to allow BP level and/or CO distribution to adjust renal blood flow (RBF) and GF to the increase of metabolites resulting from the augmenting corporal mass.

After full development is reached, two periods should be considered in relation to the level of BP: one in which it remains within the normal range; another which starts after middle age (35/40 years), when BP tends to augment in an increasing number of apparently normal persons. During the first stage, BP and flow distribution satisfy kidney functional demands and PRA remains at levels which are compatible with the maintenance of GP-TPR feed-back and sodium space. As to the second period, much has been speculated about the participation of the kidney and the origin and mechanisms involved in the increase in TPR. The increases in BP after middle age and the incidence of hypertension in the aging population led us to analyze the possibility that the TPR increase may be another manifestation of aging of the vascular tree.

Well known is the appearance with age of architectural, structural and functional changes in the arterial vessels, and their hemodynamic repercussions (10). Comparative studies of normotensive and hypertensive populations of the same age show that alterations in both groups only differ in magnitude and that there is overlapping amongst them. The decreased distensibility of the arterial tree, as well as the increases in maximal and differential pressures which appear with age, have been extensively studied. On the contrary, scarce attention has been given to the influence of such changes in the genesis of increased TPR and in the structural changes of resistance vessels and preglomerular arteries appearing with age (7).

From a physical point of view, the increases in velocity and amplitude of the pulse wave imply an increase in its potency. Since the pulse wave must dissipate before reaching the precapillary arteriole to preserve the capillaries integrity, as the potency of the pulse wave increases the resistance, vessels must increase their tonus to reduce its impact. Anatomo-clinical investigations have shown structural changes in small arteries –thickening of muscular layers and/or remodelation– which modify the relation wall-lumen (5). These alterations have been observed in vessels around 300 μm in diameter, but not in vessels of 100 μm diameter (11).

The combination of all the above facts opens the possibility –yet not considered– that the increased pulse wave potency may cause a Bayliss type of response (1) in resistance vessels, which secondarily originates the structural changes which should fix the increase in TPR, characteristic of age hypertension.

The increase of systemic peripheral resistance on one side and renal alteration on the other could establish the feed-back responsible for the hypertension evolution. The therapeutic effect of drugs that interfere with angiotensin II on the structure of the resistance vessels (12) supports the participation of the RAS as mediator of the vascular remodelation previously mentioned (Fig 1).

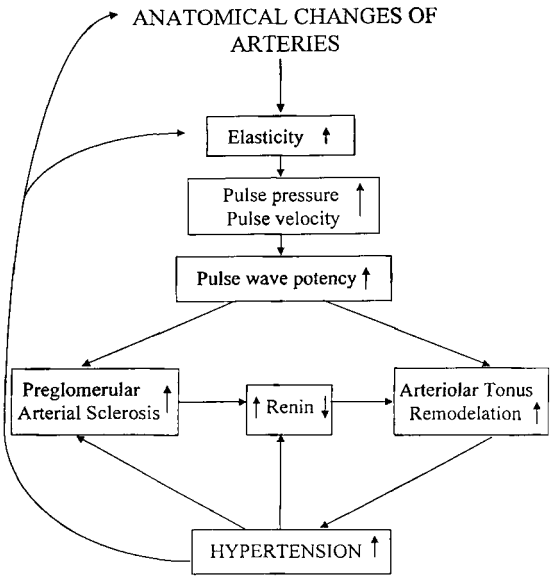

Fig 1. Diagram of the sequence of events involved in the genesis of hypertension.

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