Arterial hypertension participates actively in the development and progression of cardiovascular risk (CVR). The kidney plays a double role of culprit in the development of arterial hypertension and victim, when it suffers the consequences of persistently elevated blood pressure. On the other hand, it has been clearly demonstrated that as soon as the kidney is damaged by arterial hypertension, there is a concomitant rise in global CVR that accounts for an enhanced prevalence of fatal and non-fatal cardiovascular events currently observed in patients with chronic kidney disease (CKD). The increase in clinical expression of cardiovascular disease must be preceded by an asymptomatic stage, in which an enhanced presence of target organ damage can be potentially detected.

Different theories have come to explain how the kidney can participate in the origin of elevated blood pressure [1], but the existence of a defective handling of sodium and the consequent alteration in body fluid volumes has been, since its description by Guyton [2], the most widely accepted. It is also well-established that the renin-angiotensin system (RAS), and its final effector angiotensin II, participates in the control of blood pressure and its consequences expressed as target organ damage [e.g. albuminuria and left ventricular hypertrophy (LVH)]. A recently published paper [3] has come to confirm the role of the kidney in the genesis of hypertension while demonstrating its participation in the development of non-renal consequences of elevated blood pressure. The authors also suggest that the major mechanism of action of RAS inhibitors in hypertension is the attenuation of angiotensin II effects on the kidney.

To come to these conclusions, the authors have used a cross-transplantation model in which they address the question of the impact of renal AT1 receptor on the pathogenesis of hypertension and LVH. Four groups of mice were generated attempting to separate the actions of AT1 receptor pools in the kidney from those in systemic tissues. The authors used genetically matched F1(C57BL/6 × 129) wild type (WT) mice and F1(C57BL/6 × 129) mice homozygous for a targeted disruption of the Atr1a gene locus encoding the AT1aR (AT1aR-KO mice). Hypertension was induced by continuous infusion of angiotensin II. The analysis of blood pressure evolution revealed that only those animals carrying a WT kidney developed hypertension. Animals expressing the receptor in the periphery (KO mice), but not in the transplanted kidney, did not develop hypertension, while those animals expressing the receptor in the transplanted kidney, but not in the periphery, did in a degree similar to that seen in the WT animal. The authors found that the mechanism after the increase in blood pressure during angiotensin II infusion was an increase in sodium reabsorption by the kidney.

The authors also investigated the development of LVH and concluded that this was primarily dependent on blood pressure elevation, because systemic KO mice developed hypertension and LVH in the absence of AT1R expression in the heart when they received a kidney from a WT animal expressing the receptor. On the contrary, the WT animal receiving a kidney from a KO animal developed neither hypertension nor LVH. In conclusion, in the animal model described by Crowley et al. [3] and during the infusion of angiotensin II, the renal expression of AT1 receptors is required for the development of arterial hypertension (facilitated by an increased tubular sodium reabsorption) and LVH.

Can these results be applied to human hypertensive subjects? Human hypertension is far more complex than the model presented in this interesting article. The authors have played with only two factors, angiotensin II infusion and presence or absence of renal and/or systemic expression of AT1 receptors. In humans, KO models for AT1 receptor do not exist and hypertension due to an isolated increase in angiotensin II formation

**Keywords**: angiotensin II; arterial hypertension; AT1 receptor; kidney; left ventricular hypertrophy; natriuresis

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**Comment on Crowley SD, Gurley SB, Herrera MJ et al.**

Angiotensin II causes hypertension and cardiac hypertrophy through its receptors in the kidney. *PNAS* 2006; 103: 17985–17990.
is very rarely seen in renin-secreting tumours and in a few cases of renovascular hypertension. The presence in these cases of LVH is always accompanied by systemic and renal expression of AT1 receptors and the response to RAS suppression tends to be positive.

In the great majority of hypertensive patients, the role of the kidney in the development of arterial hypertension could be a consequence of the renal effects of an increased activity of the central nervous system [4], facilitating an increase in renal vasoconstriction, which in turn would facilitate an increase in urinary sodium reabsorption [5]. Regression of LVH is particularly positive when suppression of the RAS system is used in hypertensive patients [6], but it is impossible to determine whether this effect is primarily due to the blockade of the effects of angiotensin II on the renal AT1 receptors.

In summary, the paper of Crowley et al. [3] provides new insights into the pathogenesis of arterial hypertension in animal models during angiotensin II infusion and clearly relates the presence of renal AT1 receptors to the development of hypertension and its consequences. Applicability of these results to the pathogenesis of human hypertension and its consequences remains to be elucidated.

Conflict of interest statement. None declared.

References
3. Crowley SD, Gurley SB, Herrera MJ et al. Angiotensin II causes hypertension and cardiac hypertrophy through its receptors in the kidney. PNAS 2006; 103: 17985–17990

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