Evolution and Hypertension: Is the Renin System Necessary?

To the Editor:

We enjoyed very much Weder’s editorial on the evolutionary underpinnings of essential hypertension. We thoroughly agree with his thesis that sodium-conserving mechanisms, which conferred a survival advantage to our ancestors, are the main cause of hypertension in acculturated societies, where salt is readily available and abundant. In this respect, he mentions among other theories the polymorphisms in various genes relevant to enhanced sodium retention and the higher prevalence of such genetic variants in patients of African ancestry, as well as the related “slavery hypothesis,” all of which make sense and sound plausible.

However, there was nowhere mention of the renin–angiotensin–aldosterone system, which is the main effector mechanism in the maintenance of equilibrium between vascular tone and intravascular filling pressure. Consistent with evolutionary requirements, the renin–angiotensin–aldosterone system becomes activated if the intake of sodium is low and/or if the intra-arterial volume and filling pressure falls to maintain arterial pressure by both the increased angiotensin-induced constriction of vascular smooth muscles and increased angiotensin-induced stimulation of aldosterone leading to sodium retention. However, with the lifestyle of modern civilization, it seems that not only is the renin system redundant, but, actually, if it fails to remain suppressed, even its “normal” state of activity may be detrimental. This occurred to us ~30 years ago, when the first clinical trials with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers showed that longitudinal suppression of the renin system in various cardiovascular diseases produced significant benefits without evidence of long-term adverse consequences. Notably, after an initial decrease in plasma aldosterone levels with either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, there is a rebound to almost pretreatment levels, because other mechanisms seem to take over the release of aldosterone. This dissociation of renin–aldosterone levels is particularly apparent as a natural state in hypertensive subjects of African ancestry, who frequently display the so-called “idiopathic primary aldosteronism” (defined usually as a plasma aldosterone/plasma renin activity ratio of >30 in the absence of adrenal tumor). Again, this seems to be an evolutionary trait that evidently must have conferred a survival advantage in the distant past but has become a liability in modern times. And yet, even in these patients with extreme suppression of renin (often to undetectable levels), treatment with angiotensin-converting enzyme inhibitors or ARBs produces a lowering of blood pressure, albeit lesser than in the average essential hypertension, indicating that the renin system is still functional. Indeed, after vigorous sodium depletion, it can become reactivated rendering many of these patients “resistant” to the antihypertensive effect of diuretics.

Does that mean that the renin–angiotensin system (at least in the postnatal period) is no longer necessary and is indeed nefarious? If it were permanently obliterated in patients with essential hypertension, would that prevent a significant number of cardiovascular and renal complications? If so, a new therapeutical approach might be developed to cure hypertension by inducing irreversible inhibition of renin secretory mechanisms.

Disclosures

None.

Haralambo Gavras
Hypertension and Atherosclerosis Section
Department of Medicine
Boston University School of Medicine
Boston, Mass

Hans R. Brunner
Division of Hypertension and Vascular Medicine
Centre Hospitalier Universitaire Vaudois
Lausanne, Switzerland

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Haralambos Gavras and Hans R. Brunner

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