Sodium and calcium homeostasis are tightly regulated by endocrine systems. Of particular importance are effects of the renin–angiotensin–aldosterone system (RAAS) on sodium and of parathyroid hormone (PTH) and vitamin D on calcium homeostasis.

Although previous investigations studied the relationship between the RAAS and PTH in the setting of either absolute aldosterone excess, that is, primary aldosteronism (PA), or absolute PTH excess, that is, primary hyperparathyroidism, Brown et al addressed this issue in study participants without absolute PTH excess, that is, primary hyperparathyroidism, aldosterone excess, that is, primary aldosteronism (PA), or between the RAAS and PTH in the setting of either absolute homeostasis.

With this in line, MR antagonists by blockers or of the American Heart Association.

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MR-related mechanisms. With this in line, MR antagonists by
et al, it is tempting to speculate that decreased levels of PTH after MR antagonism may be, in part, the result of an attenuated interplay between aldosterone and AngII.

In patients with PA, treatment with either MR antagonists or adrenalectomy does not only normalize elevated PTH levels but is also associated with improved bone mineral density and decreased fracture risk. Whether beneficial effects of MR antagonism on cardiovascular health are related to its PTH modifying effect remains, however, to be evaluated in further studies. Apart from this, PTH levels may also serve as an additional tool for the diagnosis of PA, and in particular for aldosterone-producing adenomas.

Another mechanism explaining the mutual interplay between the RAAS and PTH was proposed by Maniero et al: patients with PA show an increased responsiveness of the parathyroid glands to hypocalcemia. This research group further demonstrated the expression of both type 1 PTH receptors in the aldosterone-producing adenocortical nodules, as well as expression of the MR in the nuclei of parathyroid adenoma and even in normal parathyroid cells. The presence of the MR in the nuclei of parathyroid cells indicates that aldosterone may modulate PTH secretion. In addition to this, Brown et al suggest that there may be a direct effect of the RAAS on PTH secretion probably mediated by AngII. Although the above-mentioned mechanisms may all work in concert to affect PTH, the situation seems to be even more complex when considering that Vaidya et al have previously shown that there exists an interaction with vitamin D status, that is, that the effect of the RAAS on PTH differs according to the prevailing vitamin D status. The authors suggested that according to their previous findings, vitamin D3 therapy might augment the tissue (vascular and adrenal) response to AngII infusion and marginalized the influence of an ACE inhibition on PTH. This interaction is also of interest because activation of the vitamin D receptor has been shown to directly suppress renin expression in the kidneys.

In conclusion, there exists accumulating evidence for a mutual interplay between the RAAS and the vitamin D-PTH axis. The pathophysiological background of the high prevalence of cardiovascular disease found in patients with inappropriately elevated aldosterone and PTH levels, in parallel to low vitamin D, is an ongoing research issue with high clinical relevance in different settings.

Considering the wide use of RAAS blocking agents, the results of ongoing randomized controlled trials evaluating
the clinical effects of ACE-inhibitors or MR antagonists on PTH, bone metabolism and cardiovascular disease are awaited with high interest. One study currently investigates the effects of Vitamin D Administration on Plasma Renin Activity in Patients With Stable Chronic Heart Failure (VitD-CHF). The Renin-Angiotensin-Aldosterone System and Parathyroid Hormone Control (RAAS-PARC) Study examines PTH-lowering effects of ACE-inhibitors. Another study explores the acute modulating effect of cinacalcet on the RAAS in healthy volunteers. Finally, the Effect of Eplerenone on Parathyroid Hormone (EPATH) Study evaluates the effect of MR antagonism by eplerenone on PTH levels and cardiovascular risk factors in patients with primary hyperparathyroidism.10

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