**Title: Aldosterone and parathyroid hormone: a complex and clinically relevant relationship**

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We read with interest the article by Paik et al who studied non-classical determinants of parathyroid hormone (PTH) levels in 1,288 women from the Nurses Health Study II [1]. Smoking, body mass index, low vitamin A intake and winter season were associated with higher PTH levels. These results are of particular importance when considering the crucial role of PTH for the diagnosis and treatment of bone and mineral disorders [2] and the accumulating data on PTH and cardiovascular risk [3-5]. With our letter we seek to guide the attention towards previous data suggesting that the renin-angiotensinaldosterone system (RAAS) may also have a significant impact on PTH levels [5-9]. Towards this, we and others have shown that high aldosterone levels are associated with high PTH levels [5-9]. In experimental studies it has been demonstrated that aldosterone excess increases renal and fecal loss of calcium [8-10]. This in turn results in secondary hyperparathyroidism which could be effectively treated by mineralocorticoid receptor (MR) blocking therapy in rats [8,9]. The complex interplay of calcium, PTH and the RAAS is further underlined by data indicating that both calcium as well as PTH participate in the complex regulation of the RAAS [11-13]. In this context it has been observed that aldosterone levels were elevated and positively correlated with PTH levels in patients with primary hyperparathyroidism [14,15]. Hence, primary hyperparathyroidism is associated with high aldosterone levels and primary aldosteronism is associated with high PTH levels. Clinical data suggest that treatment of either disease is effective in normalising the levels of both hormones [6,8,9,14,15]. We therefore believe that the awareness of an interplay between PTH and aldosterone could, for selected cases, be clinically relevant for diagnostic considerations of patients with elevated levels of any of these two hormones. Apart from this, concomitant elevations of both hormones in states of either hyperparathyroidism or aldosteronism could hypothetically underlie the increased risk of mortality or cardiovascular disease associated with high PTH or aldosterone levels [2-5,16]. Whether beneficial effects of treatments of PTH or aldosterone excess are significantly mediated by an impact on both hormones warrants further studies. Of

note, vitamin D metabolites have already been shown to suppress PTH as well as the RAAS [17,18]. In conclusion, we hope that our letter can provoke attention and can further stimulate research on the relationship of PTH and the RAAS in order to better understand, diagnose and treat disturbances of both hormone systems.

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