

Rebuttal: The Case for Routine Parathyroid Hormone Monitoring

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I really enjoyed Stuart Sprague and Sharon Moe's excellent companion piece on parathyroid hormone (PTH). Their knowledge and scholarship are of course second to none; yet, as is true of all of the best scholars, they wear the mantle of their considerable learning lightly. Their article is a wonderful and lucid account of the history of uremic toxins, skeletal involvement in renal diseases, and the inadequacy of almost all of the current biomarkers at our disposal to adequately address the core issues here, namely how best to treat real patients in real clinical settings (1).

It is indeed helpful of them to recount the history of PTH. Where we are today in 2012 is precisely because of where we have come from say 30 years ago. Focusing of course on the advanced secondary and even autonomous hyperparathyroidism, we can all remember when we old(er) nephrologists were young(er). However, many residents and fellows may look with indulgence at some of our comments, as one does with elderly relatives at times, because in the modern era, what was true before is no longer so relevant today. PTH concentrations of 1000, 2000, 3000 ng/L, and beyond are just rarer, at least in countries that can afford to spend significant sums on healthcare. However, a recent visit to Brazil, a country with the fifth-largest economy in the world and probably the fifth-highest PTH concentration range too, demonstrated to me that this older paradigm can still be relevant where advances in diagnosis and therapy have lagged behind. In a modern era in which most PTH values by design have been reduced to an order of magnitude less than once was the case (2), the utility and relevance of PTH measurement is very much less than my opponents suggest. Indeed, the implications of PTH normality, or elevation, will surely be situational, depending on the clinical context. We must not fall into a similar trap with PTH as we are trying now with fibroblast growth factor 23, where it is just too easy to say all elevation is "uremic toxin" related (3). Some elevation may be physiologic, and not maladaptive. Indeed, the case for novel approaches—including novel imaging such as positron emission tomography scanning, micro magnetic resonance imaging, and high-resolution computed topography scanning more precisely to measure and calibrate bone—as well as the pressing need for newer reliable bone turnover markers have never been more urgent than now (4).

While my opponents carefully parade the *unpublished* biomarker-bone biopsy series of Malluche *et al.* (5)—and very valuable it is too as a series—to support the utility of PTH in diagnosing bone pathology, they do us all no favors at all. This large series features both extremes of bone turnover and PTH concentrations, so correlations are trivially easy to find. However, over the key and important current clinical PTH range of say 200–400 ng/L (for the sake of argument), you would do better to ask a Presidential candidate to opine on bone turnover than rely on PTH concentrations to guide you.

I prefer to take a different aspect of Hart Malluche's work, namely his appreciation of the altered current clinical paradigm we face today. The following is a direct quote from a recent *published* paper of his (6) that reported on 630 bone biopsies from adult CKD patients on dialysis:

...[T]here were racial differences; whites exhibited predominantly low turnover (62%), whereas blacks showed mostly normal or high turnover (68%). A mineralization defect was observed in only 3% of patients. In whites, cancellous bone volume was low, normal, or high in approximately the same number of patients, whereas in blacks, cancellous bone volume was high in two-thirds of the patients. More than 80% of blacks and whites with low cancellous bone volume had thin trabeculae owing to low bone formation. Cortical thickness was low in half the whites, whereas it was normal in three-quarters of blacks. Cortical porosity was high in 50% of whites, whereas three-quarters of blacks had high porosity.... Low bone volume and low bone turnover are more frequent than heretofore appreciated, whereas mineralization defects nowadays are observed rarely in adults. *These findings call for an adjustment of the current therapeutic paradigm that takes into consideration race and risk of low bone volume and turnover.* The latter have been shown to be associated with increased vascular calcifications.

The italics I have used above emphasize the soundness of the judgement expressed, in my view.

Therefore, in truth, our positions are not really quite as opposed as portrayed. My opponents would not say that science should advance no further than now, because

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we all live and work camped on Elysian Fields. I would not say either that measuring PTH is of no use, and that all biochemical laboratories that offer this service should be closed down forthwith. Detecting PTH concentrations of <100 and >1000 ng/L is of value, and action should certainly follow, although above all taking into account the clinical context and health of the patient (2) and the information we can glean in addition from calcium, phosphate, vitamin D, alkaline phosphatase concentrations, and their trends. I think we all share a passionate belief that CKD-mineral bone disease is important, notwithstanding the surprising negative outcome from the Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events study (7), and we all want to find better ways to preserve health and well-being in patients with CKD.

Disclosures

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