Rebuttal: The Case for Routine Parathyroid Hormone Monitoring

David J.A. Goldsmith

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 them.

While my opponents carefully parade the unpublished biomarker-bone biopsy series of Malluche et al.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:

There 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...
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 pas-
sonate belief that CKD-mineral bone disease is important,
notwithstanding the surprising negative outcome from the
Evaluation of Cinacalcet HCl Therapy to Lower Cardiovas-
cular Events study (7), and we all want to find better ways to
preserve health and well-being in patients with CKD.

Disclosures
D.J.A.G. has received speaking and consulting honoraria from
Abbott, Amgen, Genzyme, and Shire.

References
1. Sprague SM, Moe SM: The case for routine parathyroid hormone
monitoring [published online ahead of print October 4, 2012].
2. Jean G, Lalage-Proust MH, Soubrierielle JC, Granjon S, Lorriaux C,
Hurot JM, Mayor B, Deleaval P, Chazot C: [How to deal with those
low parathyroid hormone values in dialysis patients?] [published
nephro.2012.04.003
3. Moe OW: Fibroblast growth factor 23: Friend or foe in uremia?
4. Rajapakse CS, Leonard MB, Bhagat YA, Sun W, Magland JF,
Wehrli FW: Micro-MR imaging-based computational biome-
chanics demonstrates reduction in cortical and trabecular
bone strength after renal transplantation. Radiology 262: 912–
920, 2012
5. Malluche HH, Bellorin-Font ER, Rojas E, Carvalho AB, D’Haese
PC, Druke TB, Ferreira MA, Jorgetti V, Moe SM, Sprague SM:
Predictive value of biomarkers for bone turnover in ESKD
6. Malluche HH, Mawad HW, Monier-Faugere MC: Renal osteo-
dystrophy in the first decade of the new millennium: Analysis of
630 bone biopsies in black and white patients. J Bone Miner Res
26: 1368–1376, 2011
7. Wickman A: Amgen announces top-line results of phase 3
Sensipar/Mimpara EVOLVE trial. Available at: http://www.benzinga.
com/news/12/06/2653954/amgen-announces-top-line-results-
of-phase-3-sensipar-mimpara-evolve-trial. Accessed October 17,
2012

Published online ahead of print. Publication date available at www.
cjasn.org.

See related article, “The Case for Routine Parathyroid Hormone
Monitoring,” on pages 313–318.