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PART 1:

Journal Name:	British Journal of Medicine and Medical Research
Manuscript Number:	**MS: 2012 BJMMR 2989**
Title of the Manuscript:	**Severe Symptomatic Hypocalcemia after Denosumab Administration in an End-Stage Renal Disease Patient on Peritoneal Dialysis with Secondary Hyperparathyroidism – A Different Mechanism for Hungry Bone Syndrome.**

General guideline for Peer Review process is available in this link:
(http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline)

- This form has total 9 parts. Kindly note that you should use all the parts of this review form.

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PART 2: Review Comments

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Compulsory REVISION comments	**This case report is instructive and important. The text should be improved in numerous ways:** **Abstract:** • **What the authors mean by osteoporotic stature? Kyphosis? Were spine X-rays done? Revealing vertebral fracture(s)?** • **Please use DXA rather than DEXA** • **Report BMD T-scores for each site: femoral neck, total hip and lumbar spine (L1-L4)** • **Delete "Standard deviation below for her age and sex" since this refer to Z-scores.** • **Specify what is "activatedmor bioactive vitamin D analog", Calcitriol? Alfacalcidol?** **Case presentation:** • **Same comments as for the abstract** • **Dorsal hump and progressive height loss suggest vertebral fracture(s). Please specify if vertebral fracture(s)** • **Dose of calcium supplements should be provided as elemental calcium e.g. 500 mg as calcium acetate three times daily, 500 mg as calcium carbonate 1250 mg (rather than 2250 mg). The authors should comment on why they didn't use i.v. calcium gluconate and why such low dose of oral calcium supplements?**	

	The parallel with post-parathyroidectomy hungry bone syndrome is appropriate although the mechanisms are different. In their case report, hypocalcemia is induced by abruptly blunting the calcium efflux from bone with an extremely potent antiresorptive, denosumab, in a patient with secondary hyperparathyroidism. The same could be observed with a sudden reduction in circulating PTH after parathyroidectomy in secondary hyperparathyroidism. **In the discussion, the authors should clearly state that denosumab shouldn't be used in this type of patient: CKD with secondary hyperparathyroidism until clinical experience provide further evidence on how to prevent or manage hypocalcemia. Even when patient is adequately repleted in vitamin D (normal 25-Oh and 1-25 OH2 vit D levels) large doses of calcium supplements are required. The use of iv calcium gluconate and high doses of oral calcium supplements, 6 to 12 grams per day, should be recommended together with vitamin D repletion.**	

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