Vitamin D Treatment and Toxicity: *Primum Non Nocere*

We read with interest the recent review article on Vitamin D deficiency and treatment in childhood [1]. Intermittent dosing with Stoss regimens is effective in the treatment and prevention of vitamin D deficiency, is much more economical than daily dosing, and ensures supervised administration and compliance. However, stoss does not necessarily mean large. Stoss (German for "bump up") effect can be obtained with smaller doses than those used currently by pediatricians in India. Caution needs to be exercised as vitamin D is fat soluble and accumulates in the body. The resulting hypercalcemia can be life threatening and hypercalciuria can result in nephrocalcinosis and renal failure.

The authors quote the study of Gordon, *et al*. [2] for the use of 2000 IU daily or 50,000 IU weekly for 6 weeks. They do not mention that some of the infants on weekly dose regimen developed toxic levels of 25 OHD by the end of the study. The study of Shah and Finberg, quoted by the author did not evaluate rigorously for toxicity. Studies have demonstrated that single oral doses of 600,000 IU used to treat nutritional rickets in 3-36 months old children led to significant risk of hypercalcemia [3]. Vanstone, *et al*. [4] have documented hypervitaminosis D, hypercalcemia and hypercalciuria in infants receiving 1400 to 2000 IU of vitamin D daily for 6 to 12 weeks. Thus many expert groups now recommend caution in treating children with higher doses of vitamin D. The APEG Australasian Pediatric Endocrine Group specifically mentions that stoss therapy is not recommended for children less than 3 months of age; for older children a more conservative approach of a single initial dose of 50,000 to 150,000 IU is recommended [5].

It is time pediatricians in India stopped using regimens which employ 6 lakh units, and avoid the risk of vitamin D toxicity. More emphasis should be laid on treating children with minimally effective doses.

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REPLY

In children with symptomatic vitamin D deficiency, Stoss therapy is ideal in situations where adherence to therapy is questionable, because the doses can be observed. Basic pharmacology principles suggest that the circulating half-life is a suitable dosing interval for a drug. Because vitamin D and 25(OH)D exhibit half-lives in the body that are in the order of months and weeks, the daily administration of vitamin is probably unnecessary [1]. None of the cases of hypercalcemia attributed to vitamin D supplements reported by Vanstone, *et al*. [2]. was symptomatic, and hence their observations might not be clinically relevant. Gordon, *et al*. [3] observed a higher overall incidence of mild hypercalcemia at baseline in contrast to after treatment, and also reported that all subjects were asymptomatic.

Emel, *et al*. [4] recently compared Stoss theray (150,000 units oral) with daily dose schedule (2000 units daily for 6 weeks) in children and reported that there was no evidence about the increased risk of hypercalciuria in low-stoss therapy. Higher vitamin D levels were obtained in low-stoss therapy group. Symptomatic hypercalcemia due to Stoss therapy (in appropriate doses) in children with Vitamin D deficiency has not been reported so far. In our review, Stoss therapy was suggested as an option only for children more than 1 year of age, and particularly in situations where lack of compliance is a possibility.

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Methodological Issues in Iodine Deficiency Disorders Survey

This is in reference to the recent article on "Iodine deficiency disorder in children of Ambala, Haryana" [1]. We thank the authors for highlighting an important public health issue; we have the following concerns:

1. *Current irrelevance of the district based iodine deficiency disorders (IDD) survey*: The current district specific IDD guidelines have their historic genesis from the National Goitre Control Program (NGCP) (1962). The ban on the sale of non-iodised salt was based on district level goitre prevalence and was district specific. However, sufficient evidence has been generated since establishing IDD as ubiquitous in all states and geographical regions of India [2,3] and a national level ban on sale of non-iodised salt was implemented in the year 1997. The current district specific IDD survey guidelines lack any epidemiological rationale and cannot be collated to generate state level or national level data as these surveys are done over different time period. Further these guidelines do not conform to the internationally acceptable WHO/ UNICEF/ ICCIDD recommendations.
2. *Use of spot testing kits (STK) for salt iodine content estimation*: The iodine content of salt in the present study was estimated using STK. As the reported sensitivity and specificity of STKs is low [4] the revised guidelines recommend iodometric titration for estimating iodine content of salt.
3. *Details of the method used for urinary iodine estimation*: The authors have reported that they have used iodometric titration for iodine estimation in urine but the prescribed method to estimate urinary iodine as per the guidelines is Sandell-Kolthoff reaction [5].
4. *Need to report median urinary iodine*: In addition to reporting the percentage of individuals above and below a given cut-off value of urinary iodine, the authors should have also reported the median urinary iodine. The revised indicators prescribed by WHO/ UNICEF/ICCIDD also suggest inclusion of median urinary iodine [5].

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REPLY

We thank the authors for raising important methodological issues related to iodine deficiency disorder (IDD) survey. We clarify:

1. The sampling methodology for selection of survey sites by probability proportionale-to-size (PPS) sampling adopted in the present study are in accordance with the revised guidelines of National Iodine Deficiency Disorder Control Program (NIDDCP) [1] and WHO/UNICEF/ICCIDD [2]. This method has been found to be suitable for generating state and national level data [1].
2. For household surveys, qualitative testing of salt using a rapid test kit has been employed successfully to determine overall coverage of iodized salt and to identify geographical gaps in the program. Another