



Hypervitaminosis D in Dogs Associated with Diet

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When presented with an elevation of calcium on a chemistry profile result, the veterinarian must consider whether this is likely to be the cause of clinical signs, and if so, the possible differential diagnoses. In dogs, the list of possibilities includes hypercalcemia of malignancy, primary hyperparathyroidism, renal disease, hypervitaminosis D, and granulomatous disease. The Endocrine Section of the Diagnostic Center for Population and Animal Health (DCPAH) at Michigan State University offers a variety of tests that can be used to help determine the cause of hypercalcemia. These tests include assays for parathyroid hormone, ionized calcium, parathyroid hormone-related protein (a factor produced by some tumors), and 25-hydroxyvitamin D (the prominent metabolite in the circulation that is an indicator of dietary intake of vitamin D).

Among the possible differential diagnoses of hypercalcemia in dogs, hypervitaminosis D is generally viewed as an uncommon occurrence. Reasons for hypervitaminosis D include excessive dietary intake of vitamin D or ingestion of rodenticide containing vitamin D3 (cholecalciferol) as the principal ingredient. Another related cause is ingestion of the topical crème used as an adjunct for treatment psoriasis in humans, where the principal ingredient is an analog of calcitriol (1,25-dihydroxyvitamin D).

Since July 2010 to the present, there has been a series of 16 test results in dogs that were indicative of hypercalcemia related to excessive intake of vitamin D, which we would regard as a high prevalence over this period of time. These test results included an elevation of ionized calcium, low-normal or low concentrations of parathyroid hormone, and/or an elevation of 25-hydroxyvitamin D. The affected dogs ranged in age from 8 months to 8 years. There were three mixed breed dogs and individuals from thirteen other purebred breeds. The samples from these dogs originated from eight states, including Michigan (4), Texas (4), Colorado (2), Wisconsin (2), and one each from California, Illinois, North Dakota, and Utah. In these 16 dogs, there was either a brief written history and/or communication by telephone with the referring veterinarian. In addition to hypercalcemia, the majority of dogs displayed increased thirst and urination and some dogs were identified as having loss of weight, loss of appetite, or azotemia. In telephone conversations with veterinarians, there was discussion as to possible sources of excess vitamin D. It soon became apparent there was a common factor in these 16 dogs. All were being fed a commercial Blue Buffalo wilderness chicken diet. Over this time period, there have been other associations with hypercalcemia and this brand of food, but with no additional testing. A veterinarian in South Carolina called to ask about an owner with two dogs were hypercalcemic and receiving food from the same company. Most recently, an email message was received from an owner in Minnesota describing hypercalcemia and increased thirst and urination in two dogs receiving food from Blue Buffalo.

Hypervitaminosis D can arise from intake of a very high dose of vitamin D in a single exposure or gradual accumulation of marginally excessive amounts over an extended period of time. When ingested, vitamin D is absorbed with chylomicrons and delivered to peripheral tissues. The lipophilic property of the vitamin D molecule facilitates accumulation in adipose tissue but it is also taken up in other tissues (1,2). Vitamin D taken up by the liver is converted to 25-hydroxyvitamin D in a process that does not appear to be regulated by a rate-limiting feedback mechanism. Studies in humans and animals demonstrate that a pronounced increase of 25-hydroxyvitamin D must be reached before the threshold from normocalcemia to hypercalcemia is crossed (2). When the source of excessive vitamin

D is withdrawn, release of vitamin D from tissue stores will maintain elevations of 25-hydroxyvitamin D for weeks or months.

References

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2. Jones G. Pharmacokinetics of vitamin D toxicity. *Am J Clin Nutr* 88(suppl):582S-586S, 2008.