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KEY POINTS

- ▶ Cobalamin (vitamin B₁₂) is critical to the function of many metabolic processes. Therefore, deficiencies in cobalamin can occur for many reasons and lead to a variety of clinical signs.
- ▶ Cobalamin deficiency can lead to poor outcomes in dogs and cats with chronic enteropathy and/or exocrine pancreatic insufficiency, and patients with cobalamin deficiency often will not respond to management of the underlying disorder unless or until cobalamin is supplemented.
- ▶ Oral cobalamin supplementation has traditionally been suggested not to be as effective as parenteral supplementation; however, recent studies show that oral supplementation is as effective as parenteral administration.
- ▶ COBALEQUIN® is an oral cobalamin supplement with the added benefit of containing 5-methyltetrahydrofolate (5-MFT), a naturally occurring form of folate that is well absorbed at varying pH levels and has minimal interactions with other drugs or supplements. COBALEQUIN® is a chewable tablet specifically formulated to provide stable cobalamin for dogs and cats.

Management of Cobalamin Deficiency in Dogs & Cats: Oral Supplementation

Cobalamin (vitamin B₁₂) is essential to multiple metabolic processes,¹ including energy production, DNA and RNA synthesis, reproduction, protein synthesis, and the homeostasis of sulfur-containing amino acids. Cobalamin is absorbed from the ileum through a complex mechanism involving multiple cobalamin carrier proteins.

Causes of Cobalamin Deficiency

Cobalamin deficiency in small animals can result from various causes,^{2,3} such as chronic GI disease, hereditary defects (reported in Chinese shar-peis and isolated families of giant schnauzers, border collies, and beagles), short-bowel syndrome, small intestinal dysbiosis, and exocrine pancreatic insufficiency.⁴ Plant foods contain little to no cobalamin; therefore, feeding a vegan diet can potentially lead to cobalamin deficiency.² Older cats are also more susceptible to cobalamin deficiency, regardless of other physical or hereditary factors.⁵ Small intestinal dysbiosis can be associated with cobalamin deficiency, although this association is not specific or sensitive.

Clinical Signs of Cobalamin Deficiency

Most dogs and cats with cobalamin deficiency show clinical signs of GI disease, such as anorexia, vomiting, and/or diarrhea, which could be a cause or effect of cobalamin deficiency. Other clinical signs include failure to thrive and both central and peripheral neuropathies.³ Laboratory findings such as nonregenerative anemia, leukopenia, hypoglycemia, and hyperammonemia have been associated with cobalamin deficiency.³ In a 2005 case study, a border collie with selective cobalamin deficiency was presented with hyperammonemic encephalopathy that fully responded to cobalamin supplementation.⁶ In another case report, an 8-year-old female cat was presented with neurologic signs and found to have hyperammonemia. Treatment with cobalamin resulted in resolution of the neurologic signs within 8 weeks.⁷

Diagnosing Cobalamin Deficiency

Although cobalamin deficiency is defined as a lack of cobalamin on a cellular level, there are no direct means of assessing cobalamin status on a cellular level. When cobalamin is lacking on a cellular level, metabolism changes and methylmalonic acid accumulates; thus, serum methylmalonic acid concentration can be used as a surrogate marker of cellular cobalamin status.^{8,9} However, measurement of this

metabolite is technically involved and time-consuming and is only available on a limited basis (see **Suggested Reading**). Because of this, measurement of serum cobalamin concentration has traditionally been used to help assess cobalamin status, although some patients with cobalamin deficiency do not have severely decreased serum cobalamin concentrations on a cellular level. Therefore, supplementation is recommended for patients with a low or low-normal serum cobalamin concentration (<400 ng/L).

Several assays for measuring serum cobalamin concentrations have been developed and validated for human use. However, all assays must also be analytically validated for use in dogs and cats before they can be used to measure serum cobalamin concentration in these species. In addition, reference intervals are not transferrable between laboratories, and each laboratory should establish its specific reference interval. Thus, veterinarians should inquire whether the assay offered has been validated in the target species and whether a laboratory-specific reference interval has been determined.

Cobalamin Supplementation

Hypocobalaminemia has been suggested to be a negative risk factor for a poor outcome in dogs and cats with chronic enteropathy. Similarly, hypocobalaminemia is a negative risk factor for a poor outcome in dogs with exocrine pancreatic insufficiency (EPI), with a median survival time for dogs with EPI and hypocobalaminemia being 3.7 years and 7.4 years for those not hypocobalaminemic.¹⁰ More importantly, patients with cobalamin deficiency often do not respond to management of the underlying disorder unless or until cobalamin is being supplemented.

The most common form of cobalamin used for supplementation is cyanocobalamin. However, hydroxocobalamin or methylcobalamin may also be used in patients, although these are typically more challenging to obtain and can be

more expensive. Traditionally, it has been suggested that oral cobalamin supplementation may not be effective, as absorption of orally administered cobalamin is complex and inhibited by cobalamin deficiency; however, European studies have suggested that high doses of cobalamin can successfully be used for oral supplementation in humans.^{11,12} Recent data have shown that oral cobalamin supplementation is as effective as parenteral administration.⁴ Dosing schedules for oral supplementation are empiric, with daily supplementation administered for 3 months and recommendations for cobalamin concentrations to be re-evaluated 3 to 4 weeks after discontinuation.¹³

COBALEQUIN[®] is an oral cobalamin supplement with the added benefits of containing 5-methyltetrahydrofolate (5-MFT), the metabolically active form of folate. COBALEQUIN[®] is a chewable tablet specifically formulated to provide stable, palatable cobalamin for dogs and cats.

In a retrospective study, 51 client-owned dogs with low-normal or decreased serum cobalamin concentrations received oral cyanocobalamin (250-1000 µg once daily) for a variable period. On follow-up, serum cobalamin concentrations had increased in all dogs.⁴ Similarly, in a retrospective study of client-owned cats with hypocobalaminemia and clinical signs of GI disease, 25 cats with initial serum cobalamin concentrations <250 pmol/L (338.8 ng/L) were administered daily oral cobalamin tablets.¹⁴ After 27 to 94 days, all cats had serum cobalamin concentrations above the upper limit of the reference interval. In another study, 18 dogs diagnosed with EPI were administered oral cyanocobalamin.¹⁵ After 19 to 199 days of oral supplementation, all dogs showed normal or even supranormal concentrations (lowest serum cobalamin concentration after supplementation, 794 ng/L) after a median follow-up period of 41 days.¹⁵

More recently, there have been 2 prospective studies related to oral cobalamin sup-

plementation. In one prospective study of 49 hypocobalaminemic dogs randomly assigned to receive either oral or parenteral cobalamin supplementation, all 49 dogs showed normocobalaminemia after supplementation at the 90-day follow-up. There was no difference between the parenteral or oral route of cobalamin administration.¹³ In another prospective study, 46 hypocobalaminemic dogs (due to either chronic enteropathy or EPI) were randomly assigned to receive either oral or subcutaneous cobalamin supplementation, with both groups showing a significant increase in serum cobalamin concentrations and a significant decrease in serum methylmalonic acid concentrations at ~80 to 90 days after initiation of supplementation.¹⁶

Conclusion

Hypocobalaminemia can have adverse clinical effects in both dogs and cats, and it is essential to recognize that there are a variety of causes of cobalamin deficiency. GI disease should be recognized as a cause and effect of cobalamin deficiency, and testing and supplementation should be initiated when indicated. Fortunately, oral cobalamin supplementation can provide serum levels comparable to parenteral supplementation for many, if not most, patients. Both retrospective and prospective studies have shown that the efficacy of oral cobalamin supplementation is similar to parenteral supplementation, regardless of the underlying etiology of either chronic enteropathy or EPI. ■

For references and suggested reading, please see [cliniciansbrief.com/article/management-cobalamin-deficiency-dogs-cats-oral-supplementation](https://www.cliniciansbrief.com/article/management-cobalamin-deficiency-dogs-cats-oral-supplementation)

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Suggested Reading

Texas A&M University Gastrointestinal Laboratory.
<https://www.vetmed.cvm.tamu.edu/gilab>