Thiamine deficiency in dogs due to the feeding of sulphite preserved meat

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Thiamine is a water soluble B vitamin (B1) required for the metabolism of carbohydrates and energy production.¹ It is minimally stored in the body and must be consistently obtained from the environment or synthesised. Thiamine in its phosphorylated form (thiamine diphosphate) is an essential cofactor for the function of the tricarboxylic acid (TCA) cycle and the pentose phosphate pathway. These pathways are the major sources of neuronal energy production.¹ The TCA cycle is also important in the synthesis of gamma aminobutyric acid (GABA), an inhibitory neurotransmitter in the CNS.¹ In the absence of supply, clinical signs of deficiency develop quickly.² Cessation of oxidative metabolism in the central nervous system forces the brain into anaerobic metabolism, which results in a build up of lactic acid. Bilaterally symmetrical haemorrhage and necrosis of the grey matter (which has a higher metabolic rate than white matter) occurs.²

Reports of thiamine deficiency are sporadic in the veterinary literature. Affected species have included ruminants,² horses,² cats,⁴ ⁵ mink,⁶ seals⁷ and foxes.⁶ The aetiology of thiamine deficiency varies between monogastrics and ruminants. Thiamine is synthesised by the normal bacterial flora in the rumen and caecum of herbivores. Thiamine deficiency only occurs in these species when alterations in the ruminal flora precipitate cessation of thiamine production. Causes of thiamine deficiency in carnivores include the ingestion of fish high in thiaminase,⁷ ⁸ inactivation of thiamine by cooking or processing⁵ and the addition of sulphur dioxide or sulphite preservatives to meat.⁴ ⁵ These include preservatives 220, 221, 223, 224, 225 and 228. Sulphating agents delay spoilage by inhibiting the oxidation of myoglobin into metmyoglobin, decreasing odour and preserving the red colour of meat.⁹ These agents also increase the shelf life and palatability of cooked meat. Thiamine is cleaved by sulphites into its inactive constituent compounds, pyrimidine and thiazole.⁹ When sulphite preserved meat is fed alone or at the same time as a thiamine source (for example commercial pet food), the thiamine in all the food is cleaved and a thiamine deficient state can result. The extent of thiamine destruction increases linearly with the amount of sulphur dioxide in the meat. A level of 400 mg of sulphur dioxide/kg depletes thiamine by 55% and 1000 mg/kg depletes it by 95%.

The feeding of sulphite treated meat to pets on a regular basis may lead to potentially fatal thiamine deficiency, however the danger does not appear to be widely recognised by pet owners or veterinarians. A 6-year-old female entire Golden Retriever, a 4-year-old female spayed Maltese Terrier and three 7-week-old American Staffordshire Terrier puppies were diagnosed with thiamine deficiency caused by feeding sulphite treated meat. The Golden Retriever presented with a history of inappetence, weight loss and vomiting which rapidly progressed to signs of multifocal intracranial disease including mental dullness, paresis, seizures, spontaneous nystagmus and strabismus. Thiamine pyrophosphate effect was elevated at 58% and magnetic resonance imaging revealed bilaterally symmetrical hyper-intensity of the caudate nucleus and rostral colliculi. The dog recovered with thiamine supplementation. The Maltese Terrier and the three American Staffordshire Terrier puppies also presented with rapidly progressive multifocal central nervous system signs including ataxia, paresis, increased muscle tone, seizures, nystagmus and exophthalmos. The 4-year-old dog made a rapid recovery with thiamine supplementation. Euthanasia and necropsy of a puppy revealed malacia of multiple brainstem nuclei and oedema of the cerebral cortex. These findings were consistent with thiamine deficiency.
The diagnosis of thiamine deficiency can be difficult antemortem. The clinical signs of thiamine deficiency in dogs have been described by Read and Harrington\(^3\) who induced thiamine deficiency experimentally in young Beagle dogs by feeding a thiamine deficient diet. Three stages were observed: i) a short phase of suboptimal growth (18 +/- 7.9 days), ii) an intermediate phase of inappetence, weight loss and coprophagia (58 +/- 37 days) and iii) a terminal short phase of neurological signs characterised by anorexia, emesis, central nervous system depression, paresis, ataxia, torticollis, circling, exophthalmos, convulsions and death. Some dogs died suddenly without recognition of the early phases. Thiamine deficiency is more commonly recognised in the cat.\(^4\), \(^5\) As well as inappetence and vomiting, clinical signs commonly recognised in this species include nystagmus, dilated, poorly responsive pupils, cervical ventroflexion, tetraparesis, mental depression and death.\(^4\), \(^5\)

In thiamine deficiency, other diagnostic tests such as haematological, biochemical and cerebrospinal fluid analysis are generally unremarkable. A thorough dietary history is important in the diagnosis. Fresh meat manufactured for pet consumption and cooked, non-refrigerated pet food rolls have often been shown to be high in sulphite preservatives.\(^9\), \(^10\) No requirements currently exist to identify the use or concentration of sulphite preservatives in meat for pet consumption. Sulphites are permitted as food additives for human consumption in some processed meats (such as sausages) but are prohibited in most others. Maximum permitted concentrations exist for processed foods and these must be labelled.\(^4\)

There are several approaches to the biochemical evaluation of vitamin status, none of which are widely available. The absolute concentration or co-enzyme form can be measured on plasma or whole blood. The validity of this method depends on the assumption that circulating concentrations reflect chronic intake and tissue concentrations.\(^11\) Functional tests for vitamin status depends on biological effects. They are a more sensitive index of absolute vitamin concentrations and are more widely used.\(^11\) The most commonly used test for thiamine deficiency in humans is the measurement of erythrocyte transketolase activity.\(^12\) The activity of transketolase decreases significantly in the early stages of thiamine deficiency and can be monitored in red blood cells. Transketolase activity can be restored by the addition of thiamine pyrophosphate in vitro.\(^12\) This finding provided the basis of the clinical test for marginal thiamine deficiency used commonly in humans, the thiamine pyrophosphate (TPP) effect.\(^12\) This test is carried out on haemolysed red blood cells. Results are expressed as TPP effect (%), which represents the amount of stimulated enzyme activity resulting from the addition of thiamine to the red cell haemolysates. An increased TPP effect is proportional to the degree of thiamine deficiency.\(^7\) This procedure has been used for more than 20 years to measure thiamine deficiency in humans. The normal range is 2 to 20%. It is assumed that abnormalities in red blood cell transketolase also reflect similar changes in the brain enzyme. Although this assumption seems reasonable, little supportive evidence exists.

The ‘TPP effect’ has not been widely used in animals. Read and Harrington\(^13\) used it as an indirect supporter of thiamine deficiency when experimentally induced in young Beagle dogs. They found the ‘TPP effect’ on erythrocyte transketolase to increase to a mean terminal value of 64%, indicating a thiamine deficient state. The controls were stable at a mean of 11%. They also found a reduction in erythrocyte transketolase activity and increased concentrations of blood and cerebrospinal fluid lactate and pyruvate. Because of the decreased activity of thiamine dependent enzymes, the intermediate metabolites of the TCA cycle and anaerobic metabolism (pyruvate and lactate respectively) accumulate in the blood.

Thiamine deficiency is a not a common disease of dogs and is easily prevented, however we are continuing to recognise it on a regular basis at our veterinary hospital. Veterinarians must assume that fresh pet meat and non-refrigerated cooked pet food rolls will contain sulphite preservatives and should be aware of the health risks to dogs and cats. It is recommended that a balanced
commercial pet food be substituted for these foods. If fresh meat must be fed, meat purchased for human consumption is preservative free. Response to treatment with thiamine is good if recognised and treated early.

References