

Title Page

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**Title: Effects of dietary mineral supplementation on dogs with thunderstorm-related anxiety**

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The intent of this document is to provide information to veterinarians who may be interested in referring clients as potential candidates for this study.

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Abstract

Thunderstorm-related fear and anxiety is common in dogs. Human and non-human animal studies appear to support the development of mood and behavioral disorders when minerals are deficient in the diet, particularly if individuals are subjected to environmental stressors. Dietary mineral supplementation seems to stabilize mood and behavior. The primary objective of this study is to determine whether mineral supplementation alleviates fearful and anxious behaviors in dogs with thunderstorm-related anxiety. Additionally the study is intended to provide a basis upon which a more in-depth investigation may be undertaken.

In a double-blind, placebo-controlled crossover study, a two groups of ten dogs each, with documented and diagnosed thunderstorm-related anxiety, will be fed either a mineral supplement (Standard Process® Organically Bound Minerals™) or placebo once daily with food. Dosage is according to Carsten (2003). Behavior assessment will be done via an owner-completed instruments at 30 and 60 days after supplementation begins. Following the 60 d mark, the groups will be reversed, with placebo dogs receiving the supplement and supplement dogs receiving the placebo. Behavior assessment will again be done via owner-completed instrument at 30 and 60 days after the crossover.

Data will be collected from personal interviews and owner-completed surveys and statistically analyzed to determine outcomes and results.

## Introduction

Thunderstorm-related fear and anxiety is common in dogs (Cottam et al 2005, Overall et al 2001). A study published in the Journal of the American Animal Hospital Association (McCobb et.al. 2001) describes the fear of thunderstorms as common, frustrating, not well-researched, and difficult to treat. While interest in this subject area appears to be increasing (Dreschel & Granger, 2005; Cottam, et.al., 2005; Levine et.al., 2005; Crowell-Davis, et.al., 2003; McCobb et.al., 2001; Overall et.al., 2001), a review of the literature in Science Direct and MEDLINE/PubMed using the search terms "anxiety AND dog AND minerals," and "anxiety AND dog AND mineral deficiency," and "anxiety AND dog AND mineral supplement," and "thunderstorm AND dog AND mineral [deficiency, supplement]" reveal no studies exploring mineral supplementation to relieve anxiety in dogs. Storm-phobic dogs incur costs including destruction of property, and physical and psychological trauma which may necessitate treatment (Crowell-Davis et al 2003). Distressing behaviors also create concerns for animal welfare. Storm-phobic dogs alienated from their families may increase the burden on the shelter system if these dogs are surrendered, and contribute to the growing concern of euthanizing otherwise healthy animals for their behavior issues.

Responses to certain sound stimuli, such as thunder, may not be learned, but rather may be architecturally determined by the structure and function of the central nervous system (LeDoux, 1996; Branson & Rogers, 2006). Age (Voith and Borchelt 1982), breed (McCobb et.al. 2001), chronic stress, pre-existing and/or concurrent anxiety conditions (Overall et.al. 2001; Shull-Seleer and Stagg 1991), endocrine disorders (Aronson, Dodds 2005), and whether there are other dogs in the home (Dreschel & Granger, 2005), may all affect structure and function, increasing anxiety and fearful behavior in dogs experiencing a thunderstorm.

Human and non-human animal studies appear to support the development of mood and behavioral disorders when minerals are deficient in the diet, particularly if individuals are subjected to environmental stressors (Penland, 2006). Magnesium has been found to help regulate the HPA system and corticotrophin releasing factor (Murck, 2002). Holsboer (2000) linked the relationship between magnesium and mood to an increase in HPA activity which characterizes depressed and anxious states. Stress increases the need for magnesium (Selig, 1994). Depoortere et.al. (1993) demonstrated that magnesium deficient rats experienced decreased slow wave sleep and increased wakefulness. Severe magnesium deficiency is characterized by states including, but not limited to, irritability, agitation, and anxiety (Durlach, 1980). Mineral deficiencies (calcium, magnesium) are implicated in the mood and behavior disorders of premenstrual syndrome (PMS) (Thys-Jacobs, 2000). In a six-month study of 13 post-menopausal women, Penland (1995) found that low magnesium intake was associated with increased electrical activity in the cortex, and that higher intakes of magnesium improved the coherence of brain wave patterns and enhanced communication between different parts of the brain. Penland's study suggests that even short (42 days) periods of marginal deficiency can affect brain wave activity, and this is consistent with the findings of Seelig, Berger & Spielholz (1975) that even marginally low serum magnesium was associated with a state

of anxiety. Frederickson et.al. (2005) explored cognitive and behavioral linkages to zinc, including its concentration in the hippocampus and amygdala, and its modulatory role in brain excitability. Chu et.al. (2003) found increased corticosterone and higher anxiety levels in zinc-deprived rats. Sterobrat-Hermelin (1998) found that hyperactive children and those diagnosed with ADHD were deficient in magnesium, copper, zinc, calcium and iron, and that magnesium deficiency was most common in these groups. Children receiving mineral supplementation showed a decrease in hyperactive behavior.

While some dogs respond favorably to desensitizing and counter conditioning using recorded storm sounds, many do not (Crowell-Davis et al, 2003). Additionally, many owners are increasingly unwilling to treat their dogs' behavior problems with the use of medication, preferring instead to seek holistic treatment options, of which many exist for treating canine storm fears and phobias (McAuliffe 2006). Anecdotal evidence appears to support the use of mineral supplementation in dogs with storm-related anxiety (McAuliffe, 2007; see Appendix B), and provides a rationale for the cross-over design of this study. Cottam, Dodman and Critzer (2005) indicate a need for alternative treatment options based on their belief that pharmacological interventions may be ineffective. As described above, dietary mineral supplementation has been shown to stabilize mood and behavior in human and non-human species, however, use of dietary mineral supplementation in canine behavioral management in general, and storm anxiety in particular, appears underexplored. The primary objective of this study is to determine whether dietary mineral supplementation alleviates fearful and anxious behaviors in dogs with thunderstorm-related anxiety. A secondary objective is to provide a basis upon which a more in-depth investigation may be undertaken.

The significance of this study lies in its potential contribution to increasing awareness that mineral deficiencies may cause or contribute to storm-related anxiety, and possibly other behavioral disorders, in companion dogs, thus providing an alternative treatment option. It may also increase awareness of mineral deficits in modern diets generally, as well as the body's need for appropriate mineral intake, thus contributing to the health of human as well as non-human species. Overall (2000) argues that some abnormal behavior patterns in dogs may parallel those of humans (generalized anxiety disorder, impulse control disorders, panic disorder). Thus the study may contribute to the body of knowledge of the effectiveness of mineral supplementation for treating behavioral disorders in mammalian animals, including humans. Finally, the study may also provide research, development, and educational opportunities for both formulators of nutritional supplements for dogs and humans and the clinicians who advocate their use.

### Recruitment and Selection

Veterinarians who wish to refer clients for participation in this study may do so via submission of a referral letter to the Principal Investigator. A copy of this letter is in Appendix C; please copy the text onto your letterhead.

The referral letter must be accompanied by results of a physical examination conducted within one month of the referral, including CBC, blood chemistry profile, 3Dx or 4Dx, urinalysis and fecal flotation.

It is expected that the client will pay for these tests as part of their dog's routine annual exam. There is no cost to the client for any interviews conducted during the study, and all materials and supplements will be provided at no charge.

Referred candidates will be interviewed by phone to determine if they meet participation criteria (Appendix A). For those who meet the criteria, an intake interview will be scheduled. Participants will be selected for the study based on the intake interview and results from completed Storm Phobia Assessment (SPA), Baseline Diary (BD), and Thunderstorm Supplemental Page Baseline Diary (SBD) (instruments used with permission, Behavior Service, College of Veterinary Medicine, University of Georgia).

### Observation and Data Gathering

Follow up interviews will be conducted in person and by telephone at 30, 60, 90 and 120 days. SPA's, BD's and SBD's will be returned at these intervals for assessment. Participants failing to complete and return assessment instruments in a timely fashion will be dismissed from the group. An exit interview will be conducted at the conclusion of the study.

### Writing and Publication of Results

This study is intended for publication in a peer-reviewed journal, and for presentation at appropriate professional meetings. All participating parties will receive a copy of the study after publication.

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Appendix A – Inclusion/Exclusion Criteria

1. Inclusion criteria:
  - a. Veterinary referral.
  - b. Owner willing and able to undertake/pay for seasonal physical exam including CBC, chem panel, appropriate testing to rule out heartworm and tick-borne diseases, urinalysis and fecal flotation.
  - c. Owner willing and able to maintain dog's current main diet for the 120 day information gathering phase of the study.
  - d. Dog not currently on any other food supplements or medications intended to reduce anxiety, e.g.,  $\omega$ -3's, B vitamins, minerals, etc.
  - e. Owner willing and able to administer supplement once daily.
  - f. Owner willing and able to participate for the full 120 day term of the study, barring unforeseen circumstances.
  - g. Owner willing and able to observe dog's behavior and complete documentation.
  - h. Owner willing and able to refrain from starting any other interventions during the 120 day information gathering phase, such as behavior modification, training, supplements and medications.
  - i. Owner willing and able to maintain current exercise routine, even if inadequate.
  - j. Owner is willing and able to sign Informed Consent.
  - k. Owner is at least 18 years old.
2. Exclusion criteria:
  - a. Dogs who are a hazard to themselves and require medication.
  - b. Injury has occurred to dog as a result of escape attempts.
  - c. Dog has separation distress.
  - d. Dog has aggression issues with or without documented bite history.
  - e. Dog has cognitive dysfunction.
  - f. Dog is on behavioral medication for any reason.
  - g. Dogs with pre-existing medical conditions (verified by veterinarian).

Appendix B – Case History: Archie

Signalment: "Archie," 22-month old neutered male Labrador/Golden Retriever mix.

Presenting problem: Archie displays anxiety in response to approaching thunderstorms. He alerts and orients to distant sounds of thunder, folds ears back, appears nervous and begins to scan. He then begins pacing while continuing to listen and scan. The intensity of anxious behaviors increases as the storm approaches. Escalation includes shadowing the owner, trying to hide under her legs, and jumping up on her lap, and hiding under the desk. The owner describes him as "just a wreck." Frantic behavior continues until the storm passes, then becomes normal and calm.

History: Archie lives with his owner (single female) and two other dogs, a 9-year old, neutered male Golden Retriever (Bailey) and a 3.5-year old neutered male Golden Retriever (Henry). He was acquired at 9 weeks of age from a rescue. The owner noted Archie was sound sensitive and describes him as a "chicken in general." Though his confidence was "shaky," he was able to "bounce back" when scared. He alerts to many sound stimuli, and if moving, such as while being walked, will stop, orient and listen for a period of time before moving on. Storm sensitivity was first noticed May 2007, at 17 months of age.

Archie had been attacked and injured several times by Henry. The aggression issues have been completely resolved with professional help. Archie appears to have no residual anxiety from his experiences with Henry. The owner provides an enriched environment which is emotionally and socially balanced.

What has been tried so far: The owner tries not to reinforce his anxiety but sometimes comforts him by saying, "It's OK." Distractions of play with the other two dogs who are calm, toys, food, and bones are unsuccessful.

Program of help and results: Standard Process® Organically Bound Minerals™, 3 tablets, once a day, were started May 2007, after the owner had noticed Archie's fear of storms where none previously existed. Within about two days of starting the supplement, a storm occurred. Archie's response had changed such that he would look up and around at the sound of thunder, but would then return to whatever he was doing. He displayed no signs of fear. If sleeping he would awaken, then go back to sleep.

In September 2007, the owner discontinued the supplement. Archie's response to two particularly severe storms about 2-3 weeks after discontinuing supplement included nervousness, pacing, ears back, trying to hide under owner's legs, and under a desk, clinginess, and shadowing. She indicated that he had completely reverted back to the previous behaviors seen in May and was possibly a little worse. She also noted that these particular storms seemed unusually severe, and that even the other two dogs appeared somewhat concerned.

Appendix C  
Veterinarian Approval Letter

Dog's Name \_\_\_\_\_ Breed \_\_\_\_\_  
Age \_\_\_\_\_ Weight \_\_\_\_\_ Gender (please circle) M F Neutered Spayed Intact

Client's Name \_\_\_\_\_  
Address \_\_\_\_\_  
Phone and Email \_\_\_\_\_

Results of Seasonal Physical Exam

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Copies of test results attached (please check as appropriate):

- CBC  
 Blood Chemistry Panel  
 3Dx or 4Dx  
 Urinalysis  
 Fecal Flotation

Please list any medications the dog is currently taking, including prophylactics.

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Please list any known behavioral conditions, including storm anxiety.

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Please list any known medical conditions.

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

This candidate meets the required criteria for participation in this study and is referred as a candidate for consideration.

\_\_\_\_\_  
Veterinarian Signature/Printed Name Date

\_\_\_\_\_  
Clinic Phone

Appendix D  
Organically Bound Minerals™  
Mineral Component Analysis of Potential Emotional and Behavioral Effects

An assay of the mineral components of this product shows the following minerals present. Many of these minerals have documented emotional and behavioral effects on various mammalian species. These effects are described as follows.

**Potassium.** Hypokalemic male langur monkeys showed signs of fatigue (Kumar, Sharma & Lohiya, 1997). In a severely agitated group of schizophrenic humans, serum potassium was significantly lower than in mildly agitated individuals, and a correlation was noted between severity of symptoms and concentration of serum potassium (Hatta et.al., 1999).

**Calcium.** Deficiency is implicated in the mood disturbances of premenstrual syndrome. Thys-Jacobs (2000) reported that many physical and emotional symptoms in women with premenstrual syndrome were relieved when calcium was supplemented in clinical trials.

**Magnesium.** Severe Mg deficiency is characterized by states including, but not limited to, irritability, agitation, and anxiety (Durlach, 1980). Depoortere et.al. (1993) demonstrated that magnesium deficient rats experienced decreased slow wave sleep and increased wakefulness. In a six-month study of 13 post-menopausal women, Penland (1995) found that low magnesium intake was associated with increased electrical activity in the cortex, and that higher intakes of magnesium improved the coherence of brain wave patterns and enhanced communication between different parts of the brain. Penland's study suggests that even short (42 days) periods of marginal deficiency can affect brain wave activity. Magnesium supplementation decreased hyperactive behavior in children (Starobrat-Hermelin, 1998). Holsboer (2000) linked the relationship between magnesium and mood to an increase in HPA activity which characterizes depressed and anxious states, and magnesium has been found to help regulate the HPA system and corticotrophin releasing factor (Murck, 2002). Eby and Eby (2006) found that diets deficient in magnesium, when combined with excess calcium and stress, may contribute to agitation, anxiety, irritability and other states of mental and emotional dysfunction. They express concern for the possibility that magnesium deficiency is implicated in major public health problems such as depression, low intelligence and addiction. Their recommendations include "immediate further study" of the subject, as well as replacing deficient magnesium in grain and drinking water with bioavailable forms to pre-twentieth century levels.

**Iron.** Beard et.al. (2002) found that iron deficiency provoked anxiety in rats. Iron appears necessary for normal myelinization and acts as a cofactor for a number of enzymes responsible for proper functioning of dopamine and serotonin systems (Burhans et.al., 2005). Eseh and Zimmerberg (2005) noted increased anxiety in newborn rats whose mother's diets were iron deficient, and reported an apparent decrease in anxiety with the inclusion of iron in the diet. Beard, Hendricks, et.al. (2005) demonstrated a

relationship between iron deficiency and higher levels of stress, depression and anxiety in poor, postpartum African mothers.

**Zinc.** Zinc deficient rats showed normal cognitive abilities but had elevated corticosterone and increased anxiety-like behavior (thigmotaxia) (Chu, Mouat et.al., 2003). Frederickson et.al. (2005) discussed the linkage between zinc and cognition and behavior, its concentration in the hippocampus and amygdala, and its modulatory role in brain excitability. Rats in the open-field test showed decreased frequency of line crossing and spent less time grooming after a two week period of zinc deprivation. Zinc-deficient rats also spent less time in the open arms of the plus-maze test, suggesting an increase in anxiety in zinc-deficient subjects. This study implicates a relationship between zinc deficiency and increased anxiety due to higher concentrations of basal free calcium in hippocampal cells, likely because of higher serum corticosteroids (Takeda, Tamano, et.al., 2007).

**Sodium, Phosphorous, Aluminum, Strontium, Boron, Manganese, Copper, Barium, Beryllium, Cadmium, Chromium, Cobalt, Molybdenum, Nickel, Vanadium:** Behavioral effects of deficiency in dogs and other species appear unexplored; no citations found.