

## Canine Epileptoid Cramping Syndrome (CECS) Update

Canine epileptoid cramping syndrome (CECS) is described as a paroxysmal dyskinesia (movement) disorder of Border Terriers. It is characterized by episodes of involuntary movements. The limbs, head and neck, and muscles of the sides may be affected. Episodes may be short (@ 5 minutes or less) or last for hours. Episodes are described by the owners include inability to stand up, shaking and stiff legs. Dogs are aware of their owners and surroundings. Contractions of the back and abdomen occur less frequently than previously reported. Additional symptoms mentioned are vomiting, balance problems and attempting to seek contact with the owner.

### Three recent studies include

**Phenotypic characterization of canine epileptoid cramping syndrome in Border Terriers.** A Black, V., Garosi, L., Lowrie, M. *et al* J. Small Anim Pract 2013; 55:102-107.

This covers the result of a survey that was done in the UK in 2012.

Based on the 2012 Survey they state that 50% of Borders with CECS respond to a Gluten free or hypoallergenic diet.

**The Clinical and Serological Effect of a Gluten-Free Diet in Border Terriers with Epileptoid Cramping Syndrome.** M. H. Lowrie, O.A. Garden, M. Hadjivassiliou, R.J. Harvey, D.S. Sanders, R. Powell, and L Garosi J Vet Intern Med 2015 <http://onlinelibrary.wiley.com/doi/10.1111/jvim.13643/epdf>

The Swedish Breed club has done a number of General Health Surveys, in 2000, 2009, and in 2015 one that specifically covered paroxysmal episodes, (CECS and Epilepsy.)

### BTs survey for Swedish BTs affected by cramps 2015

All studies say that the cause of CECS is currently unknown, and no medications have been reported that have a beneficial effect. There is general agreement among the three studies:

- There is no significant difference seen between sexes or between intact and altered Borders.
- Age of onset may vary from 6 mos to 11 yrs (or more) but the overall average in the Swedish study was 3.5 yrs. When considering dogs older than 6 the average age of onset was 4 yrs, and 85% had their 1<sup>st</sup> cramps at less than 5 yrs of age.
- Both the Swedish and UK studies report that CECS does not usually shorten the lifespan
- In the Swedish study 2/3s of the dogs have episodes that last less than 5 minutes. And about the same number of dogs have episodes less than five times a year.
- In Sweden roughly 40% of dogs are not put on a specific diet, which may be result of the diversity of the diets tried, and lack of understanding of what may be effective.
- Gluten free diet are perceived as being the most effective in both the UK and Sweden.
- Studies agree that dogs that have the longer episodes also have more frequent episodes.
- In the Swedish surveys there is an indication that there may be a correlation between cramping and gastrointestinal and or immune system problems (allergies.)
- Historically, diet change is the most successful action that produces a positive result. However, the gluten free diet may not be the exclusive one that works. In some dogs changing the protein source has been successful, in particular removing high protein treats such as bully sticks and pigs ears. In other dogs, switching to a raw diet (often with novel protein source such as rabbit or fish) have worked. Most raw diets are lower in gluten sources, but not all. To my knowledge there has been no tracking of the specific ingredients in home made diets that do work.

Celiac disease in humans is an immune-mediated enteropathy. Genetically susceptible people who ingest gluten may develop an enteropathy. They develop transglutamine-2 antibodies (TG2 IgA) detectable in serum, against an enzyme that breaks down gliadin.

Nonceliac gluten sensitivity is a group of conditions with an immune response to gluten that differs from celiac disease. (In includes dermatopathy, and neurological manifestations. In NCGS patients the best diagnostic tool is the detection of antibodies against gliadin (AGA IgG.)

## Canine Epileptoid Cramping Syndrome (CECS) Update (cont'd)

Lowrie's group looked at the therapeutic value of a gluten free diet in Border Terriers with CECS, and to see if there was serological evidence of gluten sensitivity.

This was a 9 month study that involved 6 dogs. All dogs had to have a 6 mo history of CECS and to have had at least two separate episodes on different days. The dogs in the study had history of CECS for 6 mos to 2 yrs with a frequency of weekly episodes to one ever 3 mos. Duration of episodes ranged from 5 mins to 60 mins with the mean duration being 15 mins.

All dogs has a complete physical examination by a neurologist. Each dog had a complete blood panel which included a CBC, serum biochemistry, urinalysis, and bile acids. Selected dogs had MRIs of the brain, CFS analysis for cytology and total protein and endoscopy examination and collection of biopsy samples from the stomach and duodenum.

Owners transitioned the dogs to the gluten free diet over a period of seven days. They were asked to keep a diary of their observed results. Dogs were reexamined at 3, 6, and 9 months, with a general physical, and neurological examination was done as well as a CBC and serum biochemistry.

Serum samples from these 6 dogs as well as those from other Border Terriers presented for medical conditions were collected to act as controls.

All samples were tested for the presence of (TG2 IgA) autoantibodies and for (AGA IgG) antibodies. These are diagnostic markers for gluten sensitivity in humans.

Three dogs responded immediately and had no further episodes, two dogs had 1 and 2 episodes within the first 4 weeks of the diet. One dog showed no response, and on questioning it was found that the dog ingested horse manure frequently. When the owner denied access to manure, the dog improved within 3 months. At the end of the study, two owners reported that their dogs had ingested gluten treats and relapsed, but resolved again once the strict gluten-free diet was resumed.

### **Antibody Titers:**

At the start of the study all dogs had higher TG2 IgA titers compared to the control group and over the study there was a decrease in titers that correlated with the clinical remission.

AGA IgG antibodies were also significantly increased compared to controls at the beginning of the study, but it was not felt to be significantly greater to be of clinical significance. However, the AGA IgG antibodies did decrease in the 5 dogs that had a strict gluten-free diet.

These data support the supposition that CECS may be caused by gluten sensitivity. This would be the first known paroxysmal movement disorder link in veterinary medicine.

Gluten is made up of gliadin and glutenin proteins. This study implicates antibodies to gliadin as causing CECS. The link between TG2 IgA activity and gluten sensitivity is not definitely proven, but the evidence is strong.

In humans it is standard practice to measure both markers, and these authors feel this is appropriate for dogs as well.

The presence of both antibodies in affected dogs, and the clinical and serological response to the gluten free diet is evidence of gluten sensitivity as a cause of CECS. These might be a diagnostic tool for CECS and for monitoring a gluten free diet.

This group is now planning a much larger study of dogs with CECS.

## Canine Epileptoid Cramping Syndrome (CECS) Update (cont'd)

### CECS – the genes.

Dr. Gary Johnson, and Dr. Denny O'Brien at the University of Missouri have done a whole genome scan of one CECS dog. There is an area of interest that they have found. The whole genome scan technology has grown by orders of magnitude in just the last 5 years, and the cost has decreased dramatically. Dr. Johnson has many archived samples from supposed CECS dogs, but the descriptions vary. We will be looking for recent samples with a good history.

- 1) Have the appropriate antibody tests performed if such tests become available.
- 2) Submit DNA samples from affected dogs. Videos of episodes are extremely helpful, so that episodes can be characterized as CECS, rather than a partial epileptic seizure. Full blood panels/results on affected dogs would help.
- 3) Put affected dogs on a strict gluten free diet.

As the above study indicates, it may take 3 months or more for a gluten free diet to take effect. And treats with gluten may cause an episode, as may scavenging of manure, rabbit pellets, deer poop, etc.

### Questions still to be answered:

May gluten sensitivity cause lead to protein sensitivity in some dogs? There are many reports that changing protein source may resolve CECS. Or is this because the new diet also happens to be gluten free.

Why do high protein treats such as bully sticks and pigs ears cause episodes?

Owners need to strict adhering to a gluten free diet. "Treats" may the reason many dogs are non-responsive. Preventing dogs from scavenging sources of gluten such as rabbit pellets and various manures is probably important.