



RESEARCH PROGRESS REPORT SUMMARY

Grant 01935-B: Abnormalities in the Stomach's Ability to Contract Predisposes Large-Breed Dogs to Bloat

Principal Investigator: Dr. Laura L. Nelson, D.V.M.

Research Institution: Michigan State University

Grant Amount: \$233,774.00

Start Date: 1/1/2014 **End Date:** 12/31/2015

Progress Report: End-Year 1

Report Due: 12/31/2014 **Report Received:** 2/2/2015

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Gastric dilatation-volvulus (GDV or "bloat") is a devastating disease common in large and giant-breed dogs. Occurring most frequently in older dogs with a close relative who has also suffered the condition, the stomach becomes both displaced and distended with air. Without emergency medical stabilization and surgical intervention, affected dogs quickly experience shock, damage to the stomach wall, and death. Most of the research relating to GDV has described risk factors for the disease, determinants of outcome with treatment, and the effectiveness of preventive surgery (gastropexy). However, the underlying cause of GDV remains unknown.

Abnormalities in the ability of the stomach to contract have been documented in dogs after naturally-occurring GDV. An analogous stomach condition in cattle, left-sided displacement of the abomasum (LDA) has been shown to, in some instances, be associated with abnormalities in the motilin gene. Motilin is an important driver of stomach contraction. This suggests that LDA and potentially GDV may be primarily caused by a stomach that does not properly contract, and that this condition may be inherited.

The goals of this study are to determine the relationship of abnormal stomach contraction with GDV and to define the biochemical and genetic alterations that may be associated with these stomach abnormalities. In the long term, we hope to develop a test to identify dogs at high risk



for GDV that would allow selective breeding to eliminate the condition and to determine which dogs will benefit most from prophylactic gastropexy or other preventive therapies.

Grant Objectives:

1. To evaluate fasting gastric motility in High Risk (HR), Low Risk (LR), Wild Type (WT) and Affected (AF) cohorts of large and giant-breed dogs as a potential means of determining predisposition to GDV.
2. To determine whether plasma levels of motilin and ghrelin differ between WT, LR, HR, and AF cohorts of large breed dogs.
3. To identify a causal gene mutation associated with high risk of GDV.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

We have made significant progress in the completion of this project in 2014. We have completed sampling of all unaffected Great Danes and 50% of our desired number of affected Great Danes. In addition, we have enrolled the majority of our WT controls and are beginning to contact and enroll Weimaraners and Bloodhounds, with plans to complete enrollment and sampling in spring and summer of 2015.

Results of motility evaluation at this time are preliminary, but we are observing a relationship between low fasting gastric pH and some breeds. Further sampling will help to demonstrate if this relationship is important. Use of the SmartPill wireless motility device has produced excellent studies. As we have enrolled only a small number of the GDV survivors of all breeds, we are looking forward to seeing what features of gastric motility are most common in GDV survivors. This will help us recognize if similar patterns are present at higher or lower levels in the other populations that we are evaluating.

At this time, evaluation of the relationship between GDV, GDV risk, and breed and blood levels of motilin and ghrelin (hormones that help to regulate gastric movement in the fasting state) is ongoing.

Finally, we have completed candidate gene analysis for MLN and GHRL, the genes for the motilin and ghrelin hormones, in the Great Dane. At this time, it appears that a mutation of these genes is NOT associated with GDV risk in the Great Dane.