Letter to the Editor

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Dear Drs. Hinchcliff and DiBartola

We would like to comment on the recent paper "Canine pancreatic-specific lipase concentrations in clinically healthy dogs and dogs with naturally occurring hyperadrenocorticism" by Mawby, Whittemore, and Fecteau as we cannot agree with the conclusions drawn from this study.[1] This study was designed to establish whether dogs with naturally-occurring hyperadrenocorticism and no signs of clinical pancreatitis have increased serum canine pancreatic lipase immunoreactivity concentrations (cPLI, as measured by Spec cPL®), which was shown to be the case. This is an interesting finding as there is contradictory evidence regarding a link between hyperadrenocorticism and pancreatitis in dogs. Some studies evaluating dogs with hyperadrenocorticism did not report on a high occurrence of patients with overt pancreatitis,[2,3] but two studies on dogs with pancreatitis reported hyperadrenocorticism to be a risk factor for acute pancreatitis.[4,5]

The finding that dogs with hyperadrenocorticism and no clinical sings of pancreatitis often have increased serum cPLI concentrations as shown by Mawby et al. allows for two possible explanations: 1) serum cPLI concentration is falsely increased in dogs with hyperadrenocorticism or 2) dogs with hyperadrenocorticism often have subclinical pancreatitis. Although the possibility of subclinical pancreatitis was mentioned in the discussion, the authors arbitrarily concluded that serum cPLI concentrations are falsely increased by hyperadrenocorticism. We respectfully submit that the authors do not provide any evidence to support this conclusion. Their conclusion was essentially based on the fact that the dogs did not display clinical signs of overt severe pancreatitis (e.g., vomiting, abdominal pain), which they could not do a-priori as such dogs had been excluded from the study. Canine pancreatitis can be associated with a wide range of clinical presentations, ranging from no clinical sings to severe clinical signs with systemic complications and it is widely accepted that dogs with pancreatitis may present with only mild clinical signs, such as depression or hyporexia.[6] Therefore, the possibility that the dogs with HAC and an increased cPLI concentration had mild or subclinical pancreatitis cannot be excluded. Thus, the authors' conclusion that "abnormal cPLI results should be interpreted with caution in dogs with HAC to avoid falsely diagnosing them with concurrent pancreatitis" is not supported by their data. Instead, dogs with HAC and an increased serum cPLI concentration may or may not have (subclinical or mild) pancreatitis and the present study unfortunately does not answer this question. Whether or not mild and subclinical pancreatitis are of clinical significance is a completely different question that remains to be answered because the long-term clinical significance of subclinical pancreatitis is currently unknown. Furthermore, it should be pointed out that the dogs were evaluated at a single time-point. Thus, pancreatitis could have been overt in at least some of those dogs shortly after the time of evaluation.

Furthermore, the questionnaire used in the study by Mawby et al. would suggest that clinical signs of mild pancreatitis, such as lethargy, hyporexia, or altered behavior, were not specifically asked for and may thus not have been reported on. Also, it is not apparent from their report how many of the dogs had abdominal ultrasound performed and if so whether the area of the pancreas was evaluated in detail. While abdominal ultrasound is considered to have a limited sensitivity for subclinical or mild pancreatitis, negative ultrasound findings would have been helpful.

Finally, the authors try to support their conclusion with a body of literature that simply does not speak to the issue at hand. The authors suggest that benign pancreatic hyperenzymemia is a condition in humans where enzymes of pancreatic origin are falsely increased in serum or plasma. However, not a single study on benign pancreatic hyperenzymemia has demonstrated, or even attempted to demonstrate, the pancreatic origin of amylase, lipase, and/or isoamylase (remark: despite the name, pancreatic isoamylase activity has not been shown to be specifically of pancreatic origin[7]) activities measured in serum or plasma of affected patients.[8–11] This is an important difference between studies in humans and the present study. Studies in humans have used the traditional catalytic assays for lipase that measure lipase activity regardless of cellular origin, while in the present study the assay used measures lipase concentration that is exclusively of pancreatic origin.[12] Therefore, the results of these studies in humans cannot be compared with or provide a plausible explanation for the results of the present study. The term pancreatic hyperenzymemia simply speaks to the lack of organ-specificity of serum amylase, lipase, and even pancreatic isoamylase activity assays in humans.

Thus, we would respectfully submit that the conclusion stated by Mawby et al. is not supported by the data presented. Subclinical pancreatitis cannot be excluded in the dogs described in this study and there is no data to suggest that subclinical pancreatitis is inconsequential and should be disregarded (of course we acknowledge that there is also no data to the contrary). Therefore, we believe that until such data are available, clinicians should cautiously evaluate (e.g., question owners for non-traditional clinical signs of pancreatitis, monitor cPLI concentration in response to management) and manage (e.g., ultra-low fat diets) dogs with hyperadrenocorticism and an increased serum cPLI concentration.

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