SO, ALBUMIN IS LOST IN THE DOG’S GUT…. WHAT DIAGNOSTIC TESTS SHOULD I DO BEFORE TREATMENT?
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INTRODUCTION
Protein losing enteropathy (PLE) is characterized by loss of proteins through the intestinal tract. Primary intestinal disease causing PLE mainly consists of lymphangiectesia, inflammatory infiltrates, crypt lesions and intestinal mucosal ulcerations. Gastrointestinal disease accompanied by hypoalbuminemia has been shown to have a guarded prognosis, but there is little published information on survival or optimal treatment.

Furthermore, although many studies have been published on inflammatory bowel disease including subsets of dogs suffering from PLE, there is very little literature available on large groups of dogs with PLE. For these reasons, the most recent literature available on protein losing enteropathies will be used for this session, as well as recently published abstracts.

BREEDS
Some breeds are at risk of developing PLE, which can help reaching a diagnosis. The following breeds have been described to be at increased risk: Norwegian lundehund, Yorkshire terrier, shar pei, basenji, soft-coated wheaten terrier, and German shepherd dog. A large series of rottweilers with PLE has also been described.

LABORATORY PARAMETERS
The diagnosis of PLE is achieved by ruling out other causes of protein loss. Reduced hepatic production can be ruled out with a bile acid stimulation test and significant urinary loss with a urine protein:creatinine ratio. Hypoalbuminemia because of loss of skin barrier integrity is also a possibility, but the defects have to be extensive and in such cases are expected to be obvious on physical examination. Protein-calorie malnutrition does not cause a marked decrease in albumin per se except in severe cases.

Once other causes of hypoalbuminemia have been ruled out, further laboratory testing can be used to assess the intestinal tract. These tests are listed in table 1. Folate and cobalamin can be helpful to assess proximal and distal small intestinal malabsorption respectively. Furthermore, hypocobalaminaemia has been shown to be a negative prognostic factor and supplementation would typically be recommended if detected. Prognostic value of low serum folate and usefulness of supplementation is unknown. Recently, hypovitaminosis D has also been shown to be a negative prognosis factor in dogs with chronic enteropathy (CE). Some PLE dogs also have a significantly lower vitamin D concentration, but the impact on survival in this group has not been investigated.

The canine chronic enteropathy clinical activity index (CCECAI) has been developed to take into account the negative factors associated with CE (such as hypoalbuminemia), and is particularly well adapted to determine the severity of disease in dogs with PLE.

HISTOPATHOLOGY
Although dietary and medical treatment trials are typically considered as the first step for dogs with CE, this is usually not the case in dogs with PLE as they might decompensate very quickly. For this reason, endoscopic or full thickness intestinal biopsies (with attendant risk of dehiscence) are often recommended prior to treatment, especially to rule out diffuse intestinal neoplasia such as lymphoma.

Histopathology is also needed to characterize the underlying pathology and guide treatment. Endoscopy is often used to assess the intestinal mucosa and to obtain biopsies. The importance of assessing not only the mucosal appearance, but also microscopic changes has been emphasized in a recent publication which showed that the sensitivity of endoscopy for gross diagnosis of lymphangiectesia was only 68%, with a specificity of 42%. The number of endoscopic biopsies needed depends on the quality of the samples as well as on the type of lesions. For example, 6 biopsies of adequate quality are needed to diagnose lymphangiectesia, whereas up to 13 good quality samples are needed to reach 99% confidence of detection for crypt lesions. It is very important to get enough good quality biopsies to be able to achieve a diagnosis, especially when assessing for crypt lesions, which have been found in up to 68% of the cases in one publication. Presence of crypt lesions has been reported to be a negative prognostic factor in dogs with PLE.

The histology findings can vary significantly between the duodenum and the ileum and for this reason, the author would typically recommend taking biopsies in both locations. Sampling of the ileum is also indicated in
dogs with a low cobalamin concentration. Recent literature suggests that some dogs with PLE have intestinal small cell lymphoma. The determination of clonality using polymerase chain reaction (PCR) for antigen receptor rearrangements (PARR) on biopsy samples can be helpful to diagnose these cases as will be discussed in the next session, and testing should be considered more routinely in dogs with PLE.

In summary, laboratory testing is central to confirm the origin of the albumin loss and can help identifying negative prognostic factors. Once loss in the gut is confirmed, histology is helpful to determine the underlying cause of the hypoalbuminaemia and guide treatment.

Treatment options will be discussed in the next session.

Table 1 – Laboratory parameters, which may assist with localisation of the albumin loss and/or have a negative prognostic value for dogs with chronic enteropathy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Localisation</th>
<th>Prognostic significance</th>
<th>Supplementation</th>
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<tbody>
<tr>
<td>Albumin</td>
<td>Not specific</td>
<td>Negative</td>
<td>Unclear</td>
</tr>
<tr>
<td>Folate</td>
<td>Duodenal disease</td>
<td>Unknown</td>
<td>Unclear</td>
</tr>
<tr>
<td>Cobalamin (B12)</td>
<td>Ileal disease</td>
<td>Negative</td>
<td>Recommended</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unclear</td>
</tr>
</tbody>
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References

10. Lecoindre, P., Chevallier, M. & Guerret, S. Protein-losing enteropathy of non neoplastic origin in the dog: A retrospective study of 34 cases. Schweizer Archiv für Tierheilkunde 152, 141-146 (2010).