### Treatment of uncomplicated canine IBD

Canine idiopathic IBD can be regarded as uncomplicated when the clinical signs are solely associated to the gastrointestinal tract and the patient does not show clinical or laboratory evidence of systemic complications. According to the WSAVA definition, antiparasites, GI-protectants and antibiotics have failed to resolve the signs. Furthermore, endoscopy has been performed that revealed benign inflammation of any degree from mild to severe. It has been documented that clinical CIBDAI score and histological score do not correlate in patients with IBD and that patients with food responsive (uncomplicated) enteropathy cannot be histologically differentiated from dogs with corticoid responsive immuno-suppression.

## Assessment of disease severity

The assessment of disease severity can be used for treatment decisions based on a differentiation between (a) uncomplicated IBD and (b) complicated IBD with systemic effects. Different scoring systems have been developed to assess the severity of IBD. The most commonly used clinical scoring is the canine IBD activity index (CIBDAI). The CIBDAI is the summation of the score of 6 different clinical signs including attitude/activity, appetite, vomiting, stool consistency, stool frequency, and weight loss. Recently a canine chronic enteropathy clinical activity index (CCECAI) has been introduced adding the scoring of serum-albumin concentration, peripheral edema and ascites, and severity of pruritus to the CIBDAI. The CCECAI allows a better estimation of the possible therapeutic success. High scores are associated with a high risk for negative outcome. Another laboratory parameter closely linked to the outcome is serum cobalamine. Low cobalamine concentrations correlate with a poorer prognosis. Interestingly, there are contradictory results concerning endoscopic scores. Some authors documented a correlation between disease severity and therapeutic outcome and others not. Histologic scoring systems have failed so far to predict the therapeutic outcome. However, since per definition the diagnosis of idiopathic IBD is based on the histologic evidence of benign intestinal inflammation, endoscopy or laparotomy with intestinal biopsy remains to be strongly recommended.
Concerning the treatment, uncomplicated IBD responds in most cases favorably to dietary management. Since dietary components especially proteins are suspected to play a role in the pathophysiology of chronic inflammation, it has always been recommended that diet change is a fundamental step in managing IBD. For small intestinal IBD, highly digestible, gluten-free diets with a novel protein source or hypoallergenic, hydrolyzed diets have shown to be of benefit. In most cases with uncomplicated IBD, diet change can be the only necessary treatment regardless of the initial clinical score. For IBD colitis, the use of moderately fermentable fiber (psyllium, beet pulp) has been shown to improve clinical signs due to binding of colonic irritants and normalization of colonic peristalsis. Additionally, the fermentable fibers support as "prebiotics" the development of beneficial intestinal microbiota. The resulting increased bacteriological production of short chain fatty acids is beneficial for colonic function. The use of probiotics for the treatment of canine IBD is under research. There is some evidence that they are beneficial in mild IBD. Dietary management alone is seen as successful when the initial clinical signs clearly improve or resolve within 10-14 days. The diet should be given for 14 weeks. In most cases, the gradual reintroduction of previous food sources will not cause a relapse except in patients that suffer from food intolerance or allergy. They will need continuation of the newly introduced diet.

Patients that do not respond to diet change alone but show mild to moderate clinical signs without systemic effects can receive long term oral antibiotic treatment, if not done already before the endoscopic examination. The drugs of choice are tylosin (15 mg/kg BID) and metronidazole (5-10 mg/kg BID) for about 4-6 weeks. Tylosin is thought to be immunomodulatory by supporting the development of enterococci with probiotic effects. Metronidazole affects anaerobic bacteria and protozoa, and is supposed to have immunomodulatory effects by inhibiting cell mediated immunity and leukocyte - endothelial cell adhesion. In patients with IBD colitis, 5-aminosalicylic acid (e.g. sulfasalazine: oral induction: 20-40 mg/kg, BID; maintenance: 10-15 mg/kg BID) has shown to be highly effective probably due to a decrease of pro-inflammatory leukotriene production in the colonic mucosa. However, dogs should be monitored for tear secretion at regular intervals since the drug can induce an irreversible keratoconjunctivitis sicca as a reported negative side effect. Patients that have failed to respond to dietary change with added antibiotic and immunomodulatory treatment should be considered to suffer from complicated IBD and undergo immunosuppressive treatment.

Treatment of complicated canine IBD

Complicated IBD has to be suspected when patients do not respond to treatment for uncomplicated IBD or when clinical signs and/or laboratory results show evidence of systemic disease. Clinical signs considered of negative prognostic value are pruritus, edema, and ascites/hydrothorax especially in connection with panhypoproteinemia. Lower serum albumin values can occur rather due to enteric protein loss than malabsorption, when liver failure and protein loosing nephropathy have been excluded. Low serum cobalamin has also been reported to be a negative prognostic factor. Patients that show systemic effects of IBD need a more aggressive therapeutic approach adding immunomodulatory/immunosuppressive drugs to the dietary change already at an early stage of the medical management. Induction and maintenance regimes are mainly influenced by rapidity of clinical remission, severity of side effects, compliance, and drug costs. Prednisone/prednisolone has been used as single agent or in combination with other medications to successfully control clinical signs of IBD. Even when controlled clinical studies are missing there is enough empirical evidence to justify the use of glucocorticoids for the treatment of IBD. It is generally recommended to start the treatment with an immunosuppressive dosage (2 mg/kg per day) until clinical improvement. This is followed by gradual reduction of the corticoid dose over several weeks to months. To avoid long term side effects on the pituitary-adrenal axis, maintenance treatment should be given every other day. Some patients need life long glucocorticoid treatment. Others can be gradually taken off the medication and stay clear of clinical signs without further immunosuppression. There is no other predictive parameter than repeated clinical review of the patients (e.g. every 2-6 weeks) during the induction phase and the phase of gradual dose reduction for maintenance. In case of severe side effects of glucocorticoids (polyuria, polydipsia, apathy, depression), reduction of prednisolone can be achieved by combining the glucocorticoid with metronidazole or azathioprine (2 mg/kg per day until remission, then reduction to 1 mg/kg every other day). It is necessary to check patients receiving azathioprine at least every 2 weeks for the development of an agranulocytosis as a reversible negative side effect. The use of budesonide, a poorly absorbed glucocorticoid with reduced systemic toxicity remains anecdotic or theoretical due to its high costs. In case of relapse during glucocorticoid reduction, it is advised to start again with the immunosuppressive dose and taper down until reaching the dose that is shown to be still effective. Dogs with complicated IBD, hypoproteinemia and severe histological changes should immediately receive a
combined treatment of prednisolone and azathioprine because they do have the worst prognosis for a positive treatment response.16 If the patient does not respond to the immunosuppressive therapy any more, a rescue protocol for steroid-refractory IBD with cyclosporine (5 mg/kg per day, 10 weeks) has been reported to be of benefit in some cases.17 Cobalamin supplementation (250-1000 µg/dog, weekly for 4 weeks, thereafter monthly) has been recommended for dogs with hypocobalaminemia.18 However, studies are missing that prove a positive effect on the outcome.19

References
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