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Histopathological Standards for the Diagnosis of Gastrointestinal Inflammation in Endoscopic Biopsy Samples from the Dog and Cat: A Report from the World Small Animal Veterinary Association Gastrointestinal Standardization Group

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Summary

The characterization of inflammatory change in endoscopic biopsy samples of the gastrointestinal mucosa is an increasingly important component in the diagnosis and management of canine and feline gastrointestinal disease. Interpretation has hitherto been limited by the lack of standard criteria that define morphological and inflammatory features, and the absence of such standardization has made it difficult, if not impossible, to compare results of retrospective or prospective studies. The World Small Animal Veterinary Association (WSAVA) Gastrointestinal Standardization Group was established, in part, to develop endoscopic and microscopical standards in small animal gastroenterology. This monograph presents a standardized pictorial and textual template of the major histopathological changes that occur in inflammatory disease of the canine and feline gastric body, gastric antrum, duodenum and colon. Additionally, a series of standard histopathological reporting forms is proposed, to encourage evaluation of biopsy samples in a systematic fashion. The Standardization Group believes that the international acceptance of these standard templates will advance the study of gastrointestinal disease in individual small companion animals as well as investigations that compare populations of animals.

Keywords: cat; diagnostic standards; dog; gastrointestinal biopsy; gastrointestinal inflammation

Introduction

The diagnosis and treatment of gastrointestinal disease in the dog and cat are increasingly based on the collection and interpretation of mucosal biopsy samples obtained endoscopically from one or more gastrointestinal sites. There are many stages in this process in which error may be introduced, thereby influencing the clinical outcome. These stages include the endoscopic biopsy procedure, the processing and embedding of the small and fragile tissue samples, and the microscopical interpretation of the tissue changes by the diagnostic pathologist (Willard *et al.*, 2001, 2002). For many clinicians and pathologists, the histopathological interpretation has proved to be the most contentious and frustrating step in the diagnostic sequence. This interpretation may be complicated by inadequacies in the number and quality of the tissue samples, by fragmentation and unfavourable orientation of these samples during processing, and by the lack of an internationally accepted set of standards for evaluating microscopical changes present in the tissues.

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The aims of the pathologist are to distinguish normal from diseased tissue, to characterize the nature and severity of tissue changes, and to provide an accurate morphological or aetiological diagnosis, thus facilitating formation of a prognosis and appropriate therapy. Some histopathological diagnoses, for example, the identification of adenocarcinoma or overt alimentary lymphoma, can be made relatively simply. By contrast, the interpretation of mucosal inflammatory change has proved to be far more complex. Characterization of gastrointestinal inflammation has been hampered by the lack of standard criteria for measuring the histopathological changes within a sample of mucosal tissue.

Over the past two decades, several independent groups have developed and applied classification systems for characterizing the nature and severity of gastrointestinal inflammatory changes (Jergens *et al*., 1992, 1996, 1999, 2003; Wilcock, 1992; Hart *et al*., 1994; Yamasaki *et al*., 1996; Stonehewer *et al*., 1998; Baez *et al*., 1999; German *et al*., 2000, 2001; Kull *et al*., 2001; Zentek *et al*., 2002; Waly *et al*., 2004; Peters *et al*., 2005; Wiinberg *et al*., 2005; Münster *et al*., 2006; Allenspach *et al*., 2007; Garcia-Sancho *et al*., 2007). In most of these studies, the nature of gastrointestinal inflammation is portrayed primarily by the dominant population of inflammatory cells (e.g. lymphoplasmacytic, eosinophilic or pyogranulomatous); it is recognized, however, that such populations may overlap and occur in various combinations. The severity of gastrointestinal inflammation has most often been graded with a simple four-point scale: normal, mild, moderate or marked. Although this approach would appear logical, the specific criteria defined by various groups have differed to the point at which it has become impossible to relate with certainty the histopathological changes described in different studies. Even when specific criteria are applied, there may be significant variation between pathologists in the interpretation of changes in gastrointestinal tissue samples. Thus, Willard *et al*. (2002) reported lack of uniformity in the assessment of 50% of biopsy samples examined by five veterinary pathologists. This interpretive variation may pose problems for the routine diagnosis of gastrointestinal disease or for monitoring the progress of patients receiving post-therapeutic endoscopy. Moreover, such variation impedes progress in the performance of multi-centre diagnostic or therapeutic clinical trials in small animal gastroenterology.

With this background, a Gastrointestinal Standardization Group was convened with the support of the World Small Animal Veterinary Association (WSAVA), and with the purpose of developing standards for the diagnosis and treatment of gastrointestinal disease in the dog and cat. One of the first tasks of this group was to develop a set of histopathological standards for characterizing the nature and severity of mucosal inflammatory and associated morphological changes. The current monograph presents the outcome of these deliberations, in what we hope will become an internationally accepted standard for the description of microscopical changes affecting the mucosa of the canine and feline gastric body, gastric antrum, duodenum and colon.

Materials and Methods

The WSAVA Gastrointestinal Standardization Group developed the standards presented herein over several face-to-face meetings (American College of Veterinary Internal Medicine [ACVIM] Forum, 2004, St Paul; ACVIM Forum, 2005, Baltimore; British Small Animal Veterinary Association [BSAVA] Congress, 2006, Birmingham; European College of Veterinary Internal Medicine [ECVIM] Congress, 2006, Amsterdam; ACVIM Forum, 2007, Seattle; ECVIM Congress, 2007, Budapest) and by electronic communication in between these meetings. The scope of the project was first defined by identifying the four most commonly sampled anatomical regions of the gastrointestinal mucosa: the gastric body, gastric antrum, duodenum and colon. For each of these regions, tissue changes were defined by (1) morphological abnormalities, and (2) the major types of inflammatory cell infiltrating the epithelium and lamina propria of that region. The Group included in these evaluations only those microscopical changes considered to be of greatest relevance to the inflammatory process. Minor changes that could equally be artefactual (e.g. small capillary haemorrhage, tissue oedema) were not incorporated into the standards.

The Group adopted pictorial ''templates'' of histopathological images to demonstrate the particular morphological or inflammatory change being presented. It was proposed that for each of these changes, four images would be presented, namely (1) the normal tissue morphology or baseline numbers of leucocyte subpopulations, (2) mild manifestation, (3) moderate manifestation, and (4) marked manifestation. The Standardization Group recognized that development of a single pictorial template applicable to samples taken from both the dog and the cat would be of greatest value. The fundamental inflammatory changes that occur within the stomach and intestine of these two species are in general sufficiently similar to allow this approach. A major exception, however, is the density of intraepithelial lymphocytes in the duodenum, which is significantly greater in the cat than in the dog (German *et al*., 1999; Waly *et al*., 2001). It was agreed that, for this variable, a separate template would be presented for each species.