Colitis in the horse with a focus on right dorsal (RDUC)

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Summary
Despite great progress in the management of the critically ill equine patient, colitis in horses remains a diagnostic and therapeutic challenge to the veterinarian. Irrespective of the cause of colonic injury and inflammation, diarrhoea usually has a severe and immediate impact on the health and wellbeing of the affected horse and can quickly become life-threatening if left unattended. Due to the potential for rapid disease progression and a fatal outcome, all cases of equine diarrhoea should invariably be considered a veterinary emergency. An overview of the current knowledge about equine colitis will be presented, including the most common causes, available tests to (hopefully) obtain a definitive aetiological diagnosis, the most important parameters in clinical-pathological monitoring, and the therapeutic and management strategies currently recommended when treating a horse with diarrhoea. The epidemiology, aetiology, pathogenesis, diagnosis and treatment for right dorsal ulcerative colitis (RDUC) will be discussed.

Equine Colitis
Colitis, or typhlocolitis when the caecum is involved, is defined as inflammation of the colon, which is invariably accompanied by severe damage to the colonic mucosa. Irrespective of the inciting cause of inflammation and colonic injury most forms of colitis have a similar pathogenesis and clinical manifestations including intraluminal fluid sequestration, abdominal discomfort, and profuse, watery diarrhoea as the result of abnormal fluid and ion mucosal transport, leading to hypovolaemia, severe dehydration, profound electrolyte abnormalities, endotoxaemia and leucopaenia. In acute cases, the diarrhoea can be rapidly debilitating and life-threatening due to severe fluid and electrolyte losses following deregulation in the rates of absorption and secretion in the damaged colonic mucosa. Malabsorption and uncontrolled secretory activity of mucosal epithelial cells, leads to massive fluid losses, rapid dehydration and death (>90% of untreated equine colitis cases die or require euthanasia). Fortunately, diarrhoea associated with acute equine colitis is only of sporadic occurrence.

The aetiologic causes of equine colitis include naturally occurring infections (Salmonellosis, intestinal clostridiosis, larval cyathostomiasis, proliferative enteropathy, rotavirus, coronavirus, etc), as well as non-infectious insults (carbohydrate overload, cantharidin toxicity, alimentary indiscretion, NSAID toxicity, etc).

In addition, in many horse with diarrhoea the diagnosis remains unknown or speculative at best. In recent years however, the percentage of colitis cases where and aetiology could not be identified has declined due to a better understanding of the condition and to advances in diagnostic testing. Despite the multiple aetiologies of equine colitis, the clinical and clinicopathological features in the acutely diarrhoeic horse are similar regardless of the underlying cause. Rapidly progressing dehydration accompanied by severe electrolyte abnormalities and major acid-base disturbances, rapid protein loss leading to hypoalbuminaemia.

Activation of systemic inflammation (i.e. SIRS), following absorption of bacterial products (e.g. endotoxin) and bacterial translocation, is common and may even precede the elimination of loose faeces. Because of the potential for rapid progression to a life-threatening state, colitis should always be considered an emergency requiring aggressive, immediate veterinary intervention and hospitalisation. Due to the similarities in the pathogenesis and clinical presentation, the diagnostic approach and the principles of therapy are also similar regardless of the aetiological cause. Diagnostic efforts are triaged to first assess immediately life-threatening derangements in hydration, volaemia, plasma electrolyte concentrations and acid base disturbances. If required, these potentially life-threatening alterations must be therapeutically addressed.
as an emergency. Subsequently, the systemic inflammatory response, coagulation status, plasma protein (albumin) concentration, organ function, and likelihood of laminitis development are assessed. Where available, the structure and integrity of the intestinal wall, particularly the right dorsal and left ventral colon, should be ultrasonographically determined. In addition, while various of the pathogens mentioned above that can cause equine colitis are potentially zoonotic, and can affect various other animal species, sampling and diagnostic efforts towards the identification of an aetiologic agent are of paramount importance for the safety of other in-contact horses, humans and animals. Reaching an aetiological diagnosis is also important for more targeted treatment, as is the case for \textit{Lawsonia intracellularis} or \textit{Cyathostomum} (small strongyle) infections. However, with the exception of proliferative enteropathy caused by \textit{L. intracellularis}, \textit{Neorickettsia risticii} causing Potomac Horse Fever in North America and verminous colitis due to cyathostominosis, which require specific antibiotics and anti-helminthics respectively, the mainstay of treatment for acute diarrhoea in the horse is the same regardless of the cause. It consists primarily of fluid replacement, correction of electrolyte and acid-base imbalances, replacement of plasma protein and coagulation factors, and controlling systemic inflammation, endotoxaemia and sepsis. Specific therapeutic goals include support of cardiovascular function, reduction of colonic inflammation and promotion of mucosal repair in order to reduce intestinal hypersecretion and malabsorption, and to promote re-establishment of the normal colonic flora. In addition, distal limb cryotherapy is a must in order to prevent the development of sepsis-associated laminitis.

Non-steroidal anti-inflammatory drugs (NSAIDs) are one of the most commonly prescribed medications in horses. With chronic use, or if overdosed, NSAID toxicity ensues and manifests clinically as an acute or chronic protein-losing ulcerative colitis of the right dorsal colon (i.e. Right Dorsal Ulcerative Colitis – RDUC), characterised by anorexia, lethargy and colic. In the acute form, depression, diarrhoea, fever and endotoxaemia may be present. If RDUC is chronic, colic signs are usually intermittent, faeces remain soft and unformed, and the patient develops ventral oedema and weight loss. Extensive mucosal ulceration of the right dorsal colon results in protein-losing enteropathy and significant hypoproteinaemia attributable mainly to hypoalbuminaemia.

The decrease in plasma protein is one of the earliest alterations in RDUC; thus, peripheral oedema may

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<thead>
<tr>
<th>Principles of Therapy for Acute Diarrhoea</th>
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</thead>
<tbody>
<tr>
<td>Fluid replacement &amp; cardiovascular support</td>
</tr>
<tr>
<td>Anti-inflammatories &amp; analgesics</td>
</tr>
<tr>
<td>Synthetic prostaglandins &amp; coating agent</td>
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<tr>
<td>Amylase resistant fermentable fibre to increase production of short chain fatty acids</td>
</tr>
<tr>
<td>Antibiotics</td>
</tr>
<tr>
<td>Probiotics &amp; transfaunation</td>
</tr>
<tr>
<td>Anticoagulants</td>
</tr>
<tr>
<td>Adsorbents</td>
</tr>
<tr>
<td>Nutrition</td>
</tr>
</tbody>
</table>
be the only clinical manifestation at first, and only if the hypoproteinaemia is sufficiently severe. In cases of severe ulceration and diarrhoea, and where systemic inflammation is present, dehydration, electrolyte abnormalities, neutropaenia, anaemia, azotaemia, and other serum chemistry abnormalities occur.

NSAIDs induced mucosal damage is thought to be multifactorial, with some degree of damage resulting from direct irritation, but mainly as a consequence of a reduction in prostaglandin synthesis following COX-1 and COX-2 inhibition. However, the role of prostaglandins in maintaining the integrity of the colonic mucosa and mucosal barrier function in horses is not well characterised. Regardless of the way the deleterious action is exerted, all NSAIDs appear to be capable of inducing intestinal damage. While phenylbutazone is the most frequently used NSAID in equine practice, it is not surprising that it is also the drug most frequently associated with RDUC. High doses of phenylbutazone have been experimentally associated with equine RDUC; acute toxicity following overdose is characterised by protein-losing enteropathy with hypoalbuminemia due to mucosal ulceration throughout the gastrointestinal tract, including the mouth. Renal papillary necrosis and thrombosis is also described. The widespread use of flunixin meglumine makes it the second most frequently associated NSAID in cases of RDUC. Though infrequently used in equine practice, aspirin is thought to have a higher toxicity due to irreversible COX inactivation, whereas NSAIDs with COX-2 selectivity such as meloxicam or firocoxib are thought to be less toxic (in vitro, both have been shown to be less harmful to the equine intestinal mucosa when compared to flunixin). Nevertheless, regardless of the NSAID being used, caution must be exercised and NSAID use should always be judicious. If prolonged used is required, monitoring plasma protein levels, and ideally albumin levels, is recommended, as a drop in total protein due to a decrease in albumin concentrations is the earliest indication of ensuing RDUC.

The need for regular monitoring of plasma or serum proteins is further emphasised by an apparently high variability in individual susceptibility to NSAID toxicity. Furthermore, behaviour and genetic factors, stress and variable tolerance to what would be considered a stressor, infection, and the immune status have all been proposed as contributors to this individual variation. Unfortunately, experimental or clinical data corroborating the role of the above mentioned factors as a trigger or a risk factor for RDUC is lacking.

Both experimentally and in clinical practice, horses with NSAID toxicity inducing RDUC have received inappropriately high doses. In practice, upon careful interrogation of the client, overuse of an NSAID and usually unintentional overdosing to treat e.g. an ophthalmologic problem or a performance-limiting musculoskeletal disorder is identified in the history. In cases where the client does not volunteer this information, careful examination will often identify a local inflammatory process with characteristics of chronicity. Thus, as intentional or accidental overdosing is almost invariably identified in horses suffering from RDUC and experimentally RDUC has only been induced when exceeding the recommended dose for several days in the case of phenylbutazone.

Adherence to the recommended dose regimen for NSAID use in the horse is considered safe, even when prolonged. However, multiple studies have identified a significant reduction in total serum protein and albumin concentrations, and an increase in the albumin:globulin ratio, as well as mucosal atrophy, focal erosions and ulcers in the alimentary tract. The occurrence of NSAID toxicity in normovolaemic patients receiving appropriate doses emphasises the need for close monitoring, particularly in critically ill patients, as conditions which result in haemodynamic alterations (dehydration, hypovolaemia, sepsis, etc) are thought to exacerbate NSAID toxicity to the gastrointestinal tract. Moreover, pre-existing intestinal inflammation which is typically managed with NSAID administration, is also thought to increase the likelihood of ulcer development in the alimentary tract as a result of NSAID toxicity.
As mentioned above, the clinical manifestations of RDUC in the horse depend on the severity and rapidity of disease development, ranging from only dependant oedema in cases with an insidious onset, to a severe and per-acute colic episode that might prompt emergency exploration of the abdomen. The diagnosis of RDUC is often presumptive, with chronic NSAID use or intentional or accidental overdose in the history being highly suggestive. The confirmation of a diagnosis can be achieved via trans-abdominal ultrasonography. The acoustic window for the right dorsal colon is located between the 11th to 15th or 16th intercostal spaces, where it can usually be readily identified ventral to the lung and medial to the liver. The diagnosis of RDUC is based on the measurement of colonic wall thickness (normal ≤ 0.5 cm). However, the ultrasound measurement is subject to a high level of inter and intra-operator variability and therefore has a low sensitivity. Despite the low sensitivity, a finding of a thickened right dorsal colon (> 0.5 cm) and oedema of the colonic wall, in the presence of clinical signs of RDUC will help confirm the diagnosis. If the diagnosis remains unclear, laparoscopic investigation can be used for confirmation. Most importantly, other potential causes of enterotyphlocolitis discussed earlier should be ruled out.

Once a diagnosis is confirmed or strongly suspected, RDUC is generally treated medically and may require weeks or months for mucosal repair to take place and for colonic wall thickening and oedema to subside. The principles mentioned above of therapy for diarrhoea are applied, though cardiovascular support and fluid replacement may only be required in per-acute cases. The recognition of RDUC should prompt the clinician to immediately discontinue NSAID administration, which will require the use of alternative pain relief. Another important aspect in the management of RDUC that differs from other causes of colitis is introduction of a low volume diet, which usually requires replacing hay with an alternative source of highly digestible fibre (e.g. psyllium mucilloid) and omega-3-rich vegetable oils for energy provision and anti-inflammatory effects (e.g. linseed oil). The use of synthetic prostaglandins (misoprostol®) and adsorbents (biosponge®) is also advocated, though evidence of their benefit is lacking. Surgical intervention carries an unfavourable prognosis but may be warranted in cases where colonic damage is extensive enough that a colon resection is required.

In humans NSAID toxicity results in high morbidity and mortality and has been termed “the silent epidemic”. However, data on the epidemiology of NSAID toxicity in horses, and on the impact and the benefit of medical and surgical treatment options on outcome and prognosis following management of RDUC are largely unknown.
References