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CLINICAL UPDATE: GRASS SICKNESS

Background; Equine Grass Sickness (equine dysautonomia) is a frequently fatal multi-system neuropathy of equids characterized by chromatolysis of autonomic, enteric and somatic neurons. While the aetiology is unknown, proposed causes include pasture derived mycotoxins and toxico-infection with *Clostridium botulinum* types C or D. Recent work indicates that EGS is unlikely to be caused by neurotoxins from *C. botulinum* but does not preclude involvement of other toxins from this bacterium. An identical disorder occurs in hares, dogs, cats and rabbits, and possibly in sheep and llamas.

Epidemiology; EGS occurs in most Northern European countries, Argentina, Chile, the Falkland Islands and possibly Colombia. United Kingdom has the highest incidence (kills approx. 1-2% horses annually). There is a single case report of EGS in a horse from North America. EGS predominantly affects 2-9 year old grazing horses.

EGS is categorized into acute, sub-acute and chronic forms based on disease severity. This classification is somewhat artificial, since disease severity is a continuum, but it can aid prediction of case outcome. Acute and sub-acute EGS is invariably fatal, with affected horses typically being euthanased within, respectively, 48 h and 7 days after the onset of clinical signs. Approximately 55% of horses with chronic EGS survive with supportive care.

Acute EGS; Horses typically present with inappetance and depression, but soon develop generalized gastrointestinal stasis with resultant dysphagia, salivation, dehydration, mild colic, distension of the stomach and small intestine with green-brown fluid, and firm, corrugated secondary large intestinal impactions. Despite the severity of these gastrointestinal abnormalities, signs of abdominal pain are typically mild to moderate, probably because of degeneration of visceral afferent sympathetic neurons which mediate gastrointestinal pain. Dysphagia reflects oral, pharyngeal and oesophageal dysfunction and may be evident as prolonged mastication, dropping food, pouching of food in the cheeks, salivation and reflux of water from the mouth during drinking. Food and water do not reflux via the nares, but spontaneous nasal reflux of gastric fluid occasionally occurs. *Per rectum* examination may reveal small intestinal distension, large bowel secondary impaction, a dry and tacky rectal mucosa and small, firm, dry faecal pellets coated with inspissated mucus. Acute EGS also causes tachycardia (typically 70-120 bpm), sweating, piloerection and bilateral ptosis. Fasciculations of the triceps, shoulder and flank muscles are common. Fasciculations are exaggerated by stressful stimuli, and, in contrast to those of botulism and equine motor neuron disease, do not cease when muscles are rested.

Sub-acute EGS; Horses have less severe gastrointestinal stasis and tachycardia (typically 60-80 bpm), but have an obvious loss of body condition and tucked up abdomen. Gastric and small intestinal distension is absent, but secondary large intestinal impactions are common. Mild diffuse weakness of the skeletal muscles of the neck, trunk and limbs causes horses to adopt a base narrow stance, low head and neck carriage, and with the hind quarters supported against the stable wall. Horses attempt to relieve weak postural muscles by spending increased time recumbent and by frequently shifting weight among all four limbs while standing. Rhinitis sicca, which appears to be pathognomonic for EGS, is common in sub-acute and chronic EGS, but may be absent in the early stages of EGS.

Chronic EGS; characterized by profound cachexia, generalized myasthenia, tachycardia (typically 50-60 bpm) and mild signs of gastrointestinal dysfunction. Rhinitis sicca may cause overt nasal obstruction, and 'snuffling' inspiratory and expiratory noise.

Diagnosis; Clinicians familiar with EGS can accurately diagnose most cases solely using clinical examination and historical data. However, some acute EGS cases present a diagnostic challenge because clinical signs are variable and common to many other diseases, particularly surgical colic. Definitive ante-mortem diagnosis is generally considered to require histologic demonstration of the characteristic enteric neurodegeneration in ileal biopsies obtained via midline, or less commonly, flank laparotomy. While laparotomy may be indicated to facilitate prompt differentiation of acute EGS and surgical colic cases, this invasive procedure is not advocated for the diagnosis of sub-acute and chronic EGS. Work is underway to evaluate the diagnostic utility of immunolabelled rectal and lingual biopsies. Detection of subtle bilateral

ptosis is facilitated by topical application of 0.5ml 0.5% phenylephrine eye drops into one conjunctival sac. A positive tests is evidenced by restoration of normal eyelash angulation within 20-30 mins, but is not pathognomonic for EGS. False negative and positive responses occur, with the latter occurring in some sedated horses and horses with botulism.

Treatment; Acute and sub-acute EGS are invariably fatal and affected horses should be euthanased as soon as a confident diagnosis is made. Intensive nursing is the mainstay of treatment for chronic EGS. Since the greatest obstacle to survival is generally profound inappetance, a selection of highly palatable feeds (ideally high in energy and protein) should be offered. Addition of vegetable oil will increase the energy density. Prolonged feeding via nasogastric tube does not appear to improve survival. Administration of analgesics, omeprazole, fluids and electrolytes may be beneficial. The rapidity and magnitude of body weight loss may aid prediction of survival. Complications occurring during the recovery phase of EGS include continued weight loss, debility and muscular weakness, colic, oesophageal choke, intestinal bacterial overgrowth, diarrhoea, penile prolapse, inappropriate sweating and aspiration pneumonia.

Prevention; There is no known guaranteed method to prevent EGS in high risk areas. After an occurrence of EGS, co-grazing horses may be housed for 2-4 weeks to prevent further cases. If this is impractical, co-grazing horses may be moved to a separate field. A large (~1000 horses) UK-wide randomised placebo controlled field trial of a killed *C. botulinum* type C toxoid vaccine (Botumink) for the prevention of EGS is currently underway and should be completed by 2017 (http://www.aht.org.uk/cms-display/egs_vt.html). It is hoped that the outcome of this study will definitively prove or refute the botulinum hypothesis and provide an effective prophylaxis for this devastating disease.