Equine Dysautonomia

Bruce C. McGorum, BSc, BVM&S, PhD, CEIM, FRCVS*,
R. Scott Pirie, BVM&S, PhD, CEIM, CEP, MRCVS

KEYWORDS

• Grass sickness • Dysautonomia • Ileus • Chromatolysis • Enteric nervous system

KEY POINTS

- Despite the adopted nomenclature, equine dysautonomia (ED; also known as equine grass sickness) is a multisystem neuropathy. Although the clinical phenotype is largely reflective of autonomic (including enteric) nervous system dysfunction, neuronal degeneration occurs at other nonautonomic neuroanatomic locations.
- ED primarily affects grazing equids, and several other disease-associated risk factors have been identified.
- The cause remains undetermined, although the currently favored etiologic hypotheses include *Clostridium botulinum* toxicoinfection and/or mycotoxicosis.
- Although the disease phenotype is subclassified as acute (severe), subacute (moderate), and chronic (mild), these represent different categories within a continuum of disease severities.
- The antemortem diagnostic approach relies on consideration of disease-associated risk factors, the clinical presentation of the patients, exclusion of other differential diagnoses, the adoption of appropriate ancillary diagnostic techniques, and, on occasion, histopathologic confirmation of enteric neuronal pathology.

INTRODUCTION

Equine dysautonomia (ED; also known as equine grass sickness) is a polyneuropathy affecting both the central and peripheral nervous systems of, almost exclusively, grazing horses. Following the original report of ED in 1907,[1] it has subsequently been recognized throughout most of Northern Europe.[2–11] Suspected cases have also been reported in the Falkland Islands[12] and Australia.[13] Although North America has largely been considered free of the disease, ED was recently described in a mule in the United States.[14] A clinically and pathologically identical disease, Mal Seco, is well recognized in South America.[15–18]

Despite the reported widespread neuroanatomical distribution of degenerative neuronal lesions in ED, the autonomic nervous system (ANS) and enteric nervous

The Dick Vet Equine Hospital, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush Campus, Easter Bush, Roslin, Midlothian EH25 9RG, GBR
* Corresponding author.
E-mail address: bruce.mcgorum@ed.ac.uk

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system (ENS) remain the most consistently and severely affected.[19] The spectrum of clinical signs, which define ED largely but not exclusively, reflects involvement of the ANS and ENS. The severity of disease and gross pathologic findings can largely be attributed to the extent of enteric neuronal loss (see *physical examination findings* and *pathologic findings*).

Despite extensive research efforts over the past century, the cause of ED remains elusive. Current research efforts are primarily focused on the potential role of either *Clostridium botulinum* neurotoxins (via toxicoinfection)[20–22] or ingested pasture-derived mycotoxins.[23,24] The *C botulinum* hypothesis was extensively investigated during the 1920s[25] and has recently received renewed interest. **Table 1** summarizes the factors that either support or refute the involvement of *C botulinum* in ED. In addition to the key association with grazing, the hypothesized role of pasture-derived mycotoxins in ED is largely justified by the seasonality of the disease[33,34] and the geographic and temporal clustering of cases,[35] which likely reflect climatic influences on etiologic agent exposure.[33,36]

PATIENT HISTORY

Consideration of the history of both the patients and the premises is beneficial in ED diagnosis. Appropriate questioning of the owner will allow the clinician to ascertain which of the published risk factors apply to the case and consider the diagnostic value of any relevant associations. A summary of the various published horse-, premise-, management-, and climate-level factors associated with either an increased or decreased risk of ED occurrence, or recurrence on a previously affected premise, is presented in **Table 2**. It is worth noting that, despite a general agreement between studies, occasional inconsistencies exist with regard to some of these reported associations.

As well as carefully considering the applicability of some of the risk factors in each case, a careful clinical history should also be obtained. Typically, severe (acute) cases of ED will have a sudden onset, with little prior indication of impending disease. In contrast, mild (chronic) cases will typically have an insidious onset, whereby

Table 1
Factors that support and refute involvement of *Clostridium botulinum* in equine dysautonomia

Supportive Factors	Refutative Factors
• Reportedly successful historic botulinum vaccine trial (1922 and 1923)[25]	• Disease phenotypic differences between ED and neuroparalytic botulism[24]
• Significantly greater prevalence of intestinal *C botulinum* bacteria and/or toxin in patients with ED vs control animals[20–22]	• Greater prevalence of other (non–*C botulinum*) clostridial species in intestinal tract of patients with ED vs controls (possibly reflecting generalized clostridial overgrowth)[30,31]
• Risk factors supportive of involvement of a soil-borne agent[26,27]	• Neuropathology apparently inconsistent with action of *C botulinum* neurotoxins[32]
• Inverse association between disease risk and systemic concentration of antibodies against *C botulinum* bacteria and toxin[28]	• SNARE protein expression in ED ganglion and enteric neurons inconsistent with action of *C botulinum* neurotoxins[32]
• Higher mucosal IgA against BoNT/C and D in patients with acute ED vs control animals[29]	• Lack of evidence of temporal and geographic clustering of ED and neuroparalytic botulism cases

Abbreviation: IgA, immunoglobulin A.