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We all know that horses residing at pasture spend the majority of their days grazing. But did you know that, in certain parts of the world, grazing could put a horse at risk for contracting a potentially fatal disease? And what's more, researchers still aren't sure what causes the disease, called equine grass sickness (EGS).

At the 2014 British Equine Veterinary Association Congress, held Sept. 10-13 in Birmingham, U.K., R. Scott Pirie, BVMS, PhD, CertEP, CertEM(IntMed), Dipl. ECEIM, MRCVS, reviewed the current knowledge about the causes of EGS. Pirie is a senior lecturer in equine internal medicine at the University of Edinburgh Royal (Dick) School of Veterinary Studies, in Scotland.

An often fatal neurologic disease, EGS primarily affects grazing horses. Horses with more severe forms of the disease experience colic, difficulty swallowing, reflux of stomach contents, excessive salivation, high heart rate, impacted intestines, muscle tremors, and patchy sweating. Horses with less severe forms experience sudden and extreme weight loss, drying of the nasal membranes, and difficulty swallowing. Only mild cases that receive intensive care survive.

Since its first reported occurrence in 1909 in eastern Scotland, grass sickness has appeared in most northern European countries and in South America. And, Pirie said, although "a vast array of etiological hypotheses have been proposed and addressed experimentally," the disease's cause remains unknown. Still, researchers have several ideas on what could be causing EGS.

"It is currently accepted that the epidemiology of the disease supports the role of an ingested soil-borne agent capable, under certain conditions, of producing or liberating a putative (assumed to be significant) neurotoxin" that has yet to be determined, Pirie said.

Clover Over the years, researchers have proposed that the consumption of clover—both alsike and white—could play a role in EGS development. However, Pirie said, early alsike clover feeding trials weren't able to reproduce the disease.

"More recently, research focused on the potential association with white clover, which has a relatively high cyanogenic glycoside content," he said. Cyanogenic glycoside is a type of toxin that can induce a wide variety of health problems including neurologic disease.

Researchers have determined that white clover samples collected from fields shortly after horses grazing there developed EGS had significantly higher concentrations of some cyanogenic glycosides than control fields, Pirie said. And, researchers have found evidence of increased exposure in horses grazing with the affected horses. Still, he said, "further study may be indicated to determine whether cyanogen ingestion constitutes a risk factor for EGS or is unrelated to disease development."

Climate "The climactic conditions associated with EGS have been considered as potentially consistent with the involvement of a pasture-derived mycotoxin, and several studies have focused on this etiological possibility," Pirie said.

Pirie said in the late 1990s researchers found that EGS-associated pastures appeared to have increased numbers of *Fusarium* spp. He also noted that around the same time researchers confirmed that *Fusarium* extracts exhibited neurotoxic properties *in vitro* (in the laboratory).

"Although this avenue of enquiry did not progress further at this time, the investigation into the role of *Fusaria* in EGS has recently been revisited," Pirie said. The British Food and Environment Research Agency and the University of Edinburgh are collaborating to revive this research, he said.

Clostridium botulinum Finally, Pirie said, the most recent research has focused on the potential role of *C. botulinum*—the bacterium that produces the toxin that causes botulism—in EGS, a theory initially researched shortly after the disease's first occurrence.

"As a soil-borne organism, many of the risk factors associated with EGS could theoretically support its contributory role," he said.

While researchers have pinpointed several factors that could potentially link *C. botulinum* type C to EGS, "the principal inconsistency with regard to this hypothesis is the fact that neuroparalytic botulism, resulting from *C. botulinum* toxicosis, is not associated with any identifiable histopathologic lesions," Pirie said, which are seen in all EGS cases.

"At present, especially upon consideration of the association between EGS and *C. botulinum* serological status and failure to experimentally induce EGS in a series of several challenge studies, further investigation of this hypothesis is focused on establishing, once again, whether vaccination against *C. botulinum* type C affords any protection against the disease," he relayed. "A U.K. nationwide vaccine trial is scheduled to be undertaken over the following two to three years, the results of which should definitively support or refute a role for *C. botulinum* in EGS etiopathogenesis."