Equine Coronavirus

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1. Introduction
Coronaviruses are single-stranded, positive-sense, non-segmented, enveloped RNA viruses belonging to the Coronaviridae family and the following 4 genera defined based on serological cross-reactivity and genetic homology: Alphacoronavirus, Betacoronavirus, Deltacoronavirus, and Gammacoronavirus.1 Equine coronavirus (ECoV) is classified within the Betacoronavirus 1 genus, along with human coronaviruses OC43, 4408, and HKU1; bovine coronavirus (BCoV); porcine hemagglutinating encephalomyelitis virus; canine respiratory coronavirus; mouse hepatitis virus; bubaline coronavirus; and sialodacryoadenitis rat coronavirus.2 Horses appear to be susceptible to the human severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) based on the high homology to the ACE2 receptor;3 however, there are at the present time (January 2021) no data documenting antigen or antibody detection to SARS-CoV-2 in equids. The only data available are from the closely related Middle East respiratory syndrome coronavirus (MERS)-CoV. The various studies have shown conflicting results, with one study documenting high seroprevalence in equids from endemic areas and another study reporting that experimentally infected horses developed no clinical signs, showed minimal viral shedding, and did not seroconvert.4,5

2. Clinical Presentation
Almost 12 years ago, a research group investigated an unusual outbreak of fever and enteric signs in 2- to 4-year-old racing draft horses in Tokachi, Hokkaido, Japan.6 It is of interest to note that enteric signs were only reported in 10% of the horses, and a total of 132/600 horses (22%) became diseased. The same racing venue experienced one additional outbreak with similar signs three years following the first outbreak.7 Additional outbreaks have since been observed and reported in the United States and Europe.8–11 Collectively, these outbreaks have been able to refine the clinical presentation of ECoV, one that is still perplexing considering the inconsistent development of enteric signs. Clinical information collected from various outbreaks involving 406 horses showed that 122 horses (30%) showed clinical signs.8 The main clinical signs reported were anorexia (98%), lethargy (89%), and fever (84%). The rectal temperature of febrile horses ranged from 101.5 to 105.8°F (median 103.8°F). Changes in fecal character, ranging from soft-formed to watery consistency, and colic were observed in 25% and 18% of horses, respectively. Signs of encephalopathy, including circling, head pressing, ataxia, proprioceptive deficits, nystagmus, recumbency, and seizure, have occasionally been reported in ECoV-infected horses.8,12

Although clinical disease is apparent in most ECoV-infected horses, one needs to consider that some horses remain subclinical after infection. Subclinical infection is defined as a lack of clinical disease in a horse from which ECoV is detected in feces by quantitative PCR (qPCR).11,13

NOTES
3. Laboratory Diagnosis

The antemortem diagnosis of ECoV relies on the presence of clinical signs compatible with ECoV infection, abnormal cell blood count, the exclusion of other infectious causes, and molecular detection of ECoV in feces. The consistently observed hematological abnormalities observed with ECoV infection are leukopenia due to neutropenia and/or lymphopenia.8,13–16 Additional, less consistent hematological abnormalities included the presence of band neutrophils and shifts in monocyte counts. Occasional rebound leukocytosis due to neutrophilia and monocytosis during the disease course and recovery can be observed as well. Complete blood cell count (CBC) abnormalities are expected to resolve within 5–7 days as long as no complications associated with the disruption of the gastrointestinal barrier occur. However, both the CBC and white cell differential can be unremarkable in clinically infected horses. Biochemical parameters may be unremarkable, but elevation of total and indirect bilirubin due to partial or complete anorexia, electrolyte changes consistent with enterocolitis, transient elevation of liver enzymes, and renal parameters suggested of pre-renal azotemia have been observed in some of the cases.14,16

It is judicious to measure blood ammonia in horses with suspected ECoV infection and concurrent signs of encephalopathy. Fielding and collaborators12 reported on a case of severe hyperammonemia (677 μmol/L; reference interval, ≤60 μmol/L) with encephalopathic signs that subsequently died. Hyperammonemia associated with ECoV infection is likely due to increased ammonia production within and absorption from the gastrointestinal tract due to gastrointestinal barrier breakdown. An increase in enteric ammonia production could also be the result of bacterial microbiome changes associated with ECoV infection. Historically, coronavirus detection in feces has been based on negative-stain electron microscopy (EM) and antigen-capture enzyme-linked immunosorbent assay (ELISA). However, the sensitivity and specificity of these diagnostic modalities have not been evaluated, and detection may be unsuccessful if viral particles are not present in sufficient numbers. Sensitive laboratory diagnosis of ECoV is through fecal qPCR. A recent study evaluated the overall accuracy of qPCR and determined 90% accuracy between clinical status and PCR detection of ECoV in various outbreak populations.8 The author has documented a few cases of ECoV infection that tested qPCR negative during early disease. These few horses ended up testing qPCR positive on a 24- to 48-hour recheck fecal sample. It is hypothesized that during peracute stages of infection or when diseased horses experience gastrointestinal stasis due to colic, there are not enough viral particles in the feces to be detected. Peak viral shedding is observed on day 3 to 4 after the development of clinical signs, and qPCR detection of ECoV in naturally infected horses generally lasts 3–9 days but can occasionally extend up to 25 days from onset of clinical disease.8,12,13 As with many viral infections, viral kinetics are likely influenced by viral strain, age of patient, and comorbidities. The role of subclinical shedding during an outbreak cannot be ignored, as 4% to 83% of healthy horses have been shown to test qPCR positive for ECoV in their feces.8 Such horses act as a source of infection and actively contribute to viral spread.

4. Treatment and Prevention

Most adult horses with clinical ECoV infection recover spontaneously in a few days without specific treatment. Horses with persistent elevated rectal temperature, anorexia, and lethargy are routinely treated with nonsteroidal anti-inflammatory drugs for 24 to 48 hours, as long as their hydration status is believed normal. Horses with colic, persistent lethargy and anorexia, and/or diarrhea have been treated more intensively with fluid and electrolyte per nasogastric intubation or intravenous administration of polyionic fluids until clinical signs have resolved.14,16 Additionally, antimicrobials and gastrointestinal protectants should be considered in horses developing signs of endotoxemia and/or septicemia secondary to disruption of the gastrointestinal barrier. Although hyperammonemia-associated encephalopathy only occurs in a small percentage of horses with ECoV infection, early recognition and treatment are associated with a positive outcome. Specific preventive measures are scarce, and there are yet no licensed vaccines against ECoV. Due to the close genetic homology of ECoV with BCoV, serological responses to BCoV vaccines have recently been investigated. One study used a killed-adenovirused BCoV vaccine in six healthy yearling horses and reported a measurable serological response in all horses following the administration of two vaccines given 28 days apart.17 A second study investigated the safety, humoral response, and viral shedding in horses inoculated orally, intranasally, or intrarectally with a commercially available modified-live BCoV vaccine.18 The results of that study showed that the modified-live BCoV was safe to administer to horses via various routes, caused minimal viral shedding, and resulted in detectable antibodies to BCoV in 27% of the vaccinates. Collectively, these two BCoV vaccines, although showing measurable antibody responses to BCoV, cannot be recommended at this time due to the lack of efficacy data. The cornerstone of ECoV prevention resides in strict biosecurity measures aimed at reducing the risk of introducing and disseminating ECoV on equine premises. It is important to be vigilant when working up horses presenting with fever, anorexia, and lethargy, with or without concurrent enteric signs. Such horses should be isolated until ECoV, as well as other potential infectious pathogens, has been ruled in or out. ECoV qPCR-positive horses should be isolated and stable- or herd-mates closely monitored until the outcome of past exposure has been determined. Outbreaks of ECoV are
generally short lasting, especially when strict biosecurity measures have been followed, and quarantine can routinely be lifted 2–3 weeks after the resolution of clinical signs in the last affected horse. ECoV is susceptible to common disinfectants, including sodium hypochlorite, povidone iodine, chlorhexidine gluconate, phenols, quaternary ammonium compounds, accelerated hydrogen peroxide, and peroxynitric acid. However, it is still unknown how long ECoV remains infectious in the environment.

Acknowledgments

Declaration of Ethics
The Author has adhered to the Principles of Veterinary Medical Ethics of the AVMA.

Conflict of Interest
The Author has no conflicts of interest.

References