EQUINE DISEASE QUARTERLY

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COMMENTARY

Accelerating Medical Progress on Equine Lameness

In the horse world, lameness is a major problem. On this point, everyone agrees. Whether your focus is elite equine athletes or pleasure horses, whether you are a professional or a recreational rider, whether your primary breed of interest is large or small, musculoskeletal injuries are common and potentially very serious.

Substantial progress has been made over the last several decades in areas of both lameness diagnosis and treatment. Importantly, the future holds as much promise as ever. Science and technology are continuing to drive advances in clinical disciplines.

Cell biology is a good example. With next generation sequencing applied on a genomic scale (inclusive of all DNA or all RNA), it is now possible to broadly compare gene expression between individual tissues and cell types. Data-driven scientific approaches are discovering a large number of genes that nobody realized were important. The results are providing new insights into cellular identity, normal function, and disease mechanisms in areas that have direct relevance to lameness.

New understanding about individual cell types enables diagnostic and therapeutic strategies to be refined. Consider cartilage as an example. Our bodies contain several different cartilaginous tissues—joint (articular) cartilage, non-articular structural cartilage, cartilage that is replaced by bone through a process called endochondral ossification, and others. Although all types of cartilage have features in common, an understanding of the unique cellular characteristics that define *articular* chondrocytes is clearly an important parameter to consider with joint diseases.

Going forward, veterinarians will increasingly have access to molecular biomarker panels to help refine their list of differential diagnoses, to select optimal therapies, and for patient monitoring. We already hear about these approaches with cancer patients, and the same concepts are applicable for bone, cartilage, tendon, ligament, and muscle tissues. The clinical goals include improved sensitivity in monitoring health as well as early identification of disease problems and how the patient is responding to treatment.

On a therapeutic level, cell-based approaches are generating high levels of interest and for good reasons. The term "stem cells" is mentioned frequently. Cells can be used therapeutically to deliver beneficial equine-specific growth and differentiation factors to an area of injury, to modulate the patient's immune system in helpful ways, and in some cases to directly generate a repair tissue. There is much to learn and quite a bit of misinformation being disseminated, but cell-based therapies do indeed hold a lot of promise.

Finally, we have entered the era of medical informatics. Hardware, software, and data storage options in computer science have advanced rapidly to enable "big data" analyses that resolve biomedical relationships and patterns from "-omic" and population levels that would be very hard to appreciate by looking only at an individual gene or a single patient. By analogy, consider how difficult it would be to resolve crop circles and other patterns in a grain field while standing on the ground. They are much easier to appreciate while looking out the window of an airplane. It is not an "either/or" issue—broad and targeted analyses are both important and often complementary.

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LLOYD'S

INTERNATIONAL

Third Quarter 2016

The International Collating Centre, Newmarket, United Kingdom and other sources reported the following disease outbreaks.

Republic of South Africa reported outbreaks of African horse sickness in endemic areas of the country, but none in the Western Cape controlled zone.

Equine influenza was recorded in Germany (isolated case), the U.K. (case in an unvaccinated filly), and the USA, in which the disease is endemic. Outbreaks of the disease were confirmed in California, Delaware, Florida, Kentucky, New Jersey, and New York.

Strangles was reported by France, Germany, Ireland, Singapore, and the USA. The number of outbreaks varied from four in France, twelve in Germany (all isolated cases), nineteen cases on two premises in Ireland, a single case in an imported horse in Singapore, and multiple outbreaks involving seventeen states in the USA. Outbreaks within the USA consisted of 99 cases confirmed on an estimated 36 premises, one of which represented co-infection with equine herpesvirus 4.

France and South Africa recorded outbreaks of equine herpesvirus 1 (EHV-1) infection. In the case of the former, hyperthermia was the only clinical sign observed. Clinical details were not provided for the outbreak in South Africa. Outbreaks of EHV-1 abortion were reported by Ireland, South Africa and the UK, all involving isolated cases of the disease. EHV-1 related neurologic disease was confirmed in France, South Africa and the USA, each represented by single cases of the disease.

Respiratory disease caused by EHV-4 was recorded by France (seven outbreaks), South Africa and Switzerland (single case of infection), and the UK (two outbreaks; limited number of infected horses in each instance). Germany reported a case of neurologic disease from which EHV-4 was detected from a nasal swab.

Infection with EHV-2 and/or EHV-5 was confirmed in the USA, principally associated with evidence of respiratory disease.

Equine infectious anemia was recorded in Canada and the USA. Nine cases were diagnosed on three premises in Saskatchewan Province, Canada. Two cases were confirmed on each of two premises in New York and Oklahoma, USA.

France recorded that equine piroplasmosis was endemic in the country. In the USA, *Theileria equi* infection was confirmed in Quarter horse racehorses engaged in non-sanctioned racing in Tennessee (seventeen cases) and Wyoming/Utah (21 cases).

Germany reported nine cases of CEM on eight premises, the majority in stallions and horses of the Icelandic breed.

The USA reported cases/outbreaks of salmonellosis during the third quarter. Two cases involved serogroup B *Salmonella* spp., 10 with serogroup C1 spp. and two with serogroup D1 spp.

Outbreaks of clostridial enteritis due to *Clostridium perfringens* Type A, genotyped as β-2 toxin positive, were recorded by the USA, two in Kentucky and two in Minnesota.

France and Germany confirmed limited outbreaks of rotavirus infection in foals.

One case of infection with *Lawsonia intracellularis* was diagnosed in a foal in Kentucky, USA.

Single cases of rabies were recorded in Oklahoma and Florida, USA.

The USA reported 49 cases of Eastern equine encephalomyelitis during the period under review. The greatest numbers of cases were confirmed in Florida, Wisconsin, and South Carolina.

The USA confirmed a total of 88 cases of West Nile encephalitis involving seventeen states. The vast majority were in non-vaccinated horses or those with incomplete vaccination histories.

Rhodococcus related disease was considered endemic in the USA. Notwithstanding the fact that it is very difficult to estimate the prevalence of this infection, some 40 cases were confirmed during the third quarter.

Japan confirmed eight cases of Getah virus infection on one premises, the majority having incomplete vaccination histories. Infected horses displayed typical clinical signs of the disease.

The USA reported three cases of Equine Monocytic Ehrlichiosis in Maryland and West Virginia. Isolated cases of Ehrlichiosis were also confirmed in Germany and Switzerland.

Equine Disease Quarterly

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Observation, Science, and Equine Lameness Diagnosis

A significant number of pain-related gait abnormalities in horses are evident only when the horse is ridden, and are not apparent when the horse is hand-walked or lunged. Even when these horses are ridden, the lameness may not be overt. While there have been many recent technical advancements in the objective assessment of gait, these are generally of limited value for detection of bilaterally symmetrical alterations in gait that result in reduced performance such as generalized stiffness, lack of willingness to work, alteration in quality of movements such as lack of hindlimb engagement and impulsion, and alteration in the rider's feel of the contact via the reins and bit to the horse's mouth.

A rider often assumes that these problems are attributable to thoracolumbar region pain, because the problems are only manifest when the horse is ridden. When observed on the lunge, such horses may lean into the circle—often more on one rein than the other—and show exaggerated contractions of the epaxial muscles. However, studies have shown that experimentally induced forelimb or hindlimb lameness may reduce range of motion of the thoracolumbosacral vertebral column. Radiographic examination may reveal impinging spinous processes, and this finding often results in an erroneous conclusion implicating thoracolumbar pain as the primary problem. We have demonstrated that by using diagnostic analgesia to abolish overt or subclinical lameness, the rider often appreciates an increased range of motion of the horse's back.

To investigate these clinical observations, we have studied normal horses subjectively free from lameness in hand, after flexion test, on the lunge on both soft and firm surfaces and when ridden. We objectively measured body lean on the lunge and range of movement of the thoracolumbar region using inertial measurement units placed at predefined locations on the thoracolumbar and pelvic regions. These studies established normal ranges of motion for the thoracolumbosacral spine and demonstrated that sound horses have a small degree of bilaterally symmetrical body lean on the lunge. We also measured body lean on the lunge in lame horses and demonstrated that there is frequently asymmetry between left and right reins, with greater lean compared with normal on at least one rein. Substantial improvement in lameness by performing diagnostic analgesia resulted in reduced body lean on both reins and reestablishment of symmetry between left and right reins. Likewise, when lameness was improved by diagnostic analgesia, range of motion of the thoracolumbosacral regions increased, especially in the caudal thoracic and lumbar regions.

We have observed that the tendency of a saddle to slip persistently to one side is most frequently associated with hindlimb lameness. Abolition of lameness by diagnostic analgesia results in resolution of the saddle slip. The saddle most commonly slips to the side of the lame or more lame hindlimb, but less frequently slips toward the less lame limb. Presumably saddle slip is induced by altered range of motion of the thoracolumbosacral region, which may vary among horses. Saddle slip may actually be an indicator of the likely presence of hindlimb lameness.

Overt lameness may not be apparent when a horse is trotting, but musculoskeletal pain may be manifest at a canter by the horse's tendency to become disunited or repeatedly change leading limbs behind or in front, crookedness, loss of a normal three time rhythm, placing the hindlimbs either abnormally close together spatially and temporally, or placing the limbs remarkably far apart. These observations may be apparent either on the lunge or when the horse is ridden. Abolition of baseline lameness seen in hand may paradoxically make the canter appear worse if sacroiliac pain is contributing to pain and poor performance.

These observations highlight the importance of evaluating horses with performance problems both in hand, on the lunge and ridden, preferably by the normal rider. Horses should be assessed in walk, trot, and canter, bearing in mind that while one aspect of the gait may improve with diagnostic analgesia, another may deteriorate. Horses should also be assessed performing the movements which they find most difficult, because in some horses this may be the only condition when the problem is manifest.

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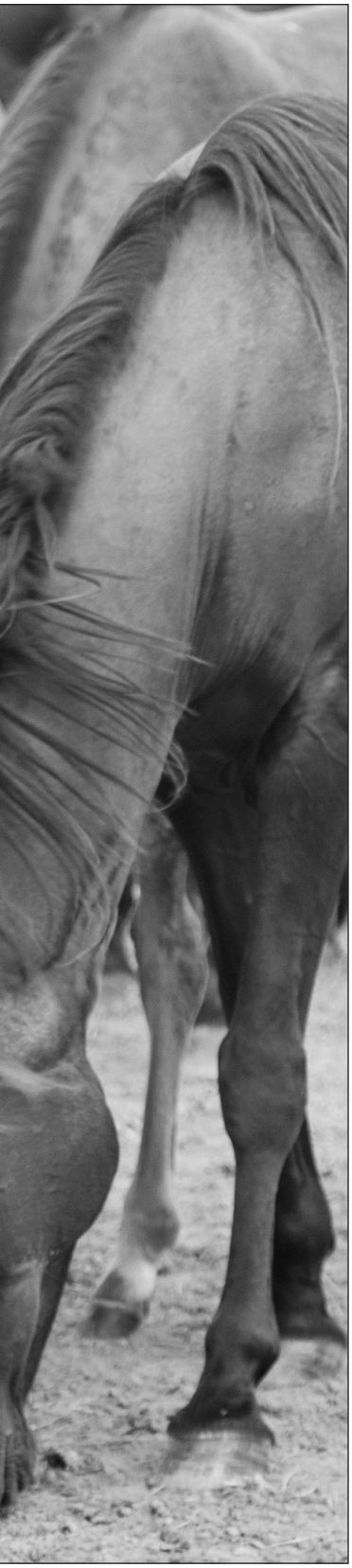

Equine Coronavirus – An Emerging Enteric Virus of Adult Horses

Equine coronavirus (ECoV) is classified within the *Betacoronavirus* genus, along with bovine coronavirus, porcine hemagglutinating encephalomyelitis virus, mouse hepatitis virus, rat coronavirus (sialodacryoadenitis virus), and certain human coronaviruses such as OC43, HKU1, Severe Acute Respiratory Syndrome coronavirus, and Middle East Respiratory Syndrome coronavirus; the latter two viruses have caused epidemic outbreaks of respiratory disease in human beings in the last decade. ECoV has been recently associated clinically and epidemiologically with emerging outbreaks of pyrogenic and enteric disease in adult horses in Japan and anorexia, lethargy, and fever in the United States.

Coronavirus infection typically begins in the proximal small intestine and subsequently spreads to the colonic epithelial cells, leading to blunting of the intestinal villi and subsequent villous atrophy. Loss of epithelial cells results in malabsorption and maldigestion of nutrients and acute diarrhea. Following a short incubation period of 48-72 hours, adult horses develop fever, anorexia, and depression. Changes in fecal character, ranging from soft-formed stools to watery consistency, and colic are seen in less than 20% of affected horses. A small number of horses develop acute neurologic signs due to hyperammonemia, which may manifest as severe depression, head pressing, ataxia, proprioceptive deficits, recumbency, nystagmus, and seizure. Common hematological abnormalities are leucopenia due to neutropenia and/or lymphopenia. ECoV infection generally resolves within 1-4 days with supportive care consisting of the administration of anti-inflammatory drugs and oral or intravenous fluids. Fatalities have been associated with septicemia, endotoxemia as well as metabolic abnormalities leading to encephalopathy (hyperammonemia).

Historically, the detection of ECoV has relied on either electron microscopy, antigen-capture ELISA, or viral isolation from the feces. All of these detection modalities lack sensitivity, especially if viral particles are not present in sufficient numbers. Quantitative polymerase chain reaction (PCR) assay for the detection of ECoV nucleic acid has supplanted many conventional virological assays, mainly due to its short turn-around-time, high throughput capability and increased analytical sensitivity and specificity. The overall agreement between clinical status and PCR results for ECoV is over 90%, making fecal PCR the diagnostic tool of choice.

Infected horses can shed ECoV up to 14 days. Due to the fecal-oral transmission route and the highly infectious nature of ECoV, common-sense biosecurity protocols should be instituted during an outbreak of ECoV. ECoV PCR positive horses (clinical or subclinical) should always be isolated from the rest of the equine population to decrease the exposure risk and environmental contamination. Potentially exposed horses should not be moved until their definitive infection status has been determined. For isolation purposes, use an empty barn or an isolation unit. In a barn situation, close one end of the barn and use it as isolation area. Caretakers and owners should wear gloves, protective clothing (coveralls or disposable gowns), and dedicated footwear.

Good hand hygiene should be instituted (faucet with warm/cold water or hand sanitizer).

Barrier nursing techniques should be established in the form of footbath or mats in front of the isolation unit and each stall. This will minimize the spread of pathogens from stalls to clean areas. It is very important to control traffic and minimize contact of affected horses with the general public. Hygiene should be maximized by regular cleaning and disinfecting.

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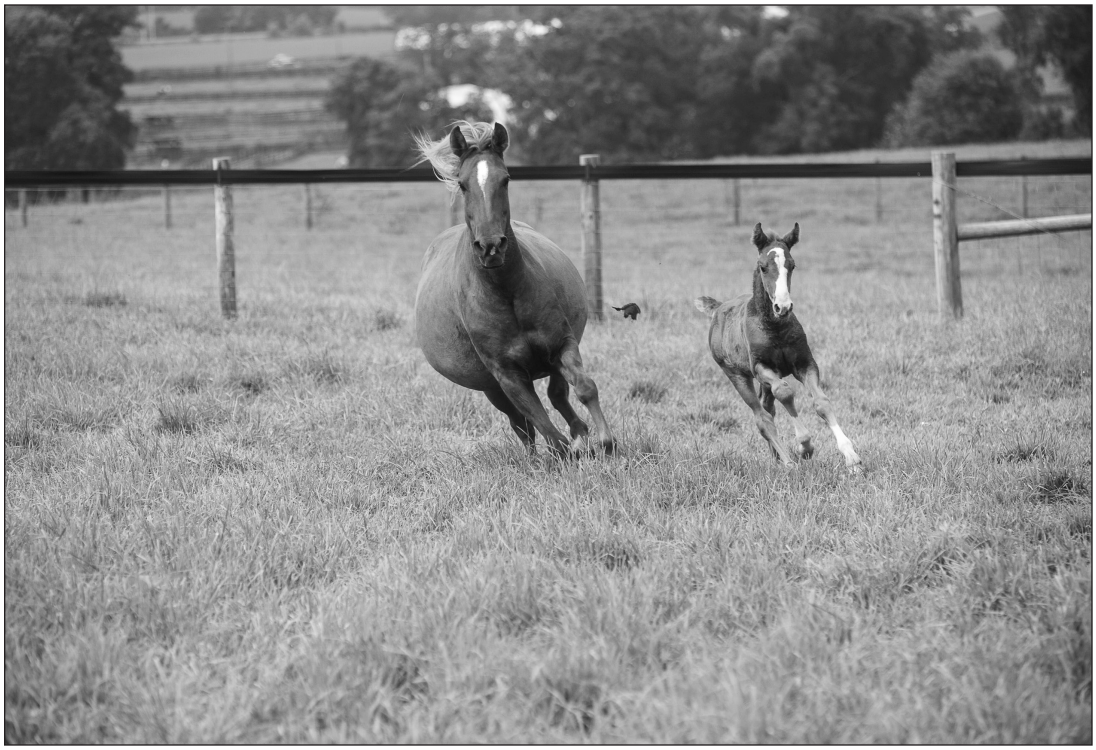
Screwworm Myiasis

Myiasis is the infestation of vertebrate animals by larvae (maggots) of any species of fly. Some fly species are specialized to use amphibian, reptilian, or avian hosts, but most usually infest mammals. In horses, the typical and most widespread of such parasites are species of internal bot flies (*Gasterophilus* spp.), but many other maggots (e.g. blow flies and/or flesh flies) may facultatively infest equines externally. Although none of these typically poses a serious threat to hosts, screwworms are a separate and often dire exception. Unlike the others, the New World screwworm, *Cochliomyia hominivorax*, is a specialized native blow fly and obligate parasite whose maggots voraciously feed only on living tissues of warm-blooded animals. It once occupied most of the Neotropical Region, including South Texas and South Florida, where it was historically the scourge of both wildlife and livestock. From its winter refuges, it spread variably northwards each summer and injured or killed thousands of victims yearly, causing substantial economic losses to animal agriculture. In the mid-1900s, USDA scientists conceived and began field-testing an innovative method aimed at eradicating screwworms as pests. The so-called sterile insect technique (SIT) involved mass-rearing millions of adult flies in captivity, sterilizing them by exposure to radiation, and over-flooding wild screwworm populations with sterile insects to the point that most local, field-mated wild females produced inviable eggs. Within several generations of such pressure, local populations died out, and progressively screwworms were extirpated, first from the USA and eventually down to Panama by 2000. Screwworms persist on a handful of Caribbean islands and in northern South America, but they are prevented from dispersing and re-infesting North America by continuous releases of sterile flies in an eastern Panamanian barrier zone. The last locally infested animal in the U.S. was seen in 1982 in Texas, and since then, dozens of screwworm incursions have been detected and dealt with on animals and humans entering the country from still-infested areas. Many of these cases involved race horses or polo ponies entering from South America, with screwworms detected in quarantine facilities. Currently, however, an active invasive population of screwworms has taken up residence in the Florida Keys. How these flies entered the country and from where is still a mystery, but the infestation is of particular concern because most of the known infested hosts have been endangered Florida Key deer on the National Key Deer Refuge. As of this writing, screwworms have killed approximately 10% of the Key deer herd, along with several local pet pigs, cats, and dogs. Since the infestation was first discovered at the end of September 2016,



Photos by Matt Barton, University of Kentucky

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personnel in a state/federal task force have instituted several strategies to contain and eliminate screwworms from the Keys, including monitoring and surveillance of fly and maggot activities to delimit the infested area, veterinary inspections of all animals leaving the Keys, preventative and curative treatments of animal hosts, and most importantly, local application of the SIT through release of over 25 million sterile flies flown in from Panama. Judicious continuation of these practices into early 2017 is expected to prevent the spread of screwworms, extirpate them, and once again, make the USA screwworm free.

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So, how can we facilitate further progress in addressing equine lameness challenges? A very important part of the answer is quality scientific research to advance knowledge. At the University of Kentucky, we have established the Equestrian Sports Research Initiative to enable multidisciplinary research teams to work together collaboratively with industry groups, clinical veterinarians, and horse professionals. Health and welfare issues in equine sports medicine are being studied from basic to clinical levels by considering horse, rider, and surface issues concurrently. As noted above, scientific and technological advances are driving progress in biomedical disciplines. Objective scientific research and the resulting new knowledge are absolutely key, and need to be a top priority.

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