UF UNIVERSITY of FLORIDA
Large Animal Hospital

The Equine Ledger

SPRING 2011 NEWS FOR HORSE OWNERS FROM THE UF COLLEGE OF VETERINARY MEDICINE ISSUE TWO

Find us on Facebook and "Like" the UF Large Animal Hospital!

Welcome to The Equine Ledger

Welcome to our second edition of the Equine Ledger! This brief newsletter is from the UF Equine Veterinary Extension Service, and will provide you with helpful information about equine health care and upcoming educational events at our college. In this issue, we have included information about a couple of our new clinical faculty, and a featured piece about EPM from our own Dr. Rob MacKay.

We also want to announce our 4th Annual Healthy Horses Conference on Saturday, April 9, 2011! Healthy Horses is an educational day with a focus on successful equine health care. The day includes lectures, lunch and live equine demonstrations. This year's topics are compiled from previous requests and will include poisonous plants for horses, lameness evaluation, colic, hoof care, non-sweaters, supplements, and emerging infectious diseases– just to name a few. We will also feature tours, a high speed treadmill demonstration, and a reproduction demonstration with pregnancy ultrasounds! The presenters will predominantly be the board certified faculty of UF's Large Animal Hospital, and a brief summary folder of the lectures will be provided to all attendees. We hope to have some of the same fantastic sponsors as last year's event, with door prizes as well! The University of Florida is dedicated to improving owner education and hope you will make this an annual event. It is a wonderful opportunity to see our hospital facility and meet veterinarians from all of our services. Plenty of time for questions will be provided. Registration is limited and can be completed online at http://conferences.dce.ufl.edu/equine, so please register soon! Please be sure to also visit our other website for additional equine event information at www.vetmed.ufl.edu/extension/equine . We hope to see you in April!

Save the Date!
Healthy Horses Conference
April 9, 2011
8:00 am - 4:30 pm
UF Veterinary Hospitals
Open House
April 16, 2011

We hope to see you at an upcoming event soon. And remember, we're here when you need us!

Sincerely,

Amanda M. House, DVM, DACVIM (Large Animal)
Assistant Professor, Large Animal Clinical Sciences

UF UNIVERSITY of FLORIDA
Large Animal Hospital

Interested in more information?
The UF Large Animal Hospital offers comprehensive diagnostic and treatment services to horses, cattle, alpacas, llamas, pigs, goats and many other large farm or food animals. Contact us at: (352) 392-2229

EPM: Pathogenesis, treatment and prevention

By Rob MacKay, DVM, PhD, DACVIM
University of Florida

Equine protozoal myeloencephalitis (EPM) is a common neurological disease of horses in the Americas. Horses with EPM most commonly have abnormalities of gait but also may present with signs of brain disease. The disease ranges in severity from mild lameness to sudden recumbency and clinical signs usually are progressive. A causative agent, Sarcocystis neurona, has been isolated from affected horses and serologic surveys suggest that up to 50% of horses in the US have been infected with this agent. EPM is considered a treatable disease although the response often is incomplete.

HISTORY AND DISTRIBUTION:

The disease was first recognized in the US in 1964 (reported in 1970), and possibly earlier in Brazil. Since 1970, EPM has been reported in horses from most of the contiguous 48 states, Panama, Canada and Brazil, and there have been unpublished reports of the occurrence of the disease in Venezuela, Argentina, and Mexico. The majority of affected horses are 1-5 years old, but older horses commonly also are affected. Although EPM has allegedly been confirmed in a 2-month-old, the disease is almost unknown in suckling foals. Prevalence of EPM by breed and gender is close to that in the general horse population; however, Standardbreds and males were over-represented in two published surveys. EPM also has been reported in a pony.

CAUSATIVE AGENT(S):

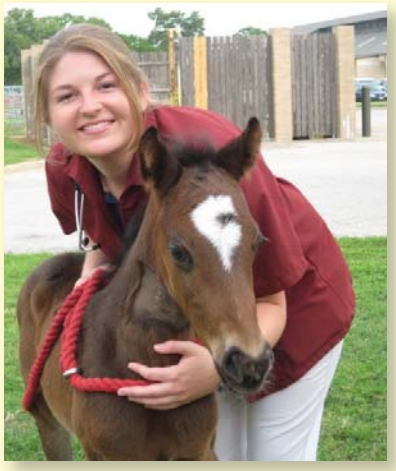
Protozoa may be found in any part of the CNS, usually in association with mixed inflammatory cellular response and neuronal destruction. Schizonts (a proliferating form of the organism), in various stages of maturation, or free merozoites are seen commonly in the cytoplasm of neurons or mononuclear phagocytes and rarely in other inflammatory or CNS cells. The parasite is in the order Apicomplexa, which includes the family Sarcocystidae. In 1991, protozoa from the spinal cord of a horse from New York state were isolated in continuous culture in a bovine monocyte cell line and named S. neurona. Since then, many additional isolates have been obtained in monocyte or endothelial cell culture from horses throughout the country (including UF). A few cases of EPM in the Americas have been associated with Neospora hughesi. Serologic surveys of horses have suggested an exposure rate to Neospora spp. of 10-25%.

LIFE CYCLE:

Species of Sarcocystis have an obligatory prey-predator two-host life cycle. The genus is named for the terminal developmental stage (sarcocyst) found in the intermediate host. The sarcocyst is the only developmental stage that is infectious for the definitive host. Because S. neurona sarcocysts have been found in only one horse (a foal), it is assumed that the horse is usually an aberrant dead-end host. Ingestion of sarcocysts by the appropriate flesh-eating (i.e., predator or scavenger) definitive host results in invasion of the small intestinal epithelium and sexual proliferation and differentiation to produce oocysts. The oocysts of Sarcocystis each contain two sporocysts which usually are released from thin-walled oocysts before they are passed with feces. Sporocysts are immediately infectious for the intermediate host. They are quite persistent in the environment and may survive for months, even during extremes of heat and cold. Intermediate hosts are infected by ingestion of contaminated feed or water.

Introducing...

Dr. Sarah Reuss



Dr. Reuss grew up in Chester County, Pennsylvania riding hunters and jumpers. She received her undergraduate degree from Pennsylvania State University, and then her veterinary degree from University of Pennsylvania School of Veterinary Medicine. After graduation, Dr. Reuss moved to Ocala where she did a 1-year rotating internship at the Equine Medical Center of Ocala. She then completed a residency in Large Animal Internal Medicine at Texas A&M University before beginning a stint in equine ambulatory practice at McKinlay and Peters Equine Service near Spokane, WA. Dr. Reuss officially joined the faculty of Large Animal Medicine on September 29, 2010. Her clinical interests include all aspects of internal medicine, but especially neonatology and critical care.§

Opossums (Didelphis virginiana in the US) has been identified as the definitive host. Several intermediate hosts including the 9-banded armadillo (Dasypus novemcinctus), the striped skunk (Mephitis mephitis), and the raccoon (Prylon locor) have been identified. Their combined geographic range covers the area where EPM occurs. The domestic cat also can support the life cycle in a laboratory setting but it seems unlikely (fortunately) that are important hosts in nature. Several other hosts of dubious significance, including the Pacific Harbor seal, the California sea otter, and farmed mink, have also been identified. The hosts for N. hughesi are not known.

DIAGNOSIS AND EPIDEMIOLOGY:

Definitive ante-mortem diagnosis of EPM is not possible. Proof of diagnosis post-mortem is demonstration of protozoa in CNS lesions, often done with immunohistochemical staining. The diagnosis frequently is made presumptively even when the organism is not seen if characteristic inflammatory changes are found.

(1) Antibody tests.

a. The Western Blot assay for S. neurona antibody is the most established diagnostic test for EPM. Serums are tested for reactivity with specific bands in transferred SDS-electrophoretograms of S neurona lysate. Recognition of these bands is taken as indication of previous or current exposure to S neurona. Results are reported as positive, weak positive, non-specific, or negative. Large serologic surveys from many states generally have shown overall seropositive rates of 25 - 65% of horses tested. Reportedly, no neonatal presuckle serum has tested positive by Western Blot; however, foals frequently become seropositive after ingestion of colostrum. Once horses seroconvert, they probably remain seropositive for months to years. Sensitivity is high (>90%) but specificity is low. On the basis of these results, a negative serum test is useful to help rule out EPM (i.e., false-negative results are uncommon) but has little value in confirming the disease (false-positive results are very common).

Compared to the serum test, Western Blot testing of undiluted CSF has somewhat better specificity for EPM although there remains a problem with false-positive results. An important cause for false-positive Western Blot results in CSF samples is contamination by serum S. neurona antibody. Serum proteins may enter CSF (1) as a result of disruption of the blood-CNS barrier (e.g., West Nile encephalomyelitis, trauma); (2) more commonly, by accidental blood contamination during CSF collection, or; (3) by "leakage" of antibody across normal blood-CNS barrier in horses with high serum titer of S. neurona IgG. It has been shown that very low level contamination of CSF with blood (equivalent to 10 RBC/μl) can turn a sample positive. Any sample that has RBC count >100/μl therefore should not be submitted. Two relatively crude measures of blood contamination are the albumin quotient and IgG index. An albumin quotient >2.2 or IgG index >0.3 indicates that there is serum protein in the sample. Clearly, when the S. neurona antibody titer in plasma is high, some false-positive results will still result from blood contamination during collection. Notwithstanding the problems outlined above, the CSF Western Blot, when used in horses that do have abnormal neurologic signs is a useful diagnostic test for EPM.

A useful additional test routinely performed by one of the commercial laboratories is the Relative Quantity CSF (RQC). This tests quantifies the amount of CSF antibody directed against an important antigen on S. neurona. Values <5 suggest low-level or doubtful infection of the CNS, whereas values >5 (5-100) are likely true positives. The RQC also can be used as a treatment guide (see below).

b. Immunofluorescent antibody test. An IFAT test for use with serum and CSF samples recently has been developed at the University of California, Davis, that shows good sensitivity and specificity when tested against a small panel of "gold standard" negatives and positives. This test is still being evaluated in the field but shows some promise. One interesting claim is that CSF testing results are unaffected by blood contamination.

(2) Polymerase Chain Reaction (PCR). Experience with the test indicates that, when used alone as a test for EPM, it has low sensitivity and high specificity (close to 100%). In the last 5 years, this test has fallen into disuse because of technical concerns about the way the test is run. Of the 3 laboratories that offer western blots (EBI and Neogen in Lexington, KY, and Michigan State University), only EBI currently offers the test.

ANCILLARY AIDS TO DIAGNOSIS:

There are abnormalities upon CSF analysis in some horses with EPM. It has been reported that as many as 35% of horses at a referral hospital have increased protein concentration (>65 mg/dl) or nucleated cell count (>7 cells/μl). My experience is that, among horses with mild clinical signs of EPM (i.e., those that typically are encountered in practice), a very low percentage have any abnormality on routine analysis. Creatine kinase (CK) activity may be high in CSF, reflecting diffusion of BB isoenzyme from damaged CNS gray matter. Unfortunately, inadvertent inclusion of a small plug of epidural fat or dura during CSF collection can dramatically elevate CK activity, thus reducing the specificity of the test.

CLINICAL SIGNS:

Because protozoa may infect

Introducing...

Dr. Audrey Kelleman

Dr. Kelleman, a native of Florida, received her undergraduate degree from Cornell University and her veterinary degree from the University of Florida in 1995. She completed her Theriogenology (animal reproduction) residency at UF in 2000 and is a Diplomate of the American College of Theriogenology. Dr. Kelleman has worked in various parts of the country and most recently hails from the University of Pennsylvania, New Bolton Center. Her professional interests are general clinical reproduction in a variety of species, including equine, camelid, and small ruminants, in addition to equine embryo transfer, semen freezing and specialty processing. Dr. Kelleman is also available on an ambulatory basis, for reproductive consultations. Please call Dr. Kelleman or the section of reproduction technician at the UF Large Animal Hospital to discuss your needs. §

EPM (cont'd)

any part of the CNS, almost any neurologic sign is possible. The disease usually begins insidiously but also may present acutely and be severe at onset. Signs of spinal cord involvement are seen more commonly than signs of brain disease.

Horses with EPM involving the spinal cord have asymmetric or symmetric truncal and limb weakness and ataxia. If all lesions are behind the second thoracic spinal cord segment (T2), only the hindlimbs are affected. If a lesion (or lesions) is located in front of T3, all four limbs may be affected. When the spinal cord behind the second sacral spinal cord segment (S2) is involved, there are signs of cauda equina syndrome, which may include degrees of rectal, anal, bladder, and penile paralysis and hypalgesia of the skin of the tail and perineum. If gray matter is damaged for more than 1-2 weeks, there may be obvious skeletal muscle atrophy (usually asymmetric) and electromyographic evidence of denervation. Common locations for atrophy in horses with EPM are gluteals, biceps femoris, infraspinatus/supraspinatus and serratus ventralis. EPM lesions in the spinal cord also may result in demarcated areas of spontaneous sweating or loss of reflexes and cutaneous sensation.

Signs noticed at the walk or during neurologic exam include any to all of the following: pelvic sway, asymmetric stride length, toe-dragging, circumduction of hindlimbs, and hypometria (also described as "floating" or "marching") of forelimbs. Other signs may only be noted during breaking and/or training. There may be frequent bucking, head-tossing, excessively high head carriage, difficulty maintaining a specific lead, and difficulty negotiating turns. Some signs which usually are attributed to primary musculoskeletal disease, such as back soreness or upward fixation of the patella(s) can be caused by weak or asymmetric use of muscle groups in horses with EPM that are in training.

The most common manifestation of brain disease in horses with EPM is a brainstem syndrome with obtundation and asymmetric vestibular (VIII) nerve dysfunction. There may also be facial paralysis (VII), dysphagia (IX, X), tongue paralysis (XII), laryngeal paralysis (X), strabismus (III, IV, VI), corneal areflexia (VI) and weak jaw tone (V). With involvement of the rostral brainstem and/or cerebrum, EPM may manifest as seizures, visual deficit/abnormal menace response, and behavioral abnormality.

Without treatment, EPM usually progresses. Progression to recumbency occurs over hours to years and may occur steadily or in a stop-start manner.

TREATMENT:

The conventional protocols for antiprotozoal therapy involve a combination of sulfonamide (usually sulfadiazine or sulfamethoxazole) and pyrimethamine given orally. These agents act synergistically to inhibit protozoal folate synthesis. Because pyrimethamine also has slight inhibitory activity for mammalian dihydrofolate reductase, there is potential for inhibition of hematopoiesis and other toxic side-effects in treated horses. An affordable FDA-approved sulfadiazine/pyrimethamine suspension (ReBalanceTM; Phoenix Scientific, St. Louis, MO) became available early this decade but has now apparently been withdrawn from the market. Compounded suspensions and pastes are offered by numerous compounding pharmacies (e.g., from Franck's Pharmacy in Ocala) usually at highly discounted rates. A single oral dose is given once daily by syringe. Because feeding, especially of alfalfa hay, has been shown to reduce absorption of pyrimethamine (or trimethoprim) by up to 50%, it is suggested that treatment is given at least an hour after and before hay is fed. Currently, it is recommended that horses with EPM are treated with sulfonamide/pyrimethamine for at least 6 months. An anti-coccidial of the triazineone family, ponazuril (Marquis®) was the first drug to win FDA approval for use in EPM. The drug is given as a dial-by-weight paste at 5 mg/kg for 28 days.

In November 2003, the 5-nitrothiazole drug, nitazoxanide (Navigator®) also was approved by the FDA but was withdrawn from the market in 2008.

Approximately 55-70% of horses improve with any of the 3 regimens, and 10-20% can be considered complete recoveries. If treatment is discontinued at that point, relapses may occur over the next several years in at least 10% of treated horses. Treatment of horses that relapse usually is less successful than treatment of initial disease.

Mild to moderate anemia (PCV 20%) is occasionally seen in horses given SDZ/PYR for 6 months. Anemia resolves within several weeks after drugs are discontinued. Rarely, neutropenia and thrombocytopenia also have been observed in treated horses. There have been isolated instances of abortions and neonatal disorders after treatment of pregnant mares, although a causal relation has not been established. Despite a theoretical concern about the fertility of stallions treated with EPM, no adverse effect has been documented. In human beings, folinic acid (5-formyl-THF), a form of bioactive tetrahydrofolate, is given to prevent or treat toxic effects of pyrimethamine. Preformed folate cannot be used by protozoa, so this practice has no effect on antimicrobial efficacy. Folic acid (the substrate of DHFR) is sometimes given to horses in an effort to prevent toxicity but on theoretical grounds probably has no positive effect and may actually be deleterious. Of far greater value is the provision of good quality folate-rich pasture or alfalfa hay. If the PCV drops below 20% or there is severe neutropenia or thrombocytopenia, antimicrobial treatment may be discontinued for 1-2 weeks until hematologic values return to an acceptable range.

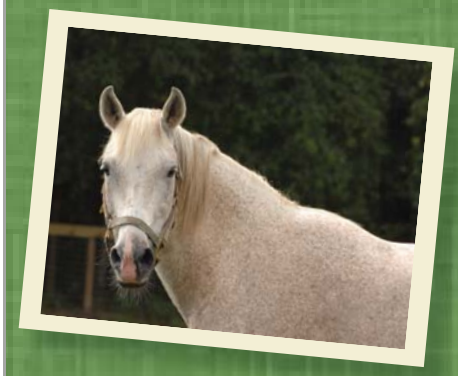
If signs are severe or rapidly progressive, anti-inflammatory/anti-oxidant therapy should be used for several days during the initial period of antimicrobial therapy or during any period of exacerbation. A reasonable protocol is flunixin meglumine (1.1 mg/kg IV), and DMSO (1 g/kg as a 10% solution given rapidly IV) twice daily for 3 days followed by flunixin once daily for 4 days. When signs of brain disease are severe or the horse is in danger of becoming recumbent at onset of therapy, a single dose of corticosteroid (e.g., dexamethasone, 0.05-0.1 mg/kg) is sometimes used. In an effort to minimize inflammatory damage and promote healing in the CNS, the antioxidant environment can be maintained throughout the treatment period by oral vitamin E supplementation (10-20 IU/kg/d). Vitamin E can easily be obtained in 1000 IU capsules which can be opened and mixed with feed. It apparently is not absorbed well in the absence of concurrent feeding.

Signs of toxicity are very rare with ponazuril treatment; however, severe colitis, fevers, and depression have been seen in horses treated with nitazoxanide. It is widely assumed that these signs occur secondary to clostridial overgrowth in the large intestine.

Some clinicians attempt to boost non-specific cell-mediated immunity by use of immunostimulants such as killed Propionibacterium acne (Eqstim), killed parapox ovis virus (Zylexis), mycobacterial cell wall extract (Equimune IV), levamisole, or alpha interferon. In persistent protozoal diseases of human beings, such as leishmaniasis, the efficacy of such approaches is established.

PREVENTION:

It is presumed that horses ingest infective opossum sporocysts with feed or water. Opossums are omnivores, and are attracted to grains, moist or dry cat or dog food, fruit or garbage. Therefore, horse feed and pet food should not be left out and open feed bags and garbage should be kept in closed galvanized metal containers, bird-feeders should be eliminated,



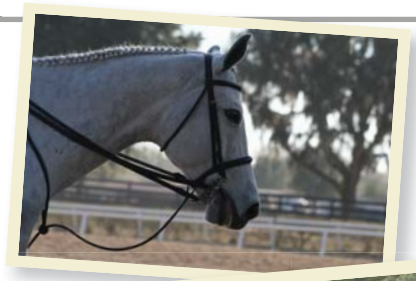
and fallen fruit should be removed. Opossums can be trapped and relocated or scared off by a patrolling big black dog. Less practically, paddocks can be opossum-proofed by placing a partially buried 2-in × 4-in-mesh fence and electric wire on the outside of existing horse fence. It is probable that sporocysts are distributed from the point of deposition by birds and/or insects, so it may be prudent to control populations of these potential vectors, at least within horse barns. Steam cleaning has been shown to kill sporocysts, so feed and water containers could be cleaned

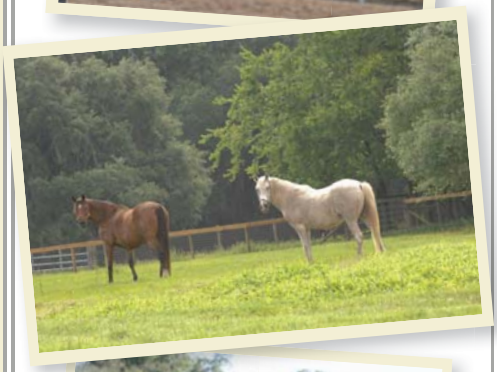
Calendar of Events

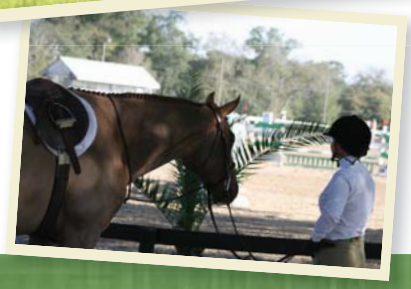
Healthy Horses Conference
April 9, 2011

UF Veterinary Hospitals
Open House
April 16, 2011

Referring Veterinarian
Appreciation Day
Conference
June 25, 2011







by this technique. An issue which hasn't been addressed is the possibility of contamination of commercially prepared feeds with S. neurona sporocysts. Because they have been heated (60 - 166 C) during preparation, "hot-processed" feeds (e.g., steam flaked, pelleted, or extruded feeds) are unlikely to harbor viable sporocysts. Because intermediate hosts do not directly infect horses, control of intermediate host populations is unlikely to be effective.

An EPM vaccine was sold under limited license by Fort Dodge Animal Health. The notably simplistic approach to vaccine development, i.e., use of killed cultured whole organisms, was criticized and the vaccine was withdrawn in 2007. §

Healthy Horses Conference Topics

- The Equine Lameness Evaluation
- Is my horse fat or does it have Metabolic Syndrome/Cushings?
- Emerging Infectious Diseases: My horse has Salmonella?
- Hoof Care
- Poisonous Plants
- Help! My horse doesn't sweat!
- Evaluating Supplements
- Live High Speed Treadmill Demonstrations
- Equine Reproduction/Pregnancy Ultrasound Demonstrations

Resources for YOU!

The Large Animal Hospital at the University of Florida is open for emergency patients 24 hours a day, 7 days a week. Please call (352) 392-2229 if you have an emergency.

A patient can be referred by the primary care veterinarian or the owner can call the hospital directly. It is critical that arrangements be made with the clinicians on-call prior to arriving at the hospital if at all possible.

All emergencies are received at our main hospital (see map). Once you arrive the patient will be stabilized and evaluated. You will then be provided with an initial medical treatment plan and will be required to leave a deposit equal to 50% of the high end of the estimate range. You and your primary care veterinarian will be updated daily and upon any changes in the patient's condition.
After 5pm Monday-Friday, on weekends, and on holidays our answering service will receive your call and connect you to the appropriate doctor based on the information provided about the medical condition of the patient.

Hours of Operation
Monday to Friday
8 a.m. to 5 p.m.

Emergencies on Saturday, Sundays and Holidays

University of Florida Large Animal Hospital
2015 SW 16th Ave.
Gainesville, FL 32610
Phone: (352) 392-2229
FAX: (352) 846-0207

Visit us at:
http://www.vetmed.ufl.edu/veterinaryhospitals/large-animal-hospital/emergencies/