Equine Proliferative Enteropathy in Horses Primarily Affects Foals

E quine proliferative enteropathy (EPE) is an emerging intestinal disease in horses that primarily affects weanling foals 4 to 7 months of age. It was first reported in horses in 1982, and since 1996 many more reports of sporadic cases in the United States, Canada, Europe, South Africa, South America and Australia have been described. The disease can cause a variety of nonspecific clinical signs, including decreased appetite, depression, weight loss, diarrhea, fever, edema and poor body condition.

EPE is caused by a bacterial pathogen, *Lawsonia intracellularis*, that affects a wide range of animals including pigs, hamsters, rabbits, fox, deer, ferrets, ostriches and nonhuman primates. The organism invades the intestinal epithelial cells and results in hyperplasia—an abnormal increase in the number of cells within the organ, which causes the organ to become enlarged. While a wide range of host species can be infected by this pathogen, the clinical features among the hosts appear to be very similar.

In the last few years, reported cases of EPE have been increasing, primarily in post-weaning foals and occasionally in adult horses. At UC Davis, the Veterinary Medical Teaching Hospital (VMTH) has seen an increased number of weanling foals with EPE. A recent case was a 7-month-old Spanish breed filly who was brought to the hospital with weight loss, poor body condition and a noticeable swelling around her abdomen.

According to the horse’s owner, the filly had been eating and drinking well and had been in good body condition until the previous week, when the owner had noticed the severe weight loss and lack of appetite. The day before coming to the VMTH, the filly had spiked a fever of 102.2°F.
Onward Into 21st Century Communication

Old dogs may not be able to learn new tricks, but old horses can. Likewise, this old horse doctor and his stable of equine publications. In the age of global communications with Internet, smart phones, iPads and the like, print is rapidly becoming passé. Many news and public information organizations are moving from their traditional formats toward electronic communication.

So, too, will the Center for Equine Health. Starting in July of this year, our Horse Report and other educational publications will be going online. A new full-color, interactive format will allow us to enhance our publications to better inform our readers on the latest in equine health.

Our gradual change from print to Web-based publication will take place between July 2010 and June 30, 2011. During that period, we will provide you with both print and Web versions of our educational materials. This will give those of you in my generation time to make the mental adjustment and obtain the necessary training from your teenage friends that will allow you to fully enjoy the new products. Beginning in July 2011, the CEH will cease production of its traditional printed Horse Report format.

So what do you need to do to get on board this new train? The first thing to do is to send your e-mail address to ljchristison@ucdavis.edu, indicating that you would like to be notified by e-mail whenever a new CEH publication is posted on the Web.

The second thing to do is be sure your computer is up to date and able to handle high-content graphic and video materials. The third is to hire that teenager I mentioned before to get you up to snuff on your computer skills. Who knows, you might even start tweeting before long.

One final word, we realize that for some few of you this move away from the printed page may create a hardship. And we don’t want to lose any of you who are interested in our work. Consequently, if you write, e-mail or call and let us know that you would like to continue to receive a printed copy, we can arrange to send you a color photocopy of our publications. Remember to ask nicely and perhaps send a few cookies to the Director. It will help ensure your request.

For the rest of you, we look forward to this latest step in our efforts to continually improve the services we provide the horse industry and its individual participants.
From the Editor . . .

The mission of the Center for Equine Health at UC Davis has not changed in over 37 years: we are here to improve the health care of horses. We do this by supporting research into the causes and treatment of equine diseases and fostering the education of future generations of equine veterinarians through grants and hands-on learning opportunities.

Perhaps equally important, the Center for Equine Health has had a long-standing commitment to providing the most current science-based information to horse enthusiasts and the veterinary profession in a timely and understandable manner. Over the years, we have published an array of educational materials, from a quarterly newsletter to research reports and special-issue publications that clarify complex topics.

The Horse Report was created in 1973 as a simple black and white newsletter and was renovated in 2004 to become a full-color larger publication. This year, we will turn the wheel again in the history of The Horse Report as we move to become an online publication. For the remainder of 2010 and through the end of June 2011, we will offer both an online version and a printed version of The Horse Report. Beginning in July 2011, we will offer only the online version.

The most obvious reason for this change is that the Center for Equine Health, along with most other individuals, schools and organizations in the country, has not escaped the economic downturn, so that printing and mailing thousands of copies of our publications are no longer practical.

Rather than look at this as an end though, we are embracing this as a new challenge that holds new possibilities. We subscribe to the philosophy that the Web is not just a paperless publishing medium, but a totally new way of sharing knowledge. Though we anticipate experiencing a learning curve, we hope to take advantage of the Web’s three-dimensional capacity to introduce audiovisual elements in the future.

For our valued readers who do not or cannot embrace this change, call or write us and request a paper publication (see Director’s Message). We will make every effort to ensure that you receive one.

However, we hope most of you will welcome this change. If you would like to be notified of a new online publication, send your e-mail address to ljchristison@ucdavis.edu. You can do this through your regular e-mail or through our website under Contact.

They say that time changes things, but you actually have to change them yourself. —Andy Warhol

Equine Proliferative Enteropathy —Continued from page 1

On presentation at UC Davis, the filly was subdued with a normal heart and respiratory rate and rectal temperature. She weighed 268 kg and was considered thin based on a low body condition score (3/9). Her heart and lungs were clear and she had good gastrointestinal motility. However, a large area of abdominal swelling was visible along the entire thorax (between the neck and abdomen). Additional swelling was noticed in the throatlatch and intermandibular (jaw) space. Overall, the filly appeared to be suffering from muscle wastage.

Blood analysis revealed low total protein and serum albumin levels, as well as a severely elevated white blood cell count (29,280/µl; reference range is 5,000-11,600/µl). An abdominal ultrasound examination was performed and feces were collected and submitted for testing for Salmonella sp., Clostridium difficile and Lawsonia intracellularis. In addition, blood was collected to test for antibodies specific to Lawsonia intracellularis.

The abdominal ultrasound examination showed thickening of the small and large intestinal wall. Fecal analysis revealed small numbers of strongyle ova. The feces tested negative for Salmonella sp. and Clostridium difficile. However, Lawsonia intracellularis was detected by molecular analysis (PCR). The serology results came back strongly positive a few days later, confirming an infection with Lawsonia intracellularis.

Hospital veterinarians provided supportive treatment via intravenous fluid, plasma and oxytetracycline —Continued on page 4
Equine Proliferative Enteropathy —Continued from page 3

to treat the *Lawsonia* infection. The filly also received omeprazole to prevent the development of gastric ulcers. Over the next few days, the foal regained her alertness as well as an appetite. After 4 days, she was discharged with an oral antibiotic to be continued at home for an additional 14 days. The owner was instructed to feed the filly a good quality hay and to continue to give her the grain supplement. We also recommended that the filly be dewormed when the antimicrobial treatment was completed.

The filly has been doing well at home and her appetite and attitude have continued to improve. A follow-up examination after one month revealed that her blood work had almost normalized except for a mildly decreased serum albumin concentration (2.6 g/dl). The filly continues to do well today.

While this case had a good outcome, animals with EPE often are not presented until the clinical signs are advanced and treatment is less effective. In weanling foals, these effects can progress rather rapidly. In addition, diagnosis of EPE can be challenging because the clinical signs are vague and there are not as yet any definitive diagnostic assays specific for EPE.

**Summary of Clinical Signs**

EPE is usually manifested in foals between 2 and 8 months of age and in North America is often seen between the months of August and January. Lethargy, lack of appetite, fever, peripheral edema (abdomen, sheath, throatlatch and distal limbs), weight loss, colic and diarrhea are among the most common clinical findings. Although diarrhea is commonly seen in affected foals and can vary from cow pie to watery, some foals may have normal fecal character.

Foals with EPE may also have concurrent health problems such as respiratory tract infections, gastric ulcerations and intestinal parasites. The clinical signs of EPE may resemble those of more common gastrointestinal disorders such as parasitism, bacterial infections (*Clostridium difficile*, *Salmonella* sp., *Rhodococcus equi*), rotavirus, coronavirus, ulcerations, sand accumulation.
and intestinal obstruction. As with pigs, EPE is often subclinical in foals—that is, it does not produce the clinical signs either because infection is in the early stages or because it is a mild case. It is unknown whether subclinical infection is associated with growth retardation or unthriftness.

**Diagnostic Evaluation**

A definitive diagnosis of EPE can be challenging and relies on a combination of several factors:

- The presence of low total blood protein levels (hypoproteinemia)
- Exclusion of common intestinal diseases
- Thickening of segments of the small intestinal wall as seen through abdominal ultrasonography
- Serum antibody testing
- Molecular (PCR) detection of *Lawsonia intracellularis* in feces

The most consistent laboratory finding has been a decrease in the levels of total blood protein and albumin. Total protein is generally less than 5.0 g/dl (normal reference range 5.8–7.7 g/dl) and albumin is usually less than 2.0 g/dl (normal reference range 2.7–4.2 g/dl). In a recent case reported in the scientific literature, low levels of albumin were the only consistent abnormalities of 57 affected foals. Affected foals may also demonstrate nonspecific blood abnormalities such as anemia or hemoconcentration.

Although abdominal ultrasonography is not very sensitive, it may show segments of thickened small intestine and excessive abdominal fluid. In these cases, abdominocentesis (a sampling of abdominal fluid) will yield a noninflammatory fluid.

Several molecular assays have been developed for detecting *L. intracellularis* in feces. PCR appears to reliably demonstrate *L. intracellularis* in the feces of clinically affected horses early in the course of the disease but often fails to detect the organism in the feces of subclinically infected animals, animals with prolonged course of disease, or foals treated with antimicrobials prior to fecal analysis.

Although no commercially available serologic assay has yet been evaluated for horses, serologic assays have generally proven useful for routine diagnosis of EPE in horses when combined with clinical signs and molecular detection of *L. intracellularis* in the feces.

**Treatment and Prevention**

It is important to treat affected animals early, before lesions (commonly seen in the ileum) become advanced, resulting in marked weight loss and critically low serum protein values (hypoproteinemia). Treatment of horses with EPE involves the use of antimicrobials such as macrolides alone or in combination with rifampin, chloramphenicol, oxytetracycline, or doxycycline administered for 3 weeks.

The choice of antimicrobial in the treatment of EPE should take into account the risk of disturbing gastrointestinal flora or inducing renal toxicity. This is especially a concern when treating older foals with severely depressed levels of serum albumin.

Supportive care such as intravenous fluids, plasma transfusion, parenteral nutrients and anti-ulcer drugs are commonly used to treat affected foals. Concurrent medical conditions should also be addressed. Although it may take weeks for the low serum protein values to resolve, rapid clinical improvement following treatment can be expected.

Prevention strategies have been best described in pigs using in-feed antimicrobials and a commercially available vaccine against *L. intracellularis*. Recent work at UC Davis has shown that a detectable antibody-mediated response was measured in foals that received an avirulent live *L. intracellularis* vaccine. However, the protection offered by this vaccine needs further investigation.
Atrial fibrillation is the most frequently reported heart rhythm abnormality in horses. It involves the two upper chambers (atria) of the heart. Its name comes from the fibrillating or quivering of the heart muscles of the atria, instead of a coordinated contraction. Normally, the heart contracts and pumps blood with a regular rhythm, for example, at a rate of 40 beats per minute in a healthy horse, and there is a beat every second. The heart may beat faster or slower with a shorter or longer interval between beats, but at any one rate the interval between beats is constant. This regular rhythm occurs as a result of regular electrical discharges, or currents, that travel through the heart and cause the muscle of the heart to contract. In atrial fibrillation, the electrical discharges are irregular and rapid and, as a result, the heart beats irregularly.

Most of the blood from the atria passes into the ventricles of the heart through passive filling (i.e., without contraction). The atrial contraction that occurs prior to the ventricles contracting is responsible only for a small percentage of blood entering into the ventricle and subsequently being passed onto the lungs and whole body circulation. Therefore, horses affected with atrial fibrillation may present with a history of poor performance at maximal exertion: during finishing or sprinting in racehorses, galloping or hill work in event horses and hunters. But horses engaged in less aerobically challenging activities, such as dressage or show jumping, may be affected and still compete at international levels. Although horses can compensate for their suboptimal heart filling and decreased cardiac output, they nevertheless attain a higher than normal heart rate at lower exercise intensity and therefore they fatigue sooner.

Before attempting any treatment of atrial fibrillation, a complete pretreatment evaluation should be performed, including an electrocardiogram (ECG), which identifies the irregular heartbeat and confirms that it is atrial fibrillation, and an echocardiogram or ultrasound of the heart to rule out any underlying heart defects as a cause for the arrhythmia. In most cases, atrial fibrillation develops without any underlying structural heart abnormality. If a horse in atrial fibrillation has an underlying structural heart problem, treatment is less successful and may be contraindicated (harmful) to the horse.

Traditionally, treatment has relied on chemical conversion, where an anti-arrhythmic drug is administered. With chemical conversion, the drug used most commonly and with the most success is quinidine sulfate. Horses are equipped with a continual ECG monitor to closely monitor for secondary arrhythmias that may develop during quinidine administration. Quinidine sulfate is administered into the stomach via a nasogastric tube. It should not be given orally because it can cause extensive ulcerations in the mouth and esophagus. Generally, the dosing is repeated every 2 hours for up to a total of 4 to 6 doses and the ECG is monitored to determine whether or not the horse converts. There are many instances where the horse does not convert after receiving 6 doses and, in those cases, conversion treatment must often be stopped since the drug can become toxic and repeated dosing can lead to complications.

When performing cardioversion with quinidine, most horses may become depressed and develop colic, laminitis or other arrhythmias. Rarely, quinidine sulfate administration can also result in Transvenous Electrical Cardioversion in Horses with Atrial Fibrillation

Carrie J. Finno, DVM, DACVIM

Dr. Carrie Finno is a resident in large animal internal medicine at the UC Davis Veterinary Medical Teaching Hospital. She was recently awarded the Louis R. Rowan Fellowship by the California Thoroughbred Foundation. Since 2007, she has been a United States Equestrian Federation (USEF) official veterinarian, performing drug testing at USEF-recognized horse shows.
in sudden death. At UC Davis, we monitor horses continually for any development of potentially life-threatening arrhythmias so that we can immediately administer treatment. We also have the unique ability to measure quinidine concentrations in the blood, which helps us to ensure that quinidine levels are maintained within the therapeutic range and are not approaching toxic levels, at which point quinidine therapy would be discontinued.

In the past 5 years, there has been another alternative treatment designed for converting horses in atrial fibrillation. The treatment is called transvenous electrical cardioversion (TVEC). This technique was established for treating atrial fibrillation in humans, and Dr. Kim McGurrin from the University of Guelph developed a similar technique for use in horses.

TVEC is different from delivering shocks across the chest with defibrillation paddles as is often seen in medical television shows. Transthoracic (across the chest) treatment is challenging in horses because it is difficult to deliver enough energy through the thick body wall of the horse to alter the heart rhythm. Instead, two special electrodes are inserted through catheters placed into the right jugular vein. The electrodes are then advanced carefully into the heart. One catheter goes into the pulmonary artery, which is the vessel that connects the right ventricle to the lungs, and the other is placed into the right atrium. This way, the electrical shock can be delivered directly to the heart and less energy is required than with transthoracic electrical cardioversion.

Correct placement of the catheters is essential to ensure that the shocks will be delivered specifically to the atria and not to the ventricles of the heart. Any inappropriate placement can lead to serious complications, so it is important to take great care to ensure their correct placement.

Placement of the electrodes is the most difficult part of the procedure. We place the electrodes with the horse standing under sedation and confirm their correct location by pressure wave measurements and ultrasound visualization of the electrodes within the pulmonary artery and right atrium. An x-ray is then taken to further confirm this placement.

Once we are sure the electrodes are correctly located, the horse is placed under general anesthesia and another x-ray is taken to be sure the electrodes did not shift while the horse was being induced. After the second confirmation, the electrodes are attached to a defibrillator unit, similar to the ones used in emergency rooms, and the horse is “shocked” at a specific time in the cardiac cycle as seen by an ECG.

The ECG is continuously monitored and we determine if the horse converts from atrial fibrillation to a normal rhythm. If no conversion is apparent, we wait 2 minutes and then try again at a higher energy level. We start at 50 Joules and increase (70, 100, 125, 150, 175, 200, 250, 300) until cardioversion is achieved or until a maximum energy of 300 J is applied.

A Case Study with TVEC

In August 2009, I was contacted by Jody Carlson-Astrom from Los Angeles. Jody had a horse named Massoun that had been diagnosed with atrial fibrillation. Massoun had been successfully treated with quinidine at a local veterinary clinic but had reverted back shortly after treatment. Jody was interested in having TVEC performed on Massoun.

We immediately decided to enlist the help of Dr. McGurrin, the world’s leading expert in this procedure. Dr. McGurrin had graciously helped us with two previous TVEC procedures in 2007. Her willingness to share her expertise and wisdom is matched only by our desire to learn and master the technique. Dr. McGurrin was once again extremely accommodating and excited to visit UC Davis, so the visit was arranged.

Performing TVEC on a horse requires an extensive and knowledgeable team. In addition to Dr. McGurrin and myself, our team included

—Continued on page 8
The Horse Report

Volume 28, Number 1 - March 2010

Dr. Mary Beth Whitcomb of the Large Animal Ultrasound Service, who has been involved in all cases of TVEC at UC Davis. Dr. Whitcomb’s interest in cardiology stems from her fellowship training in large animal ultrasonography and cardiology at the leading institution of equine cardiology in the United States, University of Pennsylvania’s New Bolton Center.

The team was further rounded out with assistance from Dr. Gary Magdesian, Dr. Emily Higgins, Dr. Tiffany Hall, and Dr. Joanie Palmiero of Equine Internal Medicine, the Large Animal Anesthesia Service, the UC Davis Cardiology Service, the Large Animal Radiology Service, and the Equine Internal Medicine technicians. We all worked together to perform the TVEC on Massoun.

Prior to anesthesia, Massoun had a complete pretreatment work-up with the UC Davis Cardiology Service and atrial fibrillation was confirmed without any underlying structural heart abnormalities.

At 9:00 on the morning of the procedure and with the assistance of the Anesthesia Service, Radiology Service, and Dr. Whitcomb’s ultrasound-guidance, the electrodes were placed under standing sedation and Massoun was placed under general anesthesia. Placement of the electrodes was verified by our Radiology Service with an x-ray. Once Massoun was stable under anesthesia, Dr. Whitcomb was responsible for the accurately timed delivery of the shocks. Massoun successfully converted at 100 J and recovered from anesthesia without incident. The entire procedure went smoothly and Massoun was back in his stall by noon. We kept Massoun in the clinic for the next few days and confirmed that he remained in a normal rhythm with an ECG on day 3. Massoun was then transferred to our Center for Equine Health for an additional week and before returning home to Jody in Los Angeles. He has been doing well since that time and has remained in a normal rhythm.

On the same day that Massoun was converted, another horse in atrial fibrillation also was successfully converted with TVEC at UC Davis. This horse has maintained a normal sinus rhythm and has returned to training.

Once successfully converted, horses without underlying heart disease often return to the same level or an improved level of performance and require no additional treatment after...
After being anesthetized, Massoun is placed on the radiology table for another x-ray to confirm that the electrodes had not shifted while the horse was being given general anesthesia. Massoun is now ready for the electrocardioversion procedure.

This x-ray confirms the accurate placement of the first electrode into the left pulmonary artery (white arrows) and the second electrode into the right atrium (black arrows). This x-ray also helps to confirm that the electrodes are not coiled in the heart.

conversion. One of the major advantages of TVEC over chemical conversion is the avoidance of side effects and toxicity related to the drugs. In addition, TVEC has had more success than chemical conversion in horses that have been in atrial fibrillation for a long period of time.

Over the past two years, Dr. McGurrin has graciously made three trips from Canada to help us develop our skills in TVEC at UC Davis. These visits have allowed the team at UC Davis to become comfortable with all aspects of the procedure. I personally would encourage owners of horses with atrial fibrillation to consider this procedure in attempting conversion.

For further information regarding TVEC, please contact Dr. Carrie Finno at the UC Davis Veterinary Medical Teaching Hospital at (530)752-0290. *
Over 280 research scientists, veterinarians and physicians from around the globe attended the inaugural North American Veterinary Regenerative Medicine Conference, held in California’s Santa Ynez Valley March 5-6, 2010.

The meeting was presented by the UC Davis Center for Equine Health; the Alamo Pintado Equine Medical Center; and Rood & Riddle Equine Hospital and included formal presentations by 25 regenerative medicine research experts from throughout the United States and Canada.

In addition to multiple formal presentations, several open-forum roundtable discussions were held between researchers and practicing clinicians, covering a range of topics including Clinical Trial Development, Basic Research and Stem Cell Biology, Regulatory Affairs and In-practice Solutions. The event combined the latest in cutting-edge research with innovative clinical applications, featuring several practitioners discussing substantial benefits of stem cell therapy seen in their animal patients.

Attendees were enthusiastic in their appreciation for both the material presented and the interchange of ideas between scientists and the audience. “The collaborative setting provided by gatherings such as this will facilitate growth in the field of regenerative medicine,” said Dr. Doug Herthel, conference speaker and practicing veterinarian. Dr. John Peroni of the University of Georgia added that “Regenerative medicine has our
industry excited because it holds so much potential for treating conditions that were formerly thought to be untreatable."

The conference, which was moderated by Dr. Gregory Ferraro of the UC Davis Center for Equine Health, included presentations of the research work of Dr. Arnold Caplan of Case Western University, Dr. Dori Borjesson of the UC Davis School of Veterinary Medicine, Dr. Thomas Koch of the University of Guelph, Dr. Alan Nixon from Cornell University and Dr. Dennis Clegg of the University of California, Santa Barbara, among others. Subjects related to the clinical application of veterinary regenerative medicine were made by several practicing clinicians including Dr. Doug Herthel from the Alamo Pintado Equine Medical Center, Dr. Larry Galuppo from UC Davis, and Dr Laurie McDuffie from the University of Price Edward Island.

Many mainstream medical specialists presented the positive effects of regenerative medicine and cell therapy seen in their human patients, holding significant expectations for its role in the advancement of human medicine.

The conference also marked the establishment of the North American Veterinary Regenerative Medicine Association (NAVRMA). The association will be dedicated to advancing the science and clinical application of non-embryo-derived stem cell therapies and regenerative medicine techniques. The group hopes to facilitate scientific investigations with stem cells acquired from fat, bone marrow and umbilical cord sources and to combine that knowledge with other regenerative medicine technologies designed to improve the health care of animals and humans alike.

Membership in NAVRMA is open to all regenerative medicine researchers, stem cell biologists, biomedical engineers, clinicians and health technicians. Interested parties can receive information regarding membership by contacting Dr. Sean Owens at sdowens@ucdavis.edu or Dr. Gregory L. Ferraro at glierraro@ucdavis.edu.
VISIT OUR WEB SITE . . .

If you are accessing The Horse Report from our website and no longer want a paper copy, PLEASE LET US KNOW .... save us the postage; the horses will benefit!

Send an e-mail request to ljchristison@ucdavis.edu

www.vetmed.ucdavis.edu/ceh

The Center for Equine Health is supported with funds provided by the State of California Pari-Mutuel Fund and contributions by private donors.

The University of California does not discriminate in any of its policies, procedures or practices.

The University is an affirmative action/equal opportunity employer. The information you provide will be used for University business and will not be released unless required by law. To review your record, contact Advancement Services, 1480 Drew Avenue, Ste. 130, Davis, CA 95616. A portion of all gifts is used to defray the costs of administering the funds. All gifts are tax-deductible as prescribed by law.