EQUINE DISEASE QUARTERLY

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JANUARY 2014
Volume 23, Number 1

COMMENTARY

IN THIS ISSUE

A concept that has received considerable focus of late is that of One Health. What exactly is One Health? It is the recognition that the health of humans, the health of animals (both domestic and wild), and the environment are all interconnected. The health of humans is affected by that of animals and the condition of the environment, and vice versa. This concept brings physicians, veterinarians, ecologists and other scientists into a multidisciplinary collaboration to monitor diseases and the environment and to study the ways that diseases are transmitted and maintained in the environment. This concept is basically synonymous with the "One Medicine" and "One World" concepts.

While the term "One Health" has recently come into vogue, its importance has been recognized for many years, especially considering zoonotic diseases that can spread between animals and people. Likewise, changes in the environment affect both humans and animals. This includes land and water use and food supplies. The global nature of commerce and the heightened movement of both humans and animals make a combined approach to health essential. The threat of emerging diseases and pandemics that could first manifest in animals means that collaboration among physicians, public and animal health workers, and environmentalists is of critical importance to quickly recognize cross-species risks and implement protective measures. Just as importantly, the potential health impact must be considered in a collaborative manner as conservation and biodiversity programs are implemented.

How does this concept impact horses and the people who interact with them? Horses inhabit an environment that exposes them to people, other horses and domestic animals, wildlife, indoor conditions, and the outdoor environment with pasture, wooded areas, and water sources. The better the job we do in health management and planning in each of these areas, the more positive the effect on the health of our horses. For example, the ecology of wildlife, including rodents, deer, skunks, and opossums, can place horses at risk for several diseases, including Lyme disease, equine protozoal encephalomyelitis, rabies, salmonellosis, and leptospirosis. Several of these diseases also pose a zoonotic risk to people. One quickly can appreciate how environmental management can have a profound effect on the health of horses and consequently people, and how health personnel must be cognizant of these interactions.

Another example that brings the One Health concept into focus in this issue of the Quarterly is the Equine Encephalitis update. West Nile virus transmission involves the interaction of wild birds, mosquitoes, horses, and humans. Bird deaths and encephalitis in horses can signal a risk of West Nile virus infection to people via mosquito vectors. Environmental control of mosquito populations can reduce the risk. The collaborative efforts of health officials in multiple disciplines are necessary to better control diseases of these types.

We must be forward thinking in our approach to health and realize that the subjects we specialize in are not within a vacuum and that an integrated One Health concept is needed to safeguard the health of horses.

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LLOYD'S

INTERNATIONAL

Third Quarter Report 2013*

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

Contagious equine metritis (*Taylorella equigenitalis*) was reported from Germany in one mare and one stallion on separate premises.

Australia, France, Ireland, Sweden, the UK, and the USA reported outbreaks of strangles. Several outbreaks were diagnosed in New South Wales, Australia. France and Ireland confirmed seven outbreaks each, either in Thoroughbreds or Standardbreds. Sweden and the USA reported that strangles was endemic, with several outbreaks diagnosed. Two outbreaks were recorded in the UK, one involving a non-Thoroughbred and the other a gelding with a concurrent infection of equine herpesvirus-1 (EHV-1).

Equine influenza was reported by Germany, Sweden, and the UK. A single case in a Thoroughbred was confirmed in Germany. Outbreaks involving Standardbred trotters and a pony were recorded on separate premises in Sweden, one of which was a racetrack. The UK confirmed at least eight outbreaks of equine influenza in as many counties, the vast majority involving unvaccinated horses. The clinical severity of disease varied significantly among affected horses.

Equine arteritis virus was isolated from the semen of a carrier stallion in France.

Equine herpesvirus-1 and -4 related diseases were reported by France, Germany, Ireland, the UK, and the USA. Equine herpesvirus-1 respiratory disease was confirmed in Germany (one outbreak), the UK (two outbreaks involving donkeys), and the USA (several outbreaks involving a number of states). Ireland reported EHV-1 related abortion in one mare and deaths of two neonatal foals, all Thoroughbreds. Equine herpesvirus-1 neurologic disease was confirmed in France (a single case in a vaccinated Thoroughbred) and the UK (two outbreaks involving several cases in both Thoroughbred and non-Thoroughbred mares). Equine herpesvirus-4 was associated with respiratory disease in France (eight outbreaks), Germany (one outbreak), and the UK (isolated cases on three premises, with one concurrent case of strangles).

Numerous cases of infection with equine herpesvirus-2 were reported by the USA, which also confirmed a single case of equine herpesvirus-5 infection.

Reports of equine piroplasmosis were received from France (endemic), United Arab Emirates (endemic, sporadic clinical cases), and the USA. The USA reported that 231,664 horses had been tested since November 2009, of which 215 were positive either for *Theileria equi* (205) or *Babesia caballi* (10). Any recently discovered cases were in Quarter Horses competing in non-sanctioned racing in Texas.

Outbreaks of salmonellosis were reported by the USA where the disease is considered endemic. Four outbreaks involved untyped *Salmonella* spp; seven additional outbreaks involved Group B salmonellae.

Two outbreaks of rotavirus infection were confirmed in French trotters in France.

Australia (New South Wales) and the USA diagnosed a limited number of *Lawsonia intracellularis* infections.

Equine monocytic ehrlichiosis was recorded in Switzerland (one case) and the USA, with cases in Florida (one), Kentucky (39), Pennsylvania (one), and Virginia (six).

Several cases of clostridial enteritis in foals due to *Clostridium perfringens* type A were confirmed in the USA.

A single case of Hendra virus infection and two cases of bat lyssa virus infection were recorded in Queensland, Australia.

The USA confirmed 135 cases of Eastern equine encephalomyelitis involving 22 states. The greatest number of cases were reported in South Carolina, Florida, Georgia, North Carolina, and Mississippi.

West Nile virus encephalitis was recorded in Italy and the USA. Italy confirmed 26 outbreaks involving 232 horses of which 10 were clinically affected with one death. The total number of cases in the USA during the period under review was 172. These occurred in 36 states, of which Montana, Wyoming, California, Texas, and Missouri had the largest number of cases.

**Second Quarter Report for Australia*

Equine Disease Quarterly

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Trypanosoma evansi Infection in Horses

Trypanosoma evansi is the etiological agent of the disease known as *Mal das Caderas* (Latin America) or s*urra* (Asia, Africa, and Europe) in horses. This parasite, which has been reported in domestic and wild mammals, can cause considerable economic losses. The trypanosomes reproduce in the blood of the vertebrate host, and the trypomastigote forms are transmitted mechanically by bloodsucking insects from infected to uninfected animals. Hot and humid climatic conditions may contribute to outbreaks of trypanosomiasis, due to higher proliferation of insects, the main vectors of *T. evansi*.

Surra is the most commonly reported disease in some continents due to the favorable environment for insects. In recent years, several outbreaks or isolated cases have been reported in certain European countries, an atypical region for the disease. In Brazil, the disease was restricted to the Midwest (region of the Pantanal of Mato Grosso) for many years. However, in the last 10 years it has spread to all regions of the country, with isolated cases and outbreaks with high associated mortality. Wild animals such as capybaras (a large rodent) and coatis (member of the raccoon family) may act as reservoirs of *T. evansi*. Populations of these species, which are present in the same areas as these outbreaks of surra, have increased considerably in recent years.

Trypanosomiasis in horses is characterized by anemia, edema of the limbs and dependent regions, anorexia, dehydration, lethargy, fever, loss of appetite, weight loss, abortion, and incoordination, followed by paralysis of the hind limbs. Researchers divide these clinical signs in two or three stages of the disease: subacute, acute, and chronic. In the chronic stage, horses usually exhibit cachexia (chronic wasting) associated with neurological signs and limb paralysis. Neurological signs are the result of the parasite travelling to the brain, where it causes an inflammatory response leading to encephalitis and cellular necrosis.

Trypanosomiasis caused by *T. evansi* can be clinically confused with other diseases, including equine protozoal myeloencephalitis in the chronic stages. Where surra is suspected, it is important to rule out other causes of equine neurologic disease. Most available diagnostic methods include the parasitological, serological, and polymerase chain reaction (PCR). The parasitological test is fast, but it lacks specificity and sensitivity due to low numbers of the parasite in the bloodstream. Serology, employing a card agglutination test kit known as CATT/*T. evansi*, has been a method used for disease surveillance in several countries. PCR testing on blood samples is a specific and sensitive method; however, it is not 100 percent reliable since *T. evansi* may only be present in the tissues.

Like any infectious agent, *T. evansi* stimulates an immune response in the infected animal. While this response is unable to clear the infection from the host, it controls and maintains the parasitemia at low levels, resulting in the disease becoming chronic. In many countries, the disease is treated with diminazene aceturate. However this drug, even when used at the recommended dose, has no significant curative rates in the vast majority of infected animals. Quinapyramine, suramin, and melarsomine dihydrochloride are additional drugs used to treat *T. evansi* infections. Quinapyramine has been used prophylactically in endemic regions.

Surra is considered by some as an emerging disease. Even in endemic areas/regions, efforts should be made to reduce the incidence of the disease through adoption of appropriate sanitary measures.

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Multisystemic Eosinophilic Epitheliotrophic Disease

Multisystemic eosinophilic epitheliotrophic disease (MEED) is a rare, chronic wasting disease of horses, characterized by development of granulomas (nodules or masses) in numerous organs. These granulomas are composed of large numbers of inflammatory cells, especially eosinophils.

Although the cause and pathogenesis are unknown, possibilities include: an exaggerated Type 2 hypersensitivity response involving helper T lymphocytes and a hypersensitivity response to nematode parasites. MEED has also been reported in cases with concurrent lymphoma.

Affected horses rarely present with acute disease, and veterinary attention is not usually sought until chronic signs are apparent, which can take several months. Younger horses are predominantly

affected and there is no sex or breed predisposition or specific geographic incidence, with sporadic cases reported from the United States, United Kingdom, Canada, and Australia.

Presenting signs vary according to the body systems involved, with the skin and gastrointestinal tract most commonly affected. Dull demeanor, inappetance, severe weight loss, diarrhea, and dermatitis are frequently reported. Skin lesions start with dry, scaly cracks and inflammation at the coronary bands and oral mucosa, then develop into widespread crusting and exudation over the face, limbs, and ventral abdomen. Lesions may initially be pruritic and progress to hair loss and thickening and cracking of the skin. Rarely, respiratory signs, including nasal and ocular discharge, swollen submandibular lymph nodes, chronic cough, and respiratory distress can predominate.

No specific diagnostic tests exist for MEED, making it a diagnosis of exclusion. Differential diagnoses include lymphoma with dermal and systemic involvement, systemic lupus erythematosus, pemphigus foliaceus, and granulomatous enteritis.

A full clinical examination should be performed, including rectal examination to identify any mesenteric lymph node swelling. Clinical pathology commonly shows a non-specific inflammatory profile and hyperfibrinogenemia. Peripheral eosinophilia is rarely present but increased eosinophils may be found in tracheal wash, bronchoalveolar lavage, and peritoneal fluids. Hypoproteinemia, due to hypoalbuminemia, occurs when gastrointestinal lesions are present. Cases with significant intestinal infiltrate also will have evidence of partial or total malabsorption, determined by glucose absorption test. Elevations in liver enzymes, particularly gamma glutamyl transferase, are common due to hepatic and biliary involvement. Abdominal ultrasound may show enlarged liver, thickened intestine, enlarged and nodular pancreas, and enlarged mesenteric and intestinal lymph nodes. Thoracic radiographs may show an interstitial pattern and nodules.

Affected tissues, such as skin, oral mucosa, rectal mucosa, liver, and intestine, should be biopsied. Histopathology confirms chronic, fibrosing inflammatory reaction with infiltrates composed of lymphocytes, plasma cells, and eosinophils seen in multiple organs. In some tissues, the eosinophilic infiltrates form granulomas.

Treatment is symptomatic, including systemic broad-spectrum antibiotics, anthelmintics, and corticosteroids. Prolonged therapy may be necessary, and some relapses have been reported. Use of the antineoplastic drug hydroxyurea has had limited success; the thiopurine antimetabolite azathioprine has also been suggested as a potentially effective treatment.

A positive response to treatment shows as improved demeanor, weight gain, reduced pruritus, and resolution of diarrhea.

The prognosis for horses with MEED is poor, and affected horses are generally euthanized due to lack of response to treatment. Survival and resolution of clinical signs has been reported, however, so treatment should be attempted.

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NATIONAL

Progress Toward New Biomarkers for the Diagnosis of Bacterial Placentitis in Mares

Placentitis is a common cause of late-pregnancy abortion in mares and poses a significant threat to fetal and neonatal viability. Bacterial agents commonly associated with the occurrence of placentitis include *Streptococcus equi* subspecies *zooepidemicus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Leptospira* spp, nocardioform bacteria (*Crossiella equi*, *Amycolatopsis* spp) and others. Except for leptospiral and nocardioform placentitis, most cases of bacterial placentitis are thought to originate due to bacterial invasion via the cervix. Therefore, these cases of ascending placentitis usually start at the cervical star and spread from there. Infection of the placenta results in subsequent infection of the fetus and in the release of prostaglandins from the inflamed placenta, which ultimately leads to abortion or delivery of a premature foal with bacterial sepsis.

Effective treatment of placentitis requires early diagnosis prior to the appearance of clinical signs, such as premature udder development with or without the streaming of milk and/or vulvar discharge.

Currently, ultrasonographic evaluation of the placenta is used to detect early cases of placentitis and to implement treatment to prevent abortion and delay premature labor. While this practice has allowed more effective treatment and has improved the outcome in many cases, it is often not practical to ultrasound every mare repeatedly during late gestation. In addition, early stages of placentitis can be missed during ultrasonographic examination, and the technique is also prone to false positive diagnoses, resulting in unnecessary treatment.

In the absence of an accurate and practical method to detect early, subclinical cases of placentitis, it has become increasingly common to treat all pregnant mares with antibiotics for five to seven days each month during late gestation. The long-term risk of developing widespread bacterial resistance against antibiotics and the development of "superbugs" should be of great concern, not only to the breeding industry, but to veterinary medicine as well as human health. Additional diagnostic tools are therefore needed to accurately identify pregnant mares with early stages of placentitis and to specifically target these mares for treatment.

The equine placenta synthesizes and metabolizes progestagens, which are critical for pregnancy maintenance. Experimentally, mares that develop chronic placentitis often have increased plasma progestin concentrations, whereas mares with acute placentitis often demonstrate a rapid drop in plasma progestin concentrations. Repeated measurement of plasma progestin concentrations in mares with placentitis can be a useful method to identify mares at risk for abortion or premature delivery.

Serum estrogen concentrations are elevated in pregnant mares between 150-310 days of gestation. The predominant estrogens in pregnant mares include estrone, equilin, equilenin, estradiol-17ß, and estradiol-17α. Determinations of serum concentrations of estrone sulfate are useful in pregnancy diagnosis and to monitor fetal viability. Researchers have observed that mares aborting from placentitis had serum estrogen concentrations below those normally detected in pregnant mares. Preliminary studies in our laboratory indicate that in mares with experimentally induced bacterial placentitis, concentrations of estradiol-17ß sulfate may decline precipitously after infection, also suggesting that maternal estrogen concentrations may be useful as an early marker of placental insult.

In addition to endocrine monitoring, measurement of acute phase proteins in blood may also be a useful biomarker for placentitis in mares. Serum concentrations of acute phase proteins are elevated when inflammation is present. This group of proteins is mainly produced by the liver in response to an inflammatory stimulus. The major acute phase protein in the horse is serum amyloid A (SAA), whereas the minor acute phase proteins include haptoglobin and fibrinogen. In ongoing research at the Maxwell H. Gluck Equine Research Center, mares with experimentally induced placentitis have a rapid and dramatic elevation in SAA within two days after intracervical inoculation with *Streptococcus equi* subspecies *zooepidemicus.* Although SAA appears to be a very sensitive indicator for acute bacterial placentitis, it is also a very nonspecific indicator, as many other acute inflammatory conditions may result in an elevation of SAA.

Ultimately, it appears likely that more than one biomarker may be required for accurate and early detection of placentitis in the mare. Ongoing research will address these needs and evaluate the utility of these markers in mares under field conditions.

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KENTUCKY

Equine Encephalitis Cases

West Nile virus (WNV) causes disease in humans, horses, and birds. It is a mosquito-borne virus that first appeared in the United States on the East Coast in 1999. Many horses were infected and died during the following years, and WNV is now considered endemic in the US.

Infected birds develop a high viremia and serve as the source of virus to infect mosquitoes. The incubation period in horses is 7-10 days and clinical signs in horses consist of low-grade fever, anorexia, and lethargy progressing to neurologic signs that may appear suddenly and worsen over the ensuing days. Fortunately, once infected, horses

Equine Disease Quarterly Newsletter

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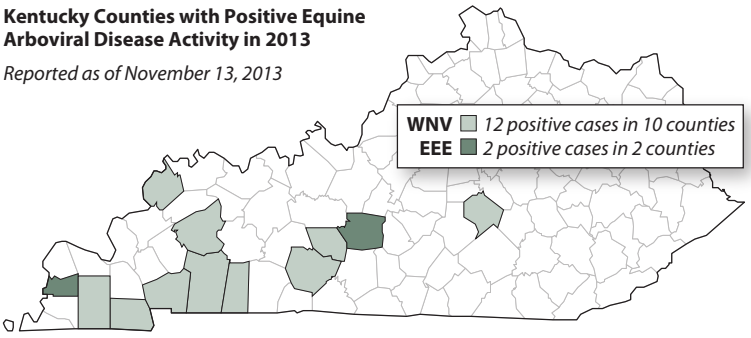
do not pose a risk to other horses, people, or birds due to low virus levels.

Since the appearance of WNV, cases have continued to be diagnosed in horses in the United States and Kentucky. As of November, Kentucky officials reported 12 cases of WNV for 2013. These cases occurred in 10 Kentucky counties. None of the 12 horses were vaccinated against WNV. Seven were Quarter Horses, two were Standardbreds, and the remaining were a Paint Horse, a Percheron cross, and a Rocky Mountain Horse. Ten of the horses survived, and two were euthanized. In 2012, 13 cases of WNV were reported versus one case in 2011. The 2012 cases were centered in Central Kentucky while in 2013 the cases were in Western Kentucky.

Eastern equine encephalomyelitis (EEE) is uncommon in Kentucky. This viral disease is also mosquito transmitted and is characterized by clinical signs similar to those seen with WNV. Eastern equine encephalomyelitis is considered to have a mortality rate approaching 90 percent. In 2013 in Kentucky, two cases of EEE were reported. One case was in a 10-year-old Tennessee Walking Horse and the other in a 17-year-old Quarter Horse.

Kentucky Counties with Positive Equine Arboviral Disease Activity in 2013

Reported as of November 13, 2013



Dr. John Poe, State Public Health Veterinarian, Frankfort, KY.

Neither had been vaccinated against EEE, and both horses died as a result of disease.

The American Association of Equine Practitioners includes WNV and EEE in their list of core vaccinations for horses. The other core vaccinations are Western equine encephalomyelitis, tetanus, and rabies.

Additional information can be found at http://www.kyagr.com/statevet/equine-infectious-diseases.html#west.

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