EQUINE DISEASE QUARTERLY

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**IN THIS ISSUE**



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LLOYD'S

# COMMENTARY

THE RECENT OUTBREAKS OF PARALYTIC equine herpesvirus-1 (EHV-1) infection at racetracks and training centers in Kentucky, Maryland, and Pennsylvania have illustrated the benefits of combining the old with the new. The old is the regular, twice-daily recording of a horse's temperature to determine if it is febrile and incubating an infection. The new is the PCR (polymerase chain reaction) test to confirm diagnosis of EHV-1 infection.

Taking a horse's temperature is a simple means of assessing an animal's state of health. Each animal has a normal temperature range which, when elevated (usually above 101.5 C), requires investigation. It is not foolproof, as older horses may not exhibit a temperature rise following infection or may do so for a short period (several hours). In the past, temperatures were invariably taken once a disease outbreak had occurred to monitor the spread of an infection. Increasingly, it has become part of the daily management routine to identify the initial case(s) of disease, enabling prompt diagnosis and prevention.

The horse that has spiked a fever within the last 24 hours is the ideal candidate from which to obtain a nasal swab and blood sample for a laboratory diagnosis. Frequently, when an outbreak of an infectious disease occurs, the laboratory is overwhelmed with samples. By identifying animals that are most likely to provide a positive result, the resources of the laboratory are put to more effective use.

The PCR test was developed several decades ago, but its application as a routine diagnostic procedure in the field for EHV-1 is recent compared to its use on postmortem material and as a research tool. PCR does not measure infectious virus but the presence of viral particles. It requires considerable technical skill on behalf of the operator, and the test system must be validated and controlled to avoid false positive and negative results. Automation can facilitate the rapid throughput of large numbers of samples, but such equipment is expensive and requires a trained, skilled operator.

If these hurdles can be overcome, the PCR provides an accurate and rapid result within 48 to 72 hours of the laboratory receiving the sample. Utilizing overnight express mail, material packaged in insulated containers reaches the laboratory within 24 hours from widely dispersed geographical areas. This express delivery to equipped laboratories is important, as not all laboratories are "geared up" to undertake PCR testing for equine pathogens.

By providing an early, reliable diagnosis, the ability to reduce the spread of a specific infection is considerably increased. Isolation of the sick horse(s) and restriction of movement minimizes the number of in-contact animals that subsequently develop illness. As observed during recent outbreaks, racing continued at affected racetracks, albeit under strict conditions of biosecurity, resulting in a slight reduction in the number of runners and the cancellation of several race days and prestigious handicap races. These limitations were primarily a consequence of restrictions of the movement of out-of-state, "ship in" horses.

With experience, application of the old and the new will be refined, allowing the attending veterinarian to provide an accurate, prompt diagnosis, thus reducing the spread of equine infectious disease and enabling the diagnostic laboratory to provide a rapid and cost effective service.

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INTERNATIONAL

## Fourth Quarter 2005

THE INTERNATIONAL COLLATING CENTRE, Newmarket, England, and other sources reported the following disease outbreaks:

Cases of abortion caused by equine herpesvirus-1 (EHV-1) were reported from New South Wales, Australia, Ireland, and the United Kingdom, with sporadic cases reported from Argentina, France, Japan, and South Africa. Neurological disease attributable to EHV-1 infection was confirmed among Thoroughbred racehorses at Turfway Park Racetrack in Northern Kentucky at the end of December. Two racehorses and an outrider pony developed severe clinical signs, resulting in euthanasia. During January 2006 EHV-1 infection was also confirmed at a Western Kentucky training facility, at two racetracks and a farm in Maryland, and at a racetrack in Pennsylvania. Several horses were euthanized after they developed severe signs of neurological disease.

Respiratory disease attributable to EHV-4 was confirmed among groups of horses in Argentina, France, and the United Kingdom. Respiratory disease attributable to equine influenza was confirmed among groups of horses in France and the United Kingdom.

Turkey reported an outbreak of leptospirosis infection, causing mild clinical disease on a Thoroughbred farm. Mild clinical cases of piroplasmosis infection were reported on several premises in Switzerland and on one premise in Turkey. Strangles was diagnosed on a farm in New South Wales, Australia, on several premises in Ireland, and in South Africa and Switzerland.

During the first week of January 2006 quarantine restrictions were lifted on the last two remaining premises testing positive for vesicular stomatitis in Colorado.

## Breed the Best to the Best

*GENOMICS* IS A BUZZWORD, EVEN AMONG scientists. The term *genomics* includes the entire complement of chromosomes, genes, and DNA sequences that make up humans and animals. Technological advances during the last 15 years have led to the entire genome sequencing for humans, mice, cattle, chickens, and dogs. Thousands of bacteria and viruses have been DNA sequenced as well. We know that vertebrates have approximately 3 billion DNA base pairs and 20,000 genes. However, the 20,000 genes account for only 3% of the DNA bases; we do not know a function for the remaining 97%. The amount of information produced by genomics is immense and has led to a wedding of biology with computer science in a field now called *bioinformatics*.

What will be the impact of genomics on horse breeding? Since the late 1600s, horse breeders have been renowned as geneticists, starting with the promotion of Thoroughbred race horses by England's King Charles II. Three hundred years of selection changed the performance and athletic abilities of the Thoroughbred. Even in the shadow of genomics, the adage remains true, "breed the best to the best and hope for the best." Why? The point is, while genomic studies focus on details of biology, the horse breeder considers the entire breeding program. So what benefits can the horse breeder derive from genomics? The answer is apparent in the large number of diagnostic tests produced from genomics research during the last decade of human medicine. They are akin to radiographs, bacterial cultures, and blood enzyme values and thus have the potential to help develop better vaccines and therapeutics.

Already, genomics studies have led to development of diagnostic tests for bacteria, viruses, and several hereditary diseases of horses (hyperkalemic periodic paralysis of Quarter horses, severe combined immunodeficiency disease of Arabian horses, glycogen branching enzyme deficiency disease of Quarter horses, overo lethal white foal syndrome of Paint horses, and epitheliogenesis imperfecta of Belgian draft horses). Furthermore, scientists are developing tests to measure how genes are controlled by nutrition; exercise; vaccination; infection; and

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disease processes such as developmental bone diseases, muscle diseases, colic, and laminitis. Every management practice has an impact on gene expression in the horse, and we will be able to measure it.

However, integrating genomics research with veterinary applications may be challenging. Research funds for horses are often earmarked to find specific treatments for specific problems. Meanwhile, genomics research does not produce drugs or vaccines by itself. Consequently, an initiative by the Morris Animal Foundation to fund teams of scientists to address important health problems for horses is particularly noteworthy.

Morris Animal Foundation accepted preproposals in February for its Equine Health Consortium initiative. The goal of the consortium approach is to encourage scientists to collaborate on large scale and solve important problems for the horse industry. Proposals were submitted covering topics from respiratory diseases to lameness to colic to hereditary diseases. Over a period of five years, $2.5 million will be raised for one consortium project. The concept is not simply to put more money into research. The goal is to bring together and harness the creative energy, individual expertise, and diverse resources of scientists working on these problems worldwide. Normally, competition is a healthy activity and stimulates creative thought. However, when resources are limited, the consortium approach assures collaboration and sharing of resources between institutions and industry, even as scientists approach problems from different angles. This initiative has potential to bring together the right teams of scientists to benefit the health and welfare of horses and possibly even include applications from the new field of genomics.

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NATIONAL

# Decreasing Risk— Utilizing Industry-Based Standards of Care

ADVERSE ANIMAL HEALTH EVENTS DO NOT occur randomly. Usually, there are identifiable causal, and possibly preventable, factors which can influence the development of disease. Depending upon whether the risk factors are already known or identified subsequent to a disease event, the management of a disease becomes basically one of either prevention or response.

For new or emerging disease conditions, it is likely that the identification of risk factors will occur only after the disease event of interest is over and a retrospective study has been completed. Consequently, these disease events tend to be prolonged and have a wider distribution among a susceptible population. As examples, Mare Reproductive Loss Syndrome (MRLS) and equine encephalitis attributable to West Nile virus initially spread unchecked due to the lack of identifiable or available interventions. Conversely, for those diseases with well delineated modes of transmission and for which standardized screening methods exist, the disease impact associated with their occurrence theoretically should be less.

From the perspective of the Thoroughbred industry, two factors that contribute to equine communicable disease spread are population densities and the frequent movement of animals for breeding or participation at performance venues. It should be no surprise that during the past three decades, communicable disease

Figure 1.

EIA Surveillance

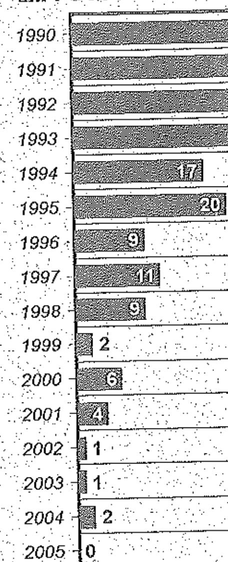
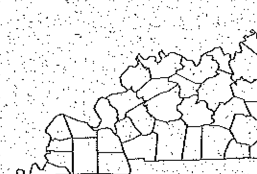



Figure 2.

2005 West Nil

*Kentucky Counties with Affected Equi*



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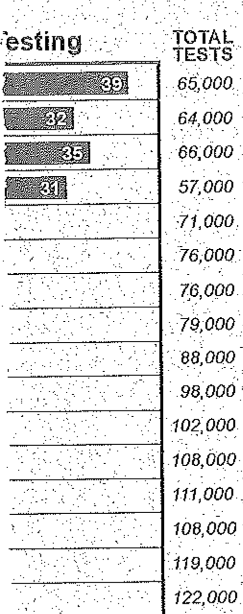
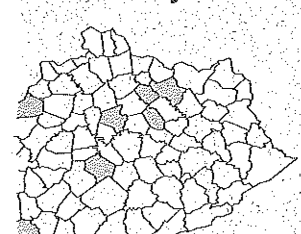



'irus Activity



events like Contagious Equine Metritis (CEM) and Equine Viral Arteritis (EVA) occurred among horses residing in Central Kentucky. This geographic area has the highest density of Thoroughbred breeding horses in the world, and the industry is dependent on the free movement of animals for its continued economic well-being. Recently, concerns over the apparent nationwide increase in equine herpesvirus-1 (EHV-1) have prompted industry advocates to propose the development of uniform methods to minimize the risk of this disease to breeding farms.

If a communicable disease is widely distributed and causes—or has the potential to cause—significant economic loss, then the institution of a uniform method of surveillance and diagnosis may be appropriate. This is usually accomplished through mandated regulatory controls or through an industrywide standard code of practice.

In general, adoption of prevention strategies can be either voluntary or regulated at the state or national level. Those imposed by regulatory authorities generally have an economic burden associated with regulation. There are monetary costs for personnel to monitor the process and financial repercussions associated with noncompliance, usually in the form of additional restrictions or fines for violations. An example of a highly regulated preventive program is the federal/state cooperative CEM program. This program has been successful in preventing the re-introduction of CEM into the United States by requiring both pre- and post-entry testing of all imported equines intended for breeding from countries where CEM is believed to exist. Since the program's inception in the late 1970s, thousands of stallions and mares have been screened, and numerous carrier animals have been prevented from directly entering the United States.

Ideally, the adoption of a voluntary yet uniform code of practice would serve to minimize risk for disease and eliminate the costs of regulation. An example of a standardized list of protocols for disease control is the widely utilized Codes of Practice published by the Horserace Betting Levy Board in the United Kingdom. These codes have been adopted by a number of member states of the European Union and provide standards for diagnosis and control of a range of economically significant equine diseases. Specifically, they include codes for CEM, equine viral arteritis (EVA), equine herpesvirus (EHV), venereal infections caused by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, and guidelines for strangles. Copies of the Codes of Practice can be downloaded from the Levy Board's home page at http://www.hblb.org.uk/. According to proponents, incidence of specific infectious disease outbreaks has decreased significantly in those countries in which they have been adopted.

Prevention of a highly contagious disease in an environment where the major species of interest is closely congregated and moves frequently depends on timely surveillance and the rapid notification of regulatory officials and other relevant parties. The adoption and utilization of well defined voluntary standards of practice as opposed to mandated controls has the value of facilitating these efforts without adding an undue regulatory burden.

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# Possible Role of Adipose Tissue in the Development of Laminitis

LAMINITIS IS ASSOCIATED WITH OBESITY as well as sepsis and postoperative conditions in horses where levels of inflammation are elevated. The precise mechanisms that lead to laminitis are unknown; however, several studies document the involvement of inflammation in the pathogenesis of laminitis. In addition, recent studies utilizing an *in vitro* approach to studying laminitis using hoof wall explants have shown that removal of glucose from the culture medium leads to rapid separation of hoof lamella tissue when subject to stress forces. A similar mechanism may occur in natural cases of laminitis where there is insulin resistance—a suppressed ability of insulin to induce glucose uptake into the cell.

While numerous mechanisms contribute to the development of insulin resistance, growing evidence points to both a correlative and causative relationship between inflammation and insulin resistance. In addition to sepsis and surgery, obesity is also considered an inflammatory state that some studies relate to a localized form of Cushing's syndrome. Circulating concentrations of inflammatory molecules including acute phase proteins and inflammatory cytokines are elevated in obese humans, with even higher elevations in obese patients with insulin resistance and type II diabetes. Further evidence indicating an inflammatory role in insulin resistance is derived from studies demonstrating a reversal of insulin resistance by administration of anti-inflammatory salicylates, such as aspirin.

Several key molecules involved in the development of insulin resistance have come to the forefront in recent years that have led researchers to investigate adipose tissue as a major player in the regulation of insulin sensitivity. Adipose tissue, once considered only a reservoir for energy storage, has emerged as an endocrine organ and an active participant in whole body energy homeostasis. A number of factors directly contributing to insulin resistance, such as the inflammatory cytokine TNFα, are synthesized and secreted by adipose tissue. Additionally, studies have shown that adipose tissue contribute a considerable percentage of the circulating inflammatory molecules IL-6 and TNFα, with degree of contribution correlating to degree of obesity in humans. Thus, the significance of excess adipose tissue as a major contributor to the development of insulin resistance cannot be understated.

Preliminary studies in our laboratory have employed a model for inducing inflammation. This model would investigate a) the relationship between inflammation and insulin resistance and b) the possible role of adipose tissue as a contributor of inflammatory molecules in insulin resistance in the horse. Administration of lipopolysaccharide (LPS), part of the cell wall of the bacteria *E. coli*, is a commonly used model for inducing inflammation. LPS induces an acute but transient inflammatory response characterized by elevation in heart rate, temperature, respiration, and insulin levels over a period of several hours. It is also well documented that administration of LPS in the horse induces increased circulating levels of the inflammatory cytokine TNFα in blood. The objectives of the study were to determine whether insulin resistance results from a direct inflammatory stimulus in the horse and measure inflammatory cytokine mRNA expression in adipose tissue in response to LPS.

Mares treated with an inflammatory stimulus not only developed a dramatic decrease in insulin sensitivity but also had marked increases in the levels of cytokine gene expression in adipose tissue. These results suggest that inflammation is associated with reduced insulin sensitivity in the horse and that adipose tissue may be a significant contributor of inflammatory cytokines in obese horses. It is clear that laminitis can be triggered in a number of different situations involving a number of different factors. However, growing evidence points to both insulin resistance and inflammation as major players in the onset of this severely debilitating disease. Impaired glucose uptake associated with inflammation in obesity and postoperative conditions may weaken the layers of the hoof lamellae and predispose the horse to laminitis. In the future, therapeutic drugs that increase insulin sensitivity and those that act as anti-inflammatory agents may work in concert to effectively treat laminitis.

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KENTUCKY

# Kentucky's EIA and West Nile Surveillance Program

DURING 2005 A TOTAL OF 121,813 SAMPLES were tested for Equine Infectious Anemia (EIA). For the first time since regulatory testing was initiated in the 1970s, no positive animals were identified (Figure 1). Private testing accounted for 101,650 samples to comply with state regulations regarding the sale and exhibition of equine in Kentucky or to meet interstate transportation requirements. Through market surveillance or other testing, 20,163 samples were collected.

West Nile virus (WNV) infection was identified in nine equine during 2005, of which six survived and three were euthanized. Eight animals had received no vaccination against WNV, and no information was available on the ninth. The distribution of the cases by county is illustrated in Figure 2.

*For more information on these or any other equine programs visit* http:/www.kyagr.com/state_vet/ah/programs/equineprogs/index.htm.

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