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IN THIS ISSUE

University of Kentucky
College of Agriculture
Department of Veterinary Science

LLOYD'S

Commentary

Five months have passed since the first reports were received of a disease outbreak occurring in central Kentucky now referred to as Mare Reproductive Loss Syndrome (MRLS). It is now possible to evaluate objectively where the scientific investigations into the cause(s) and the horse industry which suffered major adverse consequences are positioned.

Although answers to what caused the problem have proved elusive, a vast amount of valuable data has been accumulated. Clinical cases, whether reproductive losses or the eye and heart conditions, ceased by the end of June. While sporadic cases of reproductive loss continue to be reported under intense veterinary scrutiny, a small number of early and late fetal losses would have occurred even in the absence of MRLS.

A study is underway to monitor on a monthly basis the reproductive status of approximately 100 pregnant mares covered during the early part of the season. Only when these mares foal in early 2002 will definitive information on the health status of their offspring become available.

The various avenues of investigation assisted by the extensive epidemiological study on 133 farms have eliminated several possibilities, including known infectious agents, mycotoxins, ergot alkaloids, and phytoestrogens. Yet-unidentified potential agents could have caused the problem.

The "working hypothesis" developed in late May of cyanide toxicity based on the presence of cherry trees continues to be investigated. Proving or disproving this hypothesis is providing Dr. Tom Tobin's toxicology group with an arduous challenge.

The intense interest of the press, radio, and television at local, national, and international levels entirely justified establishing the MRLS Web site that can be accessed at **www.ca.uky.edu**. Since May 8 there have been over 28,500 "hits." The number of updates provided is now fewer than during the initial phase of the outbreak.

Perhaps the most interesting and valuable information is the weather data for the month of April 2001, which closely resemble that of the spring of 1981, when many agree a similar syndrome occurred.

In deciding what needs to be achieved, defining the cause would be a major step forward, but even without an answer, several practical questions must be addressed. Owners are asking if the syndrome is likely to be repeated in 2002. One lesson from 2001 is that it is unwise to speculate. However, history relates the risk of a combination of the bizarre set of circumstances that contributed to MRLS in 2001and repeating in 2002 is likely to be very low.

This will not satisfy everyone, and additional safeguards need to be in place. Close monitoring of a variety of environmental parameters will provide safeguards for 2001 and future years. This will require detailed planning and coordination with farm managers, veterinarians, scientists, and analytical laboratories. The remainder of 2001 will allow time to implement a plan providing reassurance for the success of the 2002 breeding season. ■

CONTACT
Dr. David Powell, (859) 257-2756
dgpowe2@uky.edu
Department of Veterinary Science
University of Kentucky, Lexington, Kentucky

Equine Disease Quarterly

Editors
Roberta Dwyer
David Powell
Neil Williams

Staff
Diane Furry
Linda Millercox
Libby Noble

Correspondence should be addressed to the editors,
Department of Veterinary Science
Gluck Equine Research Center
University of Kentucky
Lexington, KY 40546-0099
Telephone (859) 257-4757
Fax (859) 257-8542.

Internet address:
http://www.uky.edu/Agriculture/VetScience/gluck1.htm

International

Second Quarter 2001

The International Collating Centre, Newmarket reported the following disease outbreaks.

Coital exanthema attributable to equine herpes virus-type 3 (EHV-3) was diagnosed on two occasions in the United Kingdom among Thoroughbreds and non-Thoroughbreds. The respiratory form of equine herpes virus infection was widely reported from France in both Thoroughbreds and non-Thoroughbreds and among a single group of foals in Japan. Abortion attributable to EHV-1 was diagnosed Australia, Germany, Ireland, Japan, Sweden, and the United Kingdom. The majority were individual cases on a single premise. The paralytic form of EHV-1 infection was confirmed among a stable of show jumping horses in Denmark.

Equine viral arteritis (EVA) was diagnosed on the basis of positive serology among mares and yearlings on a single premise in the United Kingdom associated with an unvaccinated non-Thoroughbred stallion.

Reports of influenza infection were received from only one country, France, among several breeds of horses. Strangles was diagnosed among horses in Australia, Ireland, Sweden, Switzerland, and the United Kingdom. Tetanus was the cause of death of two foals in Japan.

Turkey reported the results of a national glanders eradication program completed in March 2001. Blood samples were collected from 7,500 registered Thoroughbred, Arabian, and competition horses, all of which tested negative for glanders by the complement fixation test. Mallein tests were performed on all other horses and mules in the country. Of 235,286 horses and mules, 3,509 (1.5%) tested positive and were destroyed, although no clinical cases were observed. One donkey showing clinical signs was destroyed. ■

National

West Nile Virus Update

As of September 10, evidence of West Nile Virus (WNV) has been reported in numerous states and the District of Columbia, based on disease surveillance among humans, horses, birds, and mosquitoes, as illustrated in **Figure 1**. Fourteen human cases (1 fatal) are confirmed in Florida (4), New York (4), Connecticut (3), New Jersey (1), Maryland (1), and Georgia (1). Sixty-seven equine cases (17 fatal) have been identified in Florida (54), Georgia (5), New York (2), Pennsylvania (2), and single cases in Connecticut, Kentucky, Louisiana, and Virginia. West Nile Virus has been reported for the first time in Canada in the province of Ontario and in 10 states within the United States: Alabama, Florida, Georgia, Illinois, Indiana, Kentucky, Louisiana, Michigan, Ohio, and Wisconsin.

Among the wild bird population, the majority of cases has been observed in crows, as occurred in 1999 and 2000. From mosquito pools a variety of species have been identified as positive sources of WNV, including *Aedes*, *Anopheles*, *Coquillettidia*, *Culex*, and *Ochlerotatus*.

On August 1, the USDA and Fort Dodge Animal Health announced approval of a conditional license for an inactivated vaccine against WNV for use in horses.

Updated information can be obtained at **www.aphis.usda.gov/oa/wnv/index.html.** ■

CEM — A Continuing Threat to International Trade

Since its discovery in 1977, contagious equine metritis (CEM) has been a source of considerable concern for many countries because of the ease with which it can be spread internationally through carrier stallions or mares. Caused by *Taylorella equigenitalis*, CEM is a venereally transmissible disease of equids, characterized by infertility and, very rarely, abortion in mares and infertility in stallions. Significant economic loss can result from introduction of the disease into an immunologically naïve equine breeding population.

Categorized as a List B disease by the Office International des Epizooties (OIE), CEM continues to be the subject of stringent import regulations by all the major horse-breeding countries. Notwithstanding the rigor of such measures, however, the risk of spread of CEM remains a significant threat to horse industries worldwide. The large number of asymptomatic carrier stallions and mares imported into the U.S.A. over the past four years illustrates the seriousness of this threat.

In the period September 1997 to June 2001 alone, a total of 16 imported horses, all Warmbloods, were confirmed carriers of *T. equigenitalis* on post-importation quarantine and testing. They comprised 11 stallions and 5 mares. The majority of the carrier animals originated in Germany (10), with the remainder from the Netherlands (3), the Czech Republic (1), France (1), and the United Kingdom (1). The stallions and mares ranged from 4 to 10 years in age at time of importation.

All of these stallions and mares were certified negative for CEM on pre-export bacteriological screening for the presence of *T. equigenitalis*. Presumably, this was carried out as prescribed in the OIE Manual of Standards for Diagnostic Tests & Vaccines (3rd ed.). In conformity with USDA regulations governing importation of stallions and mares from CEM-affected countries, these horses were bacteriologically tested for *T. equigenitalis* on arrival in the United States in accordance with internationally accepted protocols. Stallions were also required to be bred to two test mares and the mares monitored clinically, bacteriologically, and serologically for evidence of infection.

All five imported mares were readily confirmed clitoral carriers of *T. equigenitalis*. Of the 11 imported carrier stallions, only four were cultured positive for *T. equigenitalis* on initial post-import testing. The seven other stallions were confirmed carriers of CEM, based on transmission of infection to one or both test mares. It is worth emphasizing that five of these stallions only infected one of the two test mares they were bred to. The urethral fossa followed by the terminal urethra were the sites most frequently cultured positive for *T. equigenitalis* in the carrier stallions.

The experience of the past four years underscores the continued risk of spread of CEM through the international movement of carrier mares and, in particular, carrier stallions. Fortunately, the current USDA and state post-importation testing protocols provided the necessary safeguards that prevented CEM from being reintroduced into the United States during the period under review.

Despite proven reliability for detection of the carrier state, such measures should not be considered foolproof. In light of the increased frequency of importation of CEM positive stallions and mares into the United States since 1997, there is a heightened risk of a carrier animal, most likely a stallion, escaping detection at time of importation and reestablishing the disease in the country's fully susceptible equine breeding population.

Significant discrepancies currently exist between laboratories regarding their ability to detect the carrier animal on pre-export testing. Whether these discrepant results are linked to sample collection, transportation of swabs to the laboratory, or differences in bacteriological cultural procedures remains to be established. Clearly, the importance of test breeding stallions for detection of the carrier state cannot be over-emphasized.

It is very evident from these findings that more effective control over the international spread of CEM will require greater conformity between countries with respect to pre-export CEM testing protocols for stallions and mares. ■

CONTACT
Dr. Peter Timoney, (859) 257-1531
ptimoney@ca.uky.edu
Department of Veterinary Science
University of Kentucky, Lexington, Kentucky

Kentucky

Equine Herpes Virus Abortions

The annual monitoring of abortions attributable to equine herpes virus type 1 (EHV-1) among the Thoroughbred mare population of central Kentucky has continued for the last 42 years. The recent numbers illustrated in **Figure 2** based on accessions to the Livestock Disease Diagnostic Center (LDDC)

Figure 1.

Dark states: Human and equine cas
Lighter states: Confirmed bird and/o

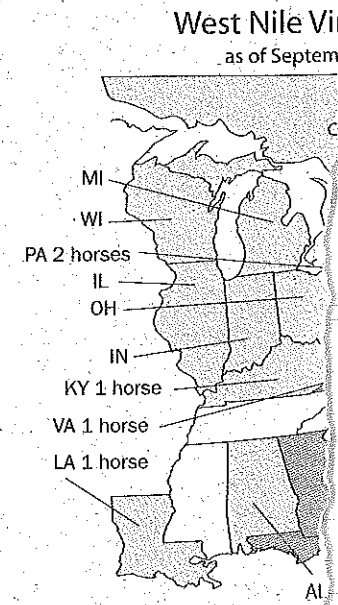

Figure 2.

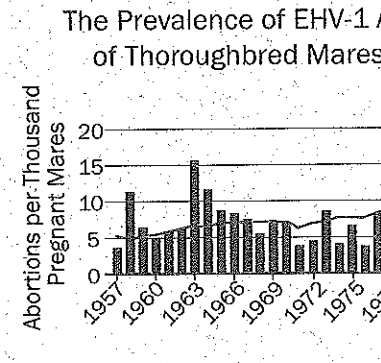

Figure 3.

Prevention of EHV -1 Abortion

- **Divide pregnant mares into group and maintain in isolation.**
- **Isolate all new arrivals for 21 da**
- **Keep first foaling mares away fro**
- **If mares removed, do not reintro**
- **Maintain vaccination program.**
- **Segregate pregnant mares from**
- **Keep foster mares away from pre**

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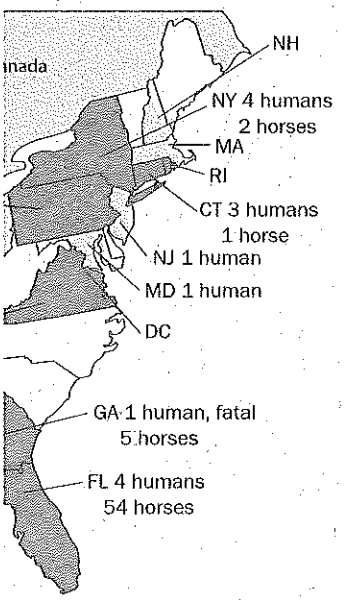
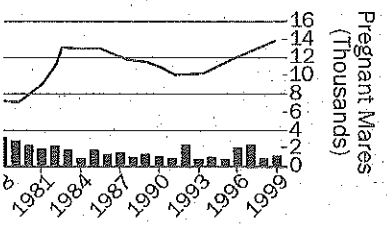
mosquito pools

us Update
ber 10, 2001



bortion and the Population
in Kentucky, 1957-1999



by stage of gestation

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older mares.
ice.

eanlings and other horses.
nant mares.

and confirmed by laboratory diagnosis are considered an accurate reflection of the field incidence. This is due to the diligence of farm managers in ensuring that all fetuses are submitted for examination.

The figure for the number of pregnant mares is derived annually from the number of foals registered by the Jockey Club, taken as 70% of mares considered in foal each year. The Jockey Club 2001 Fact Book reported 9,826 foals registered in Kentucky for 1999 (30% of the U.S. crop), which translates to 14,000 pregnant mares, the largest population over the 42-year period. The number of EHV-1 abortions per 1,000 pregnant mares has remained below 5 since 1977, despite the mare population doubling in size. Since 1977 the overall number of EHV-1 abortions per annum has ranged from a low of 11 in 1993 to a high of 47 in 1997, with 27 and 25 recorded during 2000 and 2001, respectively.

The pattern of abortions has changed significantly over the years. The majority are currently single abortions occurring on an individual farm as compared to the "abortion storms" frequently observed in the 1950s and 1960s. Multiple cases do occur even in a properly vaccinated population. In these outbreaks, the evidence frequently suggests the initial or index case was the source of infection to subsequent losses. The aborted fetus and placenta are a potent source of virus that may be sufficient to overwhelm the immunity even of a vaccinated mare.

The data strongly confirm that a combination of sound management practices, as illustrated in **Figure 3**, and annual vaccination of mares at 5, 7, and 9 months of pregnancy have contributed to this healthy state of affairs. Of greatest benefit has been the segregation of pregnant mares into small groups according to the expected foaling date and maintaining each group as a "closed herd." ■

CONTACT
Dr. Mary Lynne Vickers, (859) 253-0571
mvickers@ca.uky.edu
Livestock Disease Diagnostic Center OR
Dr. David G. Powell, (859) 257-2756
dgpowe2@uky.edu
Department of Veterinary Science, University of Kentucky
Lexington, Kentucky

Uterine Artery Rupture

Each year the University of Kentucky Livestock Disease Diagnostic Center (LDDC) receives mares that have died as result of sudden rupture of a major blood vessel of the reproductive tract, typically a uterine artery.

Mares that have suffered this type of arterial rupture are often found dead, but may be discovered in shock — exhibiting colic-type pain, sweating, trembling, pale membranes, and elevated heart rate. Many of these mares will subsequently die, but approximately 50% of the mares may survive with treatment.

Cases occur most commonly around the time of foaling but may be seen several weeks prior to or following foaling. This problem typically occurs in older mares and is believed to result from weakening of the wall of the artery as a result of advanced age and the repeated enlargement and shrinkage of the vessels associated with multiple pregnancies over the lifetime of the mare.

Antemortem diagnosis of uterine vessel rupture can be made on the basis of clinical signs and the association with parturition or pregnancy. Careful rectal palpation or ultrasound examination may reveal the presence of a hematoma in the broad ligament of the uterus and abdominocentesis will reveal free blood.

Reported treatments include a combination of quiet stall rest, sedation, analgesics, oxytocin to stimulate uterine contraction, and correction of shock through fluid or whole blood administration. Surgery is not considered a viable option in most cases due to the mares being poor anesthetic risks and the difficulty of finding and ligating the affected artery.

Mares that survive likely have a smaller arterial tear, with the hemorrhage confined to the broad ligament. In mares that live for a period of time following vessel rupture but subsequently die, it is believed that the hemorrhage is initially confined to the broad ligament; however, the pressure causes rupture of the broad ligament, allowing unchecked hemorrhage into the abdomen.

Examination of mares that die from uterine artery rupture reveals paleness of the mucosa of the gums, conjunctiva, and vulva. Upon opening of the abdominal cavity, a large volume of blood and clots are encountered. There is hemorrhage in the connective tissue

surrounding the uterus, usually with the formation of a hematoma in the broad ligament of the uterus.

Careful dissection of the arteries will reveal the site of rupture. The rupture can occur anywhere along the length of the vessel. The tear typically is 2-3 centimeters in length and oriented parallel to the long axis of the vessel. Evidence of an aneurysm is usually not observed.

The margins of the tear are ragged and clots and fibrin are usually adhered to the vessel. The tear usually involves a uterine artery but the ovarian and iliac arteries can also be affected.

Uterine vessel rupture can be a devastating occurrence and no prevention is known. Horse owners and managers can help by assisting with dystocia or quickly seeking veterinary help, especially in older mares. Aged mares should be closely monitored around the time of foaling so there can be early recognition of signs indicating internal hemorrhage in order that treatment can be quickly instituted. ■

CONTACT
Dr. Neil Williams, (859) 253-0571
nwillia@ca.uky.edu
Livestock Disease Diagnostic Center
University of Kentucky, Lexington, Kentucky

MRLS Epidemiological Study

At first glance, conducting a survey should be an easy task: ask the questions you want answers to, and tally the results. Surveying with short, five-question surveys, as was done on May 7 to members of the Kentucky Thoroughbred Farm Managers' Club, was a straightforward job: 159 e-mailed or faxed responses were returned by 10 a.m., May 10, with results disseminated the next evening. Volunteer Dr. John Walker spent some 10 hours collecting and analyzing the data via computer software.

Designing a survey to scientifically identify and analyze potentially multiple risks on farm, pasture, and individual animal bases is extremely complex. Wording survey questions is an art, since the final results must have numerators and denominators for both percentage and comparative analysis.

An outbreak emergency situation is not the time to learn how to design and analyze surveys. We asked for, and graciously received,

Timeline for MRLS Epidemiological Study

May 10 — Field epidemiology assigned to Dr. Roberta Dwyer of the Gluck Center.
May 11-12 — Epidemiology survey committee contacted:
- Robert Coleman, Ph.D., animal science nutritionist
- Ralph d'Arge, Ph.D., economist
- Barry Fitzgerald, Ph.D., reproductive physiology
- Barry Meade, D.V.M., USDA epidemiologist
- Michael Pavlick, D.V.M., USDA field veterinarian

May 14, 16 — Conference calls with USDA Centers for Epidemiology and Animal Health (CEAH), Fort Collins, Colorado; committee meets to formulate survey plans.
May 16-21 — Plans made to deliver an in-person survey to 150 farms. Question areas formulated.
May 21-25 — Dr. Lindsey Garber of CEAH comes to Lexington; survey questionnaire draft developed.
May 24 — Meeting of the Kentucky Association of Equine Practitioners Emerging Disease Committee agrees to read survey draft and make suggestions for additional areas of study.
May 26 — Final draft of survey e-mailed to CEAH.
May 25-28 — State and federal employees, volunteer veterinarians, scientists, and qualified volunteers are recruited.
May 29 — Final draft of survey received by e-mail. The 23 volunteers are assigned to 150 farms by geographic distribution. Many phone calls made to farms suggested by veterinarians to ensure they meet criteria. Survey training is planned by Drs. Pavlick and Dwyer. Initial farm visit appointments are made by Linda Javid of the Kentucky Thoroughbred Farm Manager's Club.
May 30 — Surveyors meet at the Gluck Equine Research Center for training. Farm assignments are made. Surveying begins.
May 30-June 8 — More than 100 farms are surveyed during the first eight days. Data are coded and entered by Dr. Barry Meade and electronically sent to CEAH, who develops computer program to analyze data.
June 8-18 — Surveying completed.
June 20 — KAEP general meeting on MRLS. All 80 members are requested to compile combinations of risk factors they specifically request to be analyzed.
June 26 — Data verification is completed (e.g., is it a 6 or a 0?). The final farm survey information is electronically sent to CEAH.
July 2 — Preliminary results of survey released on the Department of Veterinary Science Web site.
July 2-9 — Individual mare survey is finalized; 6 farms are randomly chosen and agree to participate with ~300 mares involved.
July 11-August 24 — Individual mare surveys completed, data are verified, coded and e-mailed to CEAH for analysis.
August 9-11 — Dr. Dwyer visits CEAH for summary of farm and pasture survey results.

the help of the USDA's Center for Epidemiology and Animal Health (CEAH) experts who design and analyze national and multidisciplinary animal surveys. The public may be more familiar with their work on the 1998 Equine National Animal Health Monitoring System (NAHMS), which has been widely quoted in lay and scientific literature and has been presented at multiple national and international meetings.

More than 200 people worked on this survey, which had the goal of identifying factors associated with MRLS early and late-term abortions in central Kentucky. These included potential risk factors, protective factors which may have helped prevent the syndrome, and those needing further investigation. Results of these studies will be published at **www.ca.uky.edu.**

This is, arguably, the best example of a large cooperative effort of farm owners, managers and their staffs, veterinarians, equine industry representatives, researchers, and state and federal agencies coming together to help solve an equine problem of immense industry and financial significance. ■

CONTACT
Dr. Roberta Dwyer, (859) 257-4285
rmdwyer@uky.edu
Department of Veterinary Science
University of Kentucky, Lexington, Kentucky

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Department of Veterinary Science
Gluck Equine Research Center
University of Kentucky
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