Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

EQUINE VIRAL ARTERITIS

Peter J. Timoney, MVB, PhD, FRCVS,
and William H. McCollum, PhD

A major sequel to the 1984 epidemic of equine viral arteritis (EVA) on Thoroughbred breeding farms in central Kentucky has been the enhanced significance with which this disease is currently regarded both nationally and internationally. Equine viral arteritis is very likely an age-old malady of horses that in the late nineteenth and early twentieth centuries was referred to by a variety of terms clinically descriptive of the disease; e.g., infectious cellulitis-pinkeye, rotlaufseuche.[1, 36] It was not until 1953, however, following an extensive outbreak of a respiratory-abortion syndrome on a Standardbred breeding farm near Bucyrus, Ohio, that EVA was identified as an etiologically distinct disease of the horse and shown to be caused by a virus that was readily distinguishable from equine rhinopneumonitis (herpesvirus 1 and 4) and equine influenza viruses.[9] In recognition of the characteristic vascular lesion associated with this infection, the etiologic agent was named equine arteritis virus (EAV). Ironically, in the approximate 30-year period from 1953 to 1984, few considered EVA a disease of veterinary medical or economic significance, notwithstanding the earlier evidence of the potential of this virus to cause abortion in mares.

Equine viral arteritis is a contagious viral disease of the horse that has been frequently confused with clinically similar diseases, especially those caused by equine herpesviruses 1 and 4 or equine influenza virus infections. Outbreaks of EVA are often associated with the movement of horses, and widespread dissemination of the virus may occur at racetracks and on breeding farms.

CLINICAL CHARACTERISTICS

Exposure to EAV may result in the development of clinical or inapparent infection, depending on the strain of virus involved, size of virus challenge, the age and physical condition of the animal(s) infected, and environmental condi-

From the Department of Veterinary Science, Gluck Equine Research Center, University of Kentucky, Lexington, Kentucky

tions.[42] Subclinical cases of infection are very common, especially in mares bred to long-term carrier stallions. Epidemiologic investigation of outbreaks of EVA has shown that the incidence of clinical to subclinical infection can vary from 1.4:1 to 1:6 in mares bred to persistently infected stallions.[39] During the 1984 epidemic in Thoroughbreds in Kentucky, it was estimated that 57% of affected farms had one or two cases of EVA, and only 14% of premises had five or more cases of the disease.[41]

The clinical signs observed in natural cases of EAV infection can vary widely in range and severity. Typical cases of the disease may present with any combination of the following: pyrexia of up to 41°C (106°F) that develops after an incubation period of 3 to 14 days (6 to 8 days after venereal exposure) that can be of 2 to 9 days duration; depression and anorexia; leukopenia; limb edema, especially of the hind limbs; stiffness of gait; nasal and lacrimal discharges; conjunctivitis and rhinitis; periorbital/supraorbital edema; mid-ventral edema involving the scrotum and prepuce of the stallion and mammary glands of the mare; urticarial-type rash that may be localized to the sides of the neck or face or generalized over most of the body; and abortion in the mare. Pyrexia and leukopenia are the most consistently observed clinical features of EVA. Less frequently observed signs include respiratory distress, coughing, diarrhea, ataxia, papular eruptions beneath the mucous membrane inside the upper lip, submaxillary lymphadenopathy, and adventitious edematous swelling in the intermandibular space, beneath the sternum, or in the shoulder region. Severity of clinical signs is likely to be greater in very young or very old horses and in debilitated animals. With rare exceptions, horses naturally affected with EVA make uneventful clinical recoveries even in the absence of symptomatic treatment. Mortality in natural cases of the disease is very uncommon and has only been reported infrequently in neonatal foals that succumbed from a fulminating interstitial pneumonia[2, 41, 49] and in foals up to a few months of age affected with a rapidly progressive pneumoenteric syndrome.[15]

Abortion due to EAV may occur late in the acute phase or early in the convalescent phase of the infection irrespective of the presence or absence of clinical signs of the disease.[9, 15, 26] Natural or experimental cases of EAV-related abortion have been recorded at anywhere from 3 to over 10 months of gestation.[5, 26] In natural outbreaks of the disease, abortion rates have varied significantly from less than 10% to between 50 and 60%.[42] An abortion rate as high as 71% was recorded in one experimental study of the transmissibility and abortigenicity of the Kentucky 1984 strain of EAV.[5] Although still unproven, there is evidence to indicate that perhaps not all strains of this virus are abortigenic.

Mares infected with EAV as a result of being bred to a shedding stallion do not appear to experience any short- or long-term virus-related fertility problems. On the other hand, stallions that have been acutely affected with the disease may undergo a period of temporary subfertility that is considered to be the result of increased testicular temperature rather than a specific side-effect of the virus. Reduced libido during the acute phase of infection is associated with decreased sperm motility, concentration, and percentage of morphologically normal sperm in ejaculates. These changes have been reported to persist for up to 6 to 7 weeks in stallions after experimental infection with EAV.[34] Although the magnitude of these changes is sufficient to cause temporary impairment of fertility in certain stallions, no long-term effects on semen quality have been observed in naturally infected stallions, even those that have remained long-term carriers of the virus for several years.[43]

A frequently encountered misconception about EVA concerns the mortality

rate associated with the disease. Apart from the potential of EAV to cause abortion in mares and, very rarely, fulminating respiratory disease in young foals, mortality does not occur following infection with naturally occurring strains of the virus. This is in sharp contrast, however, to what has been seen in horses challenged with an experimentally derived velogenic variant of the Bucyrus strain of EAV. This experimental variant of the virus can cause up to 60% mortality in adult horses exposed by the respiratory route (McCollum WH, personal communication, 1983). Much of the confusion that currently prevails regarding this disease has stemmed from incomplete and misleading descriptions of EVA in some widely referenced texts.

CAUSAL AGENT

Equine viral arteritis is caused by an RNA virus that has been classified in the genus *arterivirus* in the nonarthropod-borne group of the family *Togaviridae*.[51] Recently, The International Committee on Taxonomy of Viruses removed the genus *arterivirus* from the family *Togaviridae* and left it a free-floating genus pending the assessment of ongoing research.[37] Its natural and experimental host range would appear to be restricted to equids. Recent studies have indicated that based on organization of the viral genome, pattern of gene expression, and replication strategies, there is a strong likelihood that coronaviruses, toroviruses, and arteriviruses are ancestrally related and belong to a coronavirus-like superfamily.[8] The *arterivirus* genus has now been expanded to include the causal virus of the newly defined disease of swine; porcine reproductive and respiratory syndrome,[50] lactate dehydrogenase-elevating virus, and simian hemorrhagic fever virus.[36a]

Only one serotype of EAV has been recognized so far; the prototype Bucyrus strain, notwithstanding evidence of limited antigenic and genomic variation among North American and globally distributed isolates of the virus.[13, 32, 33] Although the information available on variation in pathogenicity between strains of EAV is, as yet, incomplete, it is nonetheless evident that the ability of strains to produce disease can vary greatly.[41]

Equine arteritis virus possesses a complement-fixing antigen but no hemagglutinin. It is easily inactivated by lipid solvents and disinfectants, and although relatively thermolabile, can survive for years at low temperatures.

DISTRIBUTION

It is evident from the results of various serologic surveys that EAV is widely distributed in horse populations throughout the world, having been reported in countries in North and South America, Europe, Africa, Asia, Australia, and New Zealand.[42] Notwithstanding its widespread distribution, there have been relatively few recorded occurrences of EAV-related illness since EVA was first defined as an etiologically distinct disease of the horse in 1953.[9] This may be partly because many cases of both clinical and inapparent EAV infection go undiagnosed because of limitations in available diagnostic capability and partly because the infection can be readily confused with other clinically similar respiratory diseases of the horse. Five known epidemics of EVA have occurred in the past 40 years, all of them in North America. With the exception of the 1984 epidemic on Thoroughbred breeding farms in Kentucky, all of these occurrences took place at racetracks and were characterized by rapid spread of the virus, with several hundred horses becoming affected in each instance.[42]

The prevalence of EAV infection varies considerably both between countries and between different breeds in the same country. Various serologic surveys conducted in the United States have disclosed that between 70 and 90% of Standardbred mares and stallions are likely to be seropositive for antibodies to the virus compared to 2 to 3% in the corresponding Thoroughbred population (Timoney PJ, McCollum WH, unpublished data).[23, 28]

TRANSMISSION

The two most important modes of transmission of EAV are via the respiratory route, involving infective aerosolized respiratory tract secretions of an acutely infected horse, and venereally, by an acute or chronically infected stallion. The importance of aerosol transmission has been documented in both natural and experimental infections,[9, 24, 25] and it is very probably the primary route of dissemination of EAV during widespread outbreaks of the disease that occur infrequently at racetracks. Although virus is also shed in vaginal secretions,[12, 26] urine,[24, 26, 35] and feces,[12, 35] during the acute phase of the infection, the amount and duration of virus shedding is greatest via the respiratory tract. EAV can be found in high concentration in respiratory secretions for up to 7 to 14 days.[24] Another potential source of virus is the fetus, placenta, and placental fluids from a mare that has aborted as a result of EAV infection.[5, 11, 26] It would appear, however, that close or direct contact is required for aerosol transmission to occur from any of the aforementioned sources of infection.[6, 40]

In association with the 1984 epidemic of EVA in Kentucky, it became evident that venereal transmission of EAV also played a very significant role in the spread of the disease. Apart from the potential for dissemination of the virus by this route by both the acutely infected mare and the stallion, venereal transmission by the long-term carrier stallion represents the primary means whereby EAV is maintained in horse populations throughout the world. Such persistently infected stallions appear to shed virus solely by the venereal route and can transmit the infection to 85 to 100% of seronegative mares to which they are bred.[43]

Transmission of EAV through indirect contact with virus-contaminated fomites, such as shanks, twitches, apparel, or personnel, is thought to play a minor role in the overall spread of this infection. Though not considered significant in relation to the 1984 epidemic of EVA in Kentucky,[41] it was suspected, however, to have been of some importance with respect to an outbreak of the disease that occurred in a veterinary teaching hospital.[6] Of further potential significance with regard to virus transmission is the role the teaser stallion or nurse mare may play in dissemination of the infection. Analysis of data from the 1984 epidemic in Kentucky could not, however, confirm that either had contributed significantly to spread of the virus on the majority of the farms investigated.[41]

Although rare, congenitally acquired infection resulting from transplacental transmission of EAV can ensue when a pregnant mare is exposed to the virus very late in gestation.[49] Although there have been no reports of teratological abnormalities associated with such infections, infected foals may develop a rapidly progressive, fulminating interstitial pneumonia and a fibrinonecrotic enteritis.

Experimentally, transmission of EAV has been achieved by the intravenous, subcutaneous, intranasal, and intratracheal inoculation of lung or spleen suspensions from acutely infected horses.[9] Also, mares have been infected following artificial insemination with semen from a long-term carrier stallion.[27]

IMMUNITY

Early studies by Doll et al[9, 10] confirmed that horses could be immunized by natural or experimental infection against subsequent challenge with virulent EAV. The duration of immunity resulting from natural infection or vaccination seems to be long lasting, in sharp contrast to that seen in equine influenza and herpesvirus infections.[10, 20, 21, 29] Complement-fixing and neutralizing antibodies appear as part of the humoral response in immunized horses, with neutralizing antibodies detectable within 1 week of exposure, peaking within 1 to 2 months, and persisting for 3 years or more.[21]

Serologic responses to the current commercial modified live virus EAV vaccine (ARVAC, Equine Arteritis Vaccine, Fort Dodge Laboratories, Inc, Fort Dodge, IA) are markedly enhanced in horses following initial revaccination, with the development of high neutralizing antibody titers that remain for at least several breeding seasons (Timoney PJ, McCollum WH, Umphenour N, and Roberts AW, unpublished data).

Foals born to mares that have been immunized against EVA are protected against the disease through the passive transfer of antibodies in the colostrum. This passively acquired protection, which lasts for 2 to 6 months, was found to interfere with vaccination with a modified live EAV vaccine.[22]

PATHOGENESIS AND PATHOLOGY

Details of the pathogenesis of EAV infection are based on experimental studies in horses challenged intranasally with the virulent variant of the Bucyrus strain of the virus.[7, 24] Initial multiplication of virus takes place in bronchial macrophages in the lungs. Within 48 hours of infection, EAV can be found in the regional lymph nodes, especially the bronchial nodes. By the third day after challenge, viremia has developed, and virus is widely distributed in various body tissues and fluids. Development of the characteristic vascular lesion associated with this infection is evident initially in blood vessels in the lungs and then in the small arteries and veins throughout the body. Virus also localizes in various epithelial sites, particularly the adrenal epithelium and the epithelial cells of the seminiferous tubules, thyroid, and liver.

With the exception of the reproductive tract in certain colts and stallions, infective EAV is no longer detectable in most body fluids and tissues after day 28 postchallenge.[12, 35] The virus has been shown to persist in specific sites in the reproductive tract for up to 180 days in prepubertal colts, 450 days in peripubertal colts,[16] and for a variable period of months or years in mature stallions.[34, 43]

The most prominent gross lesions found on necropsy examination of horses clinically affected with EVA comprise edema, congestion, and hemorrhage in various tissues throughout the body.[18, 37] The distribution and extent of these lesions are largely reflective of the vascular-mediated pathology associated with this infection and the sites of viral replication.[7]

In cases of EAV-related abortion, fetuses are usually partly autolyzed at time of expulsion and may present with a variable degree of interlobular pulmonary edema.[17] A diffuse interstitial pneumonia with excess fluid in the pleural and pericardial sacs together with edema and multifocal serosal and mucosal petechiae and ecchymoses in the wall of the small intestines have been described in fatal cases of EAV infection in very young foals.[15, 49]

The characteristic microscopic lesion observed in cases of EVA is a vasculitis involving the small arteries and, to a lesser extent, the small veins throughout

the body.[7, 18] Initial changes involve the endothelial cells of the intima, which round up and become pyknotic. This is followed by fibrinoid necrosis and lymphocytic infiltration of the tunica media and, later, by edema and infiltration of the adventitia. Thrombosis resulting from these vascular lesions has rarely been observed except in the lung and intestinal tract.[18]

No significant gross or microscopic lesions have been described in the majority of fetuses from cases of natural or experimental EAV-induced abortion.[4, 5, 9, 18] However, prominent vascular lesions were observed in the placentae, brains, livers, and spleens and, to a much lesser extent, in the lungs of two cases of EVA abortion reported by Johnson et al.[17] Microscopic lesions described in fatal cases of EAV infection in young foals comprise congestion, interlobular edema, and mononuclear cell infiltration in the lungs; locally extensive areas of mucosal hemorrhage and necrosis and fibrinoid necrosis of capillary and arterial walls in the small intestine; and multifocal hemorrhage and moderate lymphoid cell depletion in the thymus, spleen, and mesenteric lymph nodes.[49]

EPIDEMIOLOGY

A wide range of factors, both intrinsic and extrinsic to the host, have been shown to be implicated in the epidemiology of EVA and the current distribution of EAV in horse populations throughout the world. Of primary importance in any consideration of this disease is the fact that the majority of cases of acute EAV infection are subclinical or inapparent.[41] As demonstrated during the 1984 epidemic in Kentucky, the incidence of clinical disease to inapparent infection can vary significantly within groups of mares bred to particular stallions acutely or chronically infected with EAV. It is felt that mares bred to many of the long-term carrier stallions develop minimal, if any, clinical signs of EVA.

Of particular interest in relation to the epidemiology of this disease is the wide disparity in prevalence of infection between certain breeds, specifically the Standardbred and Thoroughbred. Various serologic surveys conducted in the United States and other countries have shown that the infection is endemic in Standardbreds (Timoney PJ, McCollum WH, unpublished data).[23, 28, 31] Neither field nor experimental studies have demonstrated any difference in susceptibility to infection between the Standardbred breed and other breeds of horses or in the percentage of acutely infected stallions that later become chronic carriers of the virus.[42] The factors underlying this discrepancy in seroprevalence of infection between the Standardbred and other breeds, whether directly host-related or not, remain as yet undetermined.

As indicated previously, only one major serotype of EAV represented by the prototype Bucyrus strain of the virus has been identified so far.[41] Evidence of limited antigenic and genomic variation has been demonstrated between isolates of EAV from both acutely infected and long-term carrier stallions embracing a wide geographic area.[13, 33] At this point, however, no correlation has been established between these antigenic or genomic differences and the variation in pathogenicity that has been observed among certain strains of EAV. Based on currently available data, it would appear that many, but certainly not all, strains of the virus shed by persistently infected stallions give rise to clinically inapparent infections in mares to which they are bred. Emergence of strains of the virus with the ability to cause clinical illness, including abortion, remains an unpredictable event, the basis of which has not been elucidated.

Confirmation of the significance of venereal transmission in the dissemination of EAV in the aftermath of the 1984 epidemic in Kentucky greatly furthered

our understanding of the epidemiology of this infection.[39] Prior to that point, the most important mode of transmission of this virus was considered to take place via the respiratory route and to involve infective aerosolized respiratory secretions of an acutely infected horse.[24, 25] As previously indicated, transmission of EAV infection by indirect contact through the medium of virus-contaminated fomites or personnel may be possible, but this does not appear to play a major role in the transmission and epidemiology of EVA.

Although transmission by the respiratory route is primarily responsible for spread of infection among closely congregated horses, such as at racetracks, horse shows, or sales, it does not provide a means of ensuring long-term persistence of EAV in various horse populations. Of primary significance in this regard has been confirmation of the carrier state in the stallion.[46]

A relatively high percentage of stallions can become carriers and semen shedders of EAV for a period of months or years after infection with the virus. Initial exposure of such stallions is by aerosol transmission or venereal contact with an acutely infected mare. The potential for establishment of persistent infection in the entire male horse appears to be related to age or, more specifically, to state of reproductive maturity at time of exposure to the virus. Efforts to establish a long-term carrier state in sexually immature colts have been unsuccessful.[16]

The carrier stallion provides a source of EAV through venereal contact with a susceptible mare at the time of natural breeding or of artificial insemination with infective semen.[41] Establishment of clinical or inapparent infection in the mare would be associated with a period of profuse virus shedding by the respiratory tract. This, in turn, would provide the opportunity for secondary lateral transmission to occur to susceptible in-contact horses either on the stallion breeding farm or farm of origin in respect of mares that are "vanned in" to be bred. Evidence in support of this has come from certain outbreaks of EVA that have occurred in recent years. An extensive outbreak of the disease on a major Arabian farm in the United States in 1987 was closely linked to the introduction of a recently imported stallion that was likely a chronic carrier of EAV at the time of importation.[47] Signs of EVA were first observed in the initial group of mares that were artificially bred to this stallion in that breeding season. The stallion never displayed signs of EVA and was strongly seropositive and a semen shedder of the virus when sampled. This was coincidental with detection of the first cases of the disease on the farm.

In another instance involving a carrier Dutch Warmblood stallion, interstate shipment of infective semen was responsible for a series of outbreaks of EVA on farms in widely separate locations. Although initial cases of the disease occurred in mares inseminated with this semen, secondary spread of infection to in-contact pregnant mares with resultant abortion ensued in a number of instances (Timoney PJ, McCollum WH, unpublished data).

CARRIER STATE

Although existence of the carrier state appears to occur in a high proportion of stallions previously exposed to EAV, there is no evidence to date to indicate an analogous situation exists in the mare or foal.[39] Recent studies have confirmed that establishment and maintenance of the carrier state in the stallion is testosterone-dependent.[19]

Frequency of the carrier state can vary widely among different groups of stallions, with no indication of significant variation between Standardbreds and Thoroughbreds.[43] Persistent infection has been detected in from 30 to 60% of

stallions following natural infection with EAV.[42, 43] Carrier stallions usually carry moderate to high neutralizing antibody titers to the virus. The carrier state has never been confirmed in an EAV-seronegative stallion or in a stallion that has been previously vaccinated on one or more occasions with the modified live vaccine against EVA (ARVAC, Equine Arteritis Vaccine, Fort Dodge Labs, Inc, Fort Dodge, IA), notwithstanding the fact that such animals are almost invariably strongly seropositive to the virus.[42]

Duration of the carrier state can vary from weeks to months to years, perhaps even for the lifetime of particular stallions.[46] Initially, it was suspected that a short-term or convalescent carrier phase, lasting several weeks, and a long-term or chronic carrier phase persisting for years existed. Studies in recent years have confirmed that an intermediate carrier phase lasting 3 to 7 months can also occur in both naturally infected stallions (Timoney PJ, McCollum WH, unpublished data) and in prepubertal colts experimentally challenged with the virus.[16] Although the majority of long-term carrier stallions continue to harbor EAV, there have been a number of confirmed cases of persistently infected animals ceasing to shed virus after periods ranging from 1.5 to 10 years, with no indication of reversion to a shedding state at a later date (Timoney PJ, McCollum WH, unpublished data). Review of these cases has not provided any clear-cut evidence that spontaneous clearance of the carrier state was seasonally related.

Carrier stallions shed EAV constantly in the semen, and transmission of the virus appears to occur solely by the venereal route.[43] Virus has not been detected in the nasopharyngeal secretions, urine, or blood of carrier animals. EAV is localized to the reproductive tract, and the primary site of virus persistence in the stallion is the ampulla of the vas deferens, with other accessory sex glands and portions of the lower genitourinary tract of secondary importance.[35] Virus is shed in the sperm-rich portion of the ejaculate, but is not present in the preejaculatory fluids.[43] Although it varies among stallions, some animals shed virus in very high concentrations in the semen. Extended field studies have provided no evidence that carrier stallions are or can become intermittent shedders of the virus or of the existence of latency in the persistently infected horse.[44] There appears to be 85 to 100% transmission of EAV to seronegative mares bred to long-term carrier stallions, with mares seroconverting within 28 days after breeding.[41]

ECONOMIC SIGNIFICANCE

The most significant consequences associated with occurrence of EAV infection in susceptible horses are the possibility of abortion in the mare and the establishment of the carrier state in the stallion. Of prime economic importance to the horse industry are the direct financial losses attributable to outbreaks of EAV-related abortion and the denied export markets for carrier stallions and, in the case of some countries, other categories of horses naturally seropositive for antibodies to the virus.[42] Where extensive outbreaks of EVA have occurred at racetracks, there have been attendant financial losses associated with disruption of training schedules, reduced race entries, and even race fixture cancellations.

The 1984 epidemic of EVA on Thoroughbred breeding farms in Kentucky resulted in some of the severest restrictions ever imposed on the export of horses from the United States to many of the other bloodstock-raising countries of the world.[41] Horses carrying stable, naturally acquired antibody titers to EAV, although presenting no epidemiologic risk of introducing virus into the horse population of the importing country, were stigmatized as a result of these meas-

ures and precluded from export. This has been especially financially punitive for the Standardbred industry, because the seroprevalence of infection in this breed in the United States can approach 80%.

Based on the results of an ongoing program of pre-export testing of stallions, a carrier rate of 58% was found among 130 naturally infected seropositive Standardbred stallions, or approximately 42% of the total number of stallions examined (Timoney PJ, McCollum WH, unpublished data). Although it is difficult to estimate with accuracy the extent of the loss in export revenue sustained by the country's Standardbred industry during the period under review, it must have run into many millions of dollars.[42]

In addition to the foregoing, consideration must also be given to the financial consequences associated with the continued commercial use of carrier stallions in those states that have implemented specific programs for the prevention and control of EVA in their respective Thoroughbred populations, namely Kentucky and New York. Provision was made in each program to allow the continued use of these stallions subject to certain stringent requirements being met. Although these measures have provided the necessary safeguards to prevent recurrences of EVA, they have also resulted in financial losses for the stallion owners due to decreased commercial demand for these animals.[42]

DIAGNOSIS

A presumptive diagnosis of EVA cannot be made based solely on presence of the characteristic signs of the disease. A number of other infectious and noninfectious diseases of the horse can clinically mimic EVA. These include other upper respiratory tract viral infections, especially equine herpesvirus 1 and 4, both subtypes of equine influenza virus, equine infectious anemia, purpura hemorrhagica, urticaria, and toxicosis due to hoary alyssum (*Berteroa incana*).[14] Two other important viral diseases of the horse, African Horse Sickness and Getah virus infection, both of which are exotic to the United States, also need to be considered within the context of a differential diagnosis because of clinical similarities with EVA.

Of diagnostic significance in helping to differentiate abortion due to EAV from that caused by equine herpesvirus 1 or, rarely, 4, is the fact that in herpesviral infection, the mare very seldom displays any premonitory signs prior to abortion. Furthermore, herpesvirus-infected fetuses are expelled fresh and frequently have characteristic gross lesions, whereas those infected with EAV are usually partly autolysed and seldom have any pathognomonic lesions.

Confirmation of a diagnosis of acute EAV infection is currently based on virus isolation and/or corroborative serologic data derived from tests of paired (acute and convalescent) sera taken at a 21- to 28-day interval. Initial experimental findings from the application of the polymerase chain reaction assay to the diagnosis of this infection, although still at a preliminary stage, appear very promising (Belak S, Ballagi-Pordany A, Klingeborn B, Timoney P, McCollum W, unpublished data).[3]

Appropriate specimens for virus isolation from the live animal include nasopharyngeal swabs or washings, conjunctival swabs, and citrated, EDTA, or heparinized blood samples. The chances of successfully isolating virus are influenced to a significant extent by the timing and quality of specimens that are collected. Specimens should be obtained as soon as possible after the onset of illness or suspected EAV infection. Swabs should be placed immediately in a

suitable viral transport medium* and either refrigerated or, preferably, frozen at −20°C or lower.

In cases of suspect EAV-related abortion, virus isolation can be attempted from placental and fetal fluids, placenta, lymphoreticular and other tissues, especially fetal lung.[5, 40] When a suspected outbreak of EVA is associated with mortality in young foals or older horses, specimens of a wide range of tissues, especially the lymphatic glands associated with the alimentary and respiratory tracts and related organs, should be collected both for virus isolation and histopathologic examination for the characteristic vascular lesions associated with this infection.

Screening a stallion for the presence of the carrier state initially involves taking a blood sample to determine the EAV serologic status of the animal. Only horses testing positive at a serum dilution of 1:4 or greater need be considered potential carriers of the virus. Such stallions should be screened virologically either by subjecting them to a test-breeding program involving two seronegative mares and monitoring the latter for seroconversion to the virus up to 28 days after breeding, or by attempting isolation of EAV in vitro from a collection of semen.[45] The latter method has the advantages of minimal cost, safety, and timeliness of a result. Virus isolation can be attempted at any time from the semen of a putative carrier stallion, because such animals shed the virus constantly in the semen. Care should be taken to ensure that a collection contains the virus-associated sperm-rich fraction of the ejaculate.

With the exception of unclotted blood samples, which should be refrigerated and not frozen, all specimens for attempted virus isolation should be dispatched, preferably frozen, with several freezer packs or in dry ice in a suitably insulated container and sent to an appropriately qualified laboratory using an overnight delivery service.

TREATMENT

There is no specific treatment for horses affected with EVA. As virtually all acutely affected animals make uneventful clinical recoveries, the only indications for symptomatic treatment are to assuage the severity of clinical signs. This is especially relevant for stallions that become pyrexic and develop extensive scrotal edema to minimize the potential for sperm damage and a period of temporary lowered fertility. Such animals should be allowed complete rest and given nonsteroidal antiinflammatory drugs and a diuretic to control the fever and edema. A gradual return to full activity is highly desirable. Prophylactic administration of antimicrobial drugs also may be indicated in severe cases of the disease.

At this point, there are no means available of eliminating the carrier state in stallions persistently infected with EAV other than surgical castration. Attempts at hyperimmunization of a limited number of carrier animals with the modified live vaccine against EVA (ARVAC, Equine Arteritis Vaccine, Fort Dodge Labs, Inc, Fort Dodge, IA) with a view to effecting viral clearance from the reproductive tract have been unsuccessful. Temporary down-regulation of circulating testosterone levels may offer some promise as a therapeutic strategy for future investigation (Little T, personal communication, 1991).

---

*Any cell culture medium or balanced salt solution containing from 2 to 5% antibody-free serum.

PREVENTION AND CONTROL

Current knowledge of the biology of EAV and the epidemiology of EVA has enabled the formulation of effective measures for the prevention and control of this disease. It is ironic that prior to the 1984 epidemic in Thoroughbreds in Kentucky, little attention was paid to the veterinary medical significance of EVA or to the need to develop a preventive program to control the spread of this infection, either nationally or internationally. This is especially remarkable in view of the known abortifacient properties of the causal virus. The 1984 epidemic not only served to reemphasize the abortigenic potential of EAV[5, 26] but also provided the first indication that a relatively high percentage of infected stallions become long-term carriers and constant semen shedders of the virus.[41]

Integral to current preventive and control programs is the availability of a modified live vaccine against EVA (ARVAC, Equine Arteritis Vaccine, Fort Dodge Labs, Inc, Fort Dodge, IA) that has been shown to be safe and effective for stallions and nonpregnant mares.[10, 30, 48] Mild postvaccinal febrile reactions with transient lymphopenia have been observed in a very small percentage of horses vaccinated for the first time. The vaccine is not recommended for use in pregnant mares, especially during the last 2 months of gestation, or in foals less than 6 weeks of age unless under circumstances of probable high risk of exposure to natural infection.[10]

Although primary vaccination with the current vaccine provides clinical protection against EVA for at least 1 to 3 years, it does not prevent reinfection and limited replication of challenge virus.[27] The duration of virus shedding and the amount of virus shed via the nasopharynx is, however, very significantly less than in unvaccinated controls. Revaccination results in markedly enhanced serologic responses that persist for at least several breeding seasons (Timoney PJ, McCollum WH, Umphenour N, Roberts AW, unpublished data). The vaccine was used successfully to curtail the spread of EVA during the 1984 epidemic in Kentucky, and in three subsequent large-scale outbreaks of the disease that have occurred in North America. Its use as part of the EVA control programs in Kentucky and New York for the past 9 years has not been associated with any adverse sequelae.

Apart from the potential for widespread aerosol transmission of EAV at racetracks, horse shows, and sales, prevention of EVA on breeding farms can best be achieved through implementation of sound management practices and selective use of the available vaccine, including strategic vaccination of the at-risk breeding stallion population. The possibility of introducing EAV into a group of susceptible horses can be minimized by isolating all horses returning from other farms, sales, or racetracks for 3 to 4 weeks. If feasible, segregation of pregnant mares from other horses is recommended. In the event of an outbreak of EVA, restriction of movement of breeding stock, selective vaccination, and, as an extreme resort, closure of the breeding sheds have been measures that have been successful in curtailing the spread of the disease among breeding farms.[41]

Currently, very few specific programs have been developed for the control of EVA. Kentucky and New York are the only two states that have formulated preventive and control programs for their respective Thoroughbred breeding industries.[41] Both programs are predicated on the unique significance of the carrier stallion in the epidemiology of this disease. This fact and the high frequency of the carrier state in recovered stallions have underscored the importance of identifying carrier animals in any population of breeding stallions and of implementing a policy of annual vaccination of all at-risk breeding stallions at least 28 days before onset of each breeding season. There are several advantages

to this strategy, including control over establishment of the carrier state in additional stallions, and preventing possible venereal transmission of EAV in the breeding shed and precluding the need to screen mares entering the breeding shed for evidence of EAV infection. Additionally, all first-season stallions should be checked for presence of the carrier state before the start of each breeding season. Stallions that are confirmed semen shedders and carriers of EAV can continue to be used commercially, subject to certain safeguards being met. Carrier stallions should be kept physically isolated and bred only to mares that are seropositive from previous natural exposure or vaccination or, if seronegative, vaccinated not less than 3 weeks previously. After being bred, recently vaccinated mares should be kept isolated from other seronegative horses for a period of 3 weeks. These measures, when implemented fully, have been successful in preventing occurrences of EVA associated with the use of carrier stallions.

While existing programs are directed towards controlling the spread of EAV in the Thoroughbred breed, they could, with some modification, be applied to other breeds, especially the Standardbred breed, in which the infection appears to be endemic. Based on the results of recent studies confirming the testosterone-dependency of the carrier state in the stallion[19] and the inability to establish long-term infection in the reproductive tract of prepubertal colts,[16] EVA vaccination of all Standardbred colts between 6 and 12 months of age ought to be promoted as a means of preventing future establishment of the carrier state in these animals. Because there is a risk of inadvertently introducing EAV into a susceptible horse population through the use of infective fresh or frozen semen, measures need to be formulated to obviate this happening in those breeds in which artificial insemination is permitted.

Experience since the 1984 epidemic in Kentucky has shown that practical measures can be formulated to achieve effective control over the spread of EVA at the state level. It remains to be seen, however, whether the U.S. horse industry or individual breed organizations consider the past and current economic consequences of this disease of sufficient magnitude to justify embarking upon a similar type control program that would be acceptable at the national level.

SUMMARY

Equine viral arteritis is an infrequently encountered contagious viral disease of equids that has assumed increased veterinary medical and economic significance since the 1984 epidemic in Thoroughbreds in Kentucky. The most important consequences of this infection are abortion in the mare and establishment of the carrier state in the stallion. Equine arteritis virus becomes localized in the reproductive tract of a relatively high percentage of infected stallions which serve as very efficient transmitters of the infection through direct or indirect venereal contact with susceptible mares. The long-term persistently infected stallion appears to play a major epidemiologic role in the dissemination and perpetuation of the virus in horse populations throughout the world. Aspects of the pathogenesis, immunity, and epidemiology of equine arteritis virus are discussed in relation to current methods for the diagnosis, treatment, and control of this disease.

ACKNOWLEDGMENT

Financial support for some of the material presented in this article was provided by the Frederick Van Lennep Professorship Endowment Fund.

Published as paper (No. 92–4–179) by permission of the dean and director, College of Agriculture and Kentucky Agricultural Experiment Station.

References

1. Bergman AM: Beitrage zur Kenntnis der Virustrager bei Rotlaufseuche, Influenza erisipelatosa, des Pferdes. Z Infecktionskrankh 13:161, 1913
2. Carman S, Rae C, Dubovi E: Equine arteritis virus isolated from a Standardbred foal with pneumonia. Can Vet J 29:769, 1988
3. Chirnside ED, Spaan WJM: Reverse transcription and cDNA amplification by the polymerase chain reaction of equine arteritis virus (EAV). J Virol Methods 30:133, 1990
4. Coignoul FL, Cheville NF: Pathology of the maternal genital tract, placenta and fetus in equine viral arteritis. Vet Pathol 21:333, 1984
5. Cole JR, Hall RF, Gosser HS, et al: Transmissibility and abortigenic effect of equine viral arteritis in mares. J Am Vet Med Assoc 189:769, 1986
6. Collins JK, Sari S, Ralston SL, et al: Equine viral arteritis at a veterinary teaching hospital. Prev Vet Med 4:389, 1987
7. Crawford TB, Henson JB: Immunofluorescent, light microscopic and immunologic studies of equine viral arteritis. *In* Proceedings of the Third International Conference of Equine Infectious Diseases, Paris, 1973, p 282
8. den Boon JA, Snijder EJ, Chirnside ED, et al: Equine arteritis virus is not a Togavirus but belongs to the Coronavirus-like superfamily. J Virol 65:2910, 1991
9. Doll ER, Bryans JT, McCollum WH, et al: Isolation of a filterable agent causing arteritis of horses and abortion by mares. Its differentiation from the equine abortion (influenza) virus. Cornell Vet 47:3, 1957
10. Doll ER, Bryans JT, Wilson JC, et al: Immunization against equine viral arteritis using modified live virus propagated in cell cultures of rabbit kidney. Cornell Vet 48:497, 1968
11. Doll ER, Knappenberger RE, Bryans JT: An outbreak of abortion caused by the equine arteritis virus. Cornell Vet 47:69, 1957
12. Fukunaga Y, Imagawa H, Tabuchi E, et al: Clinical and virological findings on experimental equine viral arteritis in horses. Bull Equine Res Inst 18:110, 1981
13. Fukunaga Y, McCollum WH: Complement fixation reactions in equine viral arteritis. Am J Vet Res 38:2043, 1977
14. Geor RJ, Becker RL, Kanara EW, et al: Toxicosis in horses after ingestion of hoary alyssum. J Am Vet Med Assoc 201:63, 1992
15. Golnik W, Michalaska Z, Michalak T: Natural equine viral arteritis in foals. Schweiz Arch Tierheilkd 123:523, 1981
16. Holyoak GR: The relationship between onset of puberty and establishment of persistent infection with equine arteritis virus in the experimentally infected colt [PhD dissertation]. Lexington, KY, University of Kentucky, 1992
17. Johnson B, Baldwin C, Timoney P, et al: Arteritis in equine fetuses aborted due to equine viral arteritis. Vet Pathol 28:248, 1991
18. Jones TC, Doll ER, Bryans JT: The lesions of equine viral arteritis. Cornell Vet 47:52, 1957
19. Little TV, Holyoak GR, McCollum WH, et al: Output of equine arteritis virus from persistently infected stallions is testosterone-dependent. *In* Equine Infectious Diseases VI: Proceedings of the 6th International Conference, Cambridge, UK, 1991, p 225
20. McCollum WH: Development of a modified virus strain and vaccine for equine viral arteritis. J Am Vet Med Assoc 155:318, 1969
21. McCollum WH: Vaccination for equine viral arteritis. *In* Proceedings of the Second International Conference on Equine Infectious Diseases, Paris, 1970, p 143
22. McCollum WH: Studies of passive immunity in foals to equine viral arteritis. Vet Microbiol 1:45, 1976
23. McCollum WH, Bryans JT: Serological identification of infection by equine arteritis

virus in horses of several countries. *In* Proceedings of the Third International Conference of Equine Infectious Diseases, Paris, 1972, p 256
24. McCollum WH, Prickett ME, Bryans JT: Temporal distribution of equine arteritis virus in respiratory mucosa, tissues and body fluids of horses infected by inhalation. Res Vet Sci 2:459, 1971
25. McCollum WH, Swerczek TW: Studies of an epizootic of equine viral arteritis in racehorses. J Equine Med Surg 2:293, 1978
26. McCollum WH, Timoney PJ: The pathogenic qualities of the 1984 strain of equine arteritis virus. *In* Proceedings of the Grayson Foundation International Conference of Thoroughbred Breeders Organizations, Drumoland Castle, Ireland, 1984, p 34
27. McCollum WH, Timoney PJ, Roberts AW, et al: Response of vaccinated and non-vaccinated mares to artificial insemination with semen from stallions persistently infected with equine arteritis virus. *In* Powell DG (ed): Equine Infectious Diseases V: Proceedings of the Fifth International Conference, Lexington, KY, University Press of Kentucky, 1987, p 13
28. McCue PM, Hietala SK, Spensely MS, et al: Prevalence of equine viral arteritis in California horses. California Veterinarian 45:24, 1991
29. McGuire TC, Crawford TB, Henson JB: Prevalence of antibodies to herpesvirus types 1 & 2, arteritis and infectious anemia viral antigens in equine serum. Am J Vet Res 35:181, 1974
30. McKinnon AO, Colbern GT, Collins JK, et al: Vaccination of stallions with a modified live equine arteritis virus vaccine. J Equine Vet Sci 6:66, 1986
31. Moraillon R, Moraillon A: Results of an epidemiological investigation on viral arteritis in France and some other European and African countries. Ann Rech Vet 9:43, 1978
32. Murphy TW, Timoney PJ, McCollum WH: Analysis of genetic variation among strains of equine arteritis virus. *In* Powell DG (ed): Equine Infectious Diseases V, Proceedings of the Fifth International Conference, Lexington, KY, University Press of Kentucky, 1987, p 3
33. Murphy TW, Timoney PJ, McCollum WH, et al: Genomic variability among globally distributed isolates of equine arteritis virus. Vet Microbiol 32:101, 1992
34. Neu SM, Timoney PJ, Lowry SR: Changes in semen quality following experimental equine arteritis virus infection in the stallion. Theriogenology 37:407, 1992
35. Neu SM, Timoney PJ, McCollum WH: Persistent infection of the reproductive tract in stallions experimentally infected with equine arteritis virus. *In* Powell DG (ed): Equine Infectious Diseases V: Proceedings of the Fifth International Conference, Lexington, KY, University Press of Kentucky, 1987, p 149
36. Pottie A: The propagation of influenza from stallions to mares. J Comp Pathol Ther 1:37, 1888
36a. Plagemann PGW, Moennig V: Lactate dehydrogenase-elevating virus, equine arteritis virus, and simian hemorrhagic fever virus: A new group of positive-strand RNA viruses. Adv Virus Res 41:99–192, 1991
37. Prickett ME, McCollum WH, Bryans JT: The gross and microscopic pathology observed in horses experimentally infected with equine arteritis virus. *In* Proceedings of the Third International Conference of Equine Diseases, Paris, 1972, p 265
38. Pringle CR: Committee pursues medley of virus taxonomic issues. Current Topics. ASM News 58:475, 1992
39. Timoney PJ, McCollum WH: The epidemiology of equine viral arteritis. Proc AAEP 31:545, 1985
40. Timoney PJ, McCollum WH: Equine viral arteritis. Can Vet J 28:693, 1987
41. Timoney PJ, McCollum WH: Equine viral arteritis: Epidemiology and control. J Equine Vet Sci 8:54, 1988
42. Timoney PJ, McCollum WH: Equine viral arteritis: Current clinical and economic significance. Proc AAEP 36:403, 1990
43. Timoney PJ, McCollum WH, Murphy TW, et al: The carrier state in equine arteritis virus infection in the stallion with specific emphasis on the venereal mode of virus transmission. J Reprod Fertil Suppl 35:95, 1987
44. Timoney PJ, McCollum WH, Murphy TW: A longitudinal study of equine arteritis virus infection in Standardbred stallions with special reference to occurrence of the carrier state. *In* Equine Infectious Diseases VI: Proceedings of the Sixth International Conference, Cambridge, UK, 1991, p 231

45. Timoney PJ, McCollum WH, Roberts AW: Detection of the carrier state in stallions persistently infected with equine arteritis virus. Proc AAEP 32:57, 1988
46. Timoney PJ, McCollum WH, Roberts AW, et al: Demonstration of the carrier state in naturally acquired equine arteritis virus infection in the stallion. Res Vet Sci 41:279, 1986
47. Timoney PJ, McCollum WH, Roberts AW: Current strategies for the control of equine viral arteritis. *In* Proceedings of the 92nd Annual Meeting of the United States Animal Health Association, Little Rock, AR, 1988, p 211
48. Timoney PJ, Umphenour NW, McCollum WH: Safety evaluation of a commercial live equine arteritis virus for use in stallions. *In* Powell DG (ed): Equine Infectious Diseases V, Proceedings of the Fifth International Conference, Lexington, KY, University Press of Kentucky, 1987, p 19
49. Vaala WE, Hamir AN, Dubovi E, et al: Fatal, congenitally acquired equine arteritis virus infection in a neonatal Thoroughbred. Equine Vet J 24:155, 1992
50. Wensvoort G, Terpstra C, Pol JMA, et al: Mystery swine disease in the Netherlands: The isolation of Lelystad virus. Vet Q 13:121, 1991
51. Westaway EG, Brinton MA, Gaidamovich SY, et al: Togaviridae. Intervirology 24:125, 1985

Address reprint requests to

Peter J. Timoney, MVB, PhD, FRCVS
Department of Veterinary Science
Gluck Equine Research Center
University of Kentucky
Lexington, KY 40546–0099