

REVIEW ARTICLE

Equine Viral Arteritis

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Abstract. Equine viral arteritis (EVA) can cause prominent economic losses for the equine industry. The purpose of this review is to provide the pathologist some familiarity with the clinical history, lesions, pathogenesis, and diagnosis of EVA. EVA is caused by an arterivirus (equine arteritis virus, EAV), and the vascular system is the principal but not unique viral target. EVA has variable presentations, including interstitial pneumonia, panvasculitis with edema, thrombosis and hemorrhage, lymphoid necrosis, renal tubular necrosis, abortion, and inflammation of male accessory genital glands. EAV antigen (EAVAg) can be demonstrated within the cytoplasm of epithelial cells such as alveolar pneumocytes, enterocytes, adrenal cortical cells, trophoblasts, thymus stroma, renal tubular cells, and male accessory genital gland cells. It can also be demonstrated within endothelia, in vascular, myometrial, and cardiac myocytes, macrophages, dendritelike cells of lymphoid organs, and chorionic memenchymal stromal cells. In young and adult horses, following colonization of macrophages, the virus spreads systemically using circulating monocytes and enters the endothelium and tunica media of blood vessels, histiocytes, and dendritelike cells. Eventually, the virus multiplies within renal tubular cells. Lesions are uncommon in the aborted fetus; if present, they are mild, and EAVAg is frequently not detectable within fetal tissues and placenta. The clinical presentation and lesions of EVA may resemble those of other diseases. Complete pathologic examination associated with immunohistochemistry, virus isolation, and, especially in cases of abortion, serology will guarantee a directed and accurate diagnosis.

Key words: Abortion; arterivirus; equine viral arteritis; nephritis; panvasculitis; pneumonia.

Equine viral arteritis (EVA) is a global infectious disease of horses and is characterized by panvasculitis inducing edema, hemorrhage, and abortion in pregnant mares. EVA can cause severe economic losses for the equine industry. The purpose of this review is to provide the pathologist some familiarity with the clinical history, lesions, pathogenesis, and diagnosis of EVA. EVA can be confused with other equine diseases and must be considered in sporadic and epizootic respiratory syndromes, foal death associated with respiratory and/or enteric signs, or sudden death in foals. Although not frequent, velogenic isolates of equine arteritis virus (EAV) can induce severe and fatal disease in adults. Natural outbreaks of EVA characterized by transient clinical signs and abortion in pregnant mares contrast with experimental disease, which features high mortality and prominent systemic vascular necrosis. Blood vessel cells are the major, but not exclusive, target of EAV. Lung, intestine, kidney, the reproductive tract, and occasionally the placenta are important viral replication sites, which favor the spread of the virus. Complete pathologic examination associated with the available ancillary procedures will help guarantee a directed and accurate diagnosis.

The Virus

EAV is an enveloped, spherical, positive-stranded RNA virus with a diameter of 50–70 nm. The virion is comprised of an isometric core surrounded by a lipid-containing envelope from which delicate spikes protrude. The viral genomic RNA, which is encapsulated by a single nucleocapsid protein, is contained within the core particle. Within the viral envelope at least three integral membrane proteins are incorporated. EAV is a non-arthropod-borne virus classified as a member of the new order Nidovirales, including also the bigeneric family Coronaviridae, within the family Arteriviridae with porcine respiratory and reproductive syndrome virus, simian hemorrhagic fever virus, and lactate dehydrogenase elevating virus. Genetically, EAV is similar to coronaviruses but has a dissimilar viral structure and a complement-fixing antigen but no hemagglutinins. Genetic diversity is recognized among field isolates. EAV was first isolated from fetal lung collected during an epizootic of abortion in Bucyrus, Ohio (USA). In Bucyrus, horses of both sexes and various age groups experienced an acute and febrile infectious disease charac-
Cytology of pulmonary washings has been described in one foal with severe pulmonary disease characterized by dyspnea, tachypnea, hypoxemia, and hypercapnia. The condition in this foal was initially reported in the literature as a case of bronchopulmonary dysplasia. Subsequent reanalysis of the case revealed that the foal was infected with EAV, and a correction was published. Cytologic abnormalities in bronchoalveolar lavage and tracheal aspirate reported for this foal included formed fragments of granular material, mucus, fibrin, a few small macrophages, and epithelial cells demonstrating cilia loss with retention of a prominent terminal bar and squamous metaplasia. In addition, there were papillary clusters of squamoid or cuboidal cells with focal loss of cilia. These cytologic findings corresponded to proliferative bronchiointerstitial pneumonia with intraalveolar macrophages and a few neutrophils, fibrin and hyaline membrane formation, type 2 pneumocytic hypertrophy, and hyperplasia. Most foals with EVA die without cytologic evaluation of tracheal and bronchial aspirates. This case is the only one with such an evaluation and likely represents findings in severe cases.

Because the EAV pulmonary antigen is not as abundant as the antigen in EHV-1 infection, its identification within the cytologic specimens may be difficult. However, renal tubular necrosis occurring during the late phase of the EAV infection is associated with florid intraepithelial intracytoplasmic viral growth, making the urine sample a potential candidate for in vivo immunocytochemical testing. In addition to buffy coat and rhinopharyngeal swab, part of the fluid obtained with the tracheal lavage and urine should be submitted for ancillary virologic testing.

Anatomic Pathology

EAV-associated gross and histologic lesions have been described in naturally infected and experimentally infected equids. The EAV isolates differ in virulence and consequently induce lesions that differ in severity. EAV antigen (EAVAg) can be identified in various tissues and organs either associated with lesions or occasionally in the absence of them. EAVAg can be identified within the cytoplasm of the infected cell using equine polyclonal and murine monoclonal antibodies in fresh and fixed tissues.

Gross lesions

Gross lesions are the expression of the vascular pathologic changes. Edema, congestion, and hemorrhage of the subcutaneous tissues, lymph nodes, and viscera are the most frequent gross lesions in horses that die after natural or experimental EAV infection (Fig. 1). The body cavities may contain moderate to abundant amounts of yellowish clear exudate. Congestion and lymphadenomegaly, edema, and hemor-
**Fig. 1.** Lung, liver, and stomach; foal with EVA. Severe and diffuse edema of lung, Glisson hepatic capsule, and gastric mucosa, with petechiae. Bar = 8 cm. (Courtesy of J. M. King, Department of Pathology, College of Veterinary Medicine, Cornell University, Ithaca, NY.)

**Fig. 2.** Small muscular artery; foal with EVA. Fibrinoid necrosis of the tunica media and perivascular edema with lymphocytic infiltrate. HE. Bar = 80 μm.

**Fig. 3.** Lung; foal with EVA. Interstitial pneumonia with hypertrophied type 2 pneumocytes containing intracytoplasmic EAV antigen. Hematoxylin and avidin–biotin immunoperoxidase. Bar = 20 μm.

**Fig. 4.** Small muscular artery; foal with EVA. Vascular intimal and medial necrosis with perivascular lymphocytic infiltrate and edema. EAV antigen is diffusing from the endothelium to the tunica media. Hematoxylin and avidin–biotin immunoperoxidase. Bar = 120 μm.

**Fig. 5.** Kidney; mare with EVA. Severe diffuse interstitial lymphocytic nephritis with tubular necrosis and abundant EAV antigen contained in renal tubules and intraluminal casts. Hematoxylin and avidin–biotin immunoperoxidase. Bar = 300 μm.

**Fig. 6.** Chorioallantois; equine fetus with EVA. A syncytial trophoblast cell contains abundant intracytoplasmic EAV antigen. Hematoxylin and avidin–biotin immunoperoxidase. Bar = 25 μm.
rhames can be observed along the course of the colonic and cecal vessels but also are evident systemically. On the cut surface of lymph nodes, there may be a prominent subcapsular sinus and dilated medullary sinuses. Lungs, especially those of infected neonates (Fig. 1), are wet and increased in weight, with a prominent lobular pattern. The trachea may contain froth. On occasion, lungs can be multifocally or diffusely reddish because of congestion and hemorrhage. The uterine endometrial surface of aborting mares may be swollen and diffusely congested, sometimes with hemorrhages.

**Microscopic lesions**

The histologic lesions are observed in various systems of horses with EAV infection. The blood vessels are the principal target.

**Blood vessels.** All organs, including the skin, may contain vascular changes. Mild lesions include vascular and perivascular edema with occasional lymphocytic infiltrate and endothelial cell hypertrophy. Severe changes include vasculitis with fibrinoid necrosis of the tunica media, abundant vascular and perivascular lymphocytic and lesser granulocytic infiltration (Fig. 2) with karyorrhexis, frequent loss of endothelium, and formation of large fibrinocellular stratified thrombi. Occasionally, vascular portal vasculitis consists of severe inflammatory cell infiltrate that erodes the hepatocellular perportal limiting plate. Within vessels, EAVAg localizes in endothelium, medial myocytes (Fig. 4), and pericytes. Marginating macrophages containing intracytoplasmic EAVAg may be seen, occasionally associated with infected endothelial cells. Rarely, cardiac vasculitis with myocyte necrosis and associated EAVAg can be observed. Ultrastructurally, infected endothelial cells appear hypertrophied, with expansion of cytoplasmic matrix in the absence of increased cytoplasmic organelles. Endoplasmic cisternae are distended, and mitochondria are increased in volume and their cristae are affected by degenerative changes. Specific cytoplasmic alterations associated with viral colonization of endothelial cells include dense crystallloid viral particles contained within endoplasmic cisternae and membranes of endoplasmic reticulum and vacuoles containing virions. These viral particles average 58 nm in diameter and are characterized by a 25-nm core and a less dense external membrane. Capillary lumina are often obliterated by swollen endothelial cells, platelet thrombi, or neutrophils. The nervous system is generally not affected, although cerebral vascular necrosis has been reported in fetuses.

**Lungs.** Lungs may be affected by mild to severe interstitial pneumonia (Figs. 1, 3) characterized by alveolar infiltration with macrophages and lesser numbers of neutrophils, hyaline membrane formation, and fluid-filled alveoli. There is hypertrophy and hyperplasia of alveolar pneumocytes, which become rounded with a vesicular nucleus. In addition, there is pulmonary arteritis and phlebitis. Usually EAVAg localizes within the cytoplasm of pneumocytes (Fig. 3) and within alveolar macrophages. Later in the infection, EAVAg becomes identifiable within vascular endothelium and then extends to the cytoplasm of vascular myocytes.

**Lymphoid tissue.** Within lymphoid organs, it is possible to observe lymphoid follicle necrosis, edema, and slight hemorrhage with histiocytic erythrophagocytosis. Lymph node sinuses may contain prominent and sometimes highly pleomorphic histiocytic cells and lymphocytes. EAVAg is contained within stromal dendritelike cells and within the macrophages of the lymph node sinuses and spleen.

**Intestine.** In adults, distention of the submucosal lymphatics of the large intestine, with mild crypt and lamina propria necrosis, may be observed. In foals, where the pulmonary lesions generally prevail, it is also possible to observe a pneumoenteric syndrome with pathologic changes involving crypts, intestinal mucosal blood vessels, and gastrointestinal tract–associated lymphoid tissue. Infarcts may be present in cecum and colon. In these cases, EAVAg may localize within enterocytes and vascular endothelial cells.

**Adrenal glands.** The adrenal gland may present with multifocal vasculitis, hemorrhages, and infarcts. The EAVAg can localize within cortical epithelial cells and capillary endothelium of cortex and medulla.

**Kidneys.** Renal lesions, which can be severe, occur when infection is at an advanced stage and consist of tubular necrosis, lymphocytic interstitial nephritis (Fig. 5), glomerular tuft disorganization, and hypercellularity. The viral antigen can localize within morphologically intact and necrotic tubular epithelial cells, intratubular cellular hyaline casts (Fig. 5), and glomerular endothelial and perhaps mesangial cells. Sometimes, in absence of morphologic changes and before the occurrence of the tubular lesions, it is possible to observe abundant intracytoplasmic viral antigen withinstellate and fusiform cells located within the renal interstitium.

**Skin.** The dermis may be involved with vasculitis, making skin biopsy suitable for diagnostic histopathology and immunohistochemistry. The vasculitis may be associated with thrombosis and ulcerative dermatitis.

**Female reproductive tract and fetus.** Fetuses and fetal membranes are often expelled without premonitory signs of abortion and can be autolyzed or well preserved. Lesions in the fetus are only occasionally detected and when present are represented by mild perivascular lymphocytic infiltrate and mild interstitial pneumonia. Rarely, they can be severe and...
consist of vasculitis involving the allantochorion, brain, liver, spleen, and lung. EAVAg is inconsistently detectable within tissues of aborted fetuses and when present is localized within the cytoplasm of the areolar trophoblast (Fig. 6), allantochorionic mesenchyma, thymus epithelium, splenic reticular cells, endothelium of visceral blood vessels, and enterocytes.10,13,36

In mares experiencing abortion following experimental infection,7 the uterine epithelial cells are swollen, with fragmentation of cytosolic network, swollen granular mitochondria, residual bodies, and large phagolysosomes containing dense and finely granular material, membranes, and vesicles. The uterine proprium-submucosa may be edematous with infiltration of neutrophils and macrophages and endothelial cell swelling. The myometrium may contain necrotic myocytes with ribosome clusters, macrophages, and swollen endothelial cells.

**Male reproductive tract.** EVA lesions associated with the male reproductive tract were studied in experimentally infected prepubertal and peripubertal colts.22 Colts euthanized between the 7th and the 14th day following viral inoculation had throracic and abdominal effusions, lymphadenopathy, and diffuse edema of the genital organs. Histologically, necrotizing vasculitis involving testes, epididymides, vasa deferentia, ampullae, prostate glands, and vesicular and bulbourethral glands were observed. This vasculitis was characterized by severe fibrinoid necrosis of small muscular arteries with edema and hemorrhage. Colts examined between the 28th and 180th day PI had lymphocytic and plasmacytic infiltrate within the lamina propria and tunica muscularis of the epididymides and accessory genital glands. One of the prepubertal foals, persistently infected for 15 months following viral inoculation, had marked lymphoplasmacytic infiltration of ampullae.

**Experimental infection**

Lesions observed following experimental infection have been arbitrarily divided into three groups: developmental, terminal, and chronic but active.45 Lesions were subdivided on the basis of the progression of the macroscopic and histologic changes.

The developmental lesions, observed from the 4th through the 6th day PI, consist of excessive pleural and peritoneal fluid, congestion and enlargement of the lymph nodes, and edema along the course of the colonic and cecal vessels. Histologically, distention of the submucosal lymphatics of the large intestine, with mild necrosis of the mucosal epithelium, is evident. In addition, subcapsular and interstitial edema and congestion of lymph nodes, adrenal cortices, and kidneys have been reported.

The terminal lesions are considered extensions of the developmental lesions with subcutaneous edema and abundant quantities of fluid in the peritoneal and pleural cavities. All the lymph nodes of the body are swollen and hemorrhagic to some degree. Infarcts have been described in the cecum and colon. Severe submucosal edema and hemorrhage are frequent findings, and hemorrhage of the adrenal cortex has been observed. Microscopically, there is severe necrosis of the germinal centers of lymph nodes, with associated hemorrhage. Severe necrosis of the mucosa, submucosal edema, and necrotizing panvasculitis with neutrophils and lymphocytes mainly involving the small muscular arteries also has been reported. Multifocal thrombosis and infarction involving cecum and colon and hemorrhage of the renal medulla are seen. In the renal cortex, there is mild glomerulitis with swelling and disorganization of the glomerular tufts.

Chronic lesions are seen in horses from day 12 following virus inoculation. Lesions consist of mild swollen lymph nodes and excess of fluid within peritoneal and thoracic cavities. Microscopic lesions are dramatic and consist of generalized arteritis and severe glomerulonephritis with tubular necrosis and hyaline casts.

Lesions of natural EVA are rarely as severe as those observed following experimental infection.

**Pathogenesis**

It is possible to determine the pathogenesis of EAV infection in horses by following the distribution of viral antigen and lesions in experimental12,9,36,40 and natural10,13,35,36 infections (Fig. 7). Twenty-four hours PI or later, the virus invades the respiratory epithelium (Fig. 3) and alveolar macrophages. By 48 hours PI, the virus can be found in the satellite lymph nodes, especially bronchial lymph nodes. At 3 days PI, the virus replicates in bronchopulmonary lymph nodes, endothelium, and circulating monocytes. Systemic distribution of the virus follows, with localization within macrophages and dendritelike cells of lymphoid tissue. Approximately 6–8 days PI, the virus localizes within endothelium and medial myocytes of blood vessels and mesothelium. At day 10 PI, the most severe damage occurs to blood vessels. After 10 days PI, there is decrease of EAVAg in all the locations except the tunica media of small muscular arteries.19,43

The vascular lesions observed in EAV infection, particularly medial necrosis, may be due to a combi-
Pathogenesis of Equine Viral Arteritis

- **EAV Infection**
- 24 hours PI
  - EAV in macrophages
- 48 hours PI
  - EAV in satellite lymph nodes
- 3 days PI
  - EAV in endothelium and circulating monocytes
  - Systemic distribution of EAV
  - Male carrier state
- 6-8 days PI
  - EAV in blood vessel endothelium and medial myocytes
- 10 days PI
  - Severe damage to blood vessels
  - Abortion
  - Infected newborn
- 10-21 days PI
  - EVA in Renal tubular epithelium
  - Shedding of virus in urine

Fig. 7. Pathogenesis of EVA.

Virus localization may have a direct cytopathic effect on endothelium and medial myocytes. The endothelial cell damage could induce anoxia or thrombosis.

As previously speculated, abortion may occur by myometritis. Reduction of blood flow to the fetus may occur due to blood vessel compression by endometrial edema or alteration of vascular tone by various inflammatory mediators. Serum progesterone levels constantly diminish from 6 to 48 hours before abortion and are not detectable at necropsy. This decreased progesterone production from a hypoxic placenta, combined with a local release of prostaglandins, may trigger chorionic detachment. Vasculitis with associated thrombosis may also play a role inducing ischemia. Chorionic detachment and expulsion of an infected or uninfected fetus may follow (Fig. 8). In the infected fetus, EAVAg can be identified within the trophoblastic epithelium and mesenchyma and shortly after within pneumocytes, alveolar macrophages, thymic epithelium, and enterocytes.

**Diagnosis**

The diagnosis of EVA is based on demonstration of lesions and the etiologic agent and/or seroconversion.

**Serology and virology**

The detection of seroconversion with complement-dependent virus neutralization performed using the Bucyrus strain in EAV-infected animals is a reliable method for identifying EAV infection in horses. Some foals have presuckle positive serology tests for
Pathogenesis of EAV Abortion

EAV, suggestive of in utero infection. Postsuckle testing would be invalid because of passive transfer of maternal immunity in seroconverted mares.13

Tissue culture cell lines generally used to isolate EAV are RK-13 cells, Vero cells, and equine lung cells.

In addition to immunohistochemistry, other molecular techniques, such as reverse transcription polymerase chain reaction, have been used to identify the presence of EAV, especially in regard to genital transmission of the virus.46,49 The application of these techniques to identify viral RNA in tissues may be very useful for diagnostic purposes and further studies, although sensitivity and specificity for routine diagnostic use still need to be proven.

Differential diagnoses

There are several infectious and a few noninfectious diseases that should be considered as differential diagnoses for EVA.

EHV-1 and, sporadically, equine herpesvirus 4 induce late abortion and stillbirth in horses.57,60 In neonates it is difficult to distinguish between EHV and EAV pneumonia macroscopically, whereas at the microscopic level the difference is rather clear. EHV-1 induces necrotizing bronchiolitis and interstitial pneumonia with intranuclear viral inclusions, chromatin margination, and fragmentation. Large quantities of intranuclear and intracytoplasmic EHV antigen can be immunocytochemically observed within epithelial cells, macrophages, and pulmonary endothelial cells of fetuses.11,42 In addition, EHV-1–infected fetuses and neonatal foals may present with multifocal coagulative necrosis of various organs, in particular liver, intestine, and lymphoid organs, which are also the ideal specimens for histologic and immunocytochemical diagnosis.58 EHV-1 induces encephalomyelopathy secondary to vasculitis,26 with virus antigen localizing within endothelial cells, myocytes, and pericytes.12,59 Encephalomyelitis has not been associated with EAV infection. EHV-1 also may rarely induce nonneurologic fatal disease in young adult horses with severe vasculitis that is difficult to distinguish histologically from EVA infection (F. Del Piero, unpublished).

Equine adenovirus is a rare cause of death in horses and almost exclusively involves Arabian and Thoroughbred foals affected by combined immunodeficiency characterized by severe atrophy of the lymphoid...
tissues. Foals die because of a severe necrotizing bronchopneumonia. Large intranuclear basophilic Cowdry type B viral inclusions are seen within the bronchial epithelium and are also occasionally located within the exocrine pancreas. The identifiable viral antigen is present in smaller quantities than in EHV-1 and EAV infection and is almost exclusively intranuclear.

Influenza orthomyxovirus infections accompanied by bacterial infections cause interstitial and bronchopneumonia. Vasculitis is not a characteristic feature. The orthomyxovirus antigen is abundant within the cytoplasm and nucleus and can be detected in pulmonary specimens.

The acute and subacute forms of lentivirus-induced equine infectious anemia present with gross and histologic lesions that, with the exception of bone marrow hyperplasia and dyserythropoiesis, the absence of vasculitis, and the possible occurrence of granulomatous meningoencephalomyelitis, could be mistaken for EVA. Viral RNA can be identified systemically in cells of macrophage lineage.

The orbivirus of African horse sickness causes acute pulmonary, retroorbital, and muscle edema with ascites, hydrothorax, and hydropericardium. Histologically, the edema may be associated with mild perivascular mononuclear infiltrate, which may resemble an arteriitis lesion. The virus is localized within the cytoplasm of endothelium and macrophages.

The morbillivirus of Hendra disease may cause a fatal infection and induces hemorrhagic pneumonia with typical endothelial cell syncytia. Vascular lesions resembling EVA can be systemically distributed, particularly in the kidney. The viral antigen is localized within endothelial cells, and filamentous paramyxovirus structures may be identified ultrastructurally.

Getah virus, of the alphavirus subgroup of the Togaviridae, can cause fever, rhinorrhea, and occasional exanthema, limb edema, lymphopenia or monocytosis, and abortion and must be included among the differential diagnoses for EVA.

Purpura hemorrhagica and septic shock may induce systemic hemorrhages and occasionally vascular changes resembling the severe lesions of the rare fatal EVA cases.

The toxic plant hoary alyssum (Berteroa incana) induces fever, hemolysis, limb edema, laminitis, gastroenteritis, and abortion and can mimic EVA clinical presentation and gross lesions.

Differential diagnoses should also include infectious and noninfectious abortion, and each of these forms will present more or less characteristic lesions.

Conclusions

Although not frequently diagnosed as a cause of abortion, neonatal mortality, and disease in adults, EVA is an important and perhaps emerging disease that can result in severe economic losses for the equine industry. Complete pathologic examination associated with the available ancillary procedures will guarantee a directed and accurate diagnosis.

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References

1. Belak S, Stade T, Bjorklund H, Ros Bascunana C, Ciaibatti IM, Scicluna MT, Amaddeo D, McCollum WH, Paton DJ, Autorino GL, Timoney PJ, Klingeboen B: Genetic diversity among field isolated of equine arteritis virus. Proc Int Conf Equine Infect Dis 8:177–183, 1999
2. Breese SS Jr, McCollum WH: Electron-microscopic studies of tissues of horses infected by equine arteritis virus. Proc Int Conf Equine Infect Dis 3:273–281, 1972
3. Brown CC, Meyer RF, Grubman MJ: Presence of African horse sickness virus in equine tissues, as determined by in situ hybridization. Vet Pathol 31:689–694, 1994
4. Bryans JT, Doll ER, Crowe MEW, McCollum WH: The blood picture and thermal reaction in experimental viral arteritis of horses. Cornell Vet 47:42–52, 1957
5. Cavanagh D: Nidovirales: a new order comprising Coronaviridae and Arteriviridae. Arch Virol 142:629–633, 1997
6. Cavanagh D, Brien DA, Brinton M, Enjuanes L, Holmes KV, Horzinek MC, Lai MMC, Laude H, Plaggemann PGW, Siddel S, Spaan WJM, Taguchi F, Talbot PJ: Revision of the taxonomy of the coronavirus, togavirus and arterivirus genera. Arch Virol 135:227–237, 1994
7. Coignoul FL, Cheville NF: Pathology of maternal genital tract, placenta and fetus in equine viral arteritis. Vet Pathol 21:333–340, 1984
8. Cole JR, Hall RF, Gosser HS, Hendricks JB, Pursell AR, Senne DA, Pearson JE, Gipson CA: Trasmissibility and abortogenic effect of equine viral arteritis in mares. J Am Vet Med Assoc 189:769–771, 1986
9. Crawford TD, Henson JB: Immunofluorescent, light-microscopic and immunologic studies of equine viral arteritis. Proc Int Conf Equine Infect Dis 3:282–302, 1972
10. Del Piero F: Comparison of equine arteritis virus and equine herpesvirus 1 findings in aborted fetuses. J Equine Vet Sci 19:562, 1999
11. Del Piero F, Dubovi EJ: The diagnosis of equine herpesvirus 1 (EHV-1) abortion and neonatal infection with emphasis on immuno-peroxidase histochemical findings. Vet Pathol 35:444, 1998
12. Del Piero F, Wilkins PA, de Lahunta A, Nelson C, Dubovi EJ: Fifteen cases of equine herpesvirus 1 (EHV-1) encephalomyelopathy in horses: pathological and immuno-peroxidase histochemical findings. Vet Pathol 35:441, 1998
13. Del Piero F, Wilkins PA, Lopez JW, Glaser AL, Dubovi EJ, Schlafer DH, Lein DH: Equine viral arteritis in newborn foals: clinical, pathological, serological, microbi-
logical and immunohistochemical observations. Equine Vet J 29:178–185, 1997
14 de Vries AAF, Horzinek MC, Rottier PJM, de Groot RJ: The genome organization of the Nidovirales: similarities and differences between arteri-, toro-, and coronaviruses. Semin Virol 8:33–47, 1997
15 Doll ER, Bryans JT, McCollum WH, Crowe MEW: Isolation of a filterable agent causing arteritis of horses and abortion by mares. Its differentiation from the equine abortion (influenza) virus. Cornell Vet 47:3–41, 1957
16 Doll ER, Knappberger RE, Bryans JT: An outbreak of abortion caused by the equine arteritis virus. Cornell Vet 47:69–75, 1957
17 Estes PC, Cheville NF: The ultrastructure of vascular lesions in equine viral arteritis. Am J Pathol 58:235–252, 1970
18 Freeman KP, Cline JM, Simmons R, Wilkins PA, Cudd TA, Perry BJ: Recognition of broncopulmonary dysplasia in a newborn foal. Equine Vet J 21:292–296, 1989
19 Fukunaga Y, Imagawa H, Tabuchi E: Clinical and virological findings on experimental equine viral arteritis in horses. Bull Equine Res Inst 18:110–113, 1981
20 Geor RJ, Becker RL, Kanara EW, Hovda LR, Sweeney WH, Winter TF, Rorick JK, Ruth GR, Hope E, Murphy MJ: Toxicosis in horses after ingestion of hoary alyssum. J Am Vet Med Assoc 201:63–67, 1992
21 Golnik W, Michalska Z, Michalak T: Natural equine viral arteritis in foals. Schweiz Arch Tierheilkd 123:523–533, 1981
22 Holyoak GR, Giles RC, McCollum WH, Little TV, Timoney PJ: Pathological changes associated with equine arteritis virus infection of the reproductive tract in prepubertal and peripubertal colts. J Comp Pathol 109:281–293, 1993
23 Hong CB, Donahue JM, Giles RC Jr, Petrites-Murphy MB, Poonacha KB, Roberts AW, Smith BJ, Tramontin RR, Tuttle PA, Swerczeck TW: Equine abortion and stillbirth in central Kentucky during 1988 and 1989 foaling seasons. J Vet Diagn Invest 5:560–566, 1993
24 Hooper PT, Ketterer PJ, Hyatt AD, Russel GM: Lesions of experimental equine morbillivirus pneumonia in horses. Vet Pathol 34:312–322, 1997
25 Hovda LR, Rose ML: Hoary alyssum (Berterea incana) toxicity in a herd of broodmare horses. Vet Hum Toxicol 35:39–40, 1993
26 Jackson TA, Osburn BI, Cordy DR, Kendrick JW: Equine herpesvirus 1 infection of horses: studies on the experimentally induced neurologic disease. Am J Vet Res 38:709–719, 1977
27 Jones TC, Doll ER, Bryans JT: The lesions of equine viral arteritis. Cornell Vet 47:52–68, 1957
28 Jones TC, Maurer FD: The pathology of equine influenza. Am J Vet Res 4:15–31, 1943
29 Johnson B, Baldwin C, Timoney P, Ely R: Arteritis in equine fetuses aborted due to equine viral arteritis. Vet Pathol 28:248–250, 1991
30 Kamada M, Kumanomido T, Wada R, Fukunaga Y, Imagawa H, Sugiiura T: Intranasal infection of Getah virus in experimental horses. J Vet Med Sci 53:855–858, 1991
31 King AS: Studies on equine purpura hemorrhagica: 3. Morbid anatomy and histology. Br Vet J 105:35–54, 1949
32 Kirkbride CA: Laboratory Diagnosis of Livestock Abortion, 3rd ed., pp. 202–254. Iowa State University Press, Ames, IA, 1990
33 Konno S, Yamamoto H: Pathology of equine infectious anemia. Proposed classification of pathologic types of the disease. Cornell Vet 60:393–449, 1970
34 Laegreid W, Burrage TG, Stone-Marschat M, Skowronek A: Electron microscopic evidence for endothelial infection by African horse sickness virus. Vet Pathol 29:554–556, 1992
35 Lopez JW, Del Piero F, Glaser A, Finazzi M: Immunoperoxidase histochemistry as a diagnostic tool for detection of equine arteritis virus antigen in formalin fixed tissues. Equine Vet J 28:77–79, 1996
36 MacLachlan NJ, Balasuriya UB, Rossitto PV, Hullinger PA, Patton JE, Wilson WD: Fatal experimental equine arteritis virus infection of a pregnant mare: immunohistochemical staining of viral antigens. J Vet Diagn Invest 8:367–374, 1996
37 McClesney AE, England JD: Adenoviral infection in foals. J Am Vet Med Assoc 166:83–85, 1975
38 McClure JJ, Lindsay WA, Taylor W, Ochoa R, Issel CJ, Coulter SJ: Ataxia in four horses with equine infectious anemia. J Am Vet Med Assoc 180:279–283, 1982
39 McCollum WH: Pathologic features of horses given avirulent equine arteritis virus intramuscularly. Am J Vet Res 42:1218–1220, 1981
40 McCollum WH, Prickett ME, Bryans JT: Temporal distribution of equine arteritis virus in respiratory mucosa, tissues and body fluids of horses infected by inhalation. Vet Res Sci 12:459–464, 1971
41 Murray K, Selleck P, Hooper P, Hyatt A, Gould A, Gleeson L, Westbury H, Hiley L, Selvey L, Rodwell B, Ketterer P: A morbillivirus that caused fatal disease in horses and humans. Science 268:94–97, 1995
42 Murray MJ, Del Piero F, Jeffrey SC, Davis MS, Furr MO, Dubovi EJ, Mayo JA: Neonatal equine herpesvirus type 1 infection on a Thoroughbred breeding farm. J Vet Intern Med 12:36–41, 1998
43 Neu SM, Timoney PJ, McCollum WH: Persistent infection of the reproductive tract in stallions experimentally infected with equine arteritis virus. Proc Intl Conf Equine Infect Dis 5:14, 1987
44 Oaks JL, McGuire TC, Ulibarri C, Crawford TB: Equine infectious anemia virus is found in tissue macrophages during subclinical infection. J Virol 72:7260–7269, 1998
45 Prickett ME, McCollum WH, JT Bryans: The gross and microscopic pathology observed in horses experimentally infected with the equine arteritis virus. Proc Intl Conf Equine Infect Dis 3:265–272, 1972
46 Ramina A, Dalla Valle L, De Mas S, Tisato E, Zunin A, Renier M, Cuteri V, Valente C, Cancellotti FM: Detection of equine arteritis virus in semen by reverse transcriptase polymerase chain reaction–ELISA. Comp Immunol Microbiol Infect Dis 22:187–197, 1999
47 Redaelli GD, Codazza P, Finazzi M, Agrimi P, Fanchini G, Proverbio E: Osservazioni epizootologiche, cliniche ed anatomo-istopatologiche sul primo focolaio di arterite
equina negli allevamenti italiani [First outbreak of equine viral arteritis in Italy: epidemiological, clinical and pathological findings]. Clin Vet 103:566–571, 1980
48 Rooney JR, Robertson JL: Equine Pathology, 1st ed., pp. 357–358. Iowa State University Press, Ames, IA, 1996
49 Starick E: Rapid and sensitive detection of equine arteritis virus in semen and tissue samples by reverse transcription-polymerase chain reaction, dot blot hybridisation and nested polymerase chain reaction. Acta Virol 42:333–339, 1998
50 Sutton GA, Viel L, Carman PS, Boag BL: Study of the duration and distribution of equine influenza virus subtype 2 (H3N8) antigens in experimentally infected ponies in vivo. Can J Vet Res 61:113–120, 1997
51 Timoney PJ: Clinical, virological and epidemiological features of the 1984 outbreak of equine viral arteritis in the Thoroughbred population in Kentucky, USA. Proc Int Conf Thoroughbred Breed Organ: Equine Viral Arteritis 1984:24–33, 1984
52 Timoney PJ, McCollum WH: Equine viral arteritis. Vet Clin North Am Equine Pract 9:295–309, 1993
53 Timoney PJ, McCollum WH, Murphy TW: The carrier state in equine arteritis virus infection in the stallion with specific emphasis on the venereal mode of virus transmission. J Reprod Fertil 35(Suppl 1):95, 1987
54 Vaala WE, Hamir AN, Dubovi EJ, Timoney PJ, Ruiz B: Fatal congenitally acquired infection with equine arteritis virus in a neonatal Thoroughbred. Equine Vet J 24:155–158, 1992
55 Wilkins PA: Equine viral arteritis. In: 5 Minute Consult: Equine. (in press)
56 Wilkins PA, Del Piero F, Lopez J, Cline M: Immunohistochemical diagnosis of equine arteritis infection in a foal. Equine Vet J 27:398, 1995
57 Whitwell KE: Investigations into fetal and neonatal losses in the horse. Vet Clin North Am Large Anim Pract 2:313–331, 1980
58 Whitwell KE: An assessment of the criteria used to diagnose virus abortion: a review of 100 cases. J Reprod Fertil 32(Suppl 1):110, 1982
59 Whitwell KE, Blunden AS: Pathological findings in horses dying during an outbreak of the paralytic form of equid herpesvirus type 1 (EHV-1) infection. Equine Vet J 24:13–19, 1992
60 Whitwell KE, Smith KC, Sinclair R, Mumford JA: Fetal lesions in spontaneous EHV-4 abortion in mares. Proc Int Conf Equine Infect Dis 7:354, 1994
61 Wohlsein P, Pohlenz JF, Davidson FL, Salt JS, Hamblin C: Immunohistochemical demonstration of African horse sickness viral antigen in formalin-fixed equine tissues. Vet Pathol 34:568–574, 1997

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