

**The Armed Forces Institute of Pathology
Department of Veterinary Pathology
WEDNESDAY SLIDE CONFERENCE
2003-2004**

**CONFERENCE 8
5 November 2003**

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CASE I – 03-1198 (AFIP 2887461)

Signalment: 5 months, female, Large White X Landrace, *Sus scrofa*, porcine.

History: Between December 31, 2002 and January 2, 2003, thirty-one gilts, approximately 5 months of age died and 300 were lethargic and/or febrile in a group of 988. This group of gilts entered this barn as 2 ½ month old pigs in mid-October, 2002. There had been no new animal introductions since that time. The barn was one of three on a site with each barn containing approximately 1000 pigs. The pigs were considered to be negative for PRRSV and *Mycoplasma hyopneumoniae* as determined by repeated serological testing of the pigs themselves and the source herd. Prior to this severe death loss, there was only minimal death loss (less than 1.4% total from all three barns) due to swine influenza virus (H1N1) and co-infections with type 2 circovirus, *Streptococcus suis*, and *Pasteurella multocida*. A total of 182 pigs died (18.4%) in this one barn with 159 deaths (87% of total death loss) occurring between January 2, 2003 and January 10, 2003.

Gross Pathology: The entire remains of six gilts were submitted. All pigs had cloudy meninges and heavy, red, and wet lungs. Abundant fibrin covered the pleura and pericardium of one pig.

Laboratory Results: Aerobic culture of the meninges resulted in a pure or predominant growth of *Haemophilus parasuis* from all 6 pigs. The *Haemophilus parasuis* isolate was typed by enterobacterial repetitive intergenic consensus based-polymerase chain reaction (ERIC-PCR) technique as serovar 2. *Haemophilus parasuis* was also isolated from the pleural and pericardial swab of one pig, the lungs of all 6 pigs, and in mixed growth with *Pasteurella multocida* from the lungs of 3 pigs. A pooled tissue homogenate was positive for type 2 circovirus by polymerase chain reaction (PCR). Reverse-transcriptase PCR tests of the pooled tissues were negative for influenza A virus, PRRSV (North American and European strains), and pestivirus. A

PCR test of a pooled bronchial swab was negative for *Mycoplasma hyopneumoniae*. Fluorescent antibody examinations of the tonsils were negative for pseudorabies virus. Virus isolation attempts for porcine enterovirus, PRRSV and pseudorabies virus were negative after passages on PK-15, MARC-145, PAM, and BT cells. Liver mineral analyses revealed no evidence of excessive or deficient levels of arsenic, cadmium, cobalt, copper, iron, magnesium, manganese, molybdenum, lead, selenium or zinc.

Contributor's Morphologic Diagnosis: Meningitis, subacute, severe, diffuse, fibrinopurulent, with encephalitis, subacute, moderate, multifocal, perivascular, lymphoplasmacytic and histiocytic, *Haemophilus parasuis*.

Contributor's Comment: *Haemophilus parasuis* is a common bacterial infection in swine and causes polyserositis (Glasser's disease) primarily in pigs 4 to 8 weeks of age. The severity of disease in this older age pig is remarkable but has been reported in high-health status herds populated with naive pigs¹. *Haemophilus parasuis* is a gram-negative, non-spore-forming, nonmotile, microaerophilic, rod-shaped bacteria requiring heme and/or nicotinamide adenine dinucleotide (NAD) factors for growth². There are 15 serovars recognized^{2,3} with much heterogeneity within and between serovars. Virulence is associated with serovar type but also with not yet clearly classified capsule and external membrane proteins. There is evidence that certain *Haemophilus parasuis* isolates of similar genotype as determined by ERIC-PCR have tropism for the brain¹. *Haemophilus parasuis* is a frequent co-infection or opportunistic pathogen with other bacterial agents and viruses and the presence of multiple pathogens increases the severity of the disease³. In this case, at the time of severe death loss and illness, both *Pasteurella multocida* and type 2 circovirus were identified along with the *Haemophilus parasuis*. *Pasteurella multocida* is normal flora of the swine respiratory tract and its presence in the lungs is not surprising. The co-infection with type 2 circovirus is intriguing. However, it is important to note that there was no evidence of pathology associated with type 2 circovirus (histiocytic/ granulomatous lymphadenitis, lymphoid depletion, or interstitial pneumonia) noted in any pig from this case. Control and prevention of Glasser's disease is through the use of commercial vaccines, autogenous vaccines derived from homologous strains from the affected herd found to cause systemic disease, and through water and feed medication.

AFIP Diagnosis: Brain, leptomeninges: Meningitis, lymphocytic and neutrophilic, subacute, diffuse, moderate, with abundant fibrin, Large White cross Landrace, porcine.

Conference Comment: Glasser's disease causes severe meningitis, polyserositis, and/or polyarthritis in young pigs following a stressful episode. The classical gross finding with *Haemophilus parasuis* infection is fibrinous polyserositis, arthritis, and meningitis. The primary differential diagnoses for fibrinous serositis in pigs are *Mycoplasma hyorhinis*, *Streptococcus suis* type II, and septicemic salmonellosis. Like *Haemophilus parasuis*, *Mycoplasma hyorhinis* causes polyarthritis, but meningitis is usually not a feature of mycoplasmal infection. If meningitis is present, it is mild with

lymphocytic inflammation. In addition to purulent meningitis and polyarthritis, *S. suis* type II can also cause endocarditis. *Streptococcus suis* type II is zoonotic and can cause meningitis with residual deafness or septic shock and death in humans.^{4,5}

In this case, lymphocytes and neutrophils within the subarachnoid space multifocally extend into and expand Virchow-Robin space. The significance of the isolation of type 2 circovirus is unclear.

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CASE II - C03-0733 (AFIP 2887161)

Signalment: 1-year-old Male, C.B-17-SCID-Beige mouse (*Mus musculus*).

History: Streptozotocin was administered to induce diabetes mellitus at 6 months of age. Two months later, a single cell suspension of human islet cells was xenografted beneath the renal capsule. Four months later, the mouse developed an enlarged abdomen, dyspnea, ruffled haircoat, and a bluish tinge to the ventral abdominal skin.

Gross Pathology: The abdomen was enlarged due to approximately 2 ml of serosanguineous peritoneal fluid (Figures 1 and 2). The liver was also mottled tan and granular (Figure 3).

Laboratory Results:

WBC: 12.0 K/ μ L

Neutrophils: 72.2%
Lymphocytes: 6.2%
Monocytes: 16.8%
Eosinophils: 0.3%
Basophils: 4.5%
RBC: 7.66 M/ μ L
Hemoglobin: 9.56 g/dL
Hematocrit: 27.5%
Platelets: 2538 K/ μ L

Serum protein: <1 gm/dL
Serum glucose: 217 mg/dL

Negative by ELISA for: Mouse Hepatitis Virus, Sendai Virus, Mouse Encephalomyelitis Virus (strain GDVII), Pneumonia Virus of Mice, Minute Virus of Mice, Epizootic Diarrhea of Infant Mice Rotavirus, and *Mycoplasma pulmonis*.

PCR on formalin-fixed liver was performed by the Animal Diagnostic Laboratory, College of Veterinary Medicine, Cornell University for *Mycobacterium avium* complex, *M. avium* subsp. *avium*, and *M. bovis* or *tuberculosis*, all of which were negative. PCR for *Mycobacterium tuberculosis* complex on formalin-fixed liver was also performed by Focus Technologies (Cypress, CA). *M. tuberculosis* complex DNA was not detected; however, the efficacy of the Amplicor MTB test has not been determined for non-respiratory (sputum) samples.

Contributor's Morphologic Diagnosis: Liver, hepatitis, granulomatous, multifocal to widespread, marked with intrahistiocytic bacilli, hepatocellular loss and micronodular regenerative hyperplasia.

Contributor's Comment: Multifocal to coalescing aggregates of epithelioid macrophages replace normal hepatic cords throughout the sections. These macrophages contain myriad bacilli, which are gram-positive (Brown and Brenn stain, not included) and acid-fast-positive (Ziehl-Neelsen, included). Macrophages containing bacilli were also found in the lungs, submandibular lymph node, adrenal gland, kidneys, and spleen. Immunohistochemistry (IHC) was performed on paraffin sections of liver using a commercially available (DAKO), rabbit anti-human *Mycobacterium* sp. antibody, by Dr. Fabio del Piero in the Department of Pathobiology at the University of Pennsylvania, School of Veterinary Medicine. Macrophages throughout the liver were strongly immunopositive for *Mycobacterium* sp. (Figure 4). Additional lesions in the liver include an irregular capsular surface due to hepatocellular loss and micronodular regenerative hyperplasia, as well as extramedullary hematopoiesis characterized by aggregates of myeloid cells (neutrophils) at various stages of maturity around blood vessels and within sinusoids.

Mycobacteria belong to the order Actinomycetales, which also includes the genera *Actinomyces*, *Nocardia*, *Rhodococcus*, *Corynebacterium*, *Dermatophilus* and

Streptomyces. There are numerous species of *Mycobacterium*, which are pathogenic for humans and animals. Classically, tuberculosis is caused by a group of mycobacteria referred to as the *Mycobacterium tuberculosis* complex (MTC), which includes *M. tuberculosis*, *M. bovis*, *M. africanum* and *M. microti*¹. The characteristic lesion caused by these organisms is the tubercle, a classic granuloma composed of epithelioid macrophages and multinucleated giant cells surrounded by a rim of fibroblasts. Depending on the host's immune response, necrosis, calcification and ancillary inflammatory cells such as lymphocytes might also be present¹. *M. avium* and *M. intracellulare* are closely related and comprise the *M. avium-intracellulare* complex (MAIC)¹. *M. avium* includes *M. avium* subsp. *avium* and *M. avium* subsp. *silvaticum*, originally bird pathogens, as well as *M. avium* subsp. *paratuberculosis*, the cause of Johne's disease in ruminants and the purported cause of Crohn's disease in humans¹. MAIC has also recently emerged as a significant cause of morbidity and mortality in immunocompromised humans and animals. The MAIC lesion differs from that of MTC in that sheets of epithelioid macrophages contain myriad organisms¹. Leprosy in humans is caused by *M. leprae*, while feline and murine leprosy is caused by *M. lepraemurium*, both of which are characterized as either lepromatous with large numbers of lipid-laden macrophages containing large numbers of bacilli or tuberculoid¹. Finally, other saprophytic and opportunistic mycobacteria such as *M. kansasii*, *M. fortuitum*, *M. smegmatis*, *M. xenopi*, *M. chelonae*, *M. thermoresistable* and *M. phlei* are considered atypical mycobacteria, generally causing cutaneous or subcutaneous to disseminated infections in which filamentous or beaded organisms are found within lipid vacuoles¹.

Paramount to the pathogenesis of mycobacterial infections is the ability of the organism to survive and replicate within the host's macrophage. This is made possible by numerous virulence factors residing in the cell wall, which result in biological activities such as inhibition of phagosome-lysosome fusion, scavenging of oxygen radicals and altered cytokine secretion among others¹. CD4+ T cells and their secretion of interferon- γ (IFN- γ) are also important for macrophage activation and subsequent killing of the mycobacteria¹.

Although mice are used as experimental models of mycobacterial infections, naturally occurring infections are rare². Sixty-three percent of C57BL/6N mice developed lesions due to MAIC while C3H/HeN and B6C3F1 mice as well as F344 rats housed in the same room did not. The animals appeared healthy; however lesions were found in the lungs, livers, spleens and mesenteric lymph nodes. Experiments were conducted to fulfill Koch's postulates and elucidate the pathogenesis of this naturally occurring outbreak³. It was determined that the most likely source of MAIC in the outbreak was the water since the water source for affected animals differed from unaffected animals, and direct transmission could not be demonstrated.

In this case, the histology of the multisystemic lesions was compatible with mycobacteriosis and confirmed by IHC. The gram-positive acid-fast organisms most likely represent MAIC but this could not be confirmed by PCR. SCID-beige mice, which were used in this experimental protocol, are immunocompromised. SCID mice are

homozygous for the *Prkdc*^{scid} (protein kinase, DNA activated, catalytic polypeptide) mutation, resulting in a defect in V(D)J recombination and therefore a lack of T and B lymphocytes and low to undetectable immunoglobulin levels⁴. Beige mice, homologous to humans with Chediak-Higashi syndrome, have defective cytotoxic T cells and macrophages, as well as impaired natural killer cell function due to abnormally large lysosomal granules in all granule-containing cells⁵. The double mutation makes SCID-beige mice susceptible to a variety of opportunistic pathogens; however no other animals from this experimental group have been affected to date. The source of the organisms in this mouse is not apparent but is likely from the environment since MAIC organisms have been isolated from soil, water and sawdust¹, as well as sporadic canaries and finches housed in our facilities.

AFIP Diagnosis:

1. Liver: Hepatitis, granulomatous, multifocal to coalescing, moderate, with intrahistiocytic acid-fast bacilli, C.B-17-SCID-Beige mouse, rodent.
2. Liver: Nodular hyperplasia, multifocal, moderate, with biliary hyperplasia and hepatocyte atypia.
3. Liver: Granulocytic extramedullary hematopoiesis.

Conference Comment: The contributor provides an excellent review of mycobacteriosis. Conference attendees discussed the prominent nodular hyperplasia and atypical hepatocytes characterized by cytomegaly, karyomegaly, and multinucleated hepatocytes. Phone consultation with the contributor verified that this was the only animal to demonstrate these lesions, therefore these changes are not thought to be related to the experimental regimen but may be a response to the inflammation. Conference attendees also noted numerous intravascular bacilli that, upon further investigation, are gram-positive. Post-mortem overgrowth was considered, but ruled out based on the fact that the animal was euthanized via carbon dioxide and immediately necropsied. This may represent a terminal septicemia.

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<http://www.mskcc.org>

<http://www.med.cornell.edu/>

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CASE III - 03060007 (AFIP 2890741)

Signalment: Adult (exact age unknown) male black-tailed prairie dog (*Cynomys ludovicianus*).

History: An entire group of 15 prairie dogs had become ill. Ten were dead. The prairie dogs exhibit ocular discharge, swollen eyelids, coughing, sneezing, wasting away, ulcers on tongue and death.

Gross Pathology: The patient has yellow mucoid material along the eyelids. There is a small, 0.3cm in diameter ulcer in the center of the tongue. The lungs exhibit bilateral, randomly distributed foci of pneumonia. These foci were deep red, firm and wet on cut surface. All total, 40-50% of the lung was affected.

Laboratory Results: CDC reports that tissues are positive by PCR for monkeypox virus. Also, immunohistochemistry is positive on formalin fixed lung, heart, lymph node and conjunctiva for monkeypox virus.

Contributor's Morphologic Diagnosis: Severe necrotizing bronchointerstitial pneumonia with syncytia.

Contributor's Comment: Submission of this patient preceded the reports of the monkeypox outbreak in humans and prairie dogs in the United States Midwest in early June. The prairie dog originated in Illinois from a pet distributor that also kept Gambian rats (*Cricetomys gambianus*) that were also reportedly ill. In addition, the pet distributor and his wife exhibited flu-like symptoms, but did not have any skin lesions. The referring veterinarian suspected tularemia (*Francisella tularensis*). Histological examination (esp. the syncytia) suggested a viral infection. While attempts were being made to define the etiology, reports of the monkeypox outbreak surfaced and tissues were sent to the CDC where monkeypox was confirmed by PCR and immunohistochemistry.

As of this writing, most of the literature is focused on the virology and epidemiology of the disease with scant information on gross pathology or histologic lesions in prairie

dogs. Human infections have been linked to prairie dogs that in turn appear to have been exposed from sick Gambian rats.^{1,2} Apologies in advance for some of the “smudge” artifact present in the current submission. This is attributed to intrathoracic administration of euthanasia solution. However, the histological features of the pneumonia and numerous syncytial cells are still clearly present.

AFIP Diagnosis: Lung: Pneumonia, bronchointerstitial, necrotizing, subacute, diffuse, severe, with vasculitis, syncytial cells, and eosinophilic intracytoplasmic inclusion bodies, black-tailed prairie dog (*Cynomys ludovicianus*), rodent.

Conference Comment: This case was sent to the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) at Fort Detrick, Maryland for immunohistochemical staining. Researchers there used a polyclonal anti-vaccinia antibody that cross-reacts with monkeypox, cowpox, camelpox, and smallpox viral antigen. The submitted section of lung is immunohistochemically strongly positive for orthopoxviral antigen within pulmonary macrophages and respiratory epithelial cells.

Monkeypox is a member of the Orthopoxvirus genus, and, until the spring of 2003 when it appeared in Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, had primarily caused disease in parts of Central and Western Africa. Wild squirrels have been implicated as reservoirs in Africa, whereas pet prairie dogs and a giant Gambian rat were identified as the source of the U.S. Midwest outbreak.¹ There is very little information in the published literature on the disease in prairie dogs, but it is well described in cynomolgus macaques causing, among many lesions, fibrinonecrotic bronchopneumonia with necrotizing vasculitis³.

Other orthopoxviruses of veterinary importance include cowpox, camelpox, and ectromelia (mousepox). Cowpox causes disease in cows, domestic cats, humans, and zoo animals, including large felids, elephants, and rhinoceroses. Despite its name, cowpox is not endemic in cattle. It is usually self-limiting, causing lesions on the teats and udder. Cats may have more severe disease than humans or cattle, with systemic disease accompanying maculopapular eruptions in immunocompromised individuals. Camelpox causes typical pox lesions primarily concentrated around mucocutaneous junctions, but may cause more generalized skin lesions in young camelids. Ectromelia virus is of significant economic importance in mouse laboratory colonies. It causes either a rapidly fatal form of the disease, or a chronic form with ulceration, necrosis, and loss of the extremities and tail.^{4,5}

Contributor: Oklahoma State University, Department of Veterinary Pathobiology, Room 250 McElroy Hall, Stillwater, OK 74078

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Also refer to updates through CDC Morbidity and Mortality Weekly Report (MMWR) at: <http://www.cdc.gov/mmwr/>

CASE IV - 02N427 (AFIP 2888046)

Signalment: 5 1/2-year-old Arab gelding.

History: Boomer presented to the VMTH on Thursday (10/10/02) evening after a 36-hour history of lateral recumbency. He had been seen by his referring DVM on Wednesday (10/09/02), and was prescribed prednisone and trimethoprim sulfa (TMS). Upon presentation, he was found to be comatose, dehydrated, with absent pupillary light reflexes and icteric oral mucous membranes. His lung sounds were normal. He was given 15 liters of Plasmalyte and 1 liter of hypertonic saline via a jugular catheter, and then transported to the recovery stall. After stabilizing him in a sling, he was treated overnight with IV fluids, thiamin, DMSO, gentacin and potassium penicillin. At 8:00 am on 10/11/02, he was found to be tachypneic, icteric, and tachycardic. Lung sounds were absent in his left lung fields. His fluids were stopped and he was administered two boluses of furosemide. His respiratory rate decreased slightly over 30 minutes, but his breathing became agonal shortly thereafter, and he expired quietly.

Gross Pathology:

1. Lungs:
 - a. Moderate to severe pulmonary edema
 - b. Moderate pulmonary emphysema
 - c. Multifocal atelectasis
2. Urinary bladder: Multifocal mucosal petechiation
3. Integument: Multifocal abrasions
4. Brain: Multifocal petechiation (cut surface following fixation)

Laboratory Results:

Clinical Pathology Findings:

CBC: Lymphopenia (420/ μ l) with a slight left shift (140/ μ l)

Chemistry Panel:

Hyperglycemia (223 mg/dl)
Elevated BUN (49 mg/dl), creatinine (2.3 mg/dl)
Elevated AST (776 µl/ml), LDH (1630 µl/ml), total bilirubin (4.5 mg/dl), ALT (47 µl/ml), Alk phos (502 µl/ml), total protein (8.1 gm/dl), CK (6990 µl/ml)
Slightly low Na (134 mmol/l) and K (mmol/l), Total CO₂ 20 mmol/l, pH 7.245,
pCO₂ = 66.1 mm Hg., pO₂ = 39.3 mm Hg

CSF: Clear, colorless; no RBC seen; TP = 143.2 mg/dl
TNCC = 48/µl (2% PMN, 47% lymphocytes, 51 % macrophages)
Nondegenerate neutrophils, macrophages frequently vacuolated and
occasionally contain cytoplasmic leukocytes
Interpretation: mononuclear pleocytosis

Virology:

Rabies (-) IFA
West Nile Virus (-) PCR
EEE Viral RNA RT-PCR (+) & Virus Isolation (+)

Contributor's Morphologic Diagnosis: Moderate-to-severe multifocal
necrosuppurative and hemorrhagic vasculitis and meningoencephalitis with thrombosis.

Contributor's Comment: Lesions present are widespread, and disseminated throughout most if not all sections of brain. The lesions consist of meningeal infiltrates of variable intensity made up of plasma cells, lymphocytes and localized areas that have neutrophils. Meningeal vessels are moderately congested and/or blood-filled. Additionally, all blood vessels throughout all sections of the whole brain are congested and blood-filled with focal areas of perivascular hemorrhage. Surrounding some blood vessels and oftentimes extending into the adjacent parenchyma there are variable, and oftentimes large numbers of lymphocytes, plasma cells, macrophages and neutrophils. Numerous blood vessels contain this mixed inflammatory cell infiltrate within their walls. Additionally, several exhibit fibrinoid degeneration and thrombosis. Throughout the parenchyma in most sections, both white and gray matter, there are focal areas of hemorrhage with necrosis and gliosis. Many of these foci also have degenerative neutrophils. All major anatomical regions of the brain are affected to some degree.

Eastern Equine Encephalitis Virus

Equine Arboviral encephalomyelitis - member of the antigenic alpha viruses in the family *Togaviridae*, a single-stranded, enveloped RNA virus.^{1,2.}

TRANSMISSION - Primarily enzootic cycle with a wild bird reservoir, and mosquito vector (*Culiseta melanura*) that feeds on small birds that serve as maintenance and amplifying hosts; with environmental and biological changes, spills over into other species of mosquitoes that feed on mammals at which time equine and human cases can be seen. Viremia level in people and most horses are sufficiently small such that they are considered dead end hosts.¹

ZOONOTIC POTENTIAL - Major public health threat, although incidence is lower than other viral encephalitides; severe, often fatal encephalitis in people during summer and fall months with high mosquito densities. Severity of disease greatest in youngest (<10 years) often progressing to death; least in people 10-50 years of age, and the oldest group (>50 years) either had a good outcome or died. Deaths in horses or wild birds usually precede disease in people.³

OCCURRENCE - [young more susceptible] Mainly Atlantic & Gulf coasts & Caribbean. Following infection, horses may 1) develop inapparent infection, 2) develop viremia and high fever that resolves without CNS disease, or 3) develop clinical neurologic disease.²

EQUINE MORTALITY - lethal in up to 90% of the cases⁴

EQUINE CLINICAL SIGNS: Inapparent or systemic illness or CNS [reflects cerebrocortical damage] - Sensory changes, depression, cortical blindness, increased movements progressing to ataxia, circling, head pressing, hyperexcitability, recumbency, death

GROSS LESIONS: Usually none

MICROSCOPIC FINDINGS: [Grey matter, most marked cerebral cortices, thalamus, hypothalamus, milder caudally] Largely neutrophilic inflammation; microgliosis; +/- malacia w/gitter; vasculitis, thrombosis.

DIAGNOSIS: Clinical findings, epidemiological data, histopathology, serology, viral isolation, PCR.

AFIP Diagnosis: Brain: Encephalitis, necrotizing, neutrophilic, diffuse, moderate to severe, with gliosis, vasculitis, hemorrhage, and thrombosis, Arab, equine.

Conference Comment: There are numerous viral causes of equine encephalomyelitis, among which are the Alphaviruses [Eastern equine encephalomyelitis (EEE), Western equine encephalomyelitis (WEE), and Venezuelan equine encephalomyelitis (VEE)]; the Flaviviruses (West Nile virus and Japanese encephalitis virus); Rhabdovirus (rabies virus); and equine herpesvirus-1 (EHV-1).

Histologically, EEE, WEE, and VEE cause lesions predominantly in the gray matter and most severely in the cerebral cortex, thalamus, and hypothalamus, consisting of neuronal degeneration, neuronophagia, microgliosis, and perivascular and parenchymal inflammation. In EEE, the inflammatory response is mostly neutrophilic; in VEE it is a mixture of neutrophils and lymphocytes; and in WEE, it is mostly nonsuppurative. Vasculitis and thrombosis may also be present.^{4,7}

West Nile virus primarily involves the ventral and lateral horns of the thoracic and lumbar spinal cord and lower brain stem, with perivascular lymphocytic infiltrates, neuronal degeneration, neuronophagia, and hemorrhage.^{5,7}

Japanese encephalitis virus initially causes neutrophilic leptomeningitis and encephalitis that becomes nonsuppurative. It targets neurons and causes neuronal degeneration and necrosis.⁶ Rabies virus causes nonsuppurative meningoencephalitis with intraneuronal Negri bodies, but neuronal necrosis is rare. Equine herpesvirus-1 is not neurotropic but causes vasculitis, with secondary lesions in the neuroparenchyma resulting from infarcts.^{4,7}

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