Outbreak of malignant catarrhal fever among cattle associated with a state livestock exhibition

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Case Description—Severe disease and death were identified in cattle exhibited at a state fair that were naturally infected with ovine herpesvirus type 2 (OvHV-2).

Clinical Findings—Most affected cattle had anorexia, signs of depression, diarrhea, fever, and respiratory distress ultimately leading to death. Mean duration of clinical signs prior to death was 6 days (range, 1 to 26 days). Mean number of days between apparent exposure and death was 71 days (range, 46 to 139 days).

Treatment and Outcomes—19 of 132 cattle cohoused in 1 barn died of malignant catarrhal fever (MCF). The diagnosis of sheep-associated MCF was confirmed on the basis of results of an OvHV-2-specific PCR assay performed on tissue samples obtained from affected cattle. The disease was associated but not significantly with distance from the center of the barn and was not associated with distance from the center of the sheep pens.

Clinical Relevance—Outbreaks of MCF in cattle are unusual, particularly in association with livestock exhibitions. Because the clinical signs may be similar to those of some transboundary diseases, cases of MCF should be reported and investigated. Findings for this outbreak provided evidence to suggest that fair boards and veterinarians should reexamine biosecurity recommendations for livestock exhibitions. (J Am Vet Med Assoc 2010;237:87-92)

Multiple cases of MCF were identified during a 2-week period in November 2008 among cattle owned by individuals in various geographic locations within the state of Washington. The first death occurred on Thursday, November 6, 2008. A Guernsey heifer from northwest Washington (Whatcom County) died, and a necropsy was performed by the herd veterinarian. Tissue samples were submitted to the WSU-WADDL, and the state veterinarian was contacted because a presumptive diagnosis of MCF was made. The WSU-WADDL identified microscopic MCF-like lesions in tissue samples from the lungs (ie, necrotizing vasculitis), and OvHV-2 was identified in tissue samples by use of a PCR assay on Monday, November 10, 2008. Findings were reported to the office of the state veterinarian on November 11, 2008. A second animal from the same premises, a 7-month-old Holstein heifer, was found moribund with clinical signs of oral erosions, corneal opacity, and mucopurulent ocular discharge on November 3, 2008. Microscopic examination of postmortem tissue samples revealed necrotizing vasculitis in the lungs, and results of a PCR assay for OvHV-2 were positive. These findings were reported to the state veterinarian on November 12, 2008.

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ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>FAD</td>
<td>Foreign animal disease</td>
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<td>FFA</td>
<td>Future Farmers of America</td>
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<td>FMD</td>
<td>Foot-and-mouth disease</td>
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<td>MCF</td>
<td>Malignant catarrhal fever</td>
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<td>OvHV-2</td>
<td>Ovine herpesvirus type 2</td>
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<td>WSU-WADDL</td>
<td>Washington State University—Washington Animal Disease Diagnostic Laboratory</td>
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An 8-month-old Red Angus steer from a farm in western Washington (Skagit County) died on November 12, 2008, and was found to have MCF-like vasculitis in the lungs and positive PCR assay results for OvHV-2. A 3.5-year-old Angus cow from a second farm in western Washington (Thurston County) that died on November 14, 2008, also had MCF-like vasculitis in the lungs and was considered positive for OvHV-2 infection on the basis of results of a PCR assay.

Because of the unusual cattle deaths occurring in various locations throughout the state, the Washington State Department of Agriculture initially responded to the outbreak, although the USDA, APHIS, Veterinary Services also responded because clinical signs were considered potentially indicative of FAD. Diseases ruled out during the subsequent investigation included FADs and regionally endemic diseases, including FMD, vesicular stomatitis, wildebeest-associated MCF, bovine viral diarrhea, bluetongue, and epizootic hemorrhagic disease. After FADs had been ruled out and OvHV-2–associated MCF was confirmed, it was subsequently determined that all of the affected cattle had been ex-
hibited at the same livestock show, September 18 to 21, 2008. The state fair board was contacted by the state veterinarian on November 12, 2008, and assistance was sought to help contact livestock exhibitors regarding the outbreak. For the purposes of the present investigation, a case of MCF was defined as a bull, cow, steer, or calf that died with clinical signs of MCF for which infection with OvHV-2 was confirmed by use of a previously validated OvHV-2-specific, real-time PCR assay performed on tissues obtained from the affected animal. A total of 19 cattle confirmed to have OvHV-2-associated MCF and 5 cattle with probable MCF from which no tissues for diagnostic testing were available were identified between November 6, 2008, and February 7, 2009, among the 132 cattle housed in the same barn at the fair.

Veterinary practitioners submitted various tissues from 19 of the 24 probable and confirmed MCF cases to the WSU-WADDL. Diagnostic tests for MCF included gross and microscopic examination, serologic testing, and identification of viral DNA by use of a PCR assay. Histologic examinations were performed on 6 cases for which formalin-fixed tissues were submitted for examination. Gross abnormalities identified during field necropsies performed by veterinary practitioners were reported for all 24 probable and confirmed cases and included ocularonasal discharge, keratoconjunctivitis with corneal opacity (ie, classic head and eye form of MCF), mucosal erosions in the mouth, enlarged mesenteric lymph nodes, and gastroenteritis. All 6 cases in which histologic examination was performed had lymphocytic vasculitis, necrotizing vasculitis, or both in at least 1 submitted tissue. Tissues in which vasculitis was observed included the lungs, liver, kidneys, and spleen, and vasculitis was most commonly found in the lungs (Figure 1). Other microscopic lesions included necrotizing enteritis (2/6 cases), multifocal lymph node necrosis (2/6 cases), and multifocal splenic necrosis (1/6 cases). It was not possible to examine tissues for the full range of lesions that may have been present in these 6 cattle because for 4 of the 6 cattle, only spleen and lung tissues were submitted for examination. Five of the 19 cattle confirmed to have MCF also tested positive for MCF virus-specific serum antibodies by means of a competitive ELISA performed as described. No other cattle involved in the outbreak were tested for MCF virus-specific antibodies because serum was submitted for testing from only these 5 animals.

Analysis of 5 years of records obtained from the WSU-WADDL revealed that 23 cases of MCF (ie, OvHV-2 infection) in cattle, confirmed on the basis of results of laboratory testing, were identified in 2008 (19 from the present outbreak and 4 cases not associated with this outbreak); 4 were identified in 2007; and 1 each were identified in 2006, 2005, and 2004. Although MCF is endemic in Washington State, the increase in the number of MCF cases in 2008 (23 cases) was unusual. Although diagnostic laboratory submissions are not a precise reflection of disease prevalence in Washington State, these data suggested that outbreaks of this nature were unusual in this geographic region.

All of the veterinarians who reported animals with MCF; submitted tissue samples, or both were interviewed with the use of a standardized questionnaire to gather information on the clinical signs of affected animals and epidemiology of the disease. Clinical signs were reported for 17 of the 19 animals confirmed to have MCF; the most common clinical signs were anorexia (14/17 [82%]), signs of depression, diarrhea, fever, and labored breathing. For the remaining 2 animals, the diagnosis of MCF had previously been confirmed by the WSU-WADDL, and veterinarians submitting tissues from these animals did not receive a questionnaire. Mean reported highest rectal temperature for affected animals was 40.3°C (104.5°F), with a range of 39.4° to 41.1°C (102.9° to 106.0°F). For the 132 cattle cohoused at the fair, the confirmed disease rate was 14.4% (19/132).

All owners of animals exhibited at the fair were contacted to ascertain whether any of their animals had become sick or died. All owners and FFA chapters were sent a letter by mail, e-mail, or both, and some of these individuals participated in informational meetings held by the state veterinarian's office. Veterinarians who were on the Washington State Department...
of Agriculture or Washington State Veterinary Medical Association mailing list were notified of the outbreak by newsletter. No additional reports of sick or dead animals, other than 1 cow that had recovered from a fever and tested negative for MCF, were obtained. Not all of the cattle that had been cohoused at the fair were subsequently located and examined by a private practitioner or state veterinarian, including some that had been sold for beef shortly after the fair. From the last date of possible exposure at the fair, the mean number of days to death was 71, with a range of 46 to 139 days. The epidemic curve revealed that the peak number of cattle deaths occurred the week of November 16, 2008 (Figure 2), about 56 days after presumed exposure. Mean number of days an animal was reported to be sick before death was 6, with a range of 1 to 26 days (median, 4 days).

Affected cattle ranged in age from 5 to 36 months (mean, 18 months; median, 23 months). Twelve of the cattle were female. Many breeds were represented both at the fair and among the affected animals, with no apparent breed predilection. Of the affected cattle, there were 3 Herefords, 2 Guernseys, 2 Holsteins, 2 Jerseys, 8 Angus, 1 Milking Shorthorn, and 1 Angus crossbred. The cattle came from 9 different locations in the state (Figure 3). There were 18 groups of cattle exhibited at the fair, including 16 groups of cattle exhibited by FFA chapters (86 cattle), a group of 12 demonstration dairy cattle, and an open-class beef group of Highland cattle (34 cattle). The attack rate ranged from 0% to 58% for these groups.

Information on housing locations of the animals while at the fair was provided by the fair veterinarian, FFA organizer, and organizer of the open Highland cattle class. Seventy-four sheep and 49 goats were housed in the same barn at the same time as the cattle. Examination of a barn layout diagram (Figure 4) indicated that the affected cattle were not uniformly distributed within the barn. The largest concentration of affected animals had been housed toward the center of the barn. There was no nose-to-nose contact between cattle and sheep while cattle were tied in their barn locations. Two sets of outside wash racks were available for use by exhibitors.

To assess the effect of spatial distribution of animals within the fair barn, a 3-row by 7-column grid was placed over a barn layout diagram, and grid cell-specific attack rates for cattle with MCF (confirmed and suspected disease) and distances from the centroid of each grid cell to the center of the sheep pen area and to the center of the barn were calculated. Attack rate was not significantly associated with distance from the center of the barn (attack rate = $[-0.1239 \times \text{distance}] + 0.5033; R^2 = 0.27; P = 0.07$), although the $P$ value was close to our cutoff for significance, nor was it associated with distance from the center of the sheep pen area ($R^2 = 0.01; P = 0.74$).
Discussion

Malignant catarrhal fever outbreaks in cattle are often sporadic, with just a few animals in a herd that become clinically affected. The present outbreak was unusual because it was associated with an annual livestock exhibition that had historically cohoused cattle and sheep for many years without incident. The clinical signs of MCF in cattle depend on the organ systems that are most affected by this lymphoproliferative disease and can include fever, inappetence, ocular and nasal discharge, lymphadenopathy, buccal and muzzle crustation, diarrhea, corneal opacity, signs of depression, and neurologic signs. The tropism for specific organ systems is not well understood. The disease can result in death per acutely (ie, within 1 to 2 days of clinical onset) or can result in clinical signs lasting from 1 to several weeks before death. A chronic form of the disease in cattle is possible, as is apparent recovery from infection and subclinical infection.

The epidemiology of OvHV-2 infection in cattle and the reasons some cattle develop clinical signs of MCF remain unclear. Close contact with infected sheep appears to be a consistent finding in affected cattle, but other risk factors for cattle to develop clinical signs and succumb to the disease remain unknown. The disease in cattle has been reported in both sporadic and outbreak forms. In Colorado, an 850-cow dairy located next to a large sheep feedlot reported the loss of approximately 4 to 5 animals/sy as a result of MCF. In a report of high death loss (51.2%) among bison exposed to 7-month-old lambs at a feedlot, only 1 animal in 4,000 (0.025%) developed clinical MCF. It appears that European breeds of cattle are less susceptible, compared with other ruminants. However, other reports have highlighted the potential for high mortality rates. In a report from the Republic of Ireland, a 151-cow herd that was housed with lambing ewes and then shared a grazing pasture with sheep had a 38% MCF attack rate (all animals died or were culled after developing clinical signs) 2 to 5 months after initial exposure. In the United Kingdom, a herd of 77 cattle had a 15.6% MCF attack rate after being housed 75 m from a flock of ewes and ewe lambs. The attack rate reported in the present Washington State MCF outbreak may be an underestimate because some cattle may have developed mild clinical signs and recovered. Another study also found that cattle and bison could be subclinically infected; however, reactivation of the virus in subclinically infected animals leading to clinical disease was uncommon, even under stress conditions. This suggests that it is unlikely that there will be a substantial number of new MCF cases in the future among those cattle that were exposed at the fair described in the present report.

Although OvHV-2 has never been propagated in vitro, convincing evidence indicates that sheep are the reservoir for the causative virus. Virtually all sheep are infected under natural flock conditions. Transmission from sheep appears to occur predominantly via nasal secretions. Adolescent sheep approximately 6 to 9 months of age shed the virus more frequently and readily than adults. Horizontal transmission between cattle is unlikely, even with clinical disease and close exposure, because clinically susceptible species such as cattle and bison are considered dead-end hosts for the virus. A recent study further confirmed that bison with MCF do not transmit the virus or cause disease in their herdmates, even though bison are highly susceptible to clinical disease caused by MCF virus infection. As a result, separation or quarantine of clinically affected animals is unnecessary. Cattle are most likely to be infected via the respiratory route, as indicated in a study in which cattle were experimentally infected with nasal secretions from infected sheep. Although bison appear susceptible to OvHV-2 infection, in a report of an MCF outbreak involving bison, mortality rate decreased (17.5%, 6.1%, and 0.43%) as distance from feedlot lambs increased (1.6, 4.2, and 5.1 km, respectively). These findings may be relevant when developing preventive measures for application to cattle.

Postmortem examination of MCF-affected cattle may reveal erosive lesions in the nasal mucosa and digestive tract, development of pseudomembranes, petechial hemorrhages on serosal surfaces, renal infarcts or nonsuppurative interstitial nephritis, and enlarged congested lymph nodes. Samples that should be collected during field necropsy of cattle to confirm a diagnosis of MCF include formalin-fixed brain, lymph node, gastrointestinal tract (pharynx, esophagus, rumen, and small intestine), liver, adrenal gland, kidney, urinary bladder, salivary gland, and eye tissues for detection of MCF-like histologic lesions; and fresh, cooled spleen, lung, and lymph node tissues for PCR assay analysis to detect viral DNA. The disease in cattle can be a result of infection with a wildebeest-associated strain of γ-herpesvirus (A1HV-1), a sheep-associated herpesvirus (OvHV-2), or other MCF viruses. Polymerase chain reaction testing, specifically with a real-time PCR assay, should be used to confirm suspected cases of clinical MCF in all clinically susceptible species (ie, cattle, bison, and deer). Detection of viral DNA in leukocytes or tissues correlates better with clinical disease because the amounts of viral DNA are usually below the threshold of detection in most latently infected animals. Healthy cattle may be intermittently positive when tested with a nested PCR assay, and the presence of OvHV-2 DNA in healthy cattle suggests that recovery or subclinical infection is possible. A chronic form of the disease in cattle has also been described, but the factors contributing to the development of any of these forms of disease are unknown. Detection of anti-MCF viral antibody by use of an ELISA in clinically susceptible species only indicates infection but is not diagnostic for clinical disease because a substantial percentage of these animals can be latently infected with the virus and generate a humoral immune response. Therefore, a diagnosis of MCF requires identification of clinical signs and typical histologic lesions in conjunction with a positive PCR assay result for OvHV-2. The disease cannot be confirmed on the basis of clinical signs alone.

Once an outbreak of MCF in cattle is identified, control efforts will typically not be possible because of the long incubation period in cattle. There is currently no vaccine available to prevent the development of disease in susceptible species. Nose-to-nose contact...
with sheep is the most efficient method of spread, but fomite transmission has also been reported. Adolescent lambs appear to shed higher numbers of virions, and virus shedding seems to peak in late summer or fall when most of the lamb crop is 6 to 9 months old. Therefore, separating sheep from cattle appears to be the most cost-effective strategy to prevent transmission of OvHV-2. An alternative control method for OvHV-2-associated MCF involves production of MCF virus–free sheep, and this has been successful for mixed-species operations such as zoos and wildlife parks.

The outbreak described in the present report most likely developed because of exposure of cattle to sheep shedding OvHV-2 in an exhibition barn at the fair. Although anecdotal, there were several factors supporting the conclusion that this was an outbreak and not simply a result of the sporadic form of the disease. In this instance, although significant associations were not detected, the attack rate appeared to be associated with proximity to the center of the barn but not the center of the sheep pens. At the time that the cattle and sheep were in the barn, the weather was unseasonably hot and humid. In previous years, the ventilation system (a large exhaust vent at the center of the barn) was turned off because it was excessively noisy. During the 2008 fair, because of the heat, the exhaust fan operated continuously, drawing air in from the ends of the barn toward the center. In addition, there were more sheep in the barn in 2008, compared with 2007 and 2006 (n = 64 and 58, respectively), but not compared with 2005 or 2004 (n = 88 and 107, respectively). The constant airflow over the sheep pens toward the center of the exhibition barn may have concentrated MCF virions, and the unusually high humidity would have allowed virions to survive for a longer time, thus potentially increasing both the exposure time and exposure dose for cattle housed in the pens toward the center of the exhibition barn. There is no information regarding OvHV-2 survivability in the environment because the virus has never been propagated in vitro. However, extrapolation of survivability is suggested by the general properties of enveloped viruses such as herpesviruses, which survive better under moist conditions. Although the barn environment appeared to be the most likely area for transmission, the wash racks were used by both sheep and cattle exhibitors and the possibility of fomite transmission by the public and on shared equipment could not be ruled out.

Clinical signs of sheep-associated MCF may be confused with those of wildebeest-associated MCF, mucosal disease, and bluetongue as well as FMD, rinderpest, vesicular stomatitis, and infectious bovine rhinotracheitis. Several of these diseases are considered FADs or transboundary diseases in the United States. Producers and veterinarians observing these signs should report cases of unexplained animal deaths or disease to government authorities. Twenty-six states require that sheep-associated MCF be reported to state animal health officials, but 24 other states apparently do not explicitly require reporting of sheep-associated MCF. As a result of the outbreak in the present report, the Washington State Department of Agriculture is clarifying MCF reporting requirements to include all forms of MCF.

This present outbreak highlights the vulnerability of livestock to infectious diseases at exhibitions and fairs. A survey of California State Fair exhibitors identified a number of factors associated with possible disease transmission, including the number of shows or fairs attended and the fact that animals would return home between shows, that 38% of participants did not vaccinate their show animals, and that few participants used disinfectants for equipment or trailers that transported animals. These survey results were used to model the potential impact of FMD introduction at the California State Fair and led to the conclusion that despite the relatively short incubation period (4 to 7 days) for FMD, an infection would likely be undetected until animals returned home from the exhibition. The Washington outbreak of MCF associated with a state livestock exhibition described in the present report illustrates the impact that infectious disease transmission can have. With a disease such as MCF that has a long incubation period, identification of the source could potentially be difficult. An adequate history and knowledge of the disease led practitioners to suspect the livestock exhibition. The same knowledge would be critical in responding to an outbreak of FMD.

Findings for the outbreak described in the present report provide some evidence to suggest that fair boards and fair veterinarians should reexamine biosecurity recommendations for livestock exhibitions. Because of the possibility of other such outbreaks, we recommend that sheep be housed separately from cattle; that cattle and sheep exhibits be separated temporally, with cattle showing earlier and sheep showing later if the exhibition lasts several days; that people visiting various groups of livestock be encouraged to use hand sanitizers and footbaths or other means to minimize potential cross-contamination; that exhibitors not transport sheep and cattle in the same trailers; and that equipment such as wash stalls not be shared between animals.

References


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From this month's AJVR

Evaluation of orally administered robenacoxib versus ketoprofen for treatment of acute pain and inflammation associated with musculoskeletal disorders in cats

Jerome M. Giraudel et al

Objective—To evaluate the efficacy and tolerability of oral administration of robenacoxib for treatment of acute pain and inflammation associated with musculoskeletal disorders in cats.

Animals—155 cats requiring relief of signs of pain and inflammation associated with acute musculoskeletal disorders.

Procedures—The study was a multicenter, prospective, randomized, masked, noninferiority field trial. Cats were allocated randomly to 1 of 3 treatment groups: group 1 (1.0 to 2.4 mg of robenacoxib/kg, q 24 h), group 2 (1.0 to 2.4 mg of robenacoxib/kg, q 12 h [daily dosage, 2.0 to 4.8 mg/kg]), and group 3 (ketoprofen [mean dosage, 1 mg/kg, q 24 h]). All cats were administered tablets PO for 5 or 6 days. The primary efficacy endpoint was the investigator global assessment score, which was the sum of scores of signs of pain, inflammation, and mobility assessed in a masked manner by veterinary investigators at baseline, day 2, and day 4 or 5. Cat owners monitored in a nonmasked manner secondary responses by observation of cats’ activity, behavior, appetite, and interactions. Safety was assessed by monitoring adverse events, clinical signs, and hematologic and plasma biochemical variables (before and after treatment).

Results—No significant differences were detected among the 3 treatment groups for any primary or secondary efficacy endpoints or for tolerability variables. Robenacoxib tablets administered once daily were significantly more palatable than ketoprofen tablets.

Conclusions and Clinical Relevance—Robenacoxib tablets administered once daily had noninferior efficacy and tolerability, and superior palatability, compared with the active control drug, ketoprofen, for the treatment of signs of acute pain and inflammation associated with musculoskeletal disorders in cats. (Am J Vet Res 2010;71:710–719)