Malignant catarrhal fever (MCF) is the clinical manifestation of infection of certain ruminant species with one of a group of pathogenic gammaherpesviruses known as MCF viruses. Cattle and numerous exotic ruminant species are susceptible to clinical disease that may be sporadic or occasionally epidemic in nature. The most common MCF virus worldwide is ovine herpesvirus (OvHV)-2. Reservoir hosts such as sheep, carry and excrete OvHV-2, but do not develop clinical signs, while clinically susceptible species develop severe and often fatal disease. The existence of latent infection in clinically susceptible hosts is poorly understood, but is documented in some ruminant species. Twenty-six animals from a captive herd of white-tailed deer (Odocoileus virginianus) died and were examined from October 2006 to December 2010. Fifteen of these animals (58%) showed clinical signs and gross and microscopical lesions consistent with MCF, while 11 (42%) did not. Polymerase chain reaction (PCR) amplification yielded product consistent with OvHV-2 DNA in samples of spleen from all 26 deer. To examine the possibility of latent infection in this herd, peripheral blood mononuclear cells were examined by PCR for OvHV-2 DNA, and the test was positive in 23/32 (72%) clinically normal deer. Archived serum samples were used to examine the history of MCF exposure in the herd using a competitive enzyme-linked immunosorbent assay, which demonstrated that 10/40 (25%) deer tested had MCF viral antibodies, with nine deer being seropositive over multiple years. Combined with previous observations in deer and other species, these results suggest the existence of latent infection of white-tailed deer with OvHV-2.
additional members of the MCF virus group have recently been associated with clinical disease. One is an MCF virus of unknown origin that causes clinical disease in white-tailed deer (Li et al., 2000) and the second is an MCF virus endemic in domestic goats, provisionally known as caprine herpesvirus (CpHV)-2, which has been associated with chronic alopecia in sika (Cervus nippon) and white-tailed deer (Odocoileus virginianus) (Keel et al., 2003; Li et al., 2003; Vikoren et al., 2006).

In members of the Family Cervidae, clinical signs range from peracute to chronic and have been reported in numerous species including white-tailed deer, black-tailed deer (Odocoileus hemionus columbianus), mule deer (Odocoileus hemionus), reindeer (Rangifer tarandus), muntjac deer (Muntiacus spp.), sika deer, Shiras’s moose (Alces alces shirasi), Pere David’s deer (Elaphurus davidianus), swamp deer (Cervus duvauceli), rusa deer (Rusa timorensis) and red deer (Cervus elaphus) (Clark et al., 1970; Wyand et al., 1971; Sanford and Little, 1977; Heuschele et al., 1985; Brown and Bloss, 1992; Li et al., 1999). In some captive herds SAMCF can cause catastrophic losses (Clark et al., 1970, 1972; Brown and Bloss, 1992).

There is a spectrum of disease sensitivity or resistance to SAMCF among deer species, with Pere David’s deer (Muntiacus spp.), sika deer (Cervus nippon) and white-tailed deer among the most susceptible species (Li et al., 2001a). Nasal secretions are the predominant means by which virus is spread (Li et al., 2001a).

The present retrospective report describes a captive herd of white-tailed deer in which 26 animals died or were humanely destroyed between October 2006 and December 2010. Fifteen of these 26 animals (58%) showed clinical, gross (i.e. haemorrhagic enteritis or enterocolitis, and petechial to ecchymotic haemorrhages in one or more organs) and microscopical (i.e. lymphocytic to lymphoblastic vasculitis or perivascularitis of small to medium vessels in multiple organs) lesions compatible with SAMCF. Eleven of the 26 animals (42%) died or were humanely destroyed due to conditions such as trauma, pneumonia or chronic diarrhoea unresponsive to treatment and did not have clinical, gross or microscopical lesions compatible with SAMCF. Samples of spleen were collected from all 26 deer, frozen at −80°C, and tested by nested polymerase chain reaction (PCR) (Neimanis et al., 2009). PCR amplification of spleen samples from all 26 deer yielded product consistent with OvHV-2 specific DNA.

In the 15 deer with compatible gross and microscopical lesions, the clinical signs of SAMCF included listlessness or profound depression, animals separating themselves from herd mates and reluctance to move when approached. Occasionally, bloody diarrhoea was noted 12–24 h prior to death. The most common gross lesions in SAMCF affected deer consisted of haemorrhagic enterocolitis and petechial to ecchymotic haemorrhages of the kidney, spleen, myocardium, lung, lymph nodes and skeletal musculature (especially the diaphragm and intercostal muscles), with the liver, thymus, adrenal gland and urinary bladder less commonly displaying ecchymoses or petechiae. Mesenteric lymph nodes were often enlarged, oedematous and sometimes haemorrhagic. Microscopically, small to medium sized blood vessels in affected tissues were affected by lymphocytic vasculitis and perivascularitis. Vessel walls were expanded by lymphocytic infiltrates and eosinophilic amorphous material consistent with fibrinoid necrosis (Fig. 1). Fibrinocellular thrombi were sometimes present. Multifocal haemorrhages were often present in multiple organs.

In 11 of the 26 deer, DNA specific for OvHV-2 was detected in spleen samples in the absence of clinical, gross or microscopical lesions compatible with
SAMCF. Although surveys of various deer species in Germany and Austria have failed to identify OvHV-2 by PCR in healthy deer (Frolich et al., 1998; Benetka et al., 2009), detection of OvHV-2 DNA by PCR, in the absence of clinical signs, has been reported in cattle, elk, caribou, moose and various other domestic, captive and free-ranging ruminants (Lahijani et al., 1994; Heuschele and Reid, 2001; Flach et al., 2002; Zarnke et al., 2002; Powers et al., 2005).

To explore the possibility that deer in this herd were latently infected with OvHV-2, samples of whole blood were collected in EDTA tubes from 32 adult deer in the herd as part of an annual herd health examination in late 2010. Peripheral blood mononuclear cells (PBMCs) were processed for PCR at the time of collection (Li et al., 1995) using the QIAamp DNA Mini kit (QIAGEN Inc., Valencia, California, USA) to purify DNA as recommended by the manufacturer. DNA from OvHV-2 was amplified using previously described primers and thermal cycling conditions (Li et al., 1995). Amplified portions of DNA specific for OvHV-2 were detected by PCR analysis in 23/32 (72%) PBMC samples. Presence of OvHV-2 DNA in PBMCs from asymptomatic SAMCF-susceptible species has been reported previously. In the case of a SAMCF-exposed dairy herd, OvHV-2 DNA, identified by PCR, was variably and intermittently identified, suggesting fluctuating OvHV-2 loads in peripheral blood (Powers et al., 2005). Moreover, cattle recovering from clinical SAMCF remain persistently infected (i.e. have PCR detectable OvHV-2 DNA in PBMCs) for prolonged periods (e.g. up to 2 years) (O’Toole et al., 1997; Muller-Doblies et al., 1998).

To gain an insight into the history of OvHV-2 exposure in this captive deer herd, archived serum samples collected from 2006 to 2009 and maintained at −80°C were evaluated. These samples were collected as part of annual herd health examinations. None of these animals were exhibiting signs of SAMCF. This sample set comprised 90 samples from 40 different deer. Samples from multiple years were available for 31 of the 40 deer. Serum samples were analyzed for SAMCF virus antibodies using a direct competitive enzyme-linked immunosorbent assay (cELISA) as described previously (Li et al., 2001b). SAMCF virus antibodies were detected in 10/40 (25%) deer, four of which were seropositive for multiple years (Table 1). One deer was positive for SAMCF virus antibodies in each of the 4 years that it was tested (Table 1). The remaining nine deer exhibited intermittent seropositivity with 4/9 deer becoming seronegative after years of seropositivity (one deer had a sample from 1 year only). Of the 10 seropositive deer, 6/7 tested also had PCR detectable OvHV-2 DNA in PBMCs from whole blood (Table 1). Inconsistent seropositivity has been reported in dairy cattle that were asymptomatic, but resided in a herd with a history of SAMCF (Powers et al., 2005). Detection of SAMCF virus antibodies in the absence of clinical signs has also been reported previously in fallow deer, mule deer, white-tailed deer and elk (Li et al., 1996; Frolich et al., 1998; Powers et al., 2005; Benetka et al., 2009). In one survey of free-ranging and domestic ruminants in the USA, 3% of the 63 white-tailed deer tested had SAMCF virus antibodies by cELISA (Li et al., 1996). Detection of

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<th>Animal number</th>
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ND, not done; –, negative; +, positive.


Fig. 1. Myocardium from a white-tailed deer that exhibited clinical signs of SAMCF and from which OvHV-2 DNA was detected by nested PCR in a sample of spleen. Note artery with expanded tunica media and tunica adventitia due to infiltrates of lymphocytes and fibrinoid necrosis. A fibrin thrombus fills the narrowed lumen. Haematoxylin and eosin.
SAMCF virus antibodies by cELISA may be transient and intermittent; therefore, not all infected animals will have detectable antibodies at all times (O’Toole et al., 1995).

Much remains unknown concerning latent OvHV-2 infections in susceptible species. The incubation period (i.e., time from infection to the manifestation of clinical disease) is unclear and can be variable, ranging from a few weeks to several months. It is generally accepted that susceptible animals developing clinical SAMCF from OvHV-2, or animals that are latently infected, are not contagious to other clinically susceptible hosts (O’Toole et al., 1997; Heuschele and Reid, 2001), although experimental transmission from deer to deer and deer to cattle has been achieved using tissue suspensions from a clinically affected animal (Clark et al., 1972; Reid et al., 1986). Additionally, there is evidence that OvHV-2 may be spread by aerosol over significant distances. Clinical SAMCF in bison (Bison bison) has been documented with transmission over distances of 2.5–3 miles, against prevailing winds, and in the absence of common water sources, suggesting that some mechanisms of transmission remain undefined (Li et al., 2008). Latent infection could explain SAMCF in such cases where clinical disease is present in bison or cattle, but contact with sheep or other reservoir species is absent. In actuality a significant level of subclinical or latent SAMCF may be present in both cattle and bison (Clark et al., 1970; Li et al., 2001b) and recrudescence disease may occur during periods of stress (Heuschele et al., 1985; Li et al., 1999, 2001b; Powers et al., 2003).

In the present case, sheep were located in pastures approximately 50 m (at the closest point) from the deer pastures. There was no opportunity for direct interspecies contact and equipment (e.g., feeders, tractors, etc.) was not shared between the two pastures. Comparable reports of SAMCF in captive white-tailed deer have been recorded on premises located near sheep, but with no possibility of direct contact (Wobeser et al., 1973).

The retrospective nature of the present study does not allow examination of the relationship between OvHV-2 DNA in PBMCs or tissues, SAMCF virus antibodies and SAMCF compatible lesions in individual animals. However, the present study describes a herd of captive white-tailed deer with a history of clinical SAMCF, PCR detectable OvHV-2 DNA in PBMCs and tissue and MCF virus antibodies in serum from numerous clinically normal deer. Collectively, this evidence strongly suggests the existence of white-tailed deer latently infected with OvHV-2.

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