WEST NILE VIRUS UPDATE

Infection, Clinical Disease, and Vaccination in Camelids

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The vast majority of infected animals do not show any symptoms at all following transmission of the disease from an infected mosquito.

Alpacas and llamas are susceptible to a multitude of infectious agents that cause disease in other domestic animals. Serologic evidence of exposure to many viruses exists in camelids without clinical presentation of disease. Generally speaking, camelids have a low susceptibility to viral agents compared to other domestic animals; however clinical disease resulting from rabies, contagious ecthyma, equine herpes virus-1 and West Nile virus (WNV) has been reported.

West Nile virus was first described in 1937 in a woman from Uganda suffering a fever and is considered endemic throughout most parts of the Middle East, Europe, Asia, and Africa. In 1999, WNV was identified in the northeastern United States and since then it has been found in all of the continental states with the exception of Oregon. Although the principal transmitter of WNV is the Northern House Mosquito (Culex pipiens), migratory birds are the means by which WNV is transported to new areas. Birds migrating southward from the northern Midwestern states where intense transmission was occurring in 2001 carried WNV into the southern states. Similarly, the spring northward migration reintroduced the virus to northern states. Mosquitoes become infected with the virus when they feed on birds that are infected with WNV. Once the mosquito is infected, it may transmit the virus to other animals or people, but birds are the most common host. Many birds can be infected with WNV, but crows, blue jays, and ravens are most likely to die from the infection. Mammals are considered to be "dead-end hosts" because the virus does not reach high enough levels in the bloodstream to be infective through mosquitoes. However, WNV can be transmitted via organ transplant, blood transfusion, from infected mother to fetus, and through the milk.

The first reports of WNV clinical disease in camelids occurred during the 2002 epizootic, which happened to be a particularly bad year for WNV in other species as well, accounting for 284 human deaths and countless bird and horse losses. Confirmation of camelid clinical neurologic disease resulting from WNV infection was made from post-mortem testing using immunohistochemistry and reverse-transcriptase polymerase chain reaction (PCR) from cases in Ohio and Iowa, respectively. Additional proof of the pathogenicity of West Nile Virus in camelids came in August and September of 2003, when more than a dozen alpacas in Colorado, New Mexico, and Texas died from the disease confirmed by PCR.

Based on careful observations made by veterinarians treating these sick animals, it can be concluded that the clinical disease that develops from WNV infection in alpacas produces a broad range of symptoms. Most commonly observed symptoms included "Kathryn Hepburn" type facial or body tremors, head shaking, and stumbling, which progressed quickly to recumbency and death. However, vague neurologic signs such as hyperexcitability, lame-

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ness, and colic have been the only symptoms prior to death in some of the confirmed WNV cases. The presence of a fever is extremely variable, observed in less than 50% of reported cases. Of course, a number of other diseases can cause similar neurologic symptoms in camelids, including equine herpes virus-1, listeriosis, bacterial meningitis, rabies, meningeal worm migration, brain abscessation, or mycotic encephalitis.

Treatment for clinically ill animals is mainly aimed at alleviating their symptoms, which are produced from a severe inflammation of the brain known as encephalitis. This past year, however, a few animals suspected to have WNV based on their symptoms were treated with a transfusion of antibodies against the disease. The premise behind treatment with hyperimmunized plasma is to increase the circulating antibody level which will enhance the animal's ability to neutralize the infection.

There have been mixed results from treating clinically ill humans and horses with WNV hyperimmunized plasma, with the general conclusion being that early treatment before the onset of severe clinical signs is rewarding and late treatment once the patient is recumbent is unsuccessful. These experiences mirror the results reported by veterinarians treating WNV suspect animals with passive WNV immunotherapy. For example, on one farm in which two alpacas were stricken with WNV clinical infection, normal llama plasma containing high WNV antibody titers was transfused and the animal that had recently developed symptoms completely recovered while the other animal with a more advanced case died.

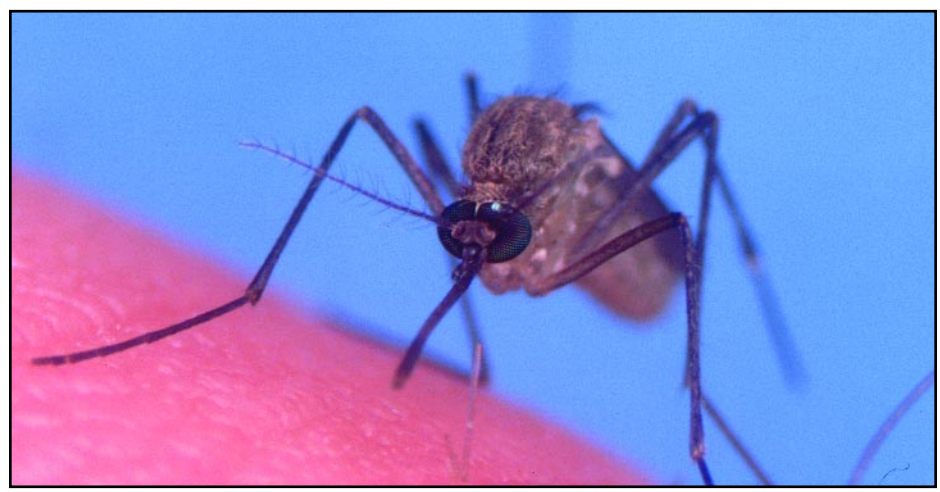
Examinations and Findings

Examination of the brain and spinal cord tissue from an infected alpaca revealed no gross lesions but on microscopic evaluation, severe inflammation in the form of lymphocytic perivascular cuffing was evident in ten different areas of the central nervous system. These findings are generally consistent with what has been reported in humans and horses with WNV encephalitis.

Postmortem testing for WNV infection is necessary to definitively confirm the disease in camelids. In humans and horses, a blood test (IgM capture ELISA) is available to determine recent exposure to WNV and differentiate between subclinical infection and clinical disease. This test does not exist for camelids. A central database has been established by the Alpaca Research Foundation to monitor WNV infection and clinical disease in camelids. The Foundation urges owners and veterinarians to report suspicious or confirmed cases of WNV infection so that the actual risk of clinical disease is better understood in this species. With the information currently available, there does not appear to be a breed, age, or sex predisposition for the development of clinical WNV disease. ARF is supporting confirmatory diagnostic testing of alpacas that have died and WNV infection was suspected.

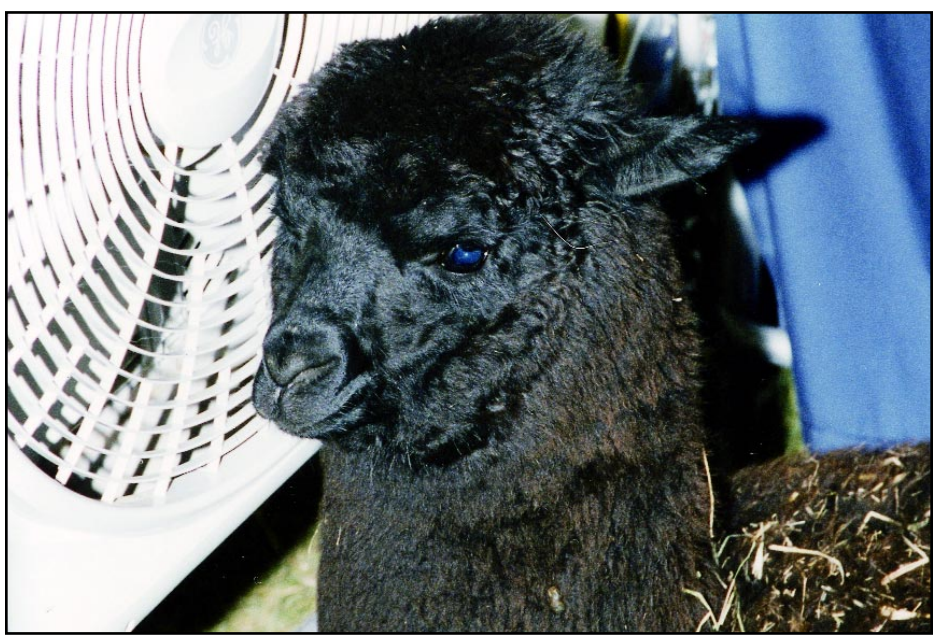
Not all animals that become infected with WNV will develop symptoms of disease. In fact, the vast majority of infected animals do not show any symptoms at all following transmission of the disease from an infected mosquito. While the Centers for Disease Control estimate that 20% of infected humans will develop symptoms of WNV disease, the incidence of clinical disease in camelids is far less. Serologic testing from alpacas on farms in Iowa, South Dakota, Colorado, and Texas has resulted in a prevalence of positive WNV antibody titers from 10-83%. None of the animals tested has ever shown any symptoms of illness, although based on their immune response, they have obviously been infected with WNV. In other countries where WNV is enzootic, antibody seropositive rates in ruminant species approach 62%, although clinical signs of WNV infection in these species are infrequent.

As stated above, the risk of developing clinical WNV disease is much greater for you than for your animals, except for birds and horses. To reduce the risk of contracting WNV, mosquito populations must be kept to a mini-



Mosquitoes become infected with the virus when they feed on birds that are infected with WNV. Once the mosquito is infected, it may transmit the virus to other animals or people.

If possible, animals should be housed indoors during peak periods of mosquito activity (dusk, evening, and dawn).



Fans can be placed in the barns to help deter mosquitoes.

mum. Every effort should be made to eliminate potential mosquito habitats on your property. Shallow standing water found in bird baths, clogged roof gutters, old tires, drainage areas, and even puddles if they persist for more than four days are ideal mosquito breeding places. Ponds containing stagnant water should be aerated or stocked with fish.

Mosquito larvicides are available in various formulations including organophosphates, bacterial larvicides (Bacillus thurigiensis israelensis) and insect growth regulators. Chemical control with larvicides is more effective and target specific than treatment with adulticides, but less permanent than habitat reduction. Applications of chemicals (e.g. organophosphates, pyrethrins, pyrethroids) to kill adult mosquitoes is the least efficient mosquito control technique. Starling, swallow, and pigeon nests that are in the barn should be removed as these birds can carry high concentrations of WNV without showing any symptoms and serve as hosts for potential infection in your animals. Dead crows, blue jays, or ravens should be reported to the local health department and removed from animal areas using gloves to handle the dead birds.

If possible, animals should be housed indoors during peak periods of mosquito activity (dusk, evening, and dawn). As mosquitoes are attracted to light, turning on outdoor lights close to animal housing during the evening and overnight should be avoided. If lighting is necessary, black lights should be used because they do not attract mosquitoes as well. In addition, lights can be placed away from where animals are kept to attract mosquitoes away. Fans can also be placed in the barns to help deter mosquitoes. Topical preparations containing mosquito repellents are available for livestock but care must be taken to read the label before using. It is interesting to point out that vitamin B and "ultrasonic" devices designed to deter mosquitoes have not been shown to prevent mosquito bites.

At Oregon State University, a WNV vaccination study was conducted using 84 alpacas and llamas that were immunologically-naïve to WNV. Using the WNV vaccine licensed for horses (Innovator, Fort Dodge), the researchers found that vaccination did not produce any local or systemic adverse reactions. Most vaccinated animals developed antibody titers following two doses of the vaccine administered intramuscularly three weeks apart. However, a third vaccination was necessary to achieve similar antibody titers as horses. Positive antibody titers were still present in the majority of animals at the time this article was written (>8 months from the initial vaccination). It is not known what antibody titer would be protective against clinical WNV disease in camelids nor has it been published for horses but it is clear from field reports by equine veterinarians that even very low titers have some protective effects.

Because of the comparatively low risk for developing clinical disease, we do not recommend that camelids be routinely vaccinated against WNV. In addition, human and veterinary epidemiologists have reported that natural exposure to WNV may provide long-term, if not lifetime, protection to clinical WNV disease. However, if a decision is made to vaccinate because

of an unusually high risk of exposure to WNV, a regimen of three intramuscular vaccinations at 3-week intervals using the horse vaccine should be followed. To ensure adequate antibody titers during periods of susceptibility, the final booster should be administered 3-6 weeks of prior to peak exposure, which is primarily in late summer and early fall but can occur year round in southern climates. Currently, there is no evidence to suggest that there is a danger in vaccinating a WNV-immune animal.

Conclusions

In summary, WNV is typically a disease between birds and mosquitoes, but can occasionally infect mammals if bitten by an infected mosquito. The vast majority of camelids that become infected with WNV show no symptoms of illness and develop protective antibodies that may provide lifelong immunity. Symptoms associated with WNV clinical disease are primarily neurologic and early treatment with passive immunotherapy in addition to anti-inflammatories and supportive care provide the best opportunity for recovery. An extra-label vaccine is available for the prevention of WNV clinical disease and has been shown to be safe and to induce a long-lasting antibody response. However, successful WNV prevention strategies should be aimed at eliminating nearby mosquito habitats and reducing opportunities for mosquito bites.

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