An underappreciated cause of neurological disease in humans and horses in SA

The West Nile Virus (WNV) may cause severe neurological disease in horses with a high death rate. Cases are frequently reported in the USA where horses are now vaccinated annually. We investigated the situation in South Africa to determine if cases are being missed in horses. We found that WNV may be an important, under-detected cause of neurological disease in South Africa and local strains can cause fatal disease in horses.

The West Nile virus (WNV) is a mosquito-transmitted virus in the flavivirus genus that is widely distributed throughout Africa, the Middle East, Asia, parts of Europe, Australia, North and South America and the Caribbean. It was first isolated in the West Nile province of Uganda from a woman with fever.

WNV circulates between birds as replication host and mosquitoes usually without causing disease. Humans and horses are incidental hosts and do not have a high enough level of the virus in the blood to infect mosquitoes. The mosquito that transmits WNV in Africa belongs to the Culex genus and is found in the vicinity of dams or standing water across the continent.

Humans and Horses
Humans and horses may experience severe disease. In humans, 20% of infections develop West Nile fever with symptoms including a rash, joint and muscle pain, fever, nausea and headache, while less than 1% of cases will develop WNV neurological disease which includes meningitis, encephalitis, polio-like paralysis in rare cases and death. Symptoms include a stiff neck, sore back, severe headache, eye sensitivity to light, weakness and changes in mental status in certain cases. In horses 20 to 30% of infections develop symptoms with as many as 90% of these developing severe neurological diseases as described below and 30 to 40% being fatal or euthanised for humane reasons.

In the USA
WNV emerged as a new pathogen in the USA in 1999 and may have been imported from birds or mosquitoes from the Middle East where identical virus strains was identified the previous year. Since then it has spread across the continent, causing more than 30 000 human cases of which 40% were neurological and more than 1 000 fatal. In horses, the largest outbreak occurred in 2002 when 15 000 cases were reported in horses over 41 states. Cases decreased in horses since the virus became endemic and a vaccine was introduced, but severe disease is still reported with about 200 cases reported every year in Texas alone.

Endemic in southern Africa
The largest outbreak occurred in humans in the Karoo in 1974 affecting about 10 000 people, with thousands visiting their local doctor with mainly WNV fever. An outbreak in humans and animals also occurred in the 1980s in the Witwatersrand affecting hundreds of people. Over the past decade, 5 to 15 cases are reported every year, although only a proportion of cases are thought to be submitted for laboratory investigation and may be largely missed as a cause of
neurological disease.
Cases of severe WNV disease have been identified, including fatal hepatitis and several non-fatal encephalitis cases in humans as well as deaths in ostrich chicks, horses and a dog. Screening of blood from horses at the annual yearling show in 2001 indicated that 11% had been exposed to WNV over a period of a year, and up to 75% of their mothers had antibodies, suggesting that WNV is still widely distributed across South Africa. Experimental infection of two horses with a local WNV strain did not cause disease, leading to the misperception that South African WNV strains are not pathogenic in horses. Today we know that only 20% of WNV infections develop symptoms and many horses in the USA get asymptomatic infections.

**Research on WNV in South Africa**
Genetic sequencing has shown that local strains all belong to genetic lineage 2 rather than lineage 1 found in the USA. However, all local cases of severe disease were caused by lineage 2 strains, and certain lineage 2 strains were just as capable of causing severe disease in laboratory animals as the lineage 1 strain from the USA.
To determine if cases of severe disease are being missed in horses in South Africa, the Zoonotic Neurological Virus Research Group, department of Medical Virology, University of Pretoria, have been working with the veterinary community to test horses with unexplained neurological disease for WNV over the past two years. We tested 123 horses of which 65 had unexplained neurological disease and the rest had fevers.
We identified WNV in 19 neurological cases (29%) and a related flavivirus (Wesselsbron Virus) in a further two. Fourteen WNV positive horses died or had to be euthanised (74%) as well as one of the two Wesselsbron Virus cases. Affected horses were four months to 19 years of age and included Thoroughbreds, Arabians, Lipizzaners, Welsh Ponies, Warmbloode, and mixed breeds. Cases were identified in Gauteng, Northern Cape, North-West, Natal and the Western Cape, occurred from March to early July, and were caused by local lineage 2 strains.

**Symptoms**
Typical symptoms in horses included stumbling in all cases, weak hind and/or forelimbs, partial loss or impaired movement, complete paralysis, partial blindness and jaundice in certain cases. Severe cases were unable to get up, had quadriplegia, limb paddling, teeth grinding, muscle twitching, chewing fits, seizures and coma before death. Fever was not always noted. Two cases that survived were sick for 21 days and had to be rested for several months, but recovered fully. Co-infections with African Horse Sickness virus (AHSV) were identified in two cases, but both had neurological symptoms that were not typical of AHSV. The WNV season coincides with the AHSV season which may be the reason that cases were missed in the past. This study suggests that WNV may be an important under-reported cause of neurological disease in horses in South Africa, and should be considered in animals with any of the described symptoms in late summer and autumn. We invite horse owners and veterinarians to let us know about cases and to send us specimens from horses with neurological disease to test. This will help us determine the true disease burden of WNV in horses in South Africa and help us make recommendations for vaccination in the future.
Points to note:

- You can protect your animals with insect repellents containing pyrethroids or DEET.
- Although the virus will not be transmitted to humans from infected horses, care should be taken when handling brain tissue or blood of infected animals.
- No specific treatment exists and symptoms are mainly treated with anti-inflammatory drugs and preventing self-injury.
- A horse vaccine is not currently available in South Africa and a human vaccine does not yet exist. **Limited availability of Horse vaccines – contact us for further details**...
- In the first few days of symptoms we can test for the virus by genetic tests in the blood or, in fatal cases, in the brain and spinal cord.
- Later on in the disease antibodies can be detected in the blood. Cases occur in late summer and autumn.
- Neurological signs include stumbling, weak hind and/or forelimbs, partial loss or impaired movement, complete paralysis, partial blindness and jaundice in certain cases. Severe cases were unable to get up, had quadriplegia, limb paddling, teeth grinding, muscle twitching, chewing fits, seizures and coma before death.

Further reading:
www.cdc.gov/ncidod/dvbid/westnile/qa/overview.htm

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