West Nile Outbreaks In Southern France Since 2000

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Abstract

In the last decade, West Nile Virus has re-emerged as an important pathogen for humans and horses, as frequent outbreaks with increased proportion of neurological disease cases have been reported. Indeed, outbreaks in Romania and Morocco in 1996, Tunisia in 1997, Italy in 1998, Russia, United States and Israel in 1999, and France, United States and Israel in 2000 presented either an increase in the number of severe human cases, an increase in the severity of neurological disease in horses or high bird mortality. Previously reported in France in 1962-65 in Camargue, West Nile (WN) disease reappeared 40 years later in 2000 and 2004 in Camargue (South of France), causing respectively 76 equine cases (21 deaths) and 33 equine cases (7 deaths). In 2003, West Nile virus caused 4 cases in humans and 4 cases in horses. The objectives of this study will be to describe the characteristics of the WN epidemics in France since 2000 and to indicate the interest of horses in the early warning system in the French epidemiological context. In particular, the passive surveillance system based on the detection of clinical cases in horses and the active surveillance system based on sentinel birds will be compared. Moreover, the results of two serosurveys conducted in 2000 and 2003 in equines will be presented; the data suggest that the specific ecology of two zones classified as "important bird areas" could allow an endemic (or frequent) circulation of the WNV.

Introduction

West Nile virus was first discovered in 1937 in the blood of a native woman of the West Nile province of Uganda who at that time was suffering from a mild febrile illness. Since then, both sporadic cases and major outbreaks of West Nile fever have been reported in Africa, the Middle East, Europe and Asia and many aspects of West Nile infection have been well documented since the early 1950's in Egypt and in Israel, in the 1960's in France and in the 1970's in South Africa. However during the last five years many reports about West Nile virus have been published, because of outbreaks occurring in Romania, Morocco, Italy, Russia and Israel but more especially with the discovery of the virus in North-America in 1999 (Dauphin et al, 2004).
In Europe, with the exception of an outbreak in France in 1962, WN fever was also considered a minor disease for humans and equines and only appeared sporadically. Since 1996, date of the first large outbreak in Romania, WN fever has become in Europe and in the Mediterranean Basin, and later in the USA a major public health concern.

In Southern France in 2000, 76 equines were laboratory-confirmed with WN virus from 131 equines presenting with neurological disorders from September to beginning of November, including 21 fatal infections. The last confirmed case was on November 3. WN virus was isolated from a horse brain biopsy. All but three cases were located in a region called "la petite Camargue" (Herault and Gard districts) harbouring several large ponds, numerous colonies of migratory and settled birds, as well as large populations of mosquitoes. No human cases were laboratory-confirmed among 51 suspected cases including 33 cases hospitalised with symptoms of encephalitis or meningo-encephalitis, and 18 other cases with fever. In contrast, WN IgM antibodies were recorded in one out of 33 healthy gamekeepers working in this area.

In France, in October 2003, both a human case and two equine cases were notified in the Var district in Southern France. Retrospective and prospective case finding of human

meningoencephalitis cases was carried out in all hospitals of the Mediterranean region. Preliminary findings confirmed several human cases in the area and 5 equine cases (with 4 meningo-encephalitis forms). In 2004, 32 equine cases were reported in the Camargue area. No human case was reported.

Objective

The objectives of this study will be to describe the characteristics of the WN epidemics in France since 2000 and to indicate the interest of horses in the early warning system in the French epidemiological context. In particular, the passive surveillance system based on the detection of clinical cases in horses and the active surveillance system based on sentinel birds will be compared. Moreover, the results of a serosurvey conducted in 2003 in equines will be presented; the data suggest that the specific ecology of two zones classified as "important bird areas" could allow an endemic (or frequent) circulation of the WNV.

Methods

2000 outbreak :

In 2000, a serological survey was undertaken in horses located within a radius of 10 km around the confirmed cases. A total of 5,133 samples of horse sera were collected between September and November 2000 from the three different districts where cases had been reported.). Animals were first tested for WN IgG antibodies and, because of logistic constraints, only positive sera were then tested for IgM antibodies. A positive animal was defined as an IgG positive animal. A positive group was defined as a group of which at least one animal was IgG positive (Durand et al, 2002).

For each animal, an individual form was filled by the vet. Among other data (date, name and address of the vet and of the animal keeper), this form mentioned the species and breed of the animal, its age and sex, the place where animal was located, and the size of the group in which the animal was included the day the sample was taken (i.e. the number of equines which were at the same place).

2003 outbreak :

In 2003, all the commercial stables located within 30 km of the first equine laboratory-confirmed case were included in the survey (racing stables, riding schools, breeders, dealers etc). In each stable, blood samples were taken from 30 randomly chosen animals (from all animals in <30 horses stables). The sera were processed and tested for anti-WNV IgG and IgM antibodies. Animals were first tested for anti-WNV IgG antibodies, positive sera being also tested for IgM antibodies. Neutralization tests were performed on a few of the first positive sera, due to the absence of other flaviviruses circulating in this Mediterranean coastal region. A geographic analysis was conducted to investigate the relationship between the seroprevalence and the nearness to natural zones that could play a specific role in the viral cycle: the areas classified as "important bird areas" (IBAs). These areas are sites of international importance for the conservation of birds (especially migrating birds), identified against a set of globally standardized scientific criteria. Two IBAs were located in the survey area.

Surveillance of bird fauna

The aim of surveillance bird fauna was to be able to rapidly detect any circulation of the West Nile virus in the Camargue in order to provide an early warning before the clinical signs had been seen in Equidae or humans and to take the appropriate measures for information, prevention and combating the disease.

Surveillance was based on:

- a "passive" system based on increased surveillance of cases of bird deaths and a virological analysis of carcasses through activation of the SAGIR network which relies on a public awareness campaign via the distribution of more than 400 posters and availability of a freecall telephone number;

- an “active” system based on serological surveillance of sentinel birds: 260 “call” ducks and domestic fowl (samples by veterinary practitioners) and controlled monthly (from June to November) on sites throughout counties of the Mediterranean area . Sentinel bird surveillance was combined with serology controls of captured wild birds (magpies and pink flamingos).

Results

2000 serosurvey :

WN IgG detection was positive for 428 (8.3%) of these samples, of which 248 (41.4%) were also IgM positive. There was a direct relationship between the number of positive clinical cases in an area and the number of positive cases included in the serological survey study.

2003 serosurvey :

Of the blood samples taken from 906 equines, 305 were WNV IgG positive (33.7%) in 33 stables (n = 41). The seroprevalence rate in IgG-positive stables ranged from 3% to 95%, and had a multi-modal distribution, half of the 33 IgG-positive stables having a >30% seroprevalence (n = 17). Of the 305 IgG-positive animals, only 23 had also IgM antibodies (7.5%), located in nine stables. In each of these nine stables, the IgG seroprevalence rate was over 30%.
The IgG seroprevalence rate showed wide geographic variations (Figure 2A), with two areas where the seroprevalence was high: nearby the IBA A and, in a lesser extent, around the IBA B. All of the stables for which the IgG seroprevalence was >30% were located ≤ 5km of an IBA (except one: a trotters racing stable, the animals of which moved frequently for races). Furthermore, around each of the two IBAs, a significant trend was found in the IgG seroprevalence by distance, with a progressive decrease of the seroprevalence when the distance to the IBA increases (Table 1). The geographic location of the IgM positive results showed a similar pattern (Figure 2B): all of the IgM-positive animals were located ≤ 3.5 km of an IBA.

Results of bird surveillance

Since 2000, no abnormal bird deaths attributable to the West Nile virus have been seen in the Camargue.
A single seroconversion (n=260) was detected in 2001 in a call duck from Bouches-du-Rhône area. Similarly in 2002, a single seroconversion (n=250) was detected in a bird from the Gard. It was concluded that the West Nile virus was present in the Camargue in 2001 and 2002 although that its circulation level was probably extremely low.
No cases of seroconversion (n=185) were seen in 2003 and the surveillance system did not therefore demonstrate the presence of the virus in the Camargue.

Discussion

During the 2000 French outbreak, the number of equine clinical cases (76 cases) was much higher than in 2003 (4 cases). Whereas studies conducted in Camargue before 2000 had shown the absence of WN antibodies in horses of the affected area, 8.5% of the animals tested there in 2000 (n = 5,107) had IgG antibodies, a much lower seroprevalence than in 2003. It is difficult to compare the IgG seroprevalence rate observed after the 1998 Italian outbreak (40%) with the 2003 French situation, as the survey perimeter is much larger in the latter case. However, the proportion of complement fixing sera found in the Italian survey (41% of the IgG-positive sera) is close to the results obtained for IgM in the 2000 French serosurvey (42%), and much higher than in the 2003 French serosurvey (7.5%). Finally, significant differences among age-specific prevalence rates were neither found in the 1998 Italian serosurvey, nor in the 2000 French serosurvey. These comparisons

suggest that the 2000 French and the Italian 1998 outbreaks were sporadic phenomena, whereas the 2003 French outbreak would better correspond to an enzootic situation.

Four independent arguments lead us to suggest the existence, in the survey area of specific zones where the WNV would frequently circulate: (i) the survey perimeter is close to an area historically described as a WNV focus; (ii) the high IgG seroprevalence and the low IgM seroprevalence suggests that many of the IgG-positive animals could have seroconverted earlier than in 2003; (iii) in the stables where the WNV has circulated in 2003 (the IgM-positive stables), an increase of the IgG seroprevalence with age suggests that the virus has also circulated in the preceding years; (iv) the natural cycle of the WNV involves birds and mosquitoes, and a close association is observed between the equine IgG seroprevalence rate and the nearness to two "important bird areas" (Durand et al, 2005).

As indicated by their name, important bird areas correspond to protected natural zones that are essential for the conservation of one or several endangered bird species. In the case of the two IBAs of the studied area, these species are migrating species that nest there. However, the connection between IBAs and seroprevalence must be interpreted cautiously. The processes it conceals are probably more complex than a simple presence/absence of some migratory bird species. Besides the avifauna, IBAs correspond to areas in which the overall biodiversity is greater than elsewhere. One can assume that it is precisely this richer biodiversity that allows the WNV cycle, easier than in other places, to develop or persist. Therefore, it is the ecology of these areas that could explain the existence of a specific epidemiological cycle, in particular because of the vector populations that live there. If birds were considered as amplifying hosts in the cycle of WNV, research would require a specific attention on competent mosquitoes, which are able to bite birds and equines and/or humans. A better understanding of the corresponding epidemiological processes could allow in the future using such areas as sentinels. Their surveillance could allow detecting the amplification of the viral cycle that can result, as it has been the case in 2003, in the occurrence of equine and human clinical cases.

Passive surveillance in Equidae, based on the national network of veterinary practitioners appears to represent a useful effective tool to detected equine clinical cases which appear to develop more or less concomitantly with human ones. Awareness and training activities for both practitioners who are specialised in equine medicine or more general practitioners would be desirable in order to provide surveillance which is of satisfactory sensitivity.

Activation of the SAGIR network on a national scale for birds should allow excess deaths due to West Nile virus infection to be identified.

An active surveillance device (in horses and/or domestic birds) which satisfied reasonable sensitivity and early warning requirements would have very high human resources and logistics costs (particularly if extended to the whole country): these costs are not commensurate with the public health consequences of the infection.

References

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