Characterization of the temporal and spatial distribution and reproductive ratio of vesicular stomatitis outbreaks in Mexico in 2008

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Objective—To characterize the temporal and spatial distribution and reproductive ratio of vesicular stomatitis (VS) outbreaks reported in Mexico in 2008.

Animals—Bovine herds in Mexico in which VS outbreaks were officially reported and confirmed from January 1 through December 31, 2008.

Procedures—The Poisson model of the space-time scan statistic was used to identify periods and geographical locations at highest risk for VS in Mexico in 2008. The herd reproductive ratio (R_h) of the epidemic was computed by use of the doubling-time method.

Results—1 significant space-time cluster of VS was detected in the state of Michoacan from September 4 through December 10, 2008. The temporal extent of the VS outbreaks and the values and pattern of decrease of the R_h were different in the endemic zone of Tabasco and Chiapas, compared with findings in the region included in the space-time cluster.

Conclusions and Clinical Relevance—The large number of VS outbreaks reported in Mexico in 2008 was associated with the spread of the disease from the endemic zone in southern Mexico to areas sporadically affected by the disease. Results suggested that implementation of a surveillance system in the endemic zone of Mexico aimed at early detection of changes in the value of R_h and space-time clustering of the disease could help predict occurrence of future VS outbreaks originating from this endemic zone. This information will help prevent VS spread into regions of Mexico and neighboring countries that are only sporadically affected by the disease. (Am J Vet Res 2011;72:233–238)

Vesicular stomatitis is a disease of livestock caused by the VSV of the family Rhabdoviridae, genus Vesiculovirus, for which 2 serotypes, New Jersey and Indiana, have been described for North America. The disease is characterized by severe vesiculation and ulceration of tongue, oral tissues, feet, and teats. The VSV infects various hosts including horses, cattle, and pigs. In certain conditions, humans and some wildlife species may also become infected. Infection with the VSV is rarely fatal, but it typically has an important impact on the economy because of the direct losses that it causes in infected herds and the imposition of quarantine restrictions that affect animal trade. Vesicular stomatitis is also important in the differential diagnosis of vesicular diseases because its clinical signs in cattle and pigs are indistinguishable from those caused by the infection with the foot-and-mouth disease virus.

The United States is regularly affected by VSV incursions, and genetic evidence suggests that viruses associated with such incursions likely originate from enzootic areas of Mexico. Diagnosis of VS became part of the passive surveillance system for vesicular diseases in Mexico in 1949. It has been suggested that VS is enzootic in certain parts of the Mexican states of Veracruz, Oaxaca, Tabasco, and Chiapas, in which the disease is most common during the rainy season. The enzootic area is characterized by tropical weather, with high levels of precipitation, and mean temperatures of 25°C. Other parts of the country such as the states of Jalisco, Michoacan, Hidalgo, Guerrero, and Colima are sporadically affected by epizootics of the disease. Unlike the enzootic zone, the epizootic area is character-
ized by arid or semiarid weather with mean temperatures of 15° to 20°C. However, despite vector-borne transmission, samples of vesicular liquid, blood serum, and epithelium are collected from animals with clinical signs of disease. The information collected for each outbreak included the location (municipality), date of first identification of VS-like lesions, date of first veterinary visit to the herd, date of diagnosis, number of susceptible animals, number of animals with VS-like lesions, animal species, number of samples collected, and presumptive and final diagnosis.

Outbreaks—Outbreaks were georeferenced by use of the centroid of the municipality in which the outbreak was located. The centroid of each municipality was obtained from databases provided by the Instituto Nacional de Estadística y Geografía. There are 2,438 municipalities in Mexico, grouped in 31 states and a Federal District (Mexico City). Most (n = 321) of the outbreaks were caused by VSNJV, whereas 4 outbreaks associated with VSIV infection. Other outbreaks caused by VSNJV were used in the analyses reported here.

Materials and Methods

Animals—A database containing the laboratory results for all VS outbreaks confirmed in 2008 was provided by the EADC. Outbreaks were defined as bovine herds with at least 1 animal with a confirmed positive test result for VSV. The information collected for each outbreak included the location (municipality), date of first identification of VS-like lesions, date of first veterinary visit to the herd, date of diagnosis, number of susceptible animals, number of animals with VS-like lesions, animal species, number of samples collected, and presumptive and final diagnosis.

General approach—The temporal and spatial distribution of VS outbreaks in Mexico in 2008 was assessed through use of the scan statistic, which is a technique for the detection of space-time clusters of disease. The basic R, which is the mean number of secondary outbreaks caused by 1 infectious herd during its entire infectious period, was estimated for each of the space-time clusters detected with the scan statistic and for the enzootic area that includes the states of Tabasco and Chiapas.

Specific approach—The Poisson model of the space-time scan statistic was used to identify significant space-time clusters of the disease. The null hypothesis was that the ratio between number of outbreaks and number of cattle per municipality was evenly distributed throughout the country. In other words, if no clustering was present, the number of outbreaks in a given municipality would be proportional to the size of the cattle population of the municipality. Therefore, and because a 1-sided statistical test was applied, rejection of the null hypothesis for a particular region and period led to the identification of space-time clusters in which the number of reported outbreaks was larger than expected on the basis of the size of the cattle population of the region.

Outbreaks were assumed to have started at the date when VS-like clinical signs were first observed in the herd. Outbreaks were aggregated into 7-day bins to account for intraweek variations in the reporting of cases, which is a type of reporting bias that has been referred to as the Monday effect. The space-time scan statistic defines cylindrical windows with the circular geographic base centered around each municipality centroid and with height corresponding to time. The base and height of the cylinder (ie, the radius of the spatial window and the duration of the cluster) were set up to vary up to a maximum of 50% of the population at risk. The expected number of outbreaks per municipality under
the null hypothesis of homogeneous distribution of the disease was assumed to be proportional to the number of cattle in the municipality. The space-time scan statistic compares the observed-to-expected ratio of outbreaks within each candidate space-time cluster with the observed-to-expected ratio of outbreaks outside the candidate cluster.\textsuperscript{1,4,13,15}

A Monte Carlo simulation process was used to test for significance of identified clusters. A large number (n = 999) of random replications of the data set were generated under the null hypothesis of outbreaks being proportional to the size of the cattle population within the candidate cluster. The maximum likelihood of the observed (n = 1) and randomly generated data (999) was then computed. Subsequently, a likelihood ratio test was used to compute, for each candidate cluster, the value of the candidate cluster was computed as $P = R/(1 + 999)$. Candidate clusters in which the condition $P < 0.05$ was estimated were assumed to represent true (significant) clusters of disease. The space-time scan statistic was calculated by use of an open-access statistical program.\textsuperscript{14,13,15}

Outbreaks were mapped by use of spatial analysis software.\textsuperscript{4}

Herd reproductive ratio ($R_h$)—The $R_h$ is an estimate of the number of herds that became infected through direct or indirect contact with an infectious herd. Thus, $R_h > 1$ indicates that the number of outbreaks is increasing; $R_h = 1$ suggests that the number of outbreaks remains constant; and $R_h < 1$ reflects a decrease in the number of outbreaks.\textsuperscript{16} In the present study, $R_h$ was calculated with the epizootic doubling-time method, so that $R_h = 1 + (\ln 2)/D$,\textsuperscript{16} in which $D$ is the duration (in days) of the infectiousness period of the herd and $t_d$ is the period (in days) in which the number of outbreaks doubled. The value of $D$ was approximated by consideration of the expert opinions of 12 veterinarians responsible for VS surveillance in Mexico. Minimum, most likely, and maximum values of $D$ equal to 15, 30, and 45 days and $D$ equal to 7, 10, and 20 days were estimated for the epizootic and enzootic areas, respectively. Because $t_d$ cannot be computed for the interval between the last day by which the number of outbreaks doubled and the end of the epizootic, a value of $R_h$ equal to 0 was assumed at the end of the epizootic.\textsuperscript{16}

Results

From January 6, 2008, through December 16, 2008, there were 321 confirmed outbreaks of VSV in Mexico. Three outbreaks were excluded from the analysis because the information on geographic location of the affected herds was missing. Thus, 318 outbreaks were included in the study. The states of Jalisco, Michoacan, and Guerrero accounted for 75% of the total number of outbreaks (Table 1). There was an increase in the number of outbreaks starting in September that continued through October and November, in which > 100 cases were reported (Figure 1).

One significant ($P < 0.001$) space-time cluster of VS outbreaks was detected by use of the spatial scan statistic. The cluster, which was centered in the municipality of Aquila, state of Michoacan, at 18.36°N, 103.19°W, lasted from September 4 through December 10, 2008, and had a radius of 403.3 km. There were 246 outbreaks confirmed within the cluster, whereas 20.5 outbreaks were expected under the null hypothesis of homogeneous distribution of VS outbreaks in Mexico (Figure 2).

The value of $R_h$ in the endemic zone that included the states of Tabasco and Chiapas increased gradually, with the peak taking place at the beginning of August, at which point the most likely value of $R_h$ was estimated.

<table>
<thead>
<tr>
<th>State</th>
<th>No. of VS outbreaks</th>
<th>No. of municipalities with VS outbreaks</th>
<th>Proportion of municipalities with VS outbreaks</th>
<th>Percentage of VS outbreaks per state</th>
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</thead>
<tbody>
<tr>
<td>Hidalgo</td>
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</tr>
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<td>0.3</td>
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<td>0.00</td>
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<td><strong>Total</strong></td>
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<td><strong>122</strong></td>
<td><strong>---</strong></td>
<td><strong>100.0</strong></td>
</tr>
</tbody>
</table>

--- = Not applicable.
to be 10 (Figure 3). By the beginning of September, the number of outbreaks in the endemic area decreased, so that the number of outbreaks did not double, and \( R_h \) approximated a value of 0 by October. The shape of the \( R_h \) pattern within the significant space-time cluster centered in the state of Michoacan was different, compared with that observed in the endemic zone. Within the Michoacan space-time cluster, outbreaks started in September (ie, approx at the time when the number of outbreaks decreased in the endemic zone). At that time, the maximum value of \( R_h \) was estimated as 6 within the cluster. The value of \( R_h \) gradually decreased and approximated a value of 0 by the end of November.

**Discussion**

The study reported here revealed that the increase in the number of VS outbreaks reported during 2008 in Mexico, compared with numbers in previous years, was associated with a significant space-time cluster of the disease in a region of central and northern Mexico, where VS does not occur every year (epizootic region) as it does in the southern region of Mexico, where VS is considered enzootic. The significant cluster of the disease, which was detected in a geographic region and time of the year different than those in which the disease typically occurs, was preceded by an increase in the \( R_h \) of the disease in the endemic area of Mexico. Implementation of real-time monitoring of space-time clustering of VS and of the \( R_h \) value as part of the surveillance system for the disease in Mexico may help to establish an early warning system for VS. It may also ultimately allow epizootic preventive measures to be established in nonendemic regions of Mexico.

A significant cluster of VS outbreaks was identified in the central part of Mexico in 2008. The cluster extended over a large area of the country (511,009 km²), which is typically considered at low risk for the disease.\(^8\) Additionally, the cluster existed from September through December and immediately after the reporting of cases in the endemic region decreased (Figure 3). These findings suggested that environmental and epidemiological factors may have acted together to favor VS spread from the endemic area into a region in which conditions are usually adverse for the transmission of the disease. The value of \( R_h \) in the endemic area gradually increased until it peaked in September and then dramatically decreased afterward. This observation is compatible with the coexistence of favorable conditions for disease transmission that were immediately followed by an adverse change in those conditions. Such favorable conditions, which resulted in the peak of the value of \( R_h \) in the endemic region in September, may have led to the spread of the disease into the epizootic region of the country by that time of the year. This hypothesis is supported by the observation that the disease spread into the epizootic region coincided with the peak in the \( R_h \) value in the endemic zone.

In the epizootic region, the disease behaved as an epidemic, with an approximate constant value of \( R_h > 1 \) through September that was followed by a gradual decrease of the transmission rate. Such a pattern in the value of \( R_h \) led to an approximately bell-shaped, short-tailed epidemic curve in the epizootic zone, with most of the outbreaks taking place immediately after the introduction of the disease (Figure 1). This observation may be associated with initial favorable conditions for disease spread followed by a change in those conditions that resulted in a short tail for the epidemiologic curve and in the extinction of the outbreaks by December. Taken together, our findings suggested that by September 2008, there may have been changes in the epidemiological or environmental conditions of Mexico that have
favored the transmission of VSV in the endemic area, as suggested by the increase in the value of R in this region and viral spread into areas that are usually not affected by the disease.

Although the factors that may have favored the spread of the disease are still to be determined, an explanation is that climatic forces may have affected the ecology of vectors involved in the spread of the disease. For example, if there were climatic conditions that resulted in an unusually high abundance of disease vectors in the endemic area, then it is also possible that, by the end of the season, the influence of those climatic conditions strong enough to favor the spread of the vectors into areas in which they are usually absent. Results of laboratory experiments have shown that minor differences in environmental factors such as light and humidity influence the feeding behavior of VS vector species. If this experimental finding holds true in natural conditions, then mechanisms for vector competence and distribution might play a role in the spread of the disease and on the selection of specific viral strains associated with specific species of vectors. Consequently, climatic changes may influence not only the abundance of the vectors in the field but also the mechanisms for competition and selection of vectors and virus strains, which may lead to different patterns of disease spread.

Results presented here may have important applications for disease surveillance in Mexico. Real-time surveillance of the disease and monitoring of the value of R in the endemic region may lead to the identification of threshold values for R that could suggest that VS spread into the epizootic region is likely to occur. Such a surveillance system could take the form of epidemiological alarms to alert the veterinary services about higher than typical risk of disease spread into regions that are usually unaffected by the disease. Although such a system may primarily help to prevent and control VS in Mexico, it could also have some potential implications for prevention of VS epizootics in the United States. In 2009, VS outbreaks were reported in Texas and New Mexico. This was the first time in 5 years that VS was reported in these regions. Interestingly, and even though the origin of the outbreak is unknown, emergence of VS in the United States was preceded by an unusual increase in the number of affected animals and distribution of the disease in central and northern Mexico. If the outbreak in the United States were associated with spread of the disease from the endemic areas of Mexico into the epizootic areas of the country in 2008, then a real-time surveillance system aimed at monitoring variations of the transmission rate in the endemic area of Mexico may help to warn of the development of the disease both in the epizootic area of Mexico and in the United States.

In the present study, certain potentially useful epidemiological data were not available for analysis. For example, information from weather stations collected during or immediately before the outbreaks could have been used to assess the relationship between disease spread and expected behavior of the vectors. Abundance and dispersion of black flies is known to be influenced by the environmental conditions in the vector’s microhabitat. However, not all the outbreaks in our study were located close to weather stations, and data from stations that were located nearby were not available to us.

For the calculation of the duration of infectiousness, expert opinion was considered more appropriate than any other source of information because official reports and the literature contained no reliable information regarding the expected infectiousness of an infected herd and on the extent and nature of the influence of epidemiological variables on the variable. For example, it was not clear to us whether the duration of herd infectiousness, which is a factor that could be influenced by disease-dependent and -independent demographic and ecological conditions, would differ between the endemic and epizootic areas. The experts consulted had > 10 years of experience in VS surveillance, and their opinion was supported by evaluation of the clinical histories of outbreaks within each region. For these reasons, the opinion of those with extended access to empirical information in the field was assumed the most accurate approximation of the true duration of infectiousness that could be obtained under the circumstances.

The study reported here showed that the large number of VS outbreaks reported in Mexico in 2008 was associated with an unusual temporal and spatial distribution of the disease in the country. Consequently, implementation of techniques for real-time detection of space-time clusters and computation of the RH as part of the surveillance program for vesicular diseases in the endemic area of Mexico may help prevent the spread of VS outbreaks into regions of Mexico and neighboring countries that are only sporadically affected by the disease.


b. SaTScan, version 8.2, Martin Kulldorff, Boston, Mass. Available at: www.satscan.org. Accessed May 13, 2009. The SaTScan software used in this study was developed under the joint auspices of Martin Kulldorff, the National Cancer Institute, and Farzad Mostashari of the New York City Department of Health and Mental Hygiene.

c. ArcGIS, version 9, ESRI Inc, Redland, Calif.

References


