

Climate, Landscape, and the Risk of Orbivirus Exposure in Cattle in Illinois and Western Indiana

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Abstract. Climate and environmental data were used to estimate the risk of testing positive for antibodies to bluetongue (BTV) and epizootic hemorrhagic disease viruses (EHDV) in cattle in Illinois and western Indiana over three transmission seasons (2000–2002). The risks of BTV and EHDV seropositivity were positively associated with temperature during every year of the study. The EHDV seropositivity was also positively associated with forest patchiness in two of the years. During 2002, a year with unusually high spring rainfall, forest patchiness was not significantly associated with EHDV but spring rainfall did have a moderating effect on temperature. Maps of predicted probability of exposure to BTV or EHDV were created using these best-fitting models and show distinctly different spatial patterns within the same cattle population.

INTRODUCTION

Bluetongue viruses (BTV) and epizootic hemorrhagic disease viruses (EHDV) are two closely related serogroups in the genus orbivirus.¹ Twenty-four serotypes of BTV have been identified of which six (BTV-1, BTV-2, BTV-10, BTV-11, BTV-13, BTV-17) have been isolated in the United States.² Of the seven EHDV serotypes identified worldwide, three (EHDV-1, EHDV-2, EHDV-6) have been isolated in the United States.³ Both serogroups infect ruminants; BTV causes a severe disease primarily in naive sheep populations while EHDV causes severe disease primarily in wild deer. Cattle can be infected by both viruses, although clinical illness in the United States has been rare. Cattle are capable of prolonged viremia after infection with both viruses and therefore may play an important role in the transmission cycles of both groups of viruses.^{4–6}

Both bluetongue disease and epizootic hemorrhagic disease are listed as notifiable diseases by the World Organization for Animal Health (OIE).⁷ The EHDV was a recent addition to the list, after outbreaks of clinical illness in cattle in Israel and Turkey led to the designation of EHDV as an emerging pathogen.^{8,9} Although BTV has been on the OIE list for decades, the recent introduction and establishment of an African strain (BTV-8) into the formerly BTV-free region of northern Europe has intensified efforts to control the spread of orbiviruses.¹⁰

The BTV and EHDV are transmitted by biting midges in the genus *Culicoides*. In the United States, *Culicoides sonorensis* is the primary vector of BTV (with the exception of Florida, where *Culicoides insignis* is the primary vector).² There is substantial evidence supporting *C. sonorensis* as a competent vector of EHDV in the United States based on oral susceptibility tests, transmission of EHDV to ruminants under experimental conditions, and isolation of EHDV from field populations of *C. sonorensis*.^{11–13} There have also been observations of *C. sonorensis* feeding on white-tailed deer (*Odocoileus virginianus*) during an epizootic of EHDV in Kentucky.¹⁴ However, studies in other regions of the United States have reported relatively small numbers of *C. sonorensis* feeding on, or trapped in the vicinity of, wild ruminants. This suggests that other

Culicoides species may play significant roles in the transmission cycle of EHDV in the United States.^{15–18}

The BTV transmission in the United States, based primarily on surveillance of slaughter cattle, occurs mostly in the southern and western states and is extremely low or absent in the northeastern states.^{19,20} The distribution of EHDV in the United States, based predominantly on wildlife surveillance, has been described as similar to that of BTV.²¹ Most descriptions of BTV and EHDV distribution in the United States tend to focus on a national scale with levels of prevalence defined by state boundaries. However, the lower Midwest, including Illinois and western Indiana, is situated in a zone where there is a transition between areas of high transmission in the south and little or no transmission in the north.^{22,23} In this transition zone area transmission is spatially and temporally variable, making precise descriptions of BTV and EHDV distribution difficult.

Improvements in geographic information systems and spatial modeling methods have led to the production of risk maps for many diseases. These methods are especially well suited for vector-borne disease because transmission by the vector can be very sensitive to environmental and climatic factors.²⁴ Bluetongue viruses have received considerable attention in this regard, although most efforts have focused on Europe, Africa, and Australia.^{25–42}

In North America there have been efforts to study the relationship between BTV in cattle and environmental or climatic variables. Seroconversion to BTV in cattle, based on a microimmunodiffusion test, was modeled using several variables related to temperature, precipitation, and humidity in Alabama.⁴³ Seroconversion was positively associated with the mean daily hours of wet vegetation and negatively associated with total precipitation during the weeks before seroconversion. Another study of cattle in Nebraska, North Dakota, and South Dakota, studied the association between seropositivity of antibodies to BTV and several environmental variables, based on a competitive enzyme-linked immunosorbent assay (ELISA) test, and found that herds at lower latitude and higher altitude had greater odds of being classified as BTV-positive herds.⁴⁴

In the peer-reviewed literature, there have been no attempts to map the distribution of BTV or EHDV based on climatic and environmental variables in the United States. Furthermore, there have been no attempts to map the risk of exposure to both BTV and EHDV within the same population. The objective of this study was to assess the relationship between prevalence of antibodies to BTV and EHDV in the cattle population

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of Illinois and western Indiana and climate and environmental variables. Underlying this study is the assumption that past exposure to BTV and EHDV is proportional to the prevalence of antibodies to those viruses in a susceptible animal population. Additionally, it is assumed that the spatial distribution of antibodies to BTV and EHDV adequately describes the spatial distributions of those two virus groups and that these distributions can be partially explained by climatic and environmental variables. We hypothesized that the distribution of exposure to both viruses would be associated with temperature but that the two viruses would differ in their relationship to other variables. Our goal was to create raster risk maps for both BTV and EHDV based on the relationships identified with climatic and environmental variables.

MATERIALS AND METHODS

Serological surveys of BTV and EHDV were carried out on dairy and beef cattle in Illinois and western Indiana as described previously.^{22,23} Briefly, blood samples were obtained from the cattle after three transmission seasons (2000, 2001, 2002). Sixty herds participated in the study during at least one of the years, 52 in Illinois and 8 in western Indiana. Approximately 50% of these herds participated during all 3 years of the study. Approximately 20% of all the animals that participated were tested more than one time over the 3 years, representing ~50% of all the test results. Selected herds were located in 34 counties. During the study period, there were ~500,000 cattle on 7,059 farms in these counties.⁴⁵ Blood sera were tested for antibodies to BTV and EHDV by competitive ELISA. Samples were collected during the winter and early spring months when no BTV or EHDV transmission was assumed to occur. All animals included in the study had spent their entire lives at the sites where they were sampled with the exception of some calves that were purchased from other locations. However, all animals that had spent any part of a transmission season at another location were excluded. All calves included in the study were at least 6 months old during the previous transmission season (June–October) to ensure that presence of maternal antibodies would not prevent seroconversion. Thus, the proportion of seropositive results for each year represents the annual cross-sectional prevalence of prior exposure to BTV and EHDV in the cattle population at these sites.

The latitude and longitude coordinates of every herd were recorded with a global positioning system (GPS) device and imported into a geographic information system (ArcGIS version 9.3) along with data layers for individual variables representing six environmental and climatic themes (Table 1). All monthly and annual spatial datasets represent the same time period of the study (2000–2002). All other datasets were generated at some time during the study period with the exception of the United States soil survey map, which was originally published in 1994 and updated in 2006, and the national elevation dataset, which is updated on a bimonthly basis. Circular buffers with radii of 2 km were created around the point locations of each herd. These buffers were used to extract summary values of each variable for every herd. Larger buffer sizes were not considered because they would have exceeded both the reported flight range of *C. sonorensis* and the reported home range of white-tailed deer in Illinois.^{46,47}

Given the importance of wild deer in the transmission cycle of EHDV, deer density should be evaluated as a predictor of

TABLE 1
Climate and environmental data considered for inclusion in the GEE models for EHDV and BTV*

Theme	Variable(s)	Source	Resolution
Temperature	Monthly mean maximum	Prism Climate Group ⁶¹	4 km
	Monthly mean minimum		
	Annual mean maximum Annual mean minimum		
Precipitation	Monthly total	Prism Climate Group ⁶¹	4 km
	Annual total		
Soil	pH	U.S. General Soil Map ⁶²	4 km
	Percent organic material		
	Cation exchange		
	Frost-free days		
	Hydrologic soil group		
	Spring soil temperature		
	Soil texture class		
	Elevation		
Livestock	Cattle density	USDA Ag. Census ⁴⁵	By County
	Sheep density		
Landcover	Percent area, each class	NLCD (2001) ⁵²	30 m
	Combined forest class only		4 km
	Number of patches		
	Mean patch size		
	Patch size coef. of variance		
	Total edge		
	Mean shape index		

*GEE = generalized estimating equation; EHDV = epizootic hemorrhagic disease virus; BTV = bluetongue virus; USDA = U.S. Department of Agriculture; NLCD = National Land Cover Database.

EHDV prevalence in cattle. However, no suitable spatial data sets of deer density are available for Illinois or Indiana. Forest landscape characteristics such as edge density and patchiness have been found to be useful in predicting deer habitat in the Midwest.^{48–51} Therefore, a combined forest data layer was created from individual forest categories in the National Land Cover Dataset (NLCD).⁵² Various landscape metrics describing aspects of forest patchiness, forest edge, and forest shape were calculated from the combined forest category using FRAGSTATS software and the Patch Analyst extension for ArcGIS.^{53,54} These forest landscape metrics were included in the analysis as proxies for deer habitat. Additionally, the percent area within each herd buffer zone composed of each of the other non-forest land cover classes were calculated and evaluated as candidate variables.

Candidate variables were initially evaluated individually in separate univariate logistic regression models for each virus and year using the positive or negative results from the cELISA tests of individual animals as the binary outcome. Variables with a *P* value > 0.2 were excluded from the final models. Plots of the log odds of BTV and EHDV seropositivity versus continuous variables were created to detect violations of the linearity assumption. Continuous variables showing a nonlinear relationship with the outcomes were categorized. For pairs of collinear variables (Pearson correlation coefficient > 0.8) the variable that had the lower *P* value in univariate analysis was retained. All monthly and annual temperature variables were highly collinear. Therefore, mean annual maximum temperatures for each year were the only temperature variables evaluated in the final models.

The variables that remained after univariate analysis were fit to six generalized estimating equation (GEE) models, one for each year and virus, assuming binomial distributions and logit link functions. Correlation caused by clustering of animals within herds was modeled using working independence combined

TABLE 2

Number of herds tested, cattle tested, seropositive cattle, percent prevalence, and 95% confidence intervals by year and virus*

Virus year	No. herds tested	No. cattle tested	No. cattle seropositive	Prevalence (%)	95% CI
EHDV 2000	54	3,555	552	15.30	14.25–16.63
EHDV 2001	43	3,155	424	13.44	12.27–14.68
EHDV 2002	41	2,651	134	5.05	4.25–5.96
BTV 2000	56	3,626	54	1.49	1.12–1.94
BTV 2001	51	4,120	40	0.97	0.69–1.32
BTV 2002	41	2,839	62	2.18	1.68–2.79

* CI = confidence interval; EHDV = epizootic hemorrhagic disease virus; BTV = bluetongue virus.

with robust Hubert-White sandwich estimators of the variance, which provide asymptotically correct estimates even when working independence is not the true underlying correlation structure.⁵⁵ The GEE models were chosen over mixed effects logistic regression models as a method to adjust for clustering of animals because GEE models of binary data provide population average estimates. Population average estimates are more appropriate for creating risk maps than the subject-specific estimates provided by mixed effects logistic regression models, which are conditional on herd membership.

The final models were selected by forcing all of the remaining variables into the full models and the significance ($P < 0.05$) of each variable was used to determine which variables should remain in the final models. To find evidence of residual spatial autocorrelation, plots of empirical variograms and simulated envelopes were created from the Pearson residuals of the six GEE models.⁵⁶ The variograms of the six models were all contained by their envelopes, suggesting that no spatial autocorrelation greater than would be expected by chance remained after adjusting for the covariates. Therefore, geostatistical models that account for spatial autocorrelation were not explored further in this study.

Risk maps displaying the predicted probability of testing positive to BTV or EHDV were created for all 3 years. Each map was created by calculating a new raster from the raster layers corresponding to the covariates included in each of the models and the regression equations for the models. The raster calculator function in the Spatial Analyst extension of ArcGIS was used to calculate the log odds of testing positive for each cell of the new rasters and then log odds was transformed to probability.

RESULTS

Over the 3 years of the study, a total of 10,585 and 9,361 cattle were tested for BTV and EHDV, respectively (Table 2). Region-wide seroprevalence (5–15%) of EHDV was significantly higher than BTV seroprevalence in all 3 years. The BTV seroprevalence remained fairly constant (1–2%) over the 3 years. However, EHDV seroprevalence dropped significantly in 2002 compared with the previous 2 years.

All six of the final GEE models included annual mean temperature; it was positively associated ($P < 0.001$) with the log odds of testing positive for BTV or EHDV antibodies (Table 3). The magnitude of the association between temperature and seropositivity was similar for both viruses and there was little year-to-year variation in the magnitudes of the coefficients for temperature. In the three BTV models, no variables other than temperature were statistically significant predictors of seropositivity. For EHDV, number of forest patches was statistically significant and positively associated with the log odds of EHDV in 2000 and 2001. In 2002, the number of forest patches was not statistically significant. However, total precipitation in May 2002 was negatively associated ($P = 0.001$) with the outcome. Additionally, there was a statistically significant interaction between temperature and precipitation. The interaction term was negative indicating that the strength of the association between EHDV seropositivity and temperature decreased with increasing precipitation. No precipitation variables were significantly associated with EHDV seropositivity in 2000 or 2001.

The fit of the six models was assessed visually using diagnostic plots created from the Pearson residuals of each model (data not shown).⁵⁵ Goodness-of-fit plots followed a generally sigmoidal shape for all models. Scatter plots of the residuals versus the linear predictors and residuals versus continuous covariates did not reveal any systematic trends that would indicate a lack of fit. However, there were outliers (residuals $> |2|$) in all six of the models. The three BTV models had no negative outliers but there were positive outliers all 3 years. The majority of these herds (11 of 14) were located at mid-latitudes but there was no east-west pattern. For EHDV, there were many more outliers. There were approximately equal numbers of positive and negative outliers and there was no discernible spatial pattern.

TABLE 3

Results of the six multivariable generalized estimating equation models for risk of being seropositive for epizootic hemorrhagic disease virus (EHDV) or bluetongue virus (BTV)*

	Variable	β	Robust P value	95% CI
2000 EHDV	Constant	-12.89	< 0.001	-16.59 to -9.19
	Temperature	0.63	< 0.001	0.41–0.85
	Forest patches	0.02	0.035	0.001–0.04
2001 EHDV	Constant	-17.69	< 0.001	-21.65 to -13.74
	Temperature	0.87	< 0.001	0.65–1.09
	Forest patches	0.03	< 0.005	0.009–0.05
2002 EHDV	Constant	-2.68	< 0.001	-3.13 to -2.23
	Temp (centered)	1.45	< 0.001	0.83–2.07
	Precip (centered)	-0.24	0.001	-0.39 to -0.10
	Temp \times precip	-0.07	0.022	-0.13 to -0.01
2000 BTV	Constant	-19.98	< 0.001	-23.30 to -16.66
	Temperature	0.90	< 0.001	0.72–1.08
2001 BTV	Constant	-23.13	< 0.001	-27.40 to -18.86
	Temperature	1.03	< 0.001	0.80–1.25
2002 BTV	Constant	-18.95	< 0.001	-21.96 to -15.94
	Temperature	0.83	< 0.001	0.68–0.98

*The higher constant term in the 2002 EHDV model was partially caused by centering the main effects on their means to reduce collinearity with the interaction term.

The BTV risk maps show the predicted probability of testing positive for BTV antibodies generally increased in a north to south gradient that coincides with an increase in temperature at lower latitudes (Figure 1). The predicted probability of seropositivity to BTV ranged from < 0.001–20% for the entire region and the probability was < 1% for nearly the entire northern half of the region in all 3 years. The EHDV maps also reveal an increase from north to south in the probability of testing positive for EHDV antibodies. However, the risk of EHDV exposure follows a more complicated pattern, influenced by forest patchiness in 2000 and 2001, and the interaction between temperature and spring rainfall in 2002. Predicted probability of seropositivity to EHDV reached as high as 90% in the southern part of the region and was > 20% for most of the southern half of the region in 2000 and 2001. The predicted risk of EHDV seropositivity was considerably lower in 2002 than in the previous 2 years with only a small area in the south of the region having a predicted probability > 50%.

DISCUSSION

The BTV and EHDV have been reported to have the same general spatial distributions in the United States.^{19–21} The

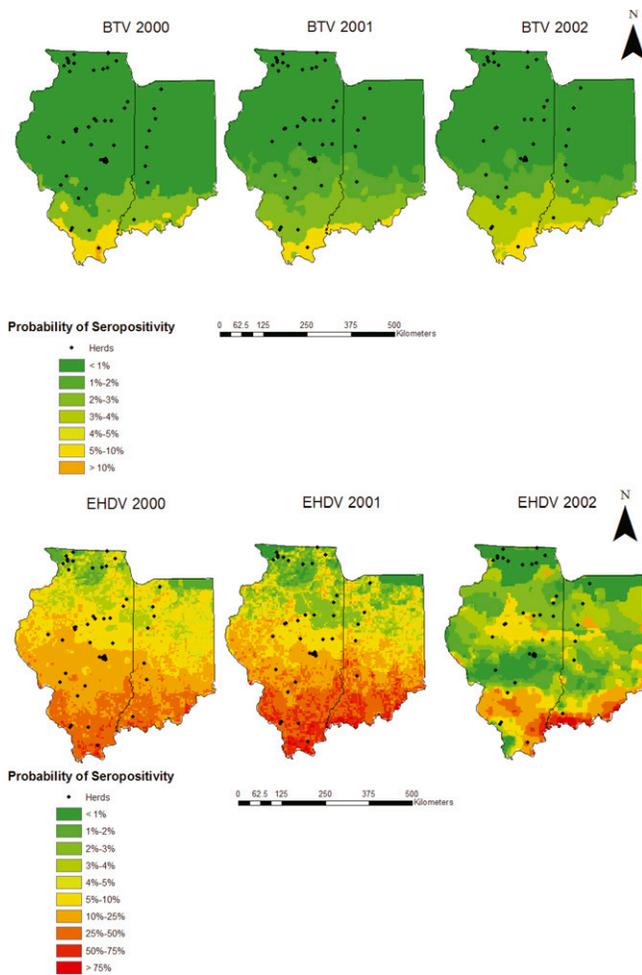


FIGURE 1. Maps of the predicted probability of testing positive for antibodies to bluetongue virus (BTV) and epizootic hemorrhagic disease virus (EHDV), 2000–2002. This figure appears in color at www.ajtmh.org.

results of this study provide evidence that, along this transition zone between areas of low and high transmission, there are considerable differences in the distributions of these two viruses, as measured by seroprevalence in cattle.

The different spatial patterns of BTV and EHDV that we identified are partially explained by forest patchiness: EHDV seropositivity was associated with patches of forest, whereas BTV was not. Forest patchiness reflects suitable habitat for deer, providing both cover and forage along forest edges and adjacent agricultural fields.^{50,51} Confirmed and suspected cases of clinical disease in cattle caused by EHDV in the United States have coincided with epizootics in deer.^{14,57} Before our study period, the last report of significant deer mortality caused by EHDV in Illinois or Indiana was during the 1998 transmission season.⁵⁸ It is possible that the higher prevalence of EHDV antibodies observed in the cattle population in our study was the result of that epizootic of EHDV in deer. The decreased prevalence observed in 2002 may be caused by waning herd immunity in the cattle population.

The decreased EHDV seroprevalence in 2002 may also be related to climatic factors. May 2002 was the eighth wettest May on record in Illinois and temperatures were below average.⁵⁹ It is possible that unusually high spring rainfall flooded *Culicoides* breeding sites resulting in a reduced population size during the peak transmission time in late summer. There was a large EHDV outbreak during the 2002 season in the eastern United States that covered a larger area than previous outbreaks, including the first ever EHDV isolations from deer in Wisconsin and Pennsylvania.⁵⁹ During this epizootic, EHDV was isolated from deer in eastern Indiana, but there were no isolations from western Indiana or Illinois. Heavy rainfall may have prevented this outbreak from spreading west into Illinois. However, BTV prevalence did not drop in 2002, suggesting that rainfall did not reduce the population of BTV vectors.

The differing spatial distributions of EHDV and BTV could be caused by the role of an unidentified vector. We found no evidence of BTV exposure among the northernmost herds of this study region during all 3 years, whereas EHDV seropositive cattle were detected in several of these herds every year. Given the number of cattle that were sampled from the northernmost herds every year, it is unlikely that seropositive animals were undetected in these herds. Additionally, there have been studies in other regions of the United States suggesting that species other than *C. sonorensis* may be more important vectors of EHDV.^{15–18} Failure to detect BTV exposure suggests that *C. sonorensis* might reach its northern limit somewhere in central Illinois and Indiana and that EHDV transmission north of this limit is sustained by another species of *Culicoides*.

Evidence does exist of BTV transmission north of this study region. Serosurveys of slaughter cattle from Wisconsin and Minnesota, using a cELISA test, detected BTV antibodies with prevalences ranging from 0.5% to 1.6% in 2000 and 2002.²⁰ The limit of transmission of BTV in the Midwest needs to be defined. As shown in the current study, knowledge of climate and landscape factors influencing distribution is useful in this regard.

To create risk maps from a regression model it is necessary to have spatial data layers for all covariates in the model. This precludes the use of non-spatial data, such as animal age, that could improve the accuracy of model predictions. The risk maps produced by these models do provide insight into the

distributions of BTV and EHDV that is not apparent when regression results are presented in a table or when prevalence is aggregated by state or zone.^{22,23} The pattern of EHDV seropositivity is suggestive of potential sites where *Culicoides* sampling could be targeted. Furthermore, the locations of outliers provide clues about where climatic and landscape variables fail to adequately explain the variation in BTV and EHDV seroprevalence. Unmeasured covariates, such as availability of suitable *Culicoides* breeding sites, variables related to herd management, or individual animal level factors, may help to further improve predictions.

A geostatistical model that incorporates residual autocorrelation can help to reduce statistical “noise” produced by unmeasured variables.⁶⁰ The lack of autocorrelation in our model residuals probably reflects the fact that most of the herds were too dispersed to be similar to each other in relation to some of these unmeasured variables. Future attempts to study the spatial distribution of BTV and EHDV seroprevalence in this transition zone should focus on herds concentrated in a smaller area, perhaps within one or a few central Illinois or Indiana counties where prevalence appears to be most variable.

Received March 1, 2010. Accepted for publication June 1, 2010.

Financial Support: Supported in part by the National Research Initiative of the USDA Cooperative State Research, Education and Extension Service, grant number 2001-35204-10153. This research was also supported in part by a Resident Fellowship from the Institute on the Environment (IonE) at the University of Minnesota (Singer).

Disclosure: The authors report no conflicts of interest.

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