A Retrospective Study of the Influence of Climatic Variables on Hemorrhagic disease in North America

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Abstract

Hemorrhagic disease (HD) is primarily caused by two related arboviruses, bluetongue virus (BTV) and epizootic hemorrhagic disease virus (EHDV). HD affects domestic and wild ruminants and is transmitted by biting midges of the genus *Culicoides*. Therefore, distribution of the disease is dependent on the survival of the midge in an area. Outbreaks in the U.S. are more common in mid-summer to late autumn, which correlates to amount of vector activity, and will decrease after the first frost. HD is the most significant disease of wild ruminants in North America and is not treatable. Currently, HD is epidemic in the western US, but it could become endemic with increased vector survivability. Countries with endemic HD experience economic impacts such as trade restrictions and the cost of surveillance, testing, and vaccination. This project examines the role of changing weather patterns such as temperature and precipitation in the prevalence of HD in North American domestic and wild animals. Drawing on information from various scholarly journals, press releases, and data from the Wyoming State Veterinary Laboratory, it was found that factors such as drought and wind speed influence HD prevalence in an endemic area. In addition, increasing temperatures have allowed the vector to expand its range and have led to infections in naïve locations, usually at northern latitudes. This research shows that cases of HD will continue to reach new areas as climate patterns change, which poses issues such as animal health and economic consequences.

Introduction

Hemorrhagic disease (HD) is an important disease of domestic and wild ruminants with a worldwide distribution. This disease system is caused by three viruses, epizootic hemorrhagic disease virus (EHDV), bluetongue virus (BTV), and *Odocoileus* adenovirus (OdAdV). The clinical signs of all three viruses are similar, which led to the general designation of "hemorrhagic disease". The focus of this project is EHDV and BTV, as they are closely related viruses. These viruses are part of the family Reoviridae, and the genus *Orbivirus.* They are nonenveloped and icosahedral, with segmented linear double stranded RNA, which means there is a greater likelihood of viral mutation and reassortment that might lead to new strains of the virus. These strains may be novel to ruminant populations, and often cause epizootic outbreaks (Rivera, 2021). BTV and EHDV were both described in the late 1800s; however, BTV was identified in Africa, while EHDV was discovered in the U.S. There are 27 serotypes of BTV, and recent phylogenetic models indicate that it originated in China or India and has been around for at least 2000 years. On the other hand, EHDV only has 7 serotypes, and is seemingly a more recent virus (Rivera, 2021).

BTV and EHDV are transmitted by midges in the genus *Culicoides*, which serve as a biological vector. Other modes of transmission have been observed rarely, including vertical transmission, through direct contact, and venereal transmission. These methods of transmission are not considered to be a significant cause of disease, and the *Culicoides* midge is the primary mode of transmission. Clinical signs of HD are variable depending on the host species, with some species experiencing severe disease, and others with subclinical infections. Common clinical signs include ulcers or lesions around the mouth and nose, edema in the head and neck region, visible and internal hemorrhage, and lethargy. Mortality can be between 0 and 100%, and sudden death without any clinical signs may occur (Rivera, 2021).

In addition to animal health concerns, other detrimental consequences can occur. Negative economic impacts can be significant due to trade restrictions, animal losses, reduced animal productivity, and measures put in place to control or prevent outbreaks. BTV is estimated to cost $3 billion annually worldwide (Speiser, 2016), while EHDV threatens the $7.9 billion commercial game farm industry in the U.S. (Sunwoo, 2020). Furthermore, HD can impact the ecology and health of threatened or endangered wild ruminants. HD is thought to be the most important viral disease of ruminants in North America, and certainly has the ability to eliminate susceptible species if introduced to naïve populations (Ruder, 2015). There is no cure or treatment for HD, so preventing viral spread is key to managing this disease. Finally, the clinical signs of HD are similar to several significant diseases, including foot-and-mouth disease, vesicular stomatitis, and anthrax. This likely contributes to the place EHDV and BTV hold on the U.S. List of Reportable Animal Diseases (Rivera, 2021).

Climate change is the most significant anthropogenic influence impacting HD. Many vector-borne diseases are impacted by climate change; notable examples are West Nile Virus and Dengue fever. The daily rate of Dengue fever infection has increased by 26% from 2007 to 2017, with climate change being one of the main contributors, assisted by urbanization and ineffective mosquito control. There are complex interactions between the components of the epidemiological triad when it comes to vector borne diseases, but generally a warmer climate is beneficial to arthropod vectors. This can allow for vector range to expand geographically to infect naïve host populations, a longer transmission season, and ecosystem changes that may or may not be beneficial (Rocklöv, 2020).

The research question was aimed at exploring how climate change has impacted the spread of HD in the U.S., with an emphasis on Wyoming. I expect to find that climatic variables that have been shown to influence HD prevalence in other areas of the United States will similarly affect the disease in Wyoming as well.

Methods

This project was designed to investigate the relationship between HD and climatic variables. A literature review was performed with peer-reviewed papers gathered from databases such as PubMed, Elsevier, and the University of Wyoming Library system. Focus was placed on recent studies, and the majority of papers reviewed for this project were published after 2014, with some exceptions that provide information that has been well established for some years. Since published studies pertaining to HD in Wyoming are limited, press releases published by the Wyoming Game and Fish Department about recent outbreaks were also used. Data from the Wyoming State Veterinary Laboratory (WSVL) in Laramie, Wyoming was gathered by querying the WSVL database (Vetstar Animal Disease Diagnostic System (VADDS)), which contains data from 2015 and later. Specifically, the database was queried for all cases of EHDV and BTV diagnosed by PCR in any species.

Results

Wind Speed

It is thought that wind speeds will be impacted by changing climate conditions, though the exact effect is not known. In fact, Zeng et al. found that since 2010, wind speeds have been increasing due to ocean-atmospheric oscillations (2019). If wind speeds continue to increase, this could have an impact upon disease transmission. The *Culicoides* midge does not migrate, but their small size allows them to be moved by the wind quite efficiently. In fact, in wind speeds of 10-40 kilometers per hour (6-24 mph), it has been found that midges may travel up to 700 kilometers from their original starting point (Wittman et al., 2002). A significant outbreak of BTV occurred in Europe in 2006, where a new serotype of the virus was introduced to the naïve hosts. A study by Sedda et al., discovered that during this outbreak, 77% of the cases were linked to midge movement by wind, both up- and downwind (2012).

Temperature

Temperature is perhaps the most significant climatic variable in this disease system. Arthropods are poikilotherms, so they are unable to regulate their internal body temperature and are subject to the environmental conditions. Every stage of the *Culicoides* life cycle is impacted by temperature, but one of the most critical stages occurs when the third stage larva over-winter before metamorphosing into adults. If winters are warmer, more larva will survive to adulthood and will be able to transmit HD (EFSA Journal, 2009).

In addition, the extrinsic incubation period (EIP) decreases as temperatures increase (Wittmann et al., 2002). The EIP is the period between an uninfected midge biting a host that is infected with HD, and when the midge can infect a naïve host. This is thought to be because temperature affects the replication of the virus within the midge (Carpenter et al., 2011). Wittmann et al. also found that as temperatures increase, the adult midge survival time decreases. However, due to the shortened EIP, the midges can transmit the viruses before they die, and disease transmission overall increases (2002).

This phenomenon is visible in several occurrences of HD. First, 2012 was the warmest year since 1985 and 19 states hit record high temperatures. There was a significant EHD outbreak in the

U.S. that year and the two events are thought to be closely related. To put this outbreak into perspective, 83 Foreign Animal Disease (FAD) Investigations resulted in a positive case in 2012, while there were 3 positive FAD cases in 2010 and 2011 combined. This outbreak was likely underreported, as clinicians started diagnosing animals based on clinical signs rather than a diagnostic lab confirmation, and reporting of cases was voluntary (Stevens et al., 2015).

Data from the WSVL shows a similar relationship between case prevalence and temperature. Although data is not available before 2015, disease prevalence has been shown to be at or near zero in the years with below average temperatures (2015 and 2019, Figure 1).

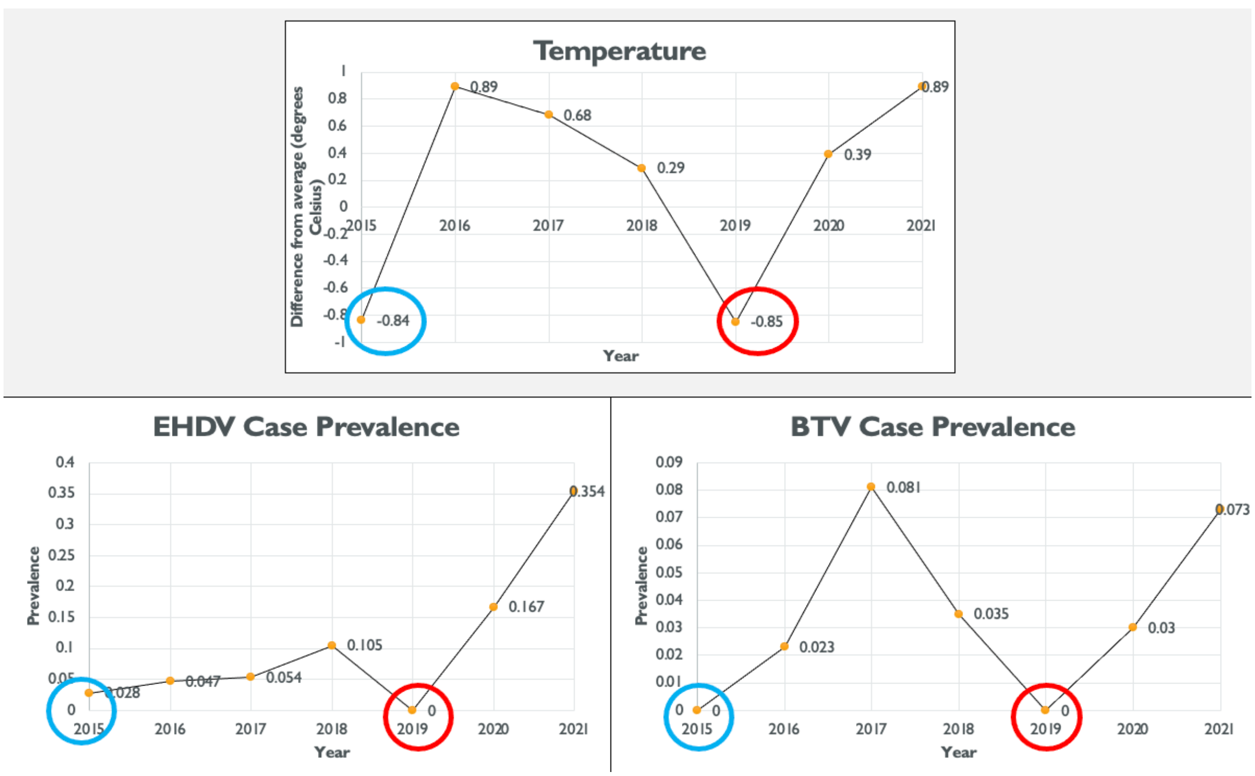

Figure 1. Data showing disease prevalence in Wyoming during years 2015-2021. Disease prevalence is lowest in years with below average temperatures.

Precipitation

Precipitation also influences the *Culicoides* midge because the life cycle of the midge requires eggs to be laid in aquatic or semi-aquatic areas. Interestingly, periods of drought have been shown to increase the prevalence of HD in a population, which could be because during drought, water begins to recede, and more mud is present when eggs are being laid. The female midge prefers to lay her eggs in mud rather than water, so drought allows for better options. Drought can also alter host behaviors, because as water sources begin to dry up, the hosts are forced to congregate at higher densities at remaining sources. HD is thought to be a density dependent disease, so when host density increases, so does disease prevalence.

A study done by Sleeman et al. explored the role of drought in HD prevalence in Virginia deer populations, where HD is endemic. Hunter harvested deer were examined to determine if hoof cracking or sloughing was present, as this is a clinical sign of deer who have survived HD infection. Since hooves grow at approximately 0.5 centimeters per month, researchers believed that if cracks were present, they were due to a HD infection that occurred during the previous year and were an accurate representation of prevalence. While this method is not flawless, since not all deer survive infection and cracked hooves could be due to another cause, they found that there was an inverse relationship between June precipitation amounts and the HD prevalence for that year (2009).

A more recent study looked deeper into the role of precipitation in an area of the U.S. that also has endemic HD. Researchers analyzed drought severity as a function of latitude or wetland cover to determine whether these variables were predictive of HD mortality. They found that in areas with increased wetland cover, there was a protective effect against HD, even as drought severity increases. To contrast, they also found that as latitude increases, the probability of HD mortality increases as drought severity worsens. This could be because as latitude increases, the incidence of HD infection becomes epidemic, rather than endemic. Hosts in these regions are more likely to be immunologically naïve and will suffer higher mortality rates following exposure to HD viruses. This study also suggested that in areas of endemic HD, herd immunity, rather than climatic variables, drives infection patterns because an animal that survives infection may have lifelong immunity (Christensen et al, 2020).

Data from the WSVL supports a relationship between precipitation and HD, as 2019 was one of the years with increased precipitation in recent history, and neither BTV nor EHDV was detected in Wyoming that year.

Conclusion

This project represents a synthesis of data on the relationship between HD and climatic variables and led to discovery of variables that are likely important to HD in Wyoming. These factors are drought and temperature, which have been shown to influence HD in other areas of the United States. This is important because HD can spread to new locations with changing climate patterns. Increasing temperatures permit expansion of the geographic range of the midge and shorten the extrinsic incubation period. This allows the midges to interact with naïve hosts and increase viral transmission. In addition, predictions about disease severity may be possible based on the climate outlook in Wyoming for a particular year. While other variables may be important, such as herd immunity, drought and temperature are likely the most critical. Since the disease cycle is epidemic in Wyoming, naïve hosts experience increased mortality during outbreaks, which can have important economic impacts such as tourism or production losses.

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