

2002

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Threat of Foreign Arthropod-Borne Pathogens to Livestock in the United States

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J. Med. Entomol. 39(3): 405–416 (2002)

ABSTRACT There are many exotic animal pathogens throughout the world that, if introduced into the United States, could have a significant detrimental impact on the health of livestock, agricultural economy, the environment, and public health. Many of these pathogens are arthropod-borne and potential vectors are readily available in the United States. A number of these arthropod-borne pathogens are discussed here as examples that illustrate the potential risk and the consequences of inadvertent introductions. Several International agencies have a role in global surveillance and in controlling animal diseases should they begin to expand their range. The risk to the United States is considerable. We propose that the United States invest in the improved infrastructure needed to reduce the risk of foreign arthropod-borne pathogens. Current U.S. programs focus on the exclusion of pathogens through regulation of animal movements and products, surveillance, especially trained animal disease diagnosticians, research support, international cooperation and, should pathogens enter our country, the resources for their prompt eradication. We suggest that the United States needs to develop a comprehensive, updated strategic plan to assess all aspects of current and future requirements, objectives, and resources needed to protect its national interests.

KEY WORDS arthropod-borne pathogens, foreign animal disease introductions, disease eradication

THERE ARE NUMEROUS exotic animal pathogens throughout the world that, if introduced to the United States, could be catastrophic for the health of livestock, our agricultural economy, the environment, and public health. Many of these pathogens are arthropod-borne and potential indigenous arthropod vectors are readily available to biologically transmit them to humans, domestic animals and wildlife in the United States. The resulting diseases could cause major production losses in livestock and livestock products, thereby reducing farm incomes and increasing costs for consumers. Some of the diseases may inhibit trade in livestock and livestock products between states or world markets, causing major losses in export income. Livestock species that are susceptible to foreign arthropod-borne pathogens include cattle, swine, sheep, goats, and horses. In addition, many species of wild animals may also succumb to pathogens transmitted by arthropods. These diseases may cause high mortality and/or morbidity resulting in chronic debilities such as reduced rates of reproduction, lowered meat and milk production, or general poor health. Other arthropod-borne

foreign diseases may be zoonotic and, thereby, have serious public health consequences. Some foreign arthropod-borne pathogens disrupt the environment through effects on wildlife. The purpose of this article is to review the threat of foreign arthropod-borne pathogens that affect livestock, their potential impact on agriculture, public health, and the environment, and the need to strengthen measures to reduce their impact.

The survival, establishment, and spread of animal diseases depend on climate, geographic factors, host species and their distribution. In addition, human efforts to prevent, control, and eradicate some animal diseases have played a role in their distribution. Unlike human diseases, animal disease control can be greatly enhanced by restricting the movement of animals and animal products both nationally and internationally. However, arthropod-borne animal pathogens pose even greater challenge. Effective management of the associated disease vectors is sometimes possible through a program of vector control or eradication. However, using animal movement restrictions may be inadequate to control an outbreak in the face of mobile arthropods.

Although expensive, it is generally more economical to eradicate epizootic animal diseases than to live, year after year, with the economic losses they impart. This approach, although successful with some infectious animal diseases, i.e., foot and mouth disease, hog cholera, and viscerotropic velogenic Newcastle disease, is especially difficult with arthropod-borne animal

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pathogens that have wildlife or vector amplification cycles that enable the pathogen to survive. The economic benefit of completely preventing the entrance of certain transmissible diseases into a country usually far outweighs the costs of the control measures. Countries devote considerable attention to preventing the introduction of disease causing pathogens through import restrictions that are one kind of nontariff trade barrier. The United States, for example, suffered nine outbreaks of foot and mouth disease in the decades preceding 1930, after which importation of meat and animals was prohibited from countries with the disease. There have been no foot and mouth disease outbreaks since that time.

Estimating costs of an exotic animal disease epizootic in a country is complex. It is made even more so by the loss of animal exports when other countries close their borders to animals and products until the epizootic is contained or eliminated. Because vaccination can mask disease, restrictions on movement are frequently maintained until vaccination against the pathogen is terminated. Export losses may far exceed those of production. Trade losses caused by the presence of strictly arthropod-borne animal diseases are normally confined to that of live animals and germplasm. Countries do not usually restrict import of meat from geographic regions in which there are animals infected with arthropod-borne diseases if the pathogen is not known to be transmitted by meat. Live animal trade, however, is also an immense international business, with millions of head of livestock crossing borders worldwide each month. In this case, severe importation restrictions may be imposed to prevent disease spread. The Office International des Epizooties (OIE) List A is composed of the 15 diseases considered as the most dangerous to livestock and poultry throughout the world. This list includes those that have the potential for rapid spread, irrespective of national borders, which are of serious socioeconomic or public health consequences, and which are of major importance in the international trade of animal and animal products (OIE 2000).

Six List A diseases are naturally transmitted by arthropods. These are African horse sickness, African swine fever, bluetongue, vesicular stomatitis, Rift Valley fever, and lumpy skin disease. The presence of any one of these pathogens in a region results in economic losses due not only to animal disease but, frequently, even greater losses in export and animal movement. There are 48 livestock diseases on the OIE List B of which 19 are arthropod-borne, while four are arthropods themselves. List B consists of transmissible diseases that are considered to be of socioeconomic and/or public health importance within countries and which are significant in the international trade of animals and animal products (OIE 2000). The lists should be recognized primarily as a means to facilitate disease reporting internationally and many of the pathogens on either List A or List B are presently exotic to the United States. Production and export losses caused by the presence of these diseases can be significant.

Several governmental and international agencies have a role in preventing the introduction and spread of animal diseases across political boundaries. Those most important to the United States are the U.S. Department of Agriculture (USDA) and OIE. Other international agencies having some responsibility in the prevention and control of animal diseases include the Food and Agriculture Organization (FAO), the International Atomic Energy Agency (IAE), and the World Health Organization (WHO) along with regional organizations such as the Pan American Health Organization and the International Institute for Cooperation in Agriculture (IICA).

The U.S. Veterinary Services (VS), part of USDA's Animal and Plant Health Inspection Service (APHIS), is charged with preventing the introduction and spread of animal diseases in this country. The regulation of the importation of animals and animal products to prevent the entrance of potentially devastating livestock diseases has been increasingly complemented by cooperation with neighboring countries and trading partners to keep these diseases from U.S. borders. This mutual cooperation began in 1947 when the USDA started to assist Mexico to successfully eradicate foot and mouth disease. There are also several arthropod-borne diseases such as Venezuelan equine encephalitis, African swine fever, and bovine babesiosis, for which cooperation has been established with other countries. Although not considered an arthropod-borne pathogen in the entomological sense, the eradication of the screwworm, *Cochliomyia hominivorax* (Coquerel), from North America, is a remarkable example of cooperation between neighboring countries to eliminate a major livestock parasite (Bram and George 2000).

The world animal health community also cooperates in the prevention and control of transmissible animal diseases. The OIE, also known as the world organization for animal health, was established in 1924 in Paris to coordinate a response to the reintroduction of rinderpest, a severe cattle disease of viral etiology, into Europe. OIE membership has since expanded from the original 28 countries to 155, including (since 1975) the United States. The OIE actively works with all other international organizations involved with animal diseases and zoonoses, including those that effect livestock, poultry, lagomorphs, aquatic animals, and honey bees.

The OIE member countries are obligated to report the presence of >100 diseases, some immediately, and describe those measures which have been taken to control them. The organization also establishes criteria for the safe international trade in animals and products through continuously revised International Animal Health Codes. Methods of diagnosis and vaccine standards for List A and List B diseases are internationally approved. In addition, OIE maintains a directory of recognized experts and institutions, as well as a compilation of countries which are free from certain diseases. The OIE seeks to reduce those nontariff barriers that needlessly interfere with international commerce.

Considering the enormous economic implications that exotic arthropod-borne pathogens could have on U.S. agriculture, it is prudent that the United States strengthen measures to guard against and to mitigate the impact of such introductions. This article will review several particularly serious exotic arthropod-borne animal pathogens as examples to illustrate their risk to the United States and the potential consequences of their introduction. We hope that this information will be useful in establishing priorities to protect the United States from dangerous exotic pathogens

Foreign Arthropod-Borne Pathogens

Although naturally occurring movements of arthropod vectors and arthropod-borne pathogens into the United States do occur, most introduced pathogens arrive as unintended byproducts of commerce, tourism, or travel. In 1999, over 70,000 vessels and over 425,000 aircraft arrived in the United States from abroad carrying humans and agricultural products. During the same period, ≈ 11.5 million animals of all classes were imported into the United States. Because of the massive influx of people, animals, and products, the risks of introducing exotic arthropod-borne pathogens are formidable.

Venezuelan Equine Encephalitis. Venezuelan equine encephalitis (VEE) viruses, RNA viruses in the genus Alphavirus, family Togaviridae, cause disease in equids and humans ranging from febrile infections to fatal encephalitis. First isolated in 1938, VEE virus has been found only in the Americas. There are six antigenically related VEE subtypes (I-VI), with five variants of subtype I (AB, C-F). Nonpathogenic subtypes IE, IF, II-VI are transmitted among rodents and mosquitoes in enzootic, nonequine cycles and may be found in regions of South and Central America and in southern Florida. Subtypes I-AB and I-C are highly pathogenic in equines, and have been the cause of several major epizootics involving horses and humans in the Americas.

The I-AB, I-C subtypes cause high viremias, and high antibody titers in equids. Viremias remain high for 4–5 d during which thousands of mosquitoes, capable of transmitting the virus, can be infected. Equids are the most important amplifying hosts of VEE epizootic subtypes; hence the disease spreads very quickly as large numbers of equines develop clinical signs. Neurologic signs can be severe in equines and include stupor, imbalance, excitation, convulsions and coma. Some strains have not been associated with epizootics because viremias in infected equines are too low to make equines good amplifying hosts. This observation is being revisited in lieu of the finding that epizootics in 1993 and 1995 in Mexico were due to subtype IE.

Many mosquito species are capable of being infected with VEE virus. These include *Psorophora confinnis* (Lynch Arribelzaga), *Aedes aegypti* (L.), *Ochlerotatus sollicitans* (Walker), *O. taeniorhynchus* (Weidemann), *Mansonia titillans* (Walker), *M. indu-*

bitans Dyar & Shannon, and *Culex tarsalis* Coquillett (Monath and Trent 1981). A 1995 VEE epidemic in South America involved at least 13,000 human cases and untold numbers of equines. Transmission in Colombia was associated with *O. taeniorhynchus* and *Ps. confinnis*. The primary vectors in enzootic foci however are species of *Culex* subgenus *Melaconion*.

The most widespread VEE epizootic began in Ecuador in 1969 and was caused by subtype I-AB. By 1971, equine and human cases had been reported in Ecuador, several Central American countries, Mexico, and in June 1971, Texas. The virus spread 4,000 km, and caused tens of thousands of human cases. Equine mortality ranged from 20 to 40%. The proportion of horses showing clinical signs that died, the case fatality rate, was 40–83%. It was estimated that 50,000 horses died and that Ecuador, alone, lost 20,000 horses (Groot 1972).

A vaccine, derived from an attenuated VEE strain TC-83, has been used during several outbreaks and has provided excellent long-term protection for equines. Vaccination of equines coupled with vector control have been used as control measures in several epizootics. However, even TC-83 is no longer used in the United States due to the denial of seropositive horses for export, fears of reversion to virulence, and transmission of the vaccine virus by mosquitoes (Walton et al. 1992b). VEE outbreaks have been attributed to reversion to virulence of live VEE vaccine strains (Weaver et al. 1999). Possible vaccine virus transmission and its reversion to virulence were major considerations for U.S. and Mexican Veterinary Services during the 1970–1971 Mexico epizootic. Because of the extensive nature of the rapidly spreading epizootic, a decision was made to include the only available vaccine, TC-83, in the eradication strategy in these two countries, although, at the time, this vaccine was still considered experimental (R.E.R., unpublished data).

VEE viruses continue to cause periodic outbreaks in South America, and suitable vectors are present in the United States. Reintroduction of the virus into the United States will have serious consequences for equine and human health. Economic losses in the millions of dollars are likely, due to resulting restrictions on interstate and international movement of U.S. equines. Mosquito control and horse protection are essential in an outbreak, and use of attenuated vaccines would be prudent in an emergency. In 1997, during a VEE outbreak in Mexico, the American Association of Equine Practitioners recommended VEE vaccination for all horses, despite possible adverse consequences, in states bordering Mexico to provide a protection buffer against the spread of VEE.

African Swine Fever. African swine fever (ASF) is caused by an unclassified virus that is the only known arthropod-borne DNA virus (Mebus 1992). It is endemic in wild swine in sub-Saharan Africa. Because of frequent incursions into domestic pigs, ASF has suppressed the development of a productive pork industry in Africa. Clinical signs of ASF infection in pigs range from chronic to hyperacute and the disease is

often fatal. Survivors may become convalescent shedders of the virus. ASF was introduced to the Iberian Peninsula in the late 1950s, after which it spread to several other European countries. With the present exception of Italy and Portugal, all the affected European countries eradicated the disease, but only after considerable cost and effort.

Other than wild and domestic swine, the only other known hosts of the virus are soft ticks of the genus *Ornithodoros* in which there is venereal and transtadial transmission (Plowright 1977). In the United States, *Ornithodoros turicata* (Dugs) has been found to be a competent vector in the laboratory (Hess et al. 1987). Thus, infected pigs and/or arthropod vectors could serve as important reservoirs to maintain virus and initiate new epizootics. Tabanid flies may transmit the virus mechanically.

Another feature that contributes to the spread of ASF virus is its persistence for months in pork products. Swine are the only omnivorous livestock. They are frequently fed meat wastes, a cause of the intercontinental spread of several epizootic ASF disease outbreaks. ASF likely spread to Europe and arrived several times in the Americas in such products. ASF occurred in Cuba in 1971 where it was eradicated by the slaughter of all swine in Havana province. A reintroduction into Cuba in 1980 was also eradicated.

African swine fever entered Brazil in 1978, and was ultimately eliminated through a successful eradication program. In the same year, the disease was introduced into the Dominican Republic, and spread to adjacent Haiti. Over the next few years the entire swine population of Hispaniola was slaughtered to eradicate the disease. The island was then repopulated with healthy swine.

The presence of ASF in a country is incompatible with an intensive, or even traditional, swine industry. Despite considerable research, there is no vaccine for ASF and affected countries have employed ambitious and costly programs based on depopulation of large swine populations to eradicate the disease (Reichard 1978).

There has been a long history of international cooperation to eradicate this feared disease from entire regions. The European Community provided substantial assistance to Spain and Portugal to eradicate the disease. The United States cooperated in the eradication programs of Brazil and the Dominican Republic. Later, Canada, the United States, and Mexico, through IICA and FAO joined in successful efforts to rid Haiti, and thus the Americas, of ASF by 1985 (Anonymus 1985). The fact that eradication was repeatedly achieved in the Americas led observers to believe that large numbers of soft ticks were not infected with the virus. The several apparently unrelated reintroductions of ASF into the Western Hemisphere demonstrates the significant and continuous risk ASF presents. If not quickly diagnosed and controlled, a U.S. ASF introduction would lead to severe consequences for the U.S. swine industry.

Heartwater. Heartwater is an infectious, virulent, transmissible, and noncontagious disease of domestic

and wild ruminants caused by the rickettsia *Cowdria ruminantium* (Cowdry). The disease is characterized by pyrexia, followed by signs of nervous disorders, hydropericardium, and often severe gastroenteritis. Mortality rates as high as 60% have been reported in herds of improved breeds of cattle (*Bos* spp.). Case mortality in sheep (*Ovis aries* L.) and goats (*Capra hircus* L.) is variable and ranges from 5% to nearly 100%. Very young animals seem resistant to infection and susceptibility increases with age during the first year of life (Camus et al. 1996). Heartwater is probably an indigenous disease of Africa where it has been diagnosed in virtually all countries from the Sahel regional transition zone southward. It has also been diagnosed in Madagascar, Mascarene Islands (Mauritius and Reunion Island), the West Africa island of Sao Tome, French West Indies (Guadeloupe and Marie Galante), and Antigua (Provost and Bezuidenhout 1987, Camus et al. 1996).

Thirteen *Amblyomma* species are known to be capable of transmitting *C. ruminantium*, but the two species considered the most important are *A. variegatum* (F.) and *A. hebraeum* Koch. Although *A. hebraeum* is the primary vector in southern Africa, *A. variegatum* is the most widespread and important vector of heartwater. *A. variegatum* was introduced with imported cattle to the Mascarene Islands and the Lesser Antilles (Sutherst and Maywald 1985), and has potential for wide extension of its present distribution, including much of the southern United States (Walker and Olwage 1987, Camus et al. 1996). Three American species, *A. maculatum* Koch, *A. cajennense* (F.), and *A. dissimile* Koch are experimental vectors of *C. ruminantium* (Barre et al. 1987, Jongejan 1992). However, *A. maculatum* is the only species with the potential for a major role in the maintenance and dissemination of heartwater if an outbreak occurred in the United States. Its efficiency as a vector is similar to that of *A. variegatum* and *A. hebraeum* (Mahan et al. 2000).

Amblyomma variegatum, colloquially known as the tropical bont tick, was introduced to the Caribbean island of Guadeloupe in the French West Indies in about 1830 on Senegalese cattle from West Africa. It spread to Marie Galante and was reported from Antigua in 1895. It is likely that *C. ruminantium* was introduced along with its vector (Uilenberg et al. 1984, Barre et al. 1995). By 1948, the tick had disseminated to Martinique. In 1967, the tick was discovered on St. Croix and over the next three decades its presence was confirmed on 11 additional islands in the eastern Caribbean, ranging from St. Vincent and Barbados in the south to as far north as Puerto Rico (Alderink and McCauley 1988, Pegram et al. 1996). The presence of livestock infected with the agent of heartwater has been documented only on Guadeloupe, Marie Galante, and Antigua. In the Caribbean, severe livestock losses due to acute dermatophilosis, the skin disease caused by the bacterium *Dermatophilus congolensis* van Saceghem, is one of the consequences and indicators of the presence of *A. variegatum* on an island (Pegram et al. 1996).

Island to island spread of *A. variegatum* could have occurred as a result of movements of tick-infested livestock or dogs, *Canis lupus* L. The cattle egret, *Bubulcus ibis* (L.), is another likely vehicle for transport of the tick (Barre et al. 1987). More than 30% of the cattle egrets examined in a survey on Guadeloupe were infested with larvae and, rarely, nymphs. The spread of *A. variegatum* in the eastern Caribbean coincided with the recent expansion of the range of the cattle egret since it became established in the region in the 1950s (Corn et al. 1993, Barre et al. 1995). The high rate of spread of *A. variegatum* in the Caribbean during the past 35 yr and the identification of cattle egrets marked in Antigua or Guadeloupe on 14 Caribbean islands and the Florida Keys fueled concerns in the United States about risks of the introduction of the tick and heartwater to the U.S. mainland (Corn et al. 1993). This knowledge helped to elicit support from the United States for efforts to create the Caribbean *Amblyomma* Program (CAP). CAP was established in 1994 with the aim of eradicating *A. variegatum* from the English speaking countries of the Caribbean (Pegram et al. 1996). This program has reached a critical stage because of persistent hot spots in both St. Kitts and St. Lucia and the questionable status of the necessary funding to support the overall effort (Uilenberg 2001).

An alarming variety of both natural and experimental vectors of heartwater, including *A. hebraeum* and *A. variegatum*, have been inadvertently introduced into the United States on wildlife imported from Africa and elsewhere during the last four decades (Bram and George 2000). Introductions of *A. variegatum*, *A. hebraeum*, *A. marmoreum*, and *A. sparsum* pose a high risk of being a source of heartwater. Even if only male *Amblyomma* are introduced on wildlife, intrastadial transmission of *C. ruminantium* by *A. hebraeum* males transferred from infected live or dead hosts occurs readily (Andrew and Norval 1989). Intrastadial transmission by other vector species is possible. *A. marmoreum* and *A. sparsum* are indigenous African species that parasitize tortoises, but are also found on ungulate wildlife species. *A. marmoreum* was found to be established in reptile facilities on eight premises in seven counties in central Florida (Burrige et al. 2000) and 15 *A. sparsum*, collected from a reptile farm in Hillsborough County, FL, tested positive for *C. ruminantium* (Florida Division of Animal Industry 1999).

Nine species of wildlife including the white-tailed deer, *Odocoileus virginianus* (Zimmerman), and a variety of ruminant species from Africa have been experimentally shown to be susceptible to *C. ruminantium* infection. Because of the importation of a great variety of African wildlife into the United States, it is important to know which species can be infected with *C. ruminantium* and the risk that wildlife pose as subclinical carriers capable of infecting ticks with the rickettsia (Burrige 1997). Andrew and Norval (1989) showed that African buffalo were carriers and Peter et al. (1998) demonstrated a carrier state for *C. ruminantium* in four other wild ruminants from Africa. This information demonstrates the substantial risk related

to the importation of wild ruminants from heartwater-endemic areas into the United States where vector-competent tick species and susceptible domestic and wild ruminants are abundant (Peter et al. 1998). Oberem and Bezuidenhout (1987) cited unpublished data that subclinical infections with *C. ruminantium* occur in the leopard tortoise (*Geochelone pardalis* Bell) and the crowned guinea fowl (*Numida meleagris* Pallas). If these unconfirmed results are correct, the leopard tortoise and crowned guinea fowl, as well as other reptiles and birds, including the cattle egret, could be carriers of heartwater.

If heartwater were to be introduced into the United States and domestic ruminants or white-tailed deer became infected, the consequences could be catastrophic. It would not be necessary for an exotic vector species, such as *A. variegatum*, to become established. Because of the superior vector efficiency of *A. maculatum* (Mahan et al. 2000) and the role of cattle and white-tailed deer as key hosts for adult Gulf Coast ticks, this indigenous vector/host combination would be a major factor in the dissemination and persistence of heartwater. The Gulf Coast tick is widespread in the southern United States along the southern Atlantic coastal states and the Gulf Coast (Keirans and Durden 1998), but the occurrence of populations of the tick in eastern Oklahoma (Semtner and Hair 1973) and southeastern Kansas are indications that the tick is extending its range northward (Goddard and Norment 1983). In the United States, the red imported fire ant, *Solenopsis invicta* Buren, is a known predator of many species of arthropods including the lone star tick, *A. americanum* (L.) (Oliver et al. 1979, Fleetwood et al. 1984) and this ant could also affect the distribution and densities of populations of *A. maculatum*. But, this was not the case in the coastal prairie area of Texas, an area long infested with the imported fire ant, where *A. maculatum* was the most prevalent of five species of larval and nymphal life stages of ticks, including *A. cajennense*, *A. inornatum* (Banks), *Hemaphysalis leporispalustris* (Packard), and *H. chordeilus* (Packard), collected on birds. Geographic differences in climate and the phenologies of the red imported fire ant and the Gulf Coast tick may result in a different predator/prey relationship in other areas cohabited by these species (Teel et al. 1998), but data on the geographic distribution and abundance of *A. maculatum* are needed for realistic assessment of the risk to U.S. cattle of an introduction of *C. ruminantium*.

West Nile Fever. West Nile (WN) viruses, the cause of WN Fever, are RNA viruses in the Japanese encephalitis group, Family Flaviviridae. WN viruses are relatives of the St. Louis encephalitis viruses that cause human cases almost annually in several southern states in the United States. WN virus is mosquito-borne and has been found in Africa, Asia, and Europe. Human epidemics have occurred in Egypt, South Africa, Israel, France, Romania, and, in 1999–2001, in the United States. The entry of WN virus into New York City in 1999 was followed by its rapid spread to 23 eastern states and the District of Columbia by October 2001.

Many avian species produce viremia sufficient to infect mosquitoes, and during the U.S. outbreaks, WN virus caused substantial bird mortality, particularly in American crows (*Corvus brachyrhynchos*). Horses, sheep, cattle, and humans are secondary hosts of WN. They are not considered good amplifying hosts and, thus, are not believed to be involved in cycling the virus in nature. The viremia in humans is low, lasting about six days. Symptoms in humans range from temporary fever to severe encephalitis and death. Only horses, among domestic animals, have been observed to develop clinical signs after infection with WN virus. Horses also have very low viremias. During the 1962–1964 WN outbreak in La Camargue, France, horses experienced 10% morbidity and a 25% mortality rate (Hayes 1989). Isolated horse cases occurred during U.S. outbreaks when case fatality rates were $\approx 20\%$ (died or were euthanized) as a result of the disease.

Mosquito species capable of being infected and transmitting WN virus include, *Culex univittatus* Theobald in Africa, *C. pipiens* L. in South Africa and Israel, and the *C. vishnui* complex of mosquitoes in India and Pakistan. The primary mosquito involved in transmission to humans during the U.S. outbreaks in the northeastern United States was *C. pipiens pipiens* (L.). However, virus was also detected in *C. restuans* Theobald, *C. salinarius* Coquillett, *Culiseta melanura* (Coquillett), *Aedes vexans* (Meigen), *Ochlerotatus japonicus japonicus* (Theobald), and *O. triseriatus* (Say) (White et al. 2001, Andreadis et al. 2001). Several other mosquito species have been detected with WN virus and are likely involved in WN transmission in different regions of the United States. WN virus was detected in *Culex nigripalpus* Theobald, *Cx. quinquefasciatus* Say, *Cx. salinarius* Coquillett, and *Culiseta melanura* (Coquillett) in Florida (M. Godsey, personal communication). Laboratory studies have also shown that several mosquito species are able to transmit WN virus (Turell et al. 2001). The role of these and other species in WN transmission in the United States is unknown. The 1999 outbreak of WN virus in New York was a classic demonstration of the impact of the introduction of an exotic, zoonotic pathogen into the United States. Sixty-two human cases occurred between August and October 1999 in the New York City metropolitan area. There were seven deaths. Twenty-five horses, of which nine died or were euthanized, were located primarily on the eastern end of Long Island, NY, were diagnosed with WN fever by October 1999. During the U.S. outbreaks, clinical signs in horses included listlessness, stumbling, weakness of limbs, ataxia, partial paralysis or death. Fever was not generally observed. In 1999, horses from the affected area were prevented from movement, and New York City airports prohibited horses from transport. Large numbers of *Ae. vexans* were observed in the region of Long Island coinciding with the appearance of the horse cases.

The United States has experienced WN virus infections in birds, horses and humans in three successive years (1999–2001) and with the finding in 2001 of WN virus in Illinois and Iowa and its arrival in Canada and

Florida, it is likely that the eastern portion of the United States is endemic for WN virus. There will likely be further appearances of WN virus, the extent and impact of which is unknown. It is probable that the virus originated in the Middle East, since the U.S. WN virus isolate is very similar to a 1998 WN isolate from a goose from Israel (Lanciotti et al. 1999). WN in the United States will impact the horse industry. Many regions of the United States have experience with the risk to horses from mosquito-borne eastern equine encephalitis (EEE) virus. The availability of an acceptable equine EEE vaccine has reduced the risk and impact of EEE on the horse industry. A similarly available and efficacious equine WN vaccine would be very useful. An equine vaccine was released for conditional use in selected regions during the summer of 2001. The safety and efficacy of this vaccine is uncertain. In addition to effects on the health and well being of equines, WN will result in economic consequences due to restrictions on interstate and international movement of equines from affected regions. Because horses do not amplify the virus, they are unlikely to serve as a means of spreading it through movement and restrictions on equine movement do not seem justified. Hence, restrictions on movement will likely be self-imposed as horse owners opt not to move horses to endemic regions. With WN virus, the United States has a new zoonotic agent that will be a challenge to animal health professionals.

Bluetongue. The bluetongue (BLU) viruses are RNA viruses, Family Orbiviridae that can infect several species of ruminants. The disease was first described in South Africa in 1902. The viruses are found worldwide between latitudes 40° N and 35° S and are transmitted by different species of biting midges of the genus *Culicoides* in different regions. There are 24 BLU serotypes, of which BLU-2, 10, 11, 13 and 17 have been found in the United States. The United States is considered endemic for BLU, particularly in western and southern states. In some states 60–80% of cattle at slaughter show BLU antibody, demonstrating previous infection with the virus (Pearson et al. 1992). Extensive surveillance by APHIS for more than 20 yr has shown no evidence of BLU transmission in north-eastern states. The remaining 19 serotypes have never been found in the United States and are considered exotic. In the Central American-Caribbean Basin BLU-1, 3, 9, 15, 16, 20, 21, and 23 have been observed, though there is little clinical disease in this region.

Although cattle can be infected with BLU virus, clinical disease is very rare (<5% of infected cases) despite a viremia that may last months. Clinical bluetongue is most severe in sheep with elevated temperature for 5–7 d, profuse salivation, swollen tongue, swelling of the buccal and nasal mucosa, oral erosions, hemorrhaging in the mouth and in the coronary bands. Oral lesions may cause sheep to vomit resulting in death through aspiration of ruminal contents and pneumonia. Sheep mortality may range from 5 to 50% in affected flocks.

The substantial impact that BLU virus can have on sheep populations has resulted in OIE recommenda-

tions for testing and certification regulations for cattle and sheep exports from endemic countries to bluetongue-free countries. It is the restrictions on trade that make BLU viruses economically important. The prolonged viremia in cattle makes them excellent reservoirs and amplification hosts. The European Union requires testing for BLU antibody or virus isolation for cattle and sheep, as well as livestock products, such as semen, from the United States. International acceptance of new diagnostic methods, such as polymerase chain reaction detection of BLU nucleic acid, will considerably ease the cost and burden of testing. The export of BLU positive animals is restricted, and U.S. economic losses due to lost trade are estimated at \$125 million annually.

The primary vector of the BLU viruses in the United States is *Culicoides sonorensis* Wirth and Jones (Tabachnick 1996, Holbrook et al. 2000). Its distribution coincides with the distribution of BLU serotypes in the west and south United States, and the species is absent from the northern states where BLU transmission does not occur. Acceptance of a BLU-free region would substantially improve the ability for U.S. livestock and its germplasm to move freely without bluetongue certification from this region (Walton et al. 1992a).

The United States is at risk for the introduction of exotic BLU serotypes, particularly from the Central American-Caribbean Basin. The primary vector in that region is *C. insignis* Lutz, which is also found in southern Florida where it overlaps with *C. sonorensis*. Preliminary laboratory studies have shown that colonized *C. sonorensis* are capable vectors for several exotic BLU serotypes (Venter et al. 1998; W.J.T. and L. H. Thompson, unpublished data). The desire to prevent exotic bluetongue serotypes from entering the United States continues to impact livestock trade. In 1998, Australian cattle exporters sought U.S. approval to export 5000 Australian feeder cattle to the United States by transshipping these animals through Mexico. USDA APHIS and the U.S. National Cattlemen and Beef Association raised several concerns. A primary concern was the danger of allowing entry of Australian cattle carrying one of the Australian bluetongue virus serotypes that are exotic to the United States. The danger of allowing entry of an exotic BLU virus would be prevented through animal quarantine regulations as specified in the U.S. Code of Federal Regulations. However, a further problem was that the animals entering through Mexico would be identified as part of the Mexican national herd, and not by their point of origin in Australia. The concern that an exotic Australian BLU could be detected in the United States as part of U.S. serological surveillance, which would not be differentiated as entry through importation, was one of the reasons for U.S. disapproval of this plan.

The danger of the bluetongue viruses to the United States is in their impact on U.S. trade in cattle, and in the potential impact of the entry of new BLU virus serotypes. Attenuated BLU vaccines are available for use against several serotypes, but these may revert to virulence, be transmitted by *Culicoides*, and the re-

sulting vaccinates face trade restrictions for export. Molecular vaccines that provide protection against BLU viruses have been tested experimentally, but have yet to be marketed. The impact of the entry of an exotic BLU serotype on the current epidemiology of BLU in the United States is difficult to predict. Any negative change in the current status of BLU virus in the United States could have serious consequences for U.S. livestock industries through further restriction on U.S. exports.

Reintroductions

Several arthropod-borne pathogens have been introduced into the United States, disappeared, and subsequently introduced again. These reintroductions reinforce the need to maintain vigilance, particularly for those organisms known to be adaptable to conditions in the United States. Following are two examples that are used to illustrate the seriousness of these occurrences.

Bovine Babesiosis. Although cattle may be infected by any one of six *Babesia* species, three species, *B. bigemina* (Smith & Kilborne), *B. divergens* M'Fadecan & Stockman, and *B. bovis* (Babes), produce clinical signs in bovines and are of particular importance to U.S. agriculture. The severity of disease in cattle varies because of differences in virulence and other attributes of the species and geographic strains, as well as host resistance. The disease is usually characterized by fever, hemolytic anemia, hemoglobinuria, and, in severe cases, death (Kuttler 1988). *Babesia bigemina* and *B. bovis* usually exist together throughout the tropical and subtropical parts of the world where their *Boophilus* tick vectors occur. In the areas of central and southern Africa, where the only *Boophilus* species is *B. decoloratus* (Koch), cattle are infected only with *B. bigemina* (Norval et al. 1983). *Babesia divergens* is found in northern Europe where *Ixodes ricinus* (L.) is the vector. In this case, both pathogen and tick vector are exotic to the United States.

Boophilus annulatus (Say) and *B. microplus* (Canestrini) were among the first ectoparasites of cattle introduced to the New World by explorers and colonists who brought tick-infested cattle with them (Hoogstraal 1986). By the latter part of the 19th century, bovine babesiosis was the major deterrent to the development of a strong cattle industry in the southern United States. When the national *Boophilus* tick eradication campaign began in the United States in 1906, the tick-infested area included all or parts of 14 southern states and a portion of southern California, an area of 1,813,000 km². By 1943 the national eradication campaign was declared complete even though *Boophilus* ticks remained in Texas, along the Rio Grande River, and the last pocket of *B. microplus* in Florida was not eliminated until 1960 (Graham and Hourigan 1977).

Today, the Cattle Fever Tick Eradication Program (CFTEP) of APHIS VS is still active in Texas where most of the problems with *B. annulatus*, the cattle tick, and *B. microplus*, the southern cattle tick, are confined

to a narrow (0.4–16 km in width) permanent Quarantine or Buffer Zone. This zone extends through parts of eight counties for ≈ 800 km along the Rio Grande River from Del Rio to Brownsville, TX (Graham and Hourrigan 1977). Both *Boophilus* species remain widespread in Mexico and incursions of tick-infested cattle, horses (*Equus caballus* L.), and ungulate wildlife across the Rio Grande River from Mexico into the Buffer Zone and the designated Free Area beyond are a constant challenge to the personnel of the CFTEP. The number of tick infestations detected in South Texas was as high as 170 in 1973. In the 6 yr from 1994 to 1999 the average of 30.5 infestations detected annually was 2.2 times greater than the average number per year reported for the previous 6 yr. Forty-six percent of the 611 stray or illegally imported cattle from Mexico that have been apprehended in the Buffer Zone since 1985 have been infested with fever ticks (Dietrich and Adams, 2000). Additionally, the annual exportation of hundreds of thousands of cattle and smaller numbers of equines from Mexico into the United States magnifies the difficulty of keeping the cattle tick and the southern cattle tick out of the United States. Inspecting all cattle and horses to ensure they are tick-free and then dipping these animals in an acaricide before their importation, is a critical part of the process of protecting the U.S. cattle industry (George 1996).

Problems in insuring that the U.S. cattle industry remains protected against fever ticks and babesiosis include the following: (1) the influence of new agreements for free trade on international quarantines; (2) intensified regulatory controls on the use and disposal of pesticides; (3) economic limitations on the development and marketing of new acaricides by animal health companies; and (4) biological problems, such as the presence in Mexico of acaricide resistant *B. microplus*, changes in plant communities that improve tick habitat, and abundant alternate hosts.

Although populations of *B. microplus* resistant to organophosphate (OP) and pyrethroid (P) acaricides are widespread in Mexico (Santamaria and Fragoso 1994), the high concentration of coumaphos used in the CFTEP is still effective. Should a *B. microplus* strain with a greater degree of OP resistance be detected, it would force the CFTEP to substitute an alternate chemical class of compounds for treating cattle. As the list of chemicals to which ticks in Mexico are resistant becomes longer, concern in the United States that acaricide-resistant ticks could spread north from the U.S.–Mexico border is justified. Previously, the small number of white-tailed deer in the southern United States contributed to the success of the eradication effort, because cattle were the only primary tick host on which the campaign needed to focus (George 1989). There are now large populations of white-tailed deer throughout the southern states. These and exotic ungulate wildlife species are confounding efforts to eradicate infestations of fever ticks (George 1996). If the CFTEP fails to contain fever tick outbreaks, white-tailed deer will be a significant factor in the dissemination of ticks back into their historical

range in the southern states. Another factor that favors the maintenance and spread of *Boophilus* tick infestations is the progressive conversion of the grassland savanna of much of the South Texas and adjacent areas of Mexico to thorn shrubland. The shrubland biotype provides a habitat more favorable to the survival of nonparasitic life stages of fever ticks (Teel 1991). Predation of *Boophilus* ticks by populations of the red imported fire ant in the southern United States may mitigate the possible ingress from Mexico and subsequent dispersal of the cattle tick and southern cattle tick. However, the degree to which the ant would reduce the risk is unknown. Butler et al. (1979) observed some predation of engorged *B. microplus* females by the fire ant, *S. geminata*, but in wooded thickets the predation rate was only 7%. These results parallel the observations of Fleetwood et al. (1984) for predation of *A. americanum* by *S. invicta*.

Direct and indirect U.S. losses attributed to the cattle tick in 1906 amounted to \$130,500,000 (James and Harwood 1969). Graham and Hourrigan (1977) estimated that this sum, in 1976 dollars, would have exceeded a billion U.S. dollars. These losses to the cattle industry were the result of enzootic babesiosis and established populations of *Boophilus* ticks. If *Babesia*-infected fever ticks spread back into the southern states, all the native yearling and adult cattle will be susceptible to a disease that may cause up to 90% mortality (Kuttler 1988). Restrictions by state and federal regulatory agencies and public attitudes pertaining to the use of acaricides would be major obstacles to any effort to eradicate fever ticks. Dense populations of white-tailed deer would invalidate the pasture vacation option used so successfully in the original eradication campaign, and the abundance of these animals, even though they are not highly susceptible hosts, would make eradication difficult. Global warming could result in an expansion of the portions of the United States with a climate favorable to tick species such as *B. annulatus* and *B. microplus* (Sutherst 1998). The risk of bovine babesiosis transmission to cattle in the southern United States continues to increase.

Vesicular Stomatitis. Vesicular stomatitis (VS) viruses are members of the genus *Vesiculovirus* of the family Rhabdoviridae. VS virus infection occurs in cattle, swine, equines, and wild animals. Cases require prompt diagnosis because they are clinically indistinguishable from foot and mouth disease (FMD). Infection can result in vesiculation, epithelial cell lysis, and severe interstitial edema. Lesions progress by extension, so that it is common for the entire epithelium of the tongue or teat to be sloughed.

Vesicular stomatitis epizootics have occurred periodically in populations of cattle and horses of the western United States. The most recent epizootics in the region were in 1995, 1997, and 1998 that included Arizona, Colorado, New Mexico, Texas, Utah, and Wyoming. There is considerable evidence that VS virus is exotic to the western United States and is probably introduced periodically into the region from Mexico and Central America. The strongest evidence

for this is the close similarity, based on nucleotide sequence analysis, between U.S. virus isolates and VS isolates made in the same year from Mexico and Central America for the past 50 yr (Nichol 1987, Nichol et al. 1993). Indeed, the finding that current U.S. and Mexican isolates are more similar than isolates from prior years suggests that the continuity of the viruses is geographic.

The 1995 epizootic was due to the New Jersey serotype of VSV (VSV-NJ), whereas the Indiana serotype (VSV-IN), after an absence from the United States of more than 30 yr, was the primary strain isolated during the 1997 epizootic. Domestic animals are not believed to be VS virus amplification hosts for insect vectors because they generally show low, transient viremias. High viral titers in skin samples associated with vesicular lesions may be a source of VS virus for nonviremic transmission by insect vectors (Stallnecht et al. 1999). Black flies (*Simulidae*) have been shown to be capable of becoming infected through nonviremic co-feeding with infected flies (Mead et al. 2000), though the epidemiological consequences of such transmission has yet to be fully explored.

Several U.S. hematophagous insect species are suspected vectors of VS virus. Virus isolations have been made from several species of *Simulidae*, *Culicoides*, *Chloropidae*, *Anthomyiidae*, and *Musca* during U.S. epizootics, and laboratory transmission has been shown for *Simulium vittatum* Zetterstedt (Cupp et al. 1992) and *Culicoides sonorensis* (A. A. Perez de Leon and W.J.T., unpublished data). However, the nature of the specific involvement of different insect species during VS epizootics in the western United States remains unclear (Schmidtman et al. 1999). There is considerable interest in the possibility that pharmacologically active substances in the saliva of hematophagous insects facilitate vertebrate infection with VS virus (Ribeiro et al. 2000, Tabachnick 2000). In addition to economic losses directly related to clinically affected animals, VS outbreaks have important economic consequences for U.S. agriculture due to quarantine of affected premises and regional, national, and international restrictions on the trade of U.S. livestock.

Attempts to control the 1995 U.S. epizootic illustrate the impact of the disease and the difficulties in reducing its impact. Efforts to prevent the spread of the disease have centered on prompt identification of clinical cases, and the imposition of quarantines on animal movement for a 16-km radius around affected premises. The quarantines and concomitant restrictions caused substantial economic losses by closing rodeos, animal fairs, and sale barns. Thirty-nine U.S. states restricted animal movement from affected states during 1995, requiring certificates from accredited veterinarians that the animals being moved had not been on VS affected premises within 30 d. Animals from affected states could not be moved to Canada or the European Union. Russia and the Republic of South Africa banned any beef from U.S. affected states. The losses due to the 1995 U.S. epizootic have been estimated as between \$50 and 100 million (W.J.T., un-

published data). The response to subsequent U.S. epizootics have been similar, though the 16-km radius quarantines were subsequently reduced to quarantining only the affected premises. Despite these efforts VS cases spread in 1995, 1997, and 1998 through several western states as they had done in past outbreaks until cold weather terminated insect transmission.

The reintroduction and spread of VS virus in the western United States is a continuing risk to the health and well being of U.S. agriculture. Of some concern, is that introduction of a new strain of VS virus could result in more substantial clinical disease in the United States. The possibility also exists that continued reintroduction of VS virus might result in the delay of diagnosis of introduced FMD before it spreads widely, which could have far more catastrophic consequences for U.S. agriculture.

Discussion

There are a number of examples of exotic diseases or their potential vectors being intercepted before they could become established in U.S. livestock populations (Bram and George 2000). However, if circumstances are suitable for the propagation of a pathogen, it can be considered fortunate if an introduced disease is detected before it spreads. Recent experiences with WN and VS viruses show that even the prompt detection efforts by the U.S. animal health community are not always effective in initiating actions to prevent the spread of these arthropod-borne pathogens. Although both viruses were closely monitored by USDA and state veterinary agencies, cases reported and investigated, quarantines implemented for VS, and insect control measures recommended, both VS and WN viruses continued to spread until natural climatic factors caused insect transmission to cease. Indeed, WN virus is now likely well established in the United States. Regardless of improved technology, attention to detection, and other important measures, there has been inadequate progress in controlling arthropod-borne diseases. Emerging arthropod-borne pathogens pose unique challenges that will require new information if we are to provide effective intervention and control (Tabachnick 1998).

It is evident that an alert animal owner, seeking diagnosis and treatment of a severe or unusual problem, is the most critical element of effective surveillance. Entomologists, too, are in position to recognize unusual occurrences of vectors or pathogens in the field. The United States has a broad network of practicing veterinarians familiar with the occurrence of endemic diseases in their areas. A system of federal accreditation of most of the country's veterinarians requires that they report notifiable diseases as well as those likely to have been introduced.

Individual states, as well as Federal government agencies, employ veterinarians and other animal health workers whose main responsibility is the prevention and control or eradication of important livestock and poultry diseases. Aware of the dangers of disease introduction, they promote the reporting of

suspicious diseases by owners and veterinarians alike and ensure that these cases are immediately investigated.

The United States has trained specialists in exotic diseases, including entomologists, whose services would be called for in the event of an emergency. Foreign animal disease diagnosticians are among these specialists, and a suspicious report can be expected to result in a prompt investigation. Usually governmental authority will halt animal and product movement pending results of such an investigation. Livestock markets and slaughterhouses, which are under state and/or Federal control, can be placed on special alert or be closed as appropriate. Two high-security USDA animal disease laboratories—the national reference laboratory in Ames, IA, and the other whose focus is only exotic diseases at Plum Island, NY—are on continuous standby to diagnose possible disease introductions. Exotic zoonotic diseases would receive similar attention by the Centers for Disease Prevention and Control in Atlanta, GA, and in Fort Collins, CO.

Despite these commendable efforts to protect the United States from the introduction of foreign animal pathogens, including those that are arthropod-borne, it is clear that U.S. agriculture still faces great risk. In addition to those foreign pathogens reviewed here, there are any number of other serious arthropod-borne diseases, such as Rift Valley fever or African horse sickness, which have the potential of entering the United States with devastating consequences. There is great need for additional information that will reduce the risk and impact of such introductions. Currently, United States Federal support of research on animal diseases is <10% of the total Federal agricultural research investment. Federal annual support for all animal agricultural research is close to \$200 million of which approximately \$50 million per year in animal diseases is invested to enhance measures that protect a \$100 billion industry. It is clear that a substantial increase in research investment is required at the Federal level to protect U.S. agriculture. Information is urgently needed on the most likely routes of invasion, strategies to inhibit invasion and an assessment of the economic costs for resulting recommendations that may impact trade and commerce. The USDA has expended considerable resources in its longstanding cooperative programs with neighboring countries to successfully control and eradicate animal diseases away from our borders. In addition, it is essential that greater emphasis be placed on promoting U.S. research projects in foreign countries. Research in foreign countries will provide information on the potential for introduction to the United States and enhance our ability to apply control strategies after an invasion. Research must be encouraged that will result in recommendations for controlling indigenous and exotic vectors and pathogens as well as the economics associated with their establishment.

There are a number of reasons why a disease may spread, regardless of conscientious efforts to diagnose and contain it. These include not only the biological variations of pathogens, vectors, host susceptibility

and density, but also the dynamic and complex livestock marketing system involving multiple and long distance animal movements. In addition to the risks resulting from accelerated worldwide movement of people and their goods, the emergence of new diseases, and global warming, there is also the potential for the introduction of new pathogens as a consequence of bioterrorism (Ban 2000).

Acknowledgments

We thank D. D. Wilson and G. S. Colgrove for their assistance in obtaining unpublished information from the archives of APHIS, Veterinary Services. We are grateful to R. B. Davey, J. F. Day, G. J. Letchworth, C. C. Lord, P. Scholl, E. T. Schmidtman, D. D. Wilson, and two anonymous reviewers for providing useful criticisms of earlier drafts of the manuscript. Publication number R-07952 of the University of Florida, IFAS, Florida Medical Entomology Laboratory, Vero Beach, FL.

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Received for publication 14 March 2001; accepted 15 November 2001.