PROTECTING PATIENTS
While research indicates that tick-borne diseases are getting worse for people and pets, preventive tools and prevalence mapping can help limit exposure.

PARASITOLOGY

It Is Always a Bad Year for Ticks: Update on Ticks and Pathogens

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Vector-borne diseases are important to the health of domestic animals, humans, and some wildlife species, and they are more than twice as likely to be emerging diseases (i.e., increasing in incidence in either new or existing populations) as non–vector-borne diseases.[1] Worldwide vector-borne diseases are increasing, and specifically in the United States, from 2004 to 2016, the number of reported human cases of tick-borne disease more than doubled.[2] Several factors are thought to contribute to the increasing incidence of diseases caused by vector-borne pathogens, including climate change; habitat changes, such as suburbanization and reforestation, that bring people, wildlife, domestic animals, and pathogens together; and an increase in certain wildlife species (e.g., rodents, deer) that support vectors and/or serve as reservoirs of infection. These factors are dynamic and, as a result, novel pathogens are expected to emerge and the incidence, prevalence, and spatial distribution of tick-borne diseases are expected to change, making monitoring essential.

TICK-BORNE PATHOGENS CONTINUE TO EMERGE

Until the early 1980s, Rocky Mountain spotted fever, caused by *Rickettsia rickettsii*, was the most commonly recognized human tick-borne disease in the U.S. However, since its initial description in the 1970s, Lyme disease, caused by *Borrelia burgdorferi*, has quickly become the most diagnosed tick-borne disease. Currently, approximately 30 000 human Lyme disease cases are confirmed annually in the U.S., but it is estimated that the actual number of cases could range from at least 300 000 to as many as 475 000.[3,4] Additionally, in the past several decades, numerous new human pathogens have been recognized (at least 9 since 2004). Many of these also infect dogs, which are commonly exposed to ticks; fewer infect cats and horses.

The diversity of tick-borne pathogens recognized in dogs has also been increasing (**TABLE 1**). Among the most common are *B burgdorferi*, *Anaplasma phagocytophilum* and *Anaplasma platys* (agents of anaplasmosis), and *Ehrlichia* species (agents of ehrlichiosis). There are 3 primary agents for canine ehrlichiosis in the U.S.: *Ehrlichia canis, Ehrlichia ewingii,* and *Ehrlichia chaffeensis*, but dogs are also susceptible to infection by *Ehrlichia muris eauclairensis*, believed to be transmitted by *Ixodes scapularis,* and the "Panola Mountain" *Ehrlichia* species, which is transmitted by *Amblyomma americanum*. In dogs, tick-borne pathogens generally cause nonspecific illness characterized by fever, lethargy, and inappetence; some may cause lameness, rash, and clinical abnormalities.

Top: Stock2468/shutterstock.com. Opposite counterclockwise from top right: Courtesy Companion Animal Parasite Council (3).

As shown in **TABLE 1**, individual tick species can be associated with several pathogens, meaning that a person or dog infested with one species of tick may be at risk of several tick-borne diseases. For example, *I scapularis* is a competent vector for *A phagocytophilum* as well as *B burgdorferi,* while *Rhipicephalus sanguineus* can transmit *E canis* and is the presumed vector for *A platys*. Similarly, *A americanum* can transmit several important pathogens. The distributions of these pathogens follow those of the associated tick vectors (**FIGURES 1–3**).

While the specific agent may not be clinically significant (e.g., treatment for *E chaffeensis* and *A phagocytophilum* is the same), accurate diagnosis is important epidemiologically, as different vectors may be involved and some tick-borne pathogens (e.g., *Babesia* species, viruses) are not susceptible to the same treatment protocols as bacterial pathogens. Also, many species of ticks may coexist on the same dog; therefore, collection and identification of one species do not rule out the presence of another species that may be responsible for the presenting disease.

TICKS ARE ON THE MOVE, AND THEY TAKE THEIR PATHOGENS WITH THEM

It is well established that several tick species are expanding their ranges and/or developing higher densities within their historical range. As ticks expand their range, they take their pathogens with them. This

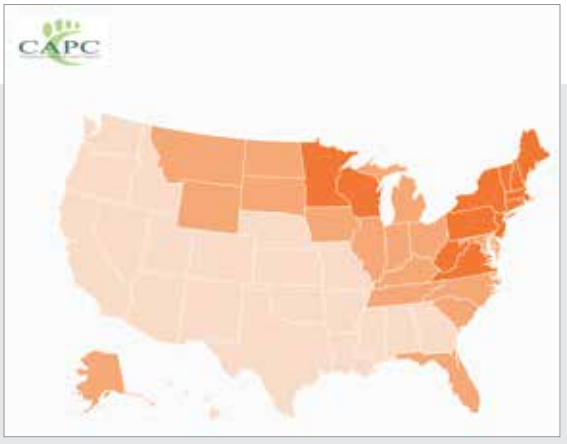

FIGURE 1. Prevalence of *Borrelia burgdorferi* antibodies in dogs in the United States for 2021. Darker shades indicate higher prevalence. Data sourced from the Companion Animal Parasite Council Parasite Prevalence Maps.

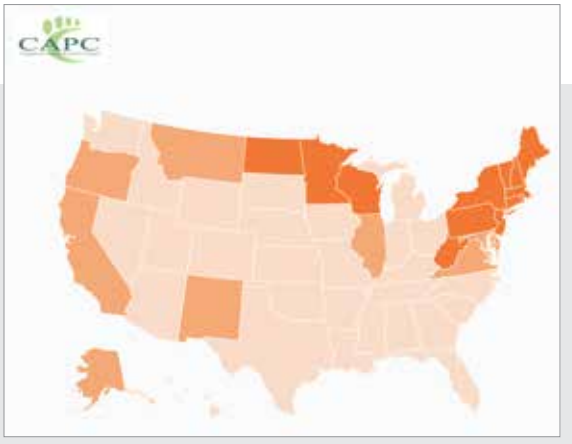

FIGURE 2. Prevalence of *Anaplasma* species antibodies in dogs in the United States for 2021. Darker shades indicate higher prevalence. Data sourced from the Companion Animal Parasite Council Parasite Prevalence Maps.

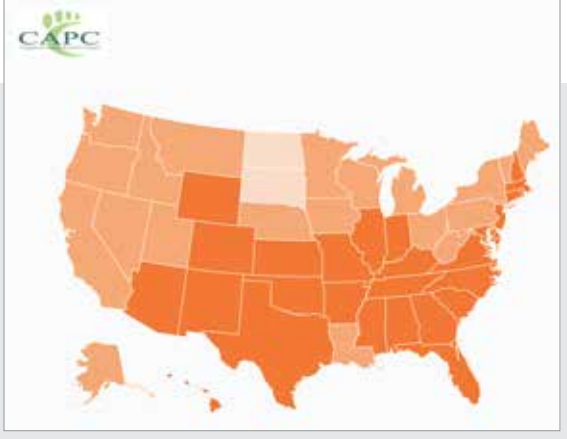

FIGURE 3. Prevalence of *Ehrlichia* species antibodies in dogs in the United States for 2021. Darker shades indicate higher prevalence. Data sourced from the Companion Animal Parasite Council Parasite Prevalence Maps.

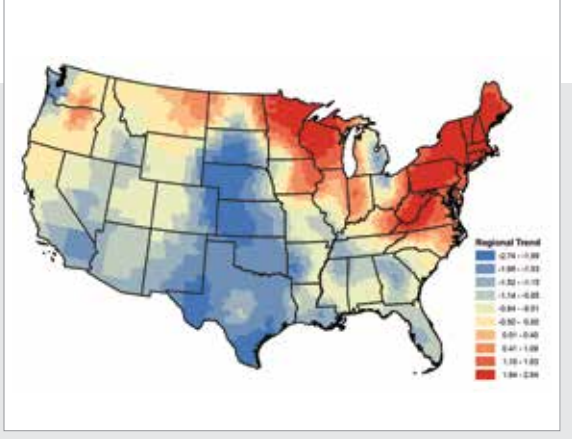

FIGURE 4. Regional change in *Borrelia burgdorferi* seroprevalence in dogs from 2012 to 2018. Regional trends range from decreases or stability of seroprevalence (blue to yellow) to increases (orange to dark red).[11]

TABLE 1 Selected Known Tick-borne Pathogens in the United States

PATHOGEN	DISEASE NAME	VECTOR	YEAR RECOGNIZED
Anaplasma phagocytophilum	Anaplasmosis	*Ixodes scapularis* (blacklegged tick) and *Ixodes pacificus* (Western blacklegged tick)	Early 1990s
Anaplasma platys	Cyclic thrombocytopenia	*Rhipicephalus sanguineus*	1970s
Babesia canis	Babesiosis	*R sanguineus*	Late 1800s
Babesia duncani	Babesiosis	*Dermacentor albipictus*	1991
Babesia gibsoni	Babesiosis	Unknown	Early 1900s
***Babesia* species (Coco)**	Babesiosis	Unknown	2004
***Babesia* species (MO1)**	Babesiosis	Unknown	1996
Babesia conradae	Babesiosis	Unknown	1990
Borrelia burgdorferi	Lyme borreliosis	*I scapularis* and *I pacificus*	1975
Borrelia mayonii	Lyme borreliosis	*I scapularis*	2012
Borrelia miyamotoi	Relapsing fever borreliosis	*I scapularis*	Described in 1994, recognized as zoonotic in 2011 in Russia, first U.S. case in 2015
Bourbon virus	Bourbon virus disease	*Amblyomma americanum* (lone star tick)	2014
Colorado tick fever virus	Colorado tick fever	*Dermacentor andersoni*	1800s to early 1900s
Ehrlichia canis	Ehrlichiosis	*R sanguineus*	1930s
Ehrlichia chaffeensis	Ehrlichiosis	*A americanum*	1986
Ehrlichia ewingii	Ewingii ehrlichiosis	*A americanum*	1998 (in people, earlier in dogs)
Ehrlichia muris eauclairensis	Ehrlichiosis	*I scapularis*	2009
Panola Mountain *Ehrlichia* species (PME)	PME ehrlichiosis	*A americanum*	2005 (in people, later in dogs)
Hepatozoon americanum	American canine hepatozoonosis	*Amblyomma maculatum* (Gulf Coast ticks)	1970s
Hepatozoon canis	Hepatozoonosis	*R sanguineus*	Early 1900s in India, first U.S. case in 2008
Heartland virus	Heartland virus disease	*A americanum*	2009
Powassan virus	Powassan	*I scapularis*	1958
Rickettsia rickettsii	Rocky Mountain spotted fever	*Dermacentor variabilis*, *D andersoni*, *R sanguineus*, and rarely other tick species	Early 1900s; *R sanguineus* recognized as new vector in 2003 in Arizona
Rickettsia parkeri	*Rickettsia parkeri rickettsiosis*	*A maculatum*	2004
***Rickettsia philippi* (*Rickettsia* species 364D)**	Pacific Coast tick fever	*Dermacentor occidentalis*	2008

CAUSES HUMAN DISEASE?	CAUSES CANINE DISEASE?	RESERVOIRS
Yes	Yes	Rodents
Not in U.S., although reported in other countries	Yes	Dogs
No	Yes	Dogs
Yes	No	Mule deer, bighorn sheep
No	Yes	Dogs
No	Yes	Dogs
Yes	No	Lagomorphs
No	Yes	Dogs
Yes	Yes	Rodents
Yes	No	Rodents
Yes	No	Rodents
Yes	No	Unknown
Yes	No	Rodents
No	Yes	Dogs
Yes	Yes	White-tailed deer
Yes	Yes	White-tailed deer
Yes	Yes	Rodents
Yes	Yes	White-tailed deer
No	Yes	Dogs, wild canids
No	Yes	Dogs
Yes	No (but antibodies have been reported)	Unknown, but antibodies detected in white-tailed deer, raccoons, horses, coyotes, and moose
Yes	No (no cases in U.S., but cases with related tick-borne encephalitis virus in Eurasia)	Various small/ medium mammals
Yes	Yes	Ticks, rodents, various species
Yes	No (but infections in wild canids)	Possibly small rodents and birds
Yes	No	Unknown

can cause diagnostic difficulties in areas where multiple pathogens may cause tick-borne diseases that present with similar signs. For example, anaplasmosis has long been endemic in dogs and humans in the northeastern U.S., but in recent years the lone star tick has expanded into the area and ehrlichiosis is now a differential in this region.

In addition, an exotic tick species, *Haemaphysalis longicornis* (Asian longhorned tick), was first detected in the U.S. in 2017 and is now widespread in the eastern states.[5] The potential for pathogen transmission by this exotic tick is a major concern. To date, there is limited evidence of natural infection of *H longicornis* with *B burgdorferi*, a variant of *A phagocytophilum*, and *Rickettsia felis*.[6] Experimentally, this tick can transmit *R rickettsii* but was not successful in transmitting *B burgdorferi* or a human variant of *A phagocytophilum*.[7-9] Additional research is clearly needed to understand the pathogen risk of this new tick, keeping in mind that this risk may change over time as the tick spreads or uses novel hosts that may be infected with different pathogens.

PREVALENCE MAPS PROVIDE REAL-TIME DATA ON PATHOGENS

Mapping the distribution of ticks and their pathogens has obvious importance, but it is complicated by many factors. A significant limitation is the great expense and logistics of gathering real-time data on the presence and density of ticks across the potential range of each tick species. For pathogens, especially multi-host pathogens, it is even more difficult to determine distribution. However, the Companion Animal Parasite Council (CAPC) provides free, interactive parasite prevalence maps for a limited group of pathogens (capcvet.org). These maps provide a local, real-time quantification of risk, and they are now being used to develop annual forecasts to allow preventive care recommendations to be proactively strengthened.

To create the maps, the CAPC receives monthly serologic data from the U.S. and Canada for several vector-borne pathogens, antigen data for heartworm (*Dirofilaria immitis*), fecal flotation data for intestinal parasites, and data on exposure to selected viruses in dogs and cats. The maps are updated monthly and data can be viewed at the national, state/province, or county level (for the U.S.) going back to January 2012, giving veterinarians expert insight into local pathogen prevalence with which to advise their clients.

Some of the pathogens included in the mapping effort are zoonotic, meaning they can infect humans. In the past, several studies have suggested and investigated the utility of domestic dogs as sentinels for where human infections may occur. Dogs live in the same general environment as their owners, often spend more time outdoors, and may have increased exposure to ideal tick habitats; therefore, their owners may be exposed to ticks that infest them. Using the very large CAPC *B burgdorferi* dataset, it was found that the mean incidence of human Lyme disease case numbers increases with canine seroprevalence until the seroprevalence in dogs reaches approximately 30%.[10] This finding reinforces the use of dogs as sentinels for human risk, especially with respect to identifying geographic areas of concern for potential human exposure.

TRENDS IN PREVALENCE OF SELECTED TICK-BORNE PATHOGENS SHOW CHANGING RISK

These data can also be used to look at trends in prevalence. Using *B burgdorferi* as an example,[11,12] modeling shows that areas with significant increases in canine *B burgdorferi* seroprevalence between January 2012 and December 2016 are the same states in which 95% of human cases occur: Maine, New Hampshire, Vermont, Massachusetts, New York, Rhode Island, Connecticut, Pennsylvania, New Jersey, Delaware, Maryland, Virginia, West Virginia, Minnesota, and Wisconsin (**FIGURE 4**). There is also a significant increase in the surrounding states: the upper peninsula and west coast of the lower peninsula of Michigan, eastern North Dakota, northeastern South Dakota, eastern Iowa, northern and eastern Illinois, Indiana, eastern Kentucky, northeastern Tennessee, eastern Ohio, North Carolina, northern California, and southern Oregon. The rate of increase in seroprevalence was highest within the high-incidence states, while seroprevalence in transitional zones immediately bordering the high-incidence regions is increasing at a slower rate.

These kinds of data are important because they show that the seroprevalence in high-incidence regions is still increasing despite the availability of acaricides and anti-*Borrelia* vaccines, which suggests that current compliance with these preventive measures is inadequate. Veterinarians and pet owners in high-incidence regions need to recognize the growing risk of exposure and implement appropriate preventive measures. Additionally, veterinarians in the areas surrounding high-incidence regions need to recognize that the seroprevalence is rising and adjust screening and preventive care protocols accordingly. Similar studies on the trends of *Anaplasma* and *Ehrlichia* species have been conducted, and they show similar trends in certain regions of the U.S.[13] When all of these pathogens are combined, it shows that dogs are at risk of a tick-borne disease in most regions of the U.S., and the risk is increasing in certain areas.

These historical prevalence data can also be combined with climatological and ecological data to construct annual forecast maps that display the expected prevalence of each pathogen in dogs for the upcoming year. These forecasts are released annually at capcvet.org and at a more "client-friendly" site, petsandparasites.org. Monthly forecasts and alerts are available at petdiseasealerts.org.

CONCLUSION

It seems veterinarians are constantly bombarded with annual warnings that "this year will be a bad tick year" or "Lyme disease cases are increasing" or "tick-borne diseases are on the rise," but importantly, the data do support a concern that tick-borne diseases are getting worse in people and pets. However, an arsenal of tools exists to help. Pet owners and veterinarians should always practice appropriate care in preventing exposure to ticks (e.g., using tick preventives, performing thorough examinations for ticks, avoiding tick habitats if possible), especially in areas with high risk. TVP

Note: This article is adapted and updated from the NAVC's 2020 VMX Conference Proceedings.

Recommended Reading

For more discussion on the pathogen exposure data used in the CAPC parasite prevalence maps and how they are developed, see: Self SCW, Liu Y, Nordone SK, et al. Canine vector-borne disease: mapping and the accuracy of forecasting using big data from the veterinary community. *Anim Health Res Rev*. 2019;20(1):47-60. doi: 10.1017/S1466252319000045

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CLEVOR®

(ropinirole ophthalmic solution)

30 mg/mL
For ophthalmic use in dogs only

Single use dropper

BRIEF SUMMARY: Before using CLEVOR® (ropinirole ophthalmic solution), please consult the product insert, a summary of which follows:

CAUTION:
Federal law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATION:
For induction of vomiting in dogs.

DOSAGE AND ADMINISTRATION:
This product should be administered by veterinary personnel.

Dosing Instructions:
Administer the appropriate number of eye drops topically according to Table 1. The number of eye drops administered corresponding to body weight results in a target dose of 3.75 mg/m^2 (dose band 2.7 - 5.4 mg/m^2). If the dog does not vomit within 20 minutes of the first dose, then a second dose may be administered.

Dose Administration
4 - 11.1 lbs (1.8 - 5 kgs), 1 drop. Example: 1 drop into either left or right eye. 11.2 - 22.1 lbs (5.1 - 10 kgs), 2 drops. Example: 1 drop into each eye. 22.2 - 44.1 lbs (10.1 - 20 kgs), 3 drops. Example: 2 drops in one eye and 1 drop in the other eye. 44.2 - 77.2 lbs (20.1 - 35 kgs), 4 drops. Example: 2 drops in each eye. 77.3 - 132.3 lbs (35.1 - 60 kgs), 6 drops. Example: an initial dose of 2 drops in each eye, followed 2 minutes later by 1 drop in each eye. 132.4 - 220.5 lbs (60.1 - 100 kgs), 8 drops. Example: an initial dose of 2 drops in each eye, followed 2 minutes later by 2 drops in each eye.

- Wear gloves and protective eye wear when handling or administering this product to prevent accidental exposure.
- Open the dropper by twisting off the tail.
- Keep the dog's head steady in a slightly upright position.
- Hold the dropper in an upright position without touching the eye.
- Rest your finger on the forehead of your dog to maintain the distance between the dropper and the eye.
- Squeeze the prescribed number of drops in to the eye(s).
- CLEVOR is a single use dropper and is light sensitive.
- After administration, with gloves on, return the dropper to the aluminum pouch and place in the carton.
- If the dog does not vomit, a second dose can be given 20 minutes after administration of the first dose.
- This second dose is the same number of drops as the first dose.
- Thirty minutes after opening, with gloves on, dispose of dropper, aluminum pouch, and carton.

Refer to the **Animal Safety Warnings** section for treatment of protracted vomiting.

CONTRAINDICATIONS:
Do not use in dogs with central nervous system depression or seizures.
Do not use in cases of ingestion of sharp foreign objects, corrosive agents (acids or alkalis), volatile substances or organic solvents.
Do not use in cases with corneal ulceration, ocular irritation, or ocular injury.
Do not use when there is a known sensitivity to ropinirole or the inactive ingredients.

WARNINGS:
Human Safety Warnings:
Not for use in humans. Keep out of reach of children.
Wear gloves and protective eye wear when handling or administering this product to prevent accidental exposure. In case of accidental eye, oral or skin exposure, flush with water. If wearing contact lenses, eyes should be rinsed first, then remove contact lenses and continue rinsing. Remove contaminated clothing. Ropinirole is a dopamine agonist. **Seek medical attention if accidental exposure occurs and show the package insert or label to the physician.**
Exposure to this drug may cause adverse reactions such as headache, nausea, vomiting, dizziness, orthostatic hypotension, and sleepiness.
Avoid contact with the product if pregnant, planning to become pregnant, or breast-feeding, as exposure has been shown to have adverse effects on embryo-fetal development based on rodent studies.

Animal Safety Warnings:
This product should be administered by veterinary personnel.
Dogs should be monitored for CLEVOR-associated clinical signs, including protracted vomiting, salivation, muscle tremors, evidence of abdominal discomfort, lethargy, transient tachycardia, transient decrease in blood pressure and signs of ocular irritation, including conjunctival hyperemia, mild blepharospasm, and protrusion of the third eyelid. These clinical signs are related to the pharmacological action of ropinirole.
To stop protracted vomiting, administer metoclopramide (dopamine D2 antagonist) at a dose of 0.5 mg/kg intravenously (IV) or subcutaneously (SQ). Metoclopramide also decreases the prevalence of most CLEVOR-associated clinical signs.

PRECAUTIONS:
The safe use of CLEVOR has not been evaluated in dogs with cardiac disease or cardiovascular compromise. CLEVOR can cause transient tachycardia and transient decreased systolic blood pressure.
The safe use of CLEVOR has not been evaluated in dogs with hepatic impairment. CLEVOR is metabolized by the liver.
The safe use of CLEVOR has not been evaluated in dogs younger than 4.5 months of age and weight less than 4 pounds.
The safe use of CLEVOR has not been evaluated in dogs that are pregnant, lactating, or intended for breeding.

ADVERSE REACTIONS:
Safety was evaluated during a field study that enrolled 132 dogs (100 in the CLEVOR group and 32 in the vehicle control group). CLEVOR was administered as drops into the eyes at the dose as directed by the dosing table (see **DOSAGE AND ADMINISTRATION**). The following table shows the number of dogs exhibiting ocular, systemic, and clinical pathology adverse reactions.
Adverse Reactions Reported During the Study (all dogs): Ocular organ system were conjunctival hyperemia, protrusion of the third eyelid, conjunctival discharge, blepharospasm, conjunctival swelling, scratching/rubbing of eyes, corneal ulceration and corneal fluorescein uptake without corneal ulceration. Systemic organ system were lethargy, tachycardia (>160 beats per minute), vomiting duration longer than one hour, salivation, trembling, diarrhea or soft stool, anxious and borborygmi. Clinicial pathology organ system were crystalluria, pyuria, increased liver enzymes, decreased blood glucose and increased prothrombin time.

To report suspected adverse events call
1(800) 835-9496, for technical assistance or to obtain a copy of the SDS, contact Vetoquinol USA, Inc. at 1 (800) 267-5707 or www.vetoquinolusa.com.

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