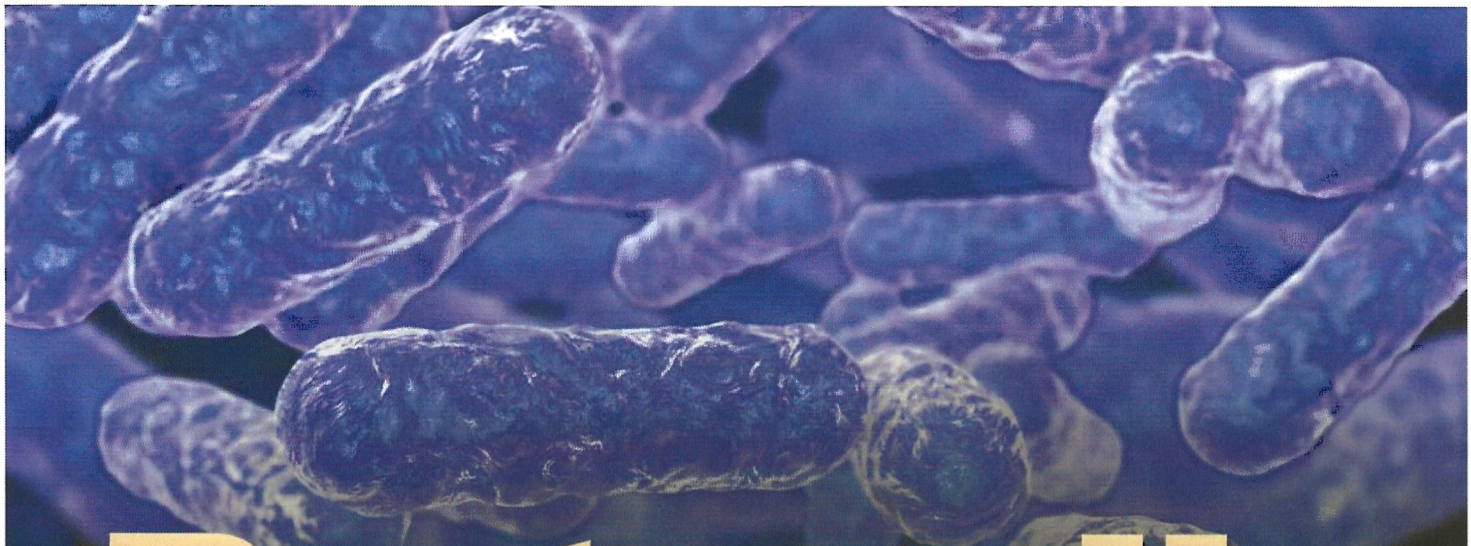


# Bartonella

## The Major Threat You've Never Heard Of

**BY SUE M. COPELAND**

This "stealth" bacteria is an emerging danger to your dog - and you. It also may be linked to the common canine cancer, hemangiosarcoma.

*Bartonella* is a stealth pathogen: it hides inside red blood cells and the cells of blood-vessel walls. Once there, it eludes the body's immune system, and often dodges detection by standard diagnostic blood tests.

above photo ©North Carolina State University

"I tell my veterinary students that, unless another infectious disease comes along that we don't yet know about, such as covid-19 did in humans, *Bartonella* will cause them more problems in their careers than anything else."

That quote is from Edward Breitschwerdt, DVM, DACVIM, Melanie S. Steele Professor of Medicine and Infectious Disease at North Carolina State University (NCSU) College of Veterinary Medicine. He's been studying the bacteria for 30 years.

"Wait, what?" you ask. "What the heck is *Bartonella?*"

It's an emerging threat that research is showing can be associated with potentially fatal conditions in your dog—and you.

Dr. Breitschwerdt should know: the bacteria infected his father 12 years ago. "If it didn't directly cause his death," he explains, "it certainly *helped* cause it." (See, "It's Personal," at page ???.)

### THE ABC'S OF *BARTONELLA*

**What it is:** A Gram-negative bacteria that causes a disease called Bartonellosis. An ancient pathogen, it has existed for thousands of years. Yet prior to 1990, there was only one named *Bartonella* species. Thanks to research by Dr. Breitschwerdt and others, there now are 40 named species, of which 17 have been associated with an expanding spectrum of disease in dogs and humans, as well as other mammals.

The bacteria lives inside blood cells and is transmitted by carriers, known as vectors, which include fleas, lice, and sand flies; *Bartonella* DNA has also been found in ticks. These vectors are found on and around such animals as dogs, cats, coyotes, raccoons, cows, foxes, horses, rodents, and bats. Bartonellosis is a zoonotic disease, meaning it can be transmitted from your pets or other mammals, to humans.

**Why it's a threat:** Bartonella is a stealth pathogen, meaning it hides inside red blood cells and the cells of bloowalls. There,

# BARTONELLA – THE MAJOR THREAT YOU'VE NEVER HEARD OF

it eludes the body's immune system—and, often, detection by standard diagnostic blood tests. (More about that, below.)

It can infect multiple areas in your dog's body, such as his cardiovascular, neurological, and skeletal systems, plus, potentially his digestive system. That means your dog may develop a heart issue (such as endocarditis, an inflammation of the heart's valves and inner lining), neurological issues (such as seizures, weakness, or paralysis), or vomiting, diarrhea, and pancreatitis-like signs.

In Dr. Breitschwerdt's AKC Canine Health Foundation-funded research (CHF; akcchf.org), *Bartonella* has also potentially been linked to hemangiosarcoma, a deadly canine cancer. (See, "The 'Hemangio' Connection," at page ???.)

"The varied presentation of symptoms reported in dogs with Bartonellosis is problematic for your veterinarian," he says. (His research team discovered the world's first identification of *Bartonella* in a dog in 1993). "Your dog may display a variety of signs from limping, to unexplained weight loss, to cancer. Or, you may say, 'My dog just isn't acting right.' Diagnostically, these problems can be caused by lots of diseases. They also can be caused by *Bartonella*."

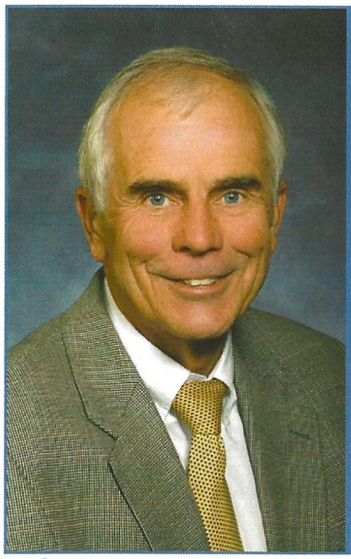
In humans, *Bartonella* is the bacteria that causes Cat Scratch Disease (CSD, also known as Cat Scratch Fever), which is characterized by fever, swollen lymph nodes, fatigue, headache, and general malaise. Recent research has shown that *Bartonella* can also cause chronic infections in humans which, over time, can damage multiple organ systems, just as the bacteria does in dogs.

"If you were to pull out current medical textbooks, they'd state that *Bartonella* is essentially two things: an infection in immunocompromised individuals, such as AIDS patients or transplant recipients," says Dr. Breitschwerdt. "Or, an infection that's transmitted by cats, which is Cat Scratch Disease. If our research holds up, which it's been doing world-wide, when combined, immunocompromise-linked disease and CSD will be just the tip of the iceberg."

"That's because there's good evidence *Bartonella* affects the human nervous system, the cardiovascular system, and the skeletal system, particularly joints, causing rheumatologic symptoms," he continues. "Immunologically, as with covid-19—the disease caused by the novel coronavirus—*Bartonella* can affect different people in very different ways."

Adds Dr. Breitschwerdt, "Not only are dogs our best friends, but naturally infected dogs continue to provide important comparative medical insights that have enhanced our understanding of human Bartonellosis."

Multiple areas of your dog's body can be infected with *Bartonella*. These include his cardiovascular, neurological, and skeletal systems. In Dr. Breitschwerdt's AKC Canine Health Foundation-funded research, the bacteria has also potentially been linked to the deadly cancer hemangiosarcoma.



**EDWARD B. BREITSCHWERDT, DVM, DACVIM**
(Small Animal Internal Medicine)

Dr. Breitschwerdt is the Melanie S. Steele Professor of Medicine and Infectious Disease at North Carolina State University (NCSU) College of Veterinary Medicine. He is also an adjunct professor of medicine at Duke University Medical Center, and a Diplomate of the American College of Veterinary Internal Medicine (ACVIM).

He directs the Intracellular Pathogens Research Laboratory in the Comparative Medicine Institute at NCSU, co-directs the Vector Borne Diseases Diagnostic Laboratory, and is the director of the NCSU-CVM Biosafety Level 3 Laboratory. A DVM graduate of the University of Georgia, he completed an internship and residency in Internal Medicine at the University of Missouri. Dr. Breitschwerdt's clinical interests include infectious disease, immunology, and nephrology. His research group has contributed to research in the areas of animal and human bartonellosis. Dr. Breitschwerdt is a strong proponent of a One Health approach to the understanding, control, and prevention of infectious diseases in animals and humans.

He has authored numerous book chapters and proceedings, and published more than 400 manuscripts in peer-reviewed scientific journals. His long list of prestigious awards includes the AKC Canine Health Foundation Asa Mays, DVM Excellence in Canine Health Research Award.

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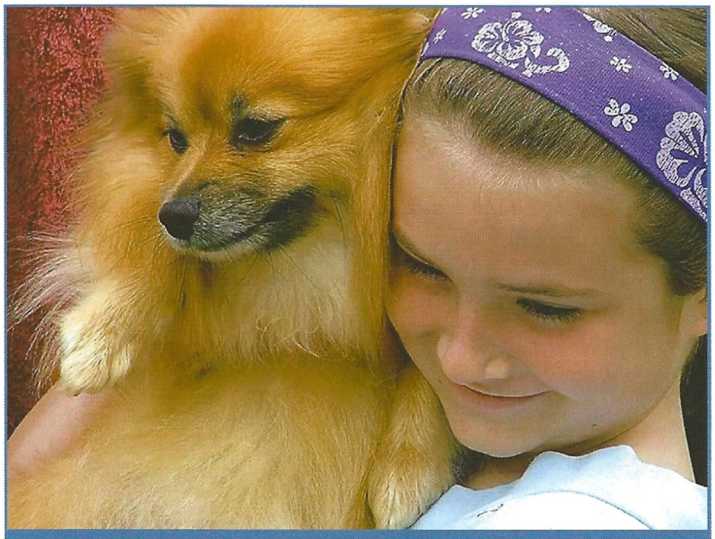

Dr. Breitschwerdt recommends rigorous pest control to help prevent Bartonellosis. "Practice flea and tick control year-round," he says. "Do it, literally, 365 days a year. Don't let up." That's because vectors can transmit Bartonella and other pathogens to your pets and to your family.

## UNDER THE RADAR

"If you were going to design the perfect pathogen to hide under the radar, *Bartonella* would be a good model," he says.

Compare it, for example, to covid-19, which he describes as a "frontal pathogen," meaning the virus immediately attacks and tries to overwhelm its victim's immune system. That way, it can cause rapid spread through respiratory secretions.

"Say you get exposed to someone who's infected with covid-19," explains Dr. Breitschwerdt. "Within days, you're a highly contagious, non-symptomatic carrier at the least, or you become ill. The disease progression may make you mildly ill, or if it's severe, you could end up on a ventilator, and perhaps even die."

"With *Bartonella*," he says, "you can literally be infected when you're 15 years old by being bitten by a tick or scratched by a flea-infested cat. But you may not develop disease until five or 10 years down the road—if ever. As a stealth pathogen, *Bartonella* doesn't severely suppress you or your dog's immune system. But if the immune system does get stressed, that may allow the bacteria to proliferate, resulting in disease."

Ironically, whereas cats carry high loads of the bacteria while rarely getting sick, dogs and humans, even those showing signs of infection, don't. In fact, infected dogs and humans have a *Bartonella* blood-bacteria level between 100 and 1,000 times lower than what is typically found in feline carriers.

That makes diagnostic detection difficult, especially with standard blood cultures. Bacterial growth from cultures can take

## IT'S PERSONAL

"My father's death still motivates me to better understand *Bartonella*," says Dr. Breitschwerdt. He thinks his father, who was found to harbor three species of the bacteria in his blood, was infected over a matter of years.

"I think Dad got one species from his barn cat, another likely came from a groundhog he'd relocated, and the third may have come from a blood transfusion. Those findings are based on DNA of three different *Bartonella* species we found in his blood," he says.

Looking back, he suspects Bartonellosis caused his father to have neurological signs, which led him to fall and break his hip. "Following hip surgery," he recalls, "he had one odd complication after another. When he got a form of esophagitis that typically only happens in people with AIDS or cancer, I wondered about an underlying cause—I was pretty sure my 86-year-old dad didn't have AIDS. And he'd been screened for cancer."

Dr. Breitschwerdt didn't immediately suspect *Bartonella*.

He'd just begun studying that bacteria in humans, so his first thought was a recurrence of the tick-borne disease caused by Ehrlichia; his father had been sickened by it in the past. That bacteria, like *Bartonella*, can present in a variety of ways. His father's neurologist agreed to provide him a blood sample for testing.

Back at his NCSU lab, Dr. Breitschwerdt's research team tested the blood. The findings startled him: It was PCR-negative for Ehrlichia, but positive for *Bartonella*. He immediately called his father's doctors.

"They started Dad on a rigorous regimen of intravenous antibiotics. He improved to the point that he could go home," he says. "Unfortunately, what I know now, that I didn't know then, is that eliminating Bartonella is hard to do. Dad relapsed several weeks after he got home." Despite further antibiotic treatment, he died.

"We share our world with vectors and mammals that can transmit or harbor Bartonella. Based on evolving research, many people may not get through life without being exposed to one or more of Bartonella species," he says. "That's what keeps me up at night. And that's why I believe we need a vaccine to protect our pets—and potentially, their owners."

20 to 40 days rather than the typical two to three days. And, despite infecting red blood cells, *Bartonella* isn't visible on blood smears. Serology antibody testing in dogs and humans is also problematic, since these stealth bacteria can persist without causing a measurable antibody response. As a result, diagnostic test results are often negative, even when infection is present. (Improved testing for *Bartonella* infection is a research area currently funded by CHF.)

Polymerase chain reaction (PCR) is a more accurate diagnostic method for *Bartonella* than standard blood tests. PCR is a molecular technique used to detect specific genetic material of a pathogen (virus, bacteria, or other) in the blood. Analysis of tissue and bodily fluids using PCR can help detect *Bartonella*, plus identify distinct genotypes among *Bartonella* species.

As with detection, treatment can be a challenge: Once inside a victim's bloodstream, the bacteria can invade a variety of cells. "So far," says Dr. Breitschwerdt, "*Bartonella* has been able to invade and live within nearly every cell in your body that an investigator has looked at. That makes it unique, because it can invade so many cells without causing substantial damage, or alerting the immune system."

In fact, a cell infected with the bacteria actually lives longer than an uninfected cell, because the organism protects that cell, its "cellular hou se," from dying. That way, it doesn't have to find another cellular house. "On an evolutionary basis," he explains, "*Bartonella* found a way to decrease programmed cell death."

In other words, this pathogen can be tough to kill. "*Bartonella* is like a bad guy in a movie—a really smart bad guy. This is not a dumb bacteria," says Dr. Breitschwerdt.

Bartonellosis in dogs, cats, and humans is generally treated with such antibiotics as doxycycline, amoxicillin, enrofloxacin, or rifampin, given for a long duration (such as four to six weeks) to reduce the bacteria load. According to the Centers For Disease Control and Prevention (CDC; cdc.gov), the ability of any antibiotic or antibiotic combination to completely clear the bacteria from the bloodstream hasn't been established.

The treatment challenge, plus the fact that *Bartonella* may be linked to cancer, caused Dr. Breitschwerdt to refocus his research. "I've gone from asking how some dogs and people get infected, and why only some get sick from it, to how to prevent people and dogs from getting infected in the first place," he says. "If we can learn how to prevent the infection, such as with a vaccine, the 'why' questions become less important."

## PREVENTION: YOUR BEST BET

Use these suggestions from Dr. Breitschwerdt to help keep your pets, and your family, safe.

- "Practice flea and tick control year-round," he says. "Do it, literally, 365 days a year. Don't let up. These vectors can transmit pathogens such as *Bartonella* to your pets, and to you. Fleas also cause allergies in your dog, which can make him itch. And, they can transmit tapeworms and other parasites."

Consult your veterinarian for the best vector-control program for your pets. Don't forget yourself: If you live in an area that has ticks and other biting insects, use topical insect repellants when you go outside.

- Talk to your veterinarian about *Bartonella*. "Our dogs are the best sentinels for understanding human Bartonellosis," says Dr. Breitschwerdt. "Veterinary workers are the best sentinels for understanding what *Bartonella* is doing in dogs."
- Donate to the AKC Canine Health Foundation (akcchg.org), to help fund more research on *Bartonella*, including for a vaccine. "Before the covid-19 pandemic, our research had finally caused people to recognize it was important to pay attention to this genus of bacteria," Dr. Breitschwerdt says. "It's a scary family of organisms. Unfortunately, pharmaceutical companies don't start to develop vaccines unless there's pressure from society. Clearly the bacteria causes endocarditis and other insidious disease in dogs and humans. We control rabies in humans, dogs, and cats by vaccinating our pets. My goal is to work toward a *Bartonella* vaccine. That way your pets are safe and protected—and can't serve as a source of transmission to you or your family."

Says CHF's Dr. Mary O. Smith, "Dr. Breitschwerdt's groundbreaking studies are just one example of the close link between canine and human health. His work to understand the mechanisms by which Bartonella causes disease in multiple organ systems in dogs is also providing key insights into the cause of human diseases."

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## THE "HEMANGIO" CONNECTION

In 2018, the AKC Canine Health Foundation (CHF; akcchf.org) launched its Hemangiosarcoma (HSA) Research Initiative to learn more about this aggressive, deadly cancer in dogs. Since 1995, CHF has provided $4.1 million in funding to support 28 grants that study HSA, in an effort to understand its causes, and improve early diagnostic and treatment protocols.

In recent CHF-funded research, Dr. Breitschwerdt and his team at North Carolina State University found a high prevalence of *Bartonella* in tumors and tissue samples from 110 dogs with HSA, using PCR analysis. A total of 73 percent of the tissue samples were positive for *Bartonella* DNA. None of the blood samples were found to be positive using the same PCR techniques. That indicates whole blood samples don't reliably reflect the pathogen's presence, according to Dr. Breitschwerdt. The research, he says, further supports another potential connection between persistent infection or inflammation, bacteria, and some types of cancer.

Like *Bartonella*, HSA is a stealth invader, most often involving blood vessels in the spleen, heart, or skin. As the cancer grows, it can go undetected, so can be at an advanced stage when discovered. For more information on the *Bartonella*-HSA connection, please go to, "The Link Between Hemangiosarcoma & Bartonella," at https://www.akcchf.org/educational-resources/library/articles/Golden-Update-Summer-2020-Hemangio-Bartonella.pdf.

Dr. Breitschwerdt is currently the principal investigator on several CHF grants:

- Grant 02550: The Role of *Bartonella* spp. Exposure and Cardiac Genetic Variation on the Clinical Expression of Arrhythmogenic Right Ventricular Cardiomyopathy in the Boxer Dog
- Grant 02519: Prevalence of *Bartonella* spp. Infection in Dogs with Cardiac and Splenic Hemangiosarcomas within and between Geographic Locations
- Grant 02787-E: 2020 Clinician-Scientist Fellowship
- Grant 02819: Identification of *Bartonella henselae In Vivo* Induced Antigens for Development of a Reliable Serodiagnostic Assay for Canine Bartonelloses

To learn more, please visit www.akcchf.org/ticks.

"The AKC Canine Health Foundation is dedicated to supporting humane research that improves the lives of dogs worldwide, and positively impacts the lives of their people," says Dr. Smith. "Dr. Breitschwerdt's groundbreaking studies are just one example of the close link between canine and human health. His work to understand the mechanisms by which *Bartonella* causes disease in multiple organ systems in dogs is also providing key insights into the cause of human diseases."

"The recent advent of SARS CoV-2 (covid-19) has been a reminder that while we await a vaccine, there are other strategies we can use to reduce infectious disease risks," says Mary O. Smith, BVM&S, PhD, DACVIM (Neurology), Vice Chairman of CHF's Board of Directors and Chairman of its Scientific Review Committee. "For covid-19, those strategies include social distancing and wearing a facial mask. For *Bartonella* and other vector-borne diseases, strategies are aimed at avoiding vectors. Talk to your veterinarian about effective flea, tick, and other external parasite control that works in your area. Remember to use products and physical barriers (such as screens) that protect both your dogs and you."

The bottom line: "*Bartonella* has been documented in cats that were buried with the Egyptian Pharaohs," says Dr. Breitschwerdt. "So we know the organism was around at least 3,000 to 4,000 years ago—and cohabitating with people and their pets. It's not a new bacteria. But it's one that's so good at flying under the radar, both human and veterinary medicine missed its existence for a long time. It will continue to complicate the lives of veterinarians and physicians—and their patients—until we find a way to prevent it."

Dr. Breitschwerdt recommends rigorous pest control to help prevent Bartonellosis. "Practice flea and tick control year-round," he says. "Do it, literally, 365 days a year. Don't let up." That's because vectors can transmit Bartonella and other pathogens to your pets and to your family.

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