

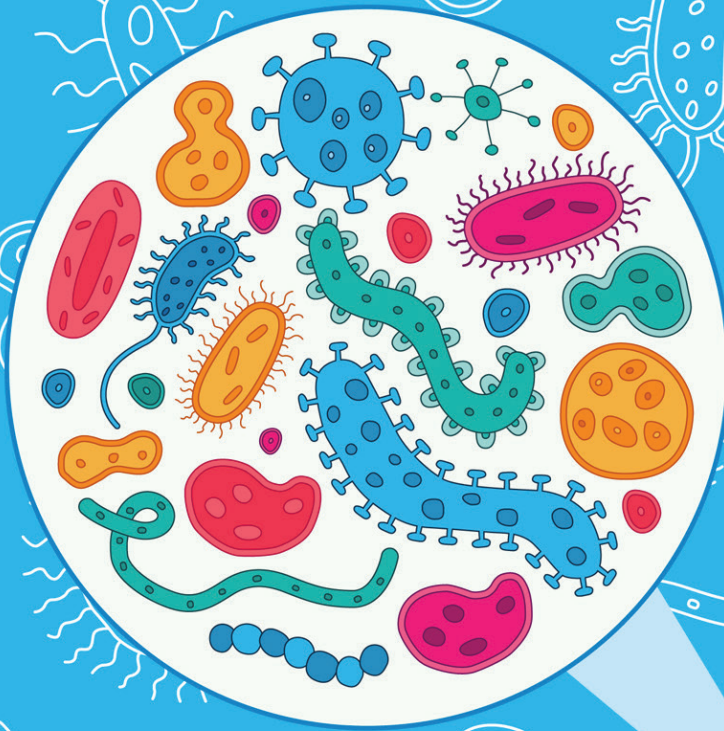
Ticks Can Transmit Multiple Infections in a Single Bite

THE LYME TIMES

The Journal of LymeDisease.org

SPECIAL ISSUE

CO-INFECTIONS



The Lyme disease community's leading source for news, insight and advocacy.



An Authority on Lyme

“LymeDisease.org Member Community is THE one place to refer anyone wanting to get accurate info about Lyme Disease. It's now more like an authority that people go to other than the CDC. We need to support you in order to keep all the issues regarding this disease relevant in the minds of all.”

— Patient

Over 30 years of content written by physicians, researchers & patients

LymeDisease.org is the largest communications network in Lyme disease. Our website draws millions of unique visitors a year. Our original print publication, the Lyme Times, has now gone digital. Our extensive reach and engagement with the Lyme community as a trusted intermediary made the launch of our big data patient registry, MyLymeData, a remarkable success.

To receive the Lyme Times, visit LymeDisease.org and become a member to help us advocate for change, raise awareness, and fund research that can improve patient's lives.

LymeTimes

The Lyme Times connects you to trustworthy information about critical research, events and treatment for Lyme and other tick-borne diseases.



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Who we are

LymeDisease.org is one of the oldest Lyme disease 501(c)(3) nonprofit organizations in the nation. We work to make the patient voice stronger, to support patient-centered research, to create legislative change, and to create a future where Lyme patients can receive the treatments they need to get well. We do this through patient empowerment and science-based advocacy—a powerful combination.

What we do

Education and outreach: Since 1989, LymeDisease.org has grown from publishing a single page newsletter into the largest communications network representing Lyme disease patients in the nation. Starting with our highly informative website, our content is widely distributed via blogs, social media, and our online quarterly journal, the Lyme Times. Members of the Board have published over 50 peer-reviewed publications.

The Lyme Times: *The Lyme Times* is our flagship publication. We inform the community about Lyme disease news, treatment approaches, research and political action through this quarterly journal.

Grassroots advocacy: Solving the critical health problems faced by Lyme patients requires grassroots involvement as well as local and national advocacy. We work with local advocates to help provide them with the tools they need for their long-term legislation efforts to succeed. For example, using our Voter Voice platform, citizens of Massachusetts sent thousands of messages to lawmakers in support of a Lyme-related insurance bill in their state. That important bill became law in August 2016. There is strength in numbers when we work together! We also promote grass-roots efforts through our nationwide network of state-based internet groups.

Research: Our patient-powered research tool, MyLymeData, allows individuals with Lyme to pool

LymeDisease.org is the
most trusted source
of information by
patients with
Lyme disease.

their personal experiences to help drive research towards a cure. Science is based on evidence. Patients need more than hope—they need proof. The estimated 1-3 million patients suffering from chronic Lyme disease today can't wait years for clinical research trials. With over 5,500 patients enrolled, MyLymeData is in the top 10% of patient registries in the nation. We have published two of our large scale surveys on access to care and quality of life in peer-reviewed journals. LDo has funded research at Stanford, the University of Connecticut at New Haven, Stony Brook, and Johns Hopkins.

Symptom checker: In 2015, LymeDisease.org launched the Symptom Checklist, which helps patients determine whether they have been exposed to Lyme disease and assess whether they should see a healthcare practitioner. The checklist is designed to educate both patients and physicians. After completing the checklist, patients can take a print out of their results to their physicians to assist in diagnosis. Over 242,000 people have used the symptom checklist to help obtain an earlier diagnosis.

Physician directory: We provide patients with referrals to healthcare providers and we provide physicians with patient education tools. The physicians in our directory have been referred by patients who have been treated by them.

Ticks Can Transmit Multiple Infections in a Single Bite

*A letter from LymeDisease.org
Founder and President*

By Phyllis Mervine

When I learned that I had Lyme disease way back in 1987, no one knew that babesiosis, ehrlichiosis, or other tick-borne infections could co-infect people and potentially exacerbate one's illness. Simply put, they weren't on anyone's radar. But it makes sense that Ixodes ticks, the primary vectors of these diseases worldwide that feed on several hundred different species of lizards, birds, and mammals, could acquire many blood-borne organisms from their hosts. In fact, a 2014 Chinese study found that locally collected ticks transmitted 237 different bacteria to lab-raised rats. The authors concluded there is "unambiguous evidence that there are as-yet unidentified pathogens associated with ticks, [which] increases the risk of multiple infections in humans, [leading] to more severe clinical manifestations."

A single bite by a nymph or adult female tick has the potential to transmit multiple infections. Doctors who look sometimes find two, three, or even four tick-borne diseases in a single patient. LymeDisease.org's published survey of over 3,000 patients with chronic Lyme found over 50% had at least one co-infection and 30% had two or more co-infections.



And, those with co-infections tend to be sicker and harder to treat. The pathogens ticks ingest during their blood meal from wildlife—Lyme disease spirochetes, Powassan virus, Bartonella, Ehrlichia, and others—develop strain- and species-specific variations as they co-evolve with their primary vertebrate hosts or tick carriers in a given geographic region. Taxonomic studies demonstrate complex interrelationships among strains and species of such pathogens around the world—not surprisingly, as many are carried by birds as well as mammals. And scientists are discovering new microbes all the time. The field of vector-borne disease is exploding. A cursory search of "tick-borne diseases" on PubMed reveals more than 700 published articles from Korea, Turkey, Uruguay, the Congo, and other countries published in the past year alone.

The fact that the picture remains incomplete has serious implications for patient care. In the best of

Special Issue

THE LYME TIMES

Published quarterly for members by
LymeDisease.org
www.lymedisease.org
Library of Congress No. 92-595999
ISSN No. 1552-7506
The Lyme Times

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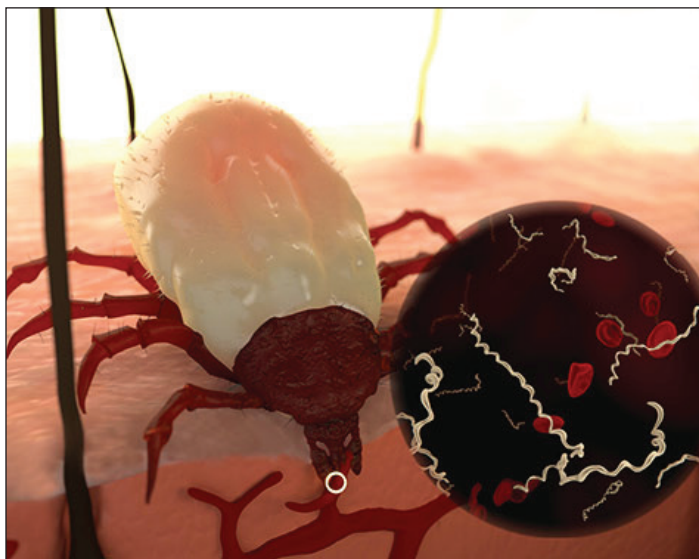
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Multiple infections from a tick bite.

times, it takes months or years for scientific research to trickle down to the trenches. For example, few physicians know that because of its great diversity of climate and vertebrate hosts, my home state — California— hosts 48 of the 86 species of ticks found in the United States. My state is also home to more species of Lyme disease and relapsing fever-group *Borrelia* than any other. Nevertheless, at the Integrated Pest Management meeting I attended in Washington, DC, in 2016, I took the microphone to complain that several of the researchers had shown only the eastern half of the country on their maps. (They promised to do better next time.) My point is, if doctors aren't informed where these diseases occur, they can't diagnose them.

If you are one of the unlucky patients having one or more co-infections, please know that there are hundreds of possible combinations just from the pathogens we already know about, to say nothing of those that await discovery. But patients often cannot obtain treatment without a positive test result and there are no commercially available tests for detecting most of these bugs! There are other obstacles.

For instance the Centers for Disease Control and Prevention (CDC) does not encourage the belief that Bartonellosis can be transmitted to humans by ticks. *Bartonella* species have been found in patients with other tick-borne diseases, but so far no one has been able to meet the official definition of “transmission” required by evidence-based scientific standards.

Hence, it is likely that millions of people afflicted by tick-borne illnesses are not being treated properly because doctors have not been able to diagnose them.

This issue of *The Lyme Times* provides an overview of some of the recent discoveries, and takes a closer look at some of the more common human co-infections. We will be adding to this issue as new information becomes available.

The important point to emphasize is that our knowledge of tick-borne infections is still in its infancy. We urgently need more sensitive tests and more effective treatments. LymeDisease.org is committed to pushing for more research, and to giving patients a voice in these vital issues that affect their lives.

“ There are hundreds of possible combinations just from the pathogens we already know about, to say nothing of those that await discovery.”

In 1989, Phyllis Mervine established the Lyme Disease Resource Center, later re-named LymeDisease.org. She also founded The Lyme Times and serves as its editor-in-chief. In an effort to help Lyme patients join together for mutual support and political action, she set up LymeDisease.org's network of online state support groups. She has collaborated with researchers studying ticks, animal reservoirs, and human infection in northern California. She has served on numerous advisory committees both locally and nationally, and is a former member of the National Institute of Health's Advisory Panel for Studies on Chronic Lyme Disease. She has had several letters and one article published in peer-reviewed medical journals, and her posters have been displayed at international Lyme conferences.

An Alphabet Soup of Co-Infections Complicates Diagnosis and Treatment

Ticks spread Pandora's box of pathogens

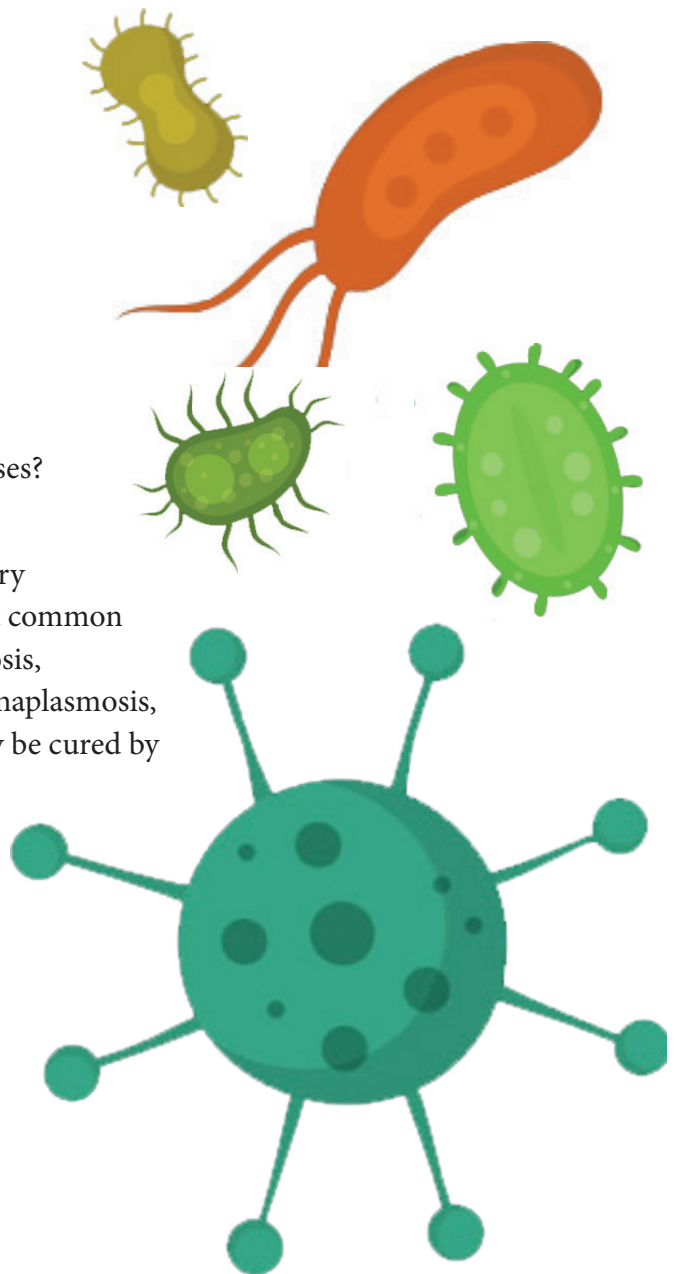
By Doug Fearn

Q

What are these “co-infections” and “associated diseases?”

A

The ticks that carry the Lyme bacteria also often carry microorganisms that cause other diseases. The most common co-infections are anaplasmosis, ehrlichiosis, babesiosis, bartonellosis, and Rocky Mountain spotted fever. Anaplasmosis, ehrlichiosis, and Rocky Mountain spotted fever may be cured by the same antibiotics that are prescribed for Lyme disease. But babesiosis is a different type of disease, caused by a blood parasite and not a bacterium. Antibiotics alone are not effective against babesiosis. Bartonellosis is a bacterial disease, but it requires different antibiotics from those used to treat Lyme disease. All are found in ticks, but some, like bartonellosis, may be spread more often from flea bites.



Q What are these new tick-borne diseases I have read about?

A There are newly-discovered species of tick-borne borrelia that can cause different symptoms. *Borrelia mayonii* causes symptoms similar to Lyme disease, but nausea and vomiting are more common with this infection and the rash is different from the bull's-eye rash of Lyme disease. It has been identified mostly in Wisconsin and Minnesota to date.

Borrelia miyamotoi causes recurrent fevers, along with other symptoms common in Lyme Disease. It has been identified mostly in the northeastern US. The effects of this disease are somewhat different and more intense than in typical Lyme disease. It can be acquired from the bite of a larval deer tick, which is too small for most people to even recognize as a tick. Doxycycline is used to initially treat both of these new Lyme disease variants. Little is known about these diseases at this time.

Powassan fever is a serious viral infection that can be fatal. Half of the patients contracting this disease will have permanent neurological damage. This disease causes serious neurological symptoms, including brain and spinal cord inflammation, severe headache, stiff neck, and seizures, as well as many of the other symptoms caused by Lyme disease. There is a diagnostic test, but few labs are capable of doing the test. There is no treatment except supportive care. According to CDC records, about 11% of patients die from Powassan fever. It is still relatively rare, with fewer than 100 cases reported to the CDC since 2004, but there may be many more undiagnosed cases. Powassan fever can be transmitted in as little as 15 minutes after a tick attaches.

Heartland and Bourbon viruses are other recently discovered tick-borne diseases, that can be deadly. They have been found mostly in Missouri and Tennessee, spread by infected lone-star ticks. There is evidence that other biting insects might also spread these diseases. There is no test and no treatment. They are still rare diseases.

Morgellons disease is an emerging disease that causes strange symptoms. It is the least understood

and most controversial of the tick-borne diseases. One unique characteristic of Morgellons is the appearance of fibers growing out of the skin, accompanied by severe itching. Morgellons patients often experience sensations of something crawling under their skin, which leads many doctors to conclude that the patient has a psychiatric problem. However, experiments have shown that dogs can have the same fibers and symptoms. New organisms such as viruses and microscopic worms are being discovered in ticks. Their role in human illness is not yet known.

Q Why do some people develop an allergy to red meat after a tick bite?

A This is a new and mysterious condition (called Alpha-gal) that seems to be related to the bite of the lone star tick. It causes some people to develop a serious, and sometimes life-threatening, reaction to eating beef, pork, and sometimes milk. It is not known yet if this is a permanent condition. Epinephrine may be required in the case of a serious reaction. Lone star ticks have spread from the South and Southwest to much of the rest of the US in recent years. They are much more aggressive than deer ticks.

Q How does my doctor know if I have these emerging co-infections?

A Few doctors are familiar with these other tick-borne diseases. They may fail to recognize the symptoms or test for these diseases, so many people are suffering from untreated infections. The lab tests for these co-infections have many of the same problems as Lyme disease tests. Often it is this combination of diseases that makes the patient so mystifyingly ill and unresponsive to treatment. If treatment for Lyme disease is unsuccessful, suspect tick-borne co-infections.

Q What are the symptoms of anaplasmosis or ehrlichiosis?

A Like Lyme disease, anaplasmosis and

ehrlichiosis infections peak during May, June, and July and the symptoms typically appear from a week to a month after infection. The initial symptoms are flu-like and can include high fever, chills, headache, fatigue, and general achiness. Fewer than half of infected people report a rash. The rash is different from a Lyme disease rash; it is usually smaller and may have raised areas. The rash is more common in children than adults. Children may also suffer from swelling of the hands and feet. Other symptoms may develop later, including nausea, diarrhea or constipation, loss of appetite, cough, stiff neck, confusion, and weight loss. Untreated, the disease can sometimes be fatal in a few weeks, especially in children.

Q How are anaplasmosis and ehrlichiosis diagnosed?

A There are blood tests for anaplasmosis and ehrlichiosis, which vary in accuracy and reliability depending on when the test is performed and the lab performing the test. It is difficult to obtain an accurate test result during the first few weeks after infection.

Q How are anaplasmosis and ehrlichiosis treated?

A Anaplasmosis and ehrlichiosis are usually treated with doxycycline. Most cases respond quickly when diagnosed and treated promptly. However, about 1-2% of these patients will die if treatment is not initiated right away. Like Lyme disease, you can get these diseases over and over again from new tick bites.

Q What are the symptoms of babesiosis?

A People with babesiosis sometimes have no symptoms at all. However, it can be life-threatening for someone with a suppressed immune system. It is also more serious for people over age 50. Symptoms are often the same as for Lyme disease, but there may also be a very high fever of up to 104°F, and anemia. Drenching night sweats, chills, severe headaches, fatigue, “air hunger,” and sleep

disturbances are common. You can also get babesiosis from a blood transfusion from an infected donor.

Q How is babesiosis diagnosed?

A There are blood tests, but test reliability declines a few weeks after infection. These tests suffer from the same lack of sensitivity that plagues Lyme disease testing. PCR tests for babesiosis can be useful if positive, but a negative result does not rule out the disease. Examining the red blood cells under a microscope may reveal the parasites, but few diagnostic laboratories are skilled at the tedious job of carefully observing the blood cells.

Q What is the treatment for babesiosis?

A It is important to remember that babesiosis is caused by a protozoan parasite and not by a bacterium, so antibiotics alone will not cure this disease. Many people appear to recover without treatment, but the disease may flare up later. Since babesiosis is closely related to malaria, anti-malarial drugs are used to treat it. Usually an atovaquone drug like Mepron or Malarone is used along with an antibiotic such as azithromycin; the combination increases the effectiveness of the treatment. As with most tick-borne diseases, you do not develop any immunity after infection and you can get Babesiosis over and over.

Q What are the symptoms of bartonellosis?

A Early bartonellosis symptoms are often similar to Lyme disease symptoms. There may be a rash, but the rash is different from a Lyme disease bull’s eye and may look like long, thin red areas, somewhat like stretch marks. In many people bartonellosis is a mild disease and the symptoms subside on their own. But in some cases, Bartonellosis may cause ongoing fatigue, depression, anxiety, headaches, swollen glands, sore soles of the feet, GI problems, arthritis, generalized aches and pains similar to those of other tick-borne diseases, seizures, neurological disorders, and even dementia.

Vision loss and eye infections may occur. As with some of the other tick-borne diseases, the symptoms of Bartonellosis tend to come and go. Some areas have a very high rate of Bartonellosis organisms in ticks, sometimes much higher than the rate for Lyme bacteria. Research has shown that Bartonellosis may be more often transmitted by fleas than by ticks.

Q
A

How is bartonellosis diagnosed?

There are blood tests, but as with other tick-borne diseases, the tests are often inaccurate. Some doctors report success with a series of PCR tests, but tick-borne bartonellosis has not been recognized long enough to have a reliable diagnostic testing procedure. Few doctors are familiar with tick-borne bartonellosis. The cause of tick-borne bartonellosis is a bacterium similar to one that causes “cat scratch disease,” which typically is far less serious and has different symptoms.

Q
A

What is the treatment for Bartonellosis?

Antibiotics are used to treat bartonellosis, but the antibiotics used to treat Lyme disease are usually not effective for bartonellosis. As with the other tick-borne diseases, treatment time can be lengthy. Since this disease has been recognized only recently, doctors are still learning which drugs are best. Levaquin, azithromycin, and Rifampin are commonly used to treat bartonellosis.

What are the symptoms of Rocky Mountain spotted fever?

Despite its name, Rocky Mountain spotted fever (RMSF) is far more prevalent in the South and East than it is in the Rocky Mountains. Like Lyme disease, it is caused by a bacterium. Untreated, it can sometimes be a fatal disease. It is spread by dog ticks as well as deer ticks. After two to fourteen days, most infected people suffer from fevers (sometimes 102°F or higher), headache, and achiness. Most people will develop a rash, which may begin around the wrists and

ankles but sometimes starts on the trunk. A classic symptom is a rash on the palms and soles of the feet, but fewer than half of the patients will have that. Untreated, about half of the people infected with RMSF will develop permanent neurological problems. If you handle a tick while removing it, be sure to wash your hands thoroughly to minimize your risk of infection with RMSF. There are reports of infection simply from contact with an infected tick.

Q
A

How is Rocky Mountain spotted fever diagnosed?

RMSF requires a clinical diagnosis, which means that it is up to your doctor to evaluate your signs and symptoms to determine if you have the disease. Early blood tests are not accurate.

Q
A

How is Rocky Mountain spotted fever treated?

Doxycycline is the recommended antibiotic for RMSF.

Q
A

Are there other co-infections?

New tick-borne diseases are being discovered all the time, and some established diseases are being diagnosed more often. New *Borrelia* species include *Borrelia miyamotoi* and *Borrelia mayonii*, which are emerging diseases that cause somewhat different symptoms than Lyme disease. Southern Tick-Associated Rash Illness (STARI) seems to share many symptoms with Lyme disease but it may be caused by a different *Borrelia* species. Colorado Tick Fever, Heartland Virus, and Powassan Virus are caused by viruses and not bacteria.

This article is excerpted from the Seventh Edition April 2017 of Lyme Disease and associated diseases The Basics, A plain-language introduction to tick-borne diseases, published by Lyme Disease Association of Southeastern Pennsylvania, Inc., a not-for-profit 501(c)(3) corporation and an affiliate of the Lyme Disease Association, Inc. Learn more at www.LymePa.org



TICK-BORNE CO-INFECTIONS ARE THE RULE, NOT THE EXCEPTION

The recognition of tick-borne pathogens that are responsible for human illness is accelerating

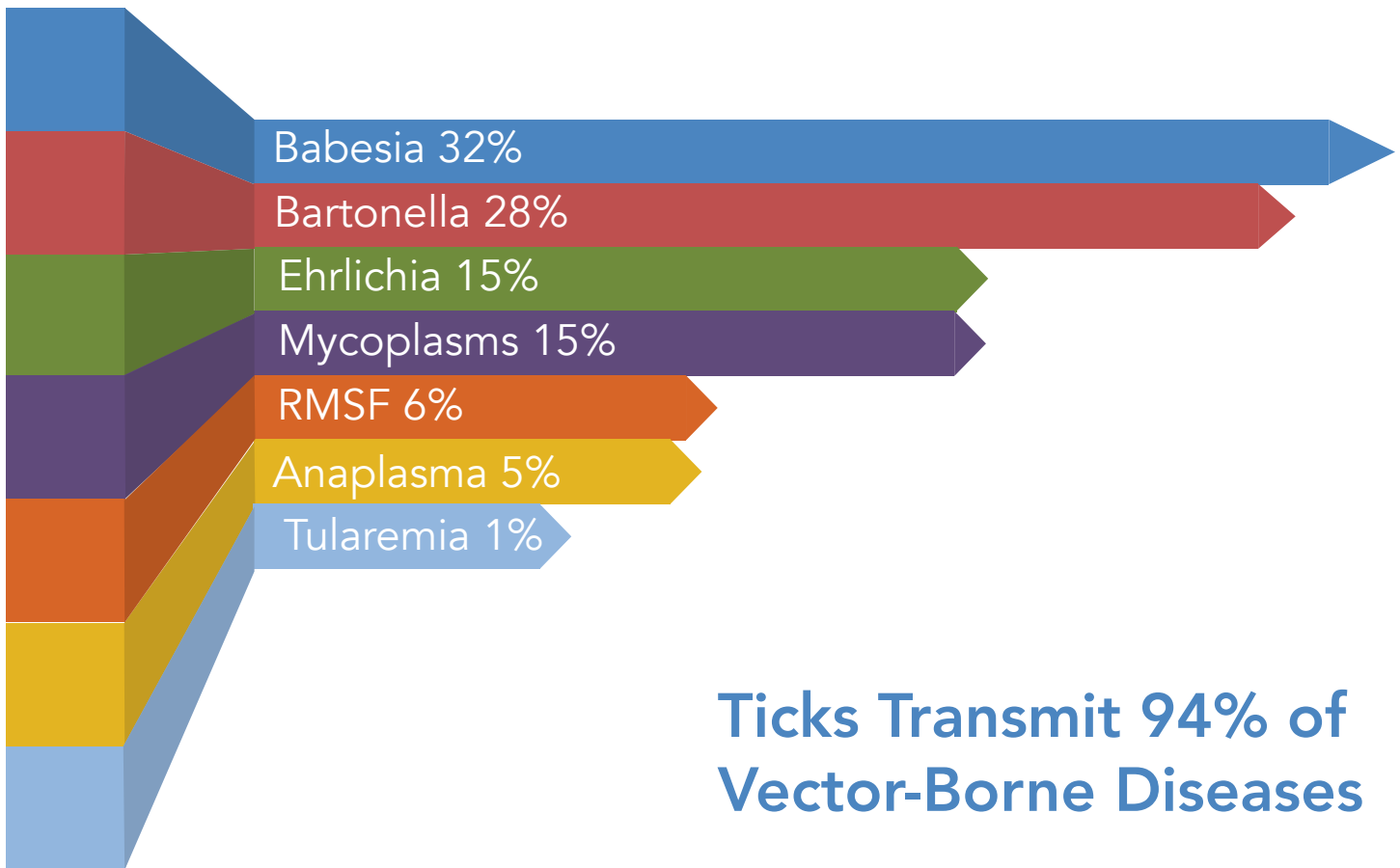
By Lonnie Marcum, PT

While Lyme disease is the fastest growing vector-borne disease in the United States, many other bacteria, parasites, and viruses can also be transmitted by ticks.

These are generally referred to as “co-infections” of Lyme, since people often have them at the same time as Lyme disease. While US cases of Lyme disease are estimated to be over 300,000 per year, no one really knows the incidence of co-infections.

In a LymeDisease.org survey of over 3,000 patients with chronic Lyme disease, more than half reported laboratory-confirmed co-infections, with 30% having two or more. According

The Most Commonly reported Co-Infections US Patients with Lyme



Ticks Transmit 94% of Vector-Borne Diseases

to Dr. Richard Horowitz, “The existence of these co-infections explains why some people with Lyme remain chronically ill even after treatment.”

The most common co-infections reported with Lyme disease are Babesia (32%), Bartonella (28%), and rickettsial illnesses (26%). Rickettsial illnesses include ehrlichiosis (15%), Rocky Mountain spotted fever (6%), and anaplasmosis (5%).

Most vector-borne diseases (VBDs) in the United States are transmitted by ticks. Of the nearly 50,000 cases of VBDs reported to the Centers for Disease Control (CDC) in 2014, 94% were tick-borne, with most of those being Lyme disease. Only 6% of VBDs were from mosquitoes. Yet, Lyme receives only a fraction of the research funding given to Zika and West Nile virus.

The recognition of tick-borne pathogens that are responsible for human illness is accelerating.

Eleven new ones have been discovered since 1960, with over half of those found since 2000.

Several factors contribute to the increase of TBDs:

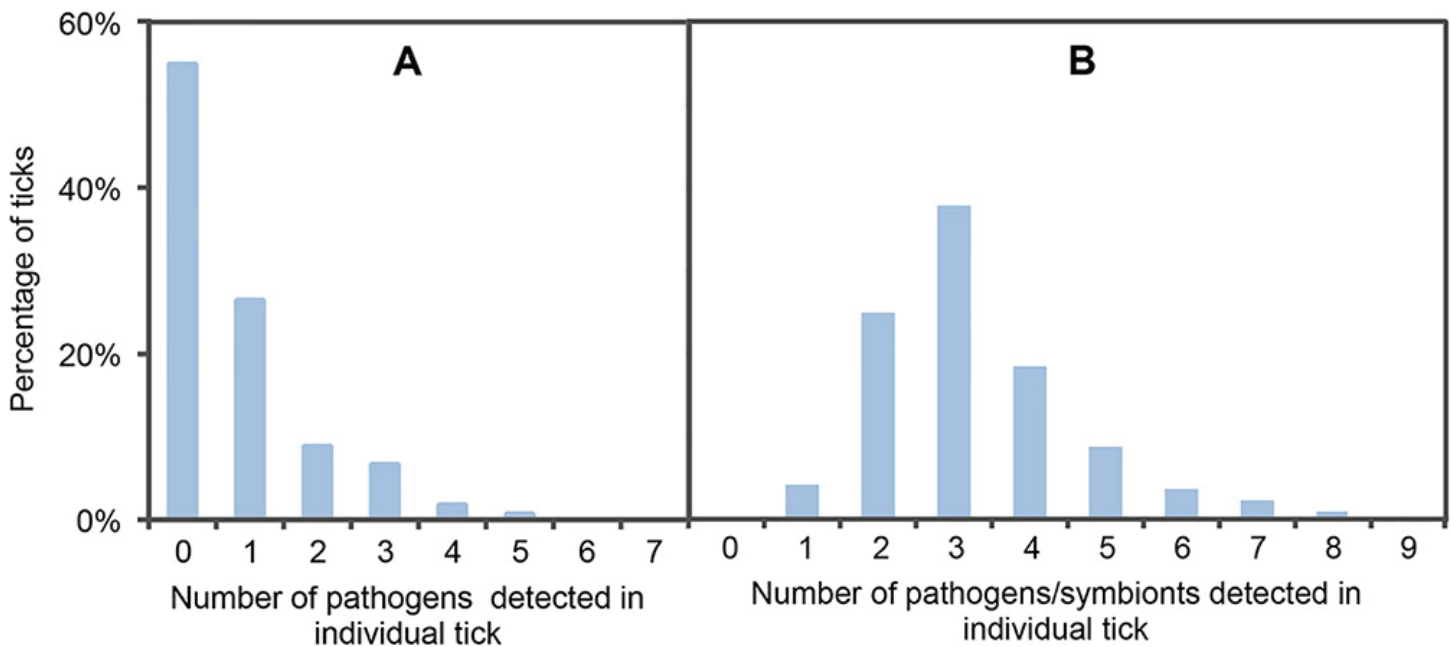
- improved diagnostics
- climatic changes (warm wet weather), reforestation and population increases of mice/deer
- range expansion and population increases of ticks
- lack of a single, effective, widely accepted preventative strategy

Ixodes (Hard-Bodied) Ticks

Of the 84 species of ticks found in the US, at least a dozen can infect humans. Ixodes (hard-bodied) ticks are the biggest culprits, known to transmit a large number of bacteria, parasites, and viruses.

According to the CDC, seven out of the 18 reportable tick-borne diseases in the US are attributable to Ixodes ticks.

The main vectors are Ixodes scapularis



Graph: Jean-Francois Cosson @jeffoscoulous (used with permission)

(blacklegged tick or deer tick) found east of the Rockies, and *Ixodes pacificus* (western blacklegged tick) found west of the Rockies.

Known pathogens transmitted by *Ixodes* ticks include:

- *Anaplasma phagocytophilum*
- *Borrelia burgdorferi*
- *Borrelia miyamotoi*
- *Borrelia mayonii*
- *Babesia microti*
- *Ehrlichia muris*
- *Powassan virus*

Co-infections Are the Rule

To better understand how many microbes can be carried by ticks, scientists are going straight to the source—the tick. One such study took a deep dive into the pathogens carried by *Ixodes* ticks. While this research was conducted in France, I believe the conclusions are applicable to *Ixodes* ticks found throughout the world. Basically, ticks carry lots of bad

stuff!

This study was the first to simultaneously test for 38 pathogens (bacteria, parasites, and viruses) and four symbionts (other microorganisms that may affect the transmission of disease). Some symbionts may make it harder for the tick to transmit pathogens, while others may make it easier.

The results were astonishing! Every tick carried at least one symbiont, and 45% were co-infected with up to five different pathogens. When you include symbionts in the count, some ticks carried as many as eight microorganisms. The study's findings are summarized in the chart above.

In conclusion, if you are bitten by a tick, know that you may have been exposed to more than just Lyme disease, and that multiple infections increase the severity of illness.

LymeSci is written by Lonnie Marcum, a licensed physical therapist and mother of a daughter with Lyme. Follow her on Twitter: @LonnieRhea. Email her at lmarcum@lymedisease.org.

References: Severity of Chronic Lyme Disease Compared to Other Chronic Conditions: A Quality of Life Survey | Image: LYMEPOLICYWONK: Study Finds Co-infections in Lyme Disease Common CDC | MMWR: Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsiosis, Ehrlichiosis, and Anaplasmosis—United States.(May 13, 2016) CDC | Public Health Grand Rounds: Emerging Tickborne Diseases | Co-infection of Ticks: The Rule Rather than the Exception | Graph: Jean-Francois Cosson @jeffoscoulous (used with permission)



Sorting out Lyme & Associated Co-infections

By Joseph Burrascano, MD

to sort it all out clinically to provide guidance in testing and treatment. Here are some clues:

In addition to *Borrelia burgdorferi* (Bb), ticks may carry and transmit other infections. Furthermore, patients with disseminated Lyme complicated by these co-infections are usually immunocompromised and may also manifest signs and symptoms of reactivated latent infections and opportunists. All can add to morbidity and may need to be treated.

Because of the large number of these other infections, the cost of reliably testing for all of them as a matter of routine is prohibitive.

Also, as in the case with Bb infection, laboratory tests for them are often insensitive. Thus there is a need

Classic Lyme (Bb infection)

- Gradual onset of initial (viral-like) symptoms—this often makes it difficult to pinpoint when the infection began
- Multisystem—almost always, in disseminated stages, involves more than one part or system (i.e., joint pain plus cognitive dysfunction)
- Migratory—first a knee will hurt, then over time this may lessen and the elbow or shoulder acts up, and later the joints calm

- down but headaches worsen
- Stiff joints and loud joint crepitus, especially the neck (“Lyme shrug”)
- Headaches are often nuchal and associated with stiff, painful, and crepitant neck
- Afternoon fevers, often unnoticed—most Lyme patients have subnormal temperatures in the morning but rise to 99+ by early to mid-afternoon, no obvious sweats
- Tiredness and limited stamina—often is a strong need to rest or even a nap in the afternoon, especially when the flushed face and elevated temperature appears
- Four-week cycles—Bb activity, and thus symptoms, wax and wane in a cycle that repeats roughly every four weeks. This cycle, if clear, can guide your treatments
- Slow response to treatment, with an initial symptom flare in most (“Herxheimer-like reaction”), then improvement over weeks, punctuated by the monthly symptom flares. Likewise, if treatment is ended too soon, an initial period of well-being will gradually be replaced by a return of symptoms over a few weeks
- EM rash in 25% to 50% of patients

Bartonella and “Bartonella-like organisms”

- Gradual onset of initial illness
- CNS symptoms are out of proportion to the musculoskeletal ones—if a patient has no or minimal joint complaints but is severely encephalopathic (see below), then think of Bartonella/BLO
- Obvious signs of CNS irritability can include muscle twitches, tremors, insomnia, seizures, agitation, anxiety, severe mood swings, outbursts, and antisocial behavior
- GI involvement may present as gastritis or abdominal pain (mesenteric adenitis)
- Sore soles, especially in the morning
- Tender subcutaneous nodules along the extremities, especially outer thigh, shins, and occasionally along the triceps
- Occasional lymphadenopathy.
- Morning fevers, usually around 99; occasionally light sweats are noted
- Elevated vascular endothelial growth factor

“ There is a need to sort it all out clinically to provide guidance in testing and treatment.”

(VEGF) occurs in a minority, but the degree of elevation correlates with activity of the infection and may be used to monitor treatment

- Rapid response to treatment changes—often symptoms improve within days after antibiotics are begun, but relapses occur also within days if medication is withdrawn early
- May have papular or linear red rashes (like stretch marks that do not always follow skin planes), especially in those with GI involvement

Babesia Species

- Rapid onset of initial illness, often with sudden onset of high fever, severe headaches, sweats, and fatigue; thus it is easy to know when infection began
- Obvious sweats, usually at night, but can be day sweats as well
- Air hunger, need to sigh and take a deep breath; dry cough without apparent reason.
- Headaches can be severe-dull, global (involves the whole head, described like the head is in a vise)
- Fatigue is prominent, does not clear with rest, and is made worse with exercise.
- Mental dullness and slowing of reactions and responses
- Dizziness—more like a tippy feeling, and not vertigo or purely orthostasis
- Symptoms cycle rapidly, with flares every four to six days
- Hypercoagulation is often associated with Babesia infections

- Rarely, splenomegaly
- Very severe Lyme disease can be a clue to Babesia infection, as it will make Lyme symptoms worse and Lyme treatments less effective

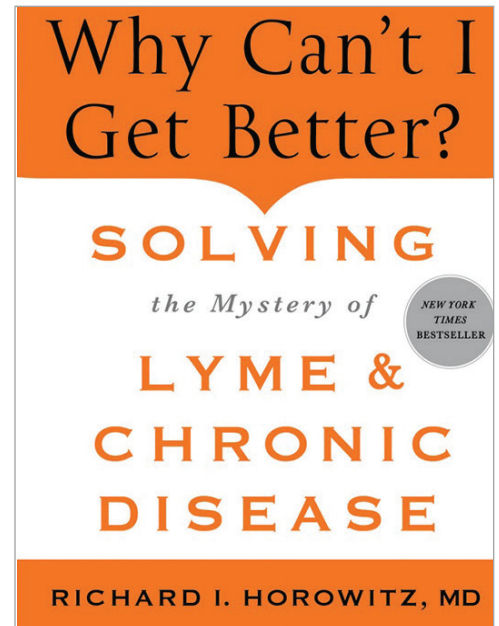
Ehrlichia/Anaplasma

- Rapid onset of initial illness with fever, headache, prostration
- Headaches are sharp, knife-like, and often behind the eyes
- Muscle pain, not joint pain, and can be mild or severe.
- Low WBC, low platelet count, elevated liver enzymes, and (rarely) inclusions seen in the WBCs
- Rarely see diffuse vasculitic rash, including palms and soles (less than 10%)
- Rapid response to treatment
- DNA Viruses (HHV-6, EBV, CMV)
- Persistent fatigue, made worse with exercise
- Sore throat, lymphadenopathy, and other viral-like complaints
- May see elevated liver enzymes and low WBCs

“ Because of the large number of these other infections, the cost of reliably testing for all of them as a matter of routine is prohibitive.

- Mycoplasma
- Gradual onset
- May be light night sweats
- Symptoms are made worse with exercise
- Major fatigue and neurological dysfunction, especially autonomic neuropathies
- Metabolic disturbances, immune damage, very low CD57 count (less than 20)
- Found in the sickest and most poorly responding Lyme patients (CFIDS-like)

In his book *Why Can't I Get Better: Solving the Mystery of Lyme and Chronic Disease*, Dr. Richard Horowitz proposes what he calls the MSIDS model. It stands for Multiple Systemic Infections Disease Syndrome and takes a broad look at how many different factors can contribute to persistent illness. In the following excerpt, he discusses several of the factors that can complicate diagnosis and treatment of Lyme disease.



WHY CAN'T I GET BETTER?

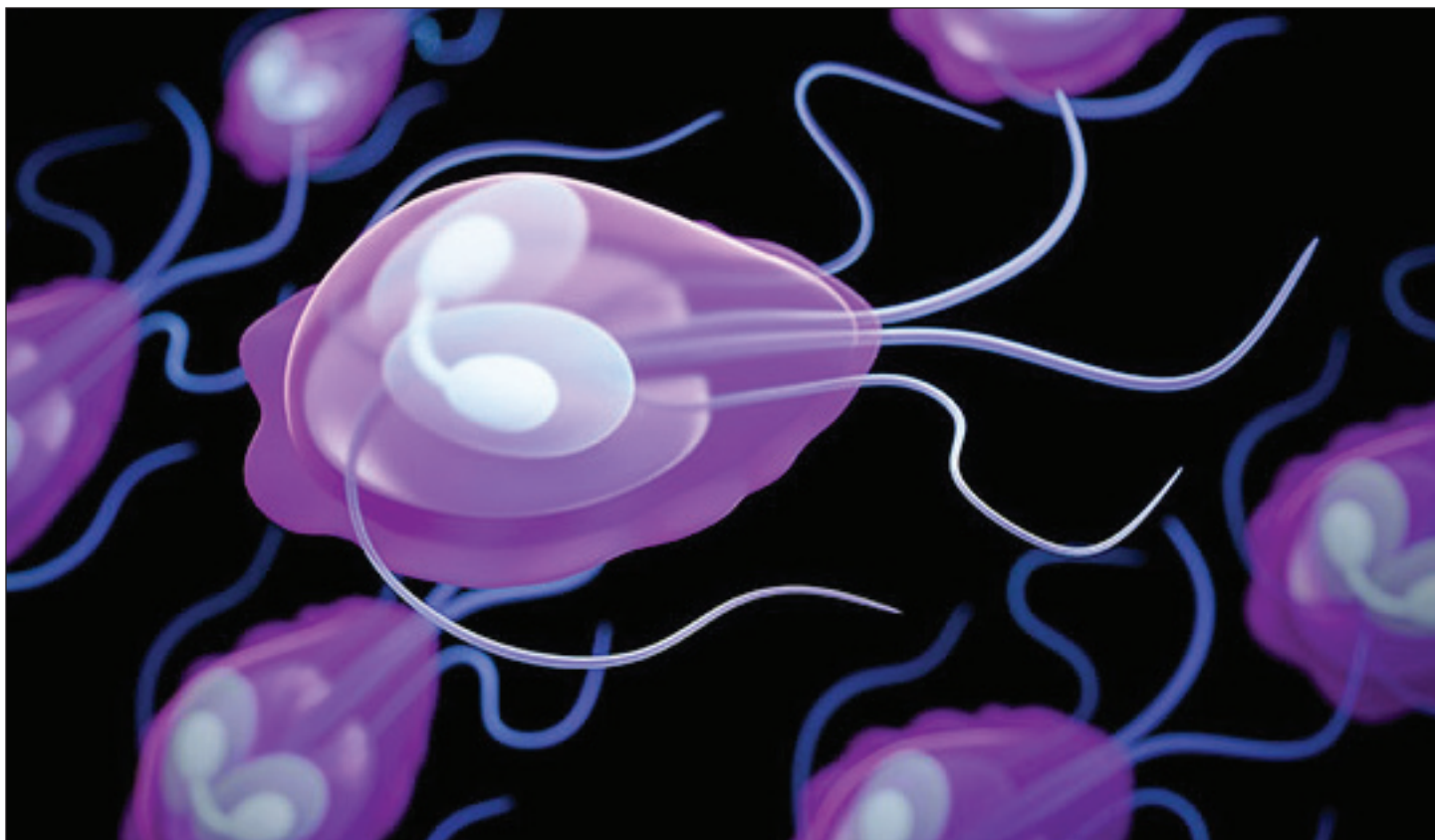
The importance of looking at parasites, viruses, yeast and fungal infections

By Richard Horowitz, MD

Parasitic Infections

Intestinal parasites like giardia, amoeba, pinworm, hookworm, schistosomiasis, and strongyloides are part of the MSIDS map. These infections are found on both serum antibody testing and stool cultures (i.e., local labs, Genova stool CDSA). Although we generally think of parasitic worms as only inhabiting the GI tract, Dr. Alan MacDonald recently found nematode filarial worms in the cerebrospinal fluid

of patients with multiple sclerosis and Alzheimer's disease at autopsy. Dr. Eva Sapi has found filarial worms in *Ixodes scapularis* ticks, and Zhang and colleagues found them in lone star ticks, so it is possible that filarial worms are being regurgitated from the gut of the tick into humans after a tick bite. Dr. Steven Fry has found parasites in the bloodstream living in biofilms, called *Protomyxoa rheumatica* (FL-1953), which are composed of up to eight different genetic types of parasites. Babesia suppresses our ability to clear other parasites, so are multiple parasites partially responsible for chronic illness in



A microscopic view of intestinal parasites giardia.

Lyme-MSIDS?

Parasites apart from Babesia can play an important role in keeping chronic Lyme patients sick, and antiparasitic regimens are often important.

Regimens including Biltricide, ivermectin, pyrantel pamoate (Pin-X), paromomycin, Alinia, and Albenza have been effective in certain patients with not only persistent GI symptoms but also fatigue, headaches, and myalgias resistant to classical tick-borne therapy. Some Morgellons patients report noticing help using antiparasitic drugs in combination with regimens against Lyme and tick-borne co-infections (like Bartonella), and some neuropsychiatric Lyme patients have seen improvement in cognition and behavior with antiparasitic drugs. Make sure you do a comprehensive parasite evaluation if you or your patient is not getting better.

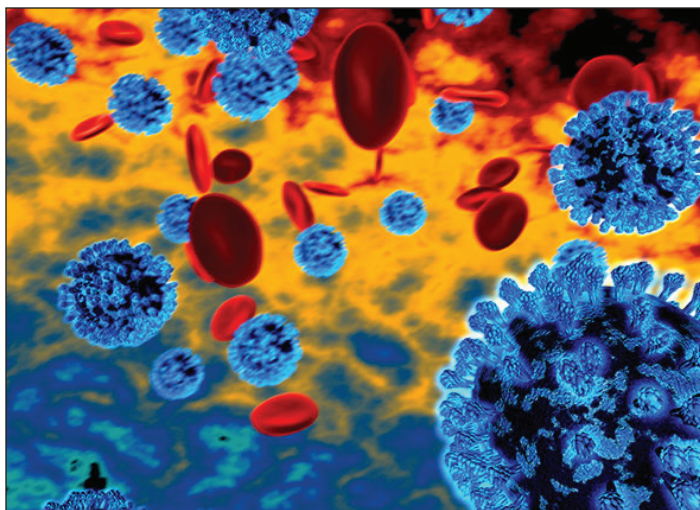
Viral Infections

Vector-borne viral infections can affect those with Lyme-MSIDS. Some of these infections are transmitted by mosquitos, such as dengue fever, Japanese encephalitis, Eastern and Western equine

encephalitis, West Nile virus, and the newer Chikungunya and Zika viruses. The Zika virus can also be transmitted by sexual contact. Others are transmitted by ticks, such as tick-borne encephalitis virus (TBEV), Omsk hemorrhagic fever, Kyasanur forest disease (KFD), Congo-Crimean hemorrhagic fever (CCHF), Powassan encephalitis, and the recently discovered Heartland and Bourbon viruses. Researchers have also isolated the Tacaribe virus, which can cause hemorrhagic disease, from 11.2 percent of Amblyomma americanum ticks in Florida. It is not known if the tick can transmit the virus to humans.

Chronic viral infections (non-tick-borne) may also explain some of the resistant symptomatology that we see among the Lyme-MSIDS population for whom antibiotic therapy fails.

Viruses do not respond to antibiotics, and some of these viruses can cause illness in patients with chronic fatigue syndrome and fibromyalgia. I often screen chronic MSIDS patients for associated viral infections, especially if they are presenting with significant fatigue, fibromyalgia, and neurological



Viral infections at the microscopic level.

symptoms. These patients may be carrying viral infections without knowing it, and once they become infected with Lyme disease and other co-infections, it may cause a reactivation of prior viral infections and an exacerbation of their condition.

The most common viral infections that we screen for include:

- Epstein-Barr
- Human herpes virus 6 (HHV-6)
- Cytomegalovirus (CMV)
- West Nile

We often find elevated levels of HHV-6, which are linked to both chronic fatigue syndrome and fibromyalgia, each of which can cause the same overlapping symptoms that we see with Lyme disease. HHV-6 also causes roseola (sixth disease) in children, and nearly 100 percent of adults today have been exposed. It can reactivate later in life secondary to immunological and environmental factors and can lead to hepatitis and meningoencephalitis, as well as being a possible cofactor in ADD, autism spectrum disorder, and multiple sclerosis.

Viruses can also affect autoimmune processes. In 2015, genetic variants of the Epstein-Barr virus were linked to multiple sclerosis, and varicella (Herpes zoster) viral infections were shown to cause an arteritis (inflammation in the arteries). Previously, CMV was shown to increase inflammation in rheumatoid arthritis.

We also will occasionally screen for HHV-8, Cocksackie virus, and parvovirus. Enteroviruses have been linked to neurological disorders with tics, implicating an immune-inflammatory reaction in

the pathoetiology of certain brain disorders (like PANS/PANDAS). We may also look for Powassan encephalitis or other types of viral encephalitis if the patient is coming in with a particularly severe neurological presentation. The Powassan virus is now found in increasing numbers of ticks in different areas of the United States (including the Lower Hudson Valley, where I practice) and can be transmitted in as little as 15 minutes of a tick attachment. It can cause fevers, seizures, focal neurological findings, neurological deficits (including loss of consciousness), hemiplegia (paralysis of half of the body), and neurological consequences, including mental status changes, visual deficits, hearing impairments, and chronic motor difficulties.

Nutritional Supplements Help with Viral Infections

Nutritional Supplements Help with Viral Infections Lyme disease patients often report that they feel worse and that their symptoms flare up when they come down with viral infections. It is as if their immune system can only effectively fight so many infections at the same time. Nutritional supplements may help, although most do not see a strong clinical shift in their symptoms. The following supplements have known scientific efficacy against viruses:

- Colostrum derivatives, such as transfer factors: antibodies that protect against disease and are produced by mammals during lactation.
- Olive leaf extract: Olive leaves and their active component, oleuropein, have been found effective in treating herpes, influenza A, Cocksackie, and other viruses.
- Mushroom derivatives, including 3–6 beta-glucan: The immune-enhancing properties of the yeast beta-glucan have been the subject of more than 60 years of research and more than 800 scientific studies.

Preclinical research has shown 3–6 beta-glucan to be efficacious against a range of infectious diseases. Beta-glucan's primary effect is to increase natural killer (NK) cells and the phagocytic capacity of immune cells, and to enhance the movement of these



Supplements to help the treatment of candida infections

cells to the site of a foreign challenge throughout the body via the liver, spleen, and lymph nodes. Clinical research has shown it to have synergistic effects with antibiotics (JH reactions are possible), and 3–6 beta-glucan has been shown to be superior to most other immune supplements. It is therefore useful for those with Lyme-MSIDS fighting bacterial and viral infections with a healthy immune system.

Treating Viral Infections

There is no specific treatment for tick-borne viral encephalopathies like Powassan encephalitis, except supportive treatment, and HIV medications are being studied as a possible option for these patients.

Anyone who does not adequately respond to appropriate antibiotic protocols while addressing the 16-point differential on the MSIDS map, and who has high viral titers and/or a positive PCR, may suffer from viral infections that may have been present and/or reactivated, and a trial of antiviral medication is warranted. This could include Valtrex, Famvir, acyclovir, or Valcyte in severe cases. In our experience, classical antiviral drugs such as Valtrex and Famvir do not have a significant clinical effect in the majority of MSIDS patients, except in preventing frequent relapses of herpes viruses. Occasionally Byron White herbal remedies against viruses, such as A-EB/H6, are helpful.

Candida And Fungal Infections

Candida syndrome with intestinal dysbiosis (a microbial imbalance in the gut) is not an uncommon health problem. It should be suspected in any MSIDS patient who has unexplained fatigue, joint and muscle

pain, and neurological symptoms such as brain fog and headaches that are unresponsive or worsen with standard treatment regimens.

I first learned about candida many years ago after one of my patients had developed a strange set of skin rashes that worsened every time she took antibiotics. She also complained of chronic fatigue, headaches, blood sugar swings, trouble concentrating, and digestive problems. In searching for answers, I came across William Crook's book, *The Yeast Connection*. In it he described my patient's symptoms perfectly. By placing her on a yeast-free diet and treating the candida with antifungal agents, we were able to reverse all of her symptoms, which had baffled dermatologists and other subspecialists who had been unable to find a cause.

Although we normally have candida organisms present in our gastrointestinal tract in limited amounts, taking antibiotics for bacterial infections will encourage an overgrowth of candida.

Antibiotics kill off the good bacteria that keep our normal level of yeast in check. Furthermore, the standard American diet, which is high in sugar and refined carbohydrates, can promote an overgrowth of yeast. Other factors that may contribute to the candida syndrome are:

- Oral contraceptives
- Immune suppression due to stress
- Severe illness or chemotherapy
- Drugs that decrease the acidity of the gastrointestinal tract, such as antacids, H2 blockers (such as Zantac), and proton pump inhibitors (such as Prilosec).

Candida can be confused with antibiotic-resistant Lyme disease. Many patients with adrenal dysfunction and associated hypoglycemia also suffer from candidiasis. These symptoms overlap with those of persistent Lyme disease (except in Lyme there is migratory pain, where symptoms come and go). The most common signs and symptoms of candidiasis include:

- Blood sugar swings with overlapping reactive hypoglycemia and a craving for sweets
- Depression



A microscopic view of a candida fungal infection.

- Dizziness with poor motor coordination
- Fatigue
- Fungal infections of the nails
- Gas and bloating, which increase with sugar/carbohydrate consumption
- Headaches
- Itching and other skin problems
- Mood swings
- Muscle and joint pain that does not migrate throughout the body
- Poor digestion with nausea
- Poor memory and concentration (brain fog)
- Rashes
- Thrush in the mouth (yeast on the tongue and buccal mucosa, which appears as a white, patchy coating)
- Vaginitis (recurrent vaginal yeast infections)

If you have been tested with both an IgE and IgG food allergy panel and found to be allergic to a multiplicity of foods, suspect overlapping candida and leaky gut syndrome, especially if there is histamine release with associated itching, sneezing, wheezing, and/or nasal congestion after eating certain foods. Pay particular attention to your diet and the acid/alkaline

balance of your foods, avoiding allergic foods by following a rotation diet. A comprehensive digestive stool analysis (CSDA) can also be performed through various labs such as Genova Diagnostics to check for bacterial and yeast overgrowth in the stool, while checking yeast sensitivities to antifungal agents.

Treating Candida and Yeast Infections

The most important dietary modifications for dealing with yeast are to eliminate malt, vinegar, simple sugars, and carbohydrates (including fruits early on in the treatment), as well as all yeast-containing foods (most breads and cheeses) and fermented foods (e.g., soy sauce, tempeh, pickles, sauerkraut, and alcoholic beverages such as wine, beer, and cider). Mushrooms should also be avoided (they are fungal, which is a form of yeast), as well as any foods to which you are either sensitive or allergic.

We prescribe nystatin prophylactically if patients need to be on longterm antibiotics, to avoid issues with yeast overgrowth, but often the tablet form of nystatin is insufficient in dealing with severe yeast problems once they have arisen. Powdered nystatin is more effective than tablets, and should be used in cases of severe candida.



***Clostridium difficile* bacteria**

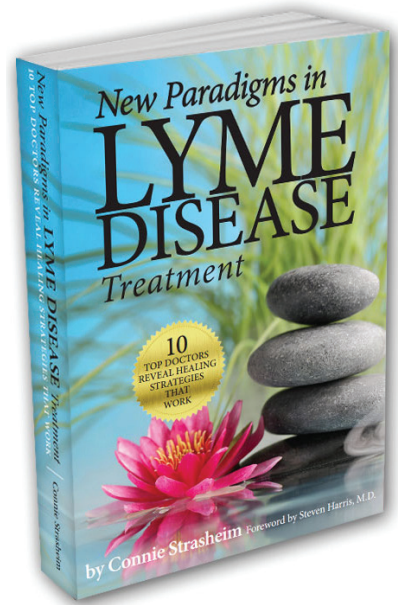
Despite explaining the necessity of a strict, sugar-free, yeast-free diet to our patients taking antibiotics, they often have a difficult time adhering to this regimen.

Therefore, we sometimes use rotations of antifungal medications such as Diflucan and, rarely, Sporanox. These medications can be very effective, but potential side effects include inflammation of the liver and cardiac symptoms (EKG abnormalities) requiring proper monitoring. If these medications are ineffective or are contraindicated, natural antifungal agents, such as caprylic acid, grapefruit seed extract, garlic, berberine, and oregano oil can be helpful. We also frequently use monolaurin, a biofilm-busting coconut oil extract with antibacterial, antiviral, and antifungal effects, as well as Biocidin with broad spectrum botanicals for intestinal dysbiosis. When combined with good-quality, high-dose probiotics (lactobacillus and/or Bifidobacterium) they can be extremely beneficial in restoring the proper balance of intestinal bacteria and yeast in the colon. We use several strains of high-potency acidophilus and choose brands that are acid resistant and/or coated with sodium alginate to increase the amount of acidophilus

that colonizes the small and large intestines.

Not all forms of yeast are detrimental. Apart from prescribing high doses of good-quality probiotics, and occasionally prebiotics containing fructooligosaccharides (FOS) to prevent antibiotic-associated diarrhea, we also give patients *Saccharomyces boulardii*, a type of beneficial yeast that has been shown to decrease the incidence of *Clostridium difficile* diarrhea. *Clostridium difficile* is a bacteria responsible for 95 percent of pseudo-membranous colitis and 30 percent of all antibiotic-associated diarrheas. *Saccharomyces* is a healthy yeast that acts as a temporary barrier protecting the intestinal mucosa. A 2009 study published in *Infection and Immunity* showed that *saccharomyces* has a protease that inhibits the effects of *Clostridium difficile* toxins A and B. *Clostridium difficile* has the potential to be life threatening. It is therefore very important to protect against this possibility by using high-dose probiotics and *Saccharomyces boulardii* during antibiotic therapy.

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Dr. Wayne Anderson Offers a Closer Look at Six Lyme-Related Infections

From *New Paradigms in Lyme Disease Treatment*

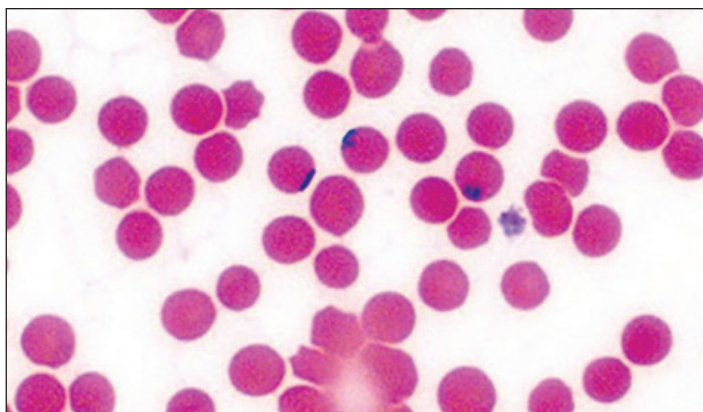
By Wayne Anderson, ND and Connie Strasheim

I've learned through experience that each Lyme disease pathogen causes a specific set of symptoms in the body, and that I can readily identify infections in my patients by analyzing their symptoms. In the following sections, I describe typical symptom patterns of six of the most common Lyme-related infections. I encourage doctors to refer to this section when trying to identify which infections are dominant in their patients.

These symptom patterns should only be used as a guideline for diagnosis since no two people are exactly

the same, and symptoms will vary from person to person. Neurotoxins from these infections all cause inflammation in the brain and nervous system and cause similar symptoms and compromise the body's function in a similar way. Yet, each microbe often will manifest its own unique traits or personality.

Understanding the different symptom patterns that the microbes cause is especially important since lab tests for Lyme disease aren't adequate (although they have improved greatly in recent years). Diagnosis also can be complicated by the fact that people's immune systems respond differently to infection, according to their life stressors and metabolic strengths and weaknesses. Doctors should look for patterns in their patients and always appreciate that treating people with Lyme disease is about shades of gray, because the infections create symptom pictures that are never black



A close up look at the Babesia bacteria.

and white.

Babesia or Babesia-like Organism (BABLO) Symptom Patterns

Babesia or Babesia-like Organism (BABLO) Babesia, or Babesia-like organisms (BABLO) primarily affect the brain and autonomic nervous system. The first words that a patient with active Babesia-like organisms in his body might say are that he can't focus or think. His cognitive function is significantly compromised, and his mood is almost always affected. Both depression and anxiety are very common. A person with Babesia has a lot of emotional upheaval; fear is a dominant symptom.

Babesia also can affect the autonomic nervous system, which is responsible for much of the "automatic" functions of the body, such as heartbeat, breathing, etc. This means that the communication between the brain and body is affected, so any physical symptoms that patients have from Babesia can be related more to autonomic nervous system dysfunction rather than the organisms themselves. For instance, Babesia can cause postural orthostatic tachycardia syndrome (POTS); a racing heart at rest and/or an irregular heartbeat and heavy pounding heart at night, but the problem isn't in the heart. The problem is that the autonomic nervous system isn't functioning properly.

Shortness of breath is also common, because people with Babesia don't regulate their oxygen-saturation flow properly due to problems in the autonomic nervous system (ANS). Such people feel a sense of "air hunger" because the ANS isn't dilating their bronchial tubes or opening their diaphragm

properly, because these parts of their body are not getting the signal to do so from the command center in brain.

Additional symptoms of Babesia include lots of drenching sweats and chills. Babesia is a relative of the malarial organism and is part protozoan and part bacteria. So as with malaria, people can get terrible chills and lots of sweats and basically feel like they are going crazy. People with Babesia are often quite chilled and can't get warm and will have to take a hot shower or jump in a bathtub to warm up. The temperature de-regulation is again related to a dysfunctional autonomic nervous system. So, people either can't get warm, or they get too hot. They turn down the thermostat at night because they are too hot, but then they get too cold while in bed and so turn it back up by a degree. They freeze when going to bed and throw the covers on; then, in the middle of the night, they get boiling hot and throw the covers off and drench their bedclothes in sweat.

Insomnia is common as Babesia affects the sleep center in the brain. Other symptoms include blurred vision, bowel-motility issues and bladder difficulties. People with Babesia will either have trouble starting their urinary stream or will go through episodes of incontinence. They may also have problems with bowel motility; usually constipation, but can also sometimes have diarrhea due to autonomic nervous system de-regulation. A dominant Babesia infection also can affect certain areas of the wrists, hands, ankles and feet. These areas can be painful, numb or experience temperature extremes.

Babesia does not generally cause pain in the body, so if a person has pain, then it's usually due to another problem. The picture is always complicated though because people with Babesia who have a compromised detoxification system will have pain in their body as a result of poor waste removal. But, the pain is not from the infection itself.

These are what I call clearly identifiable Babesia symptoms in those patients who have an immune system that is not terribly depleted or who don't have a compromised detoxification system or other conditions or infections that are currently active and which could complicate the symptom picture. The same holds true for the symptom patterns of all of the other infections described here.

Bartonella or Bartonella-Like Organism

(BLO) Symptom Patterns

Many people have Bartonella or Bartonella-like (BLO) infections in their bodies. They are perhaps the most abundant infections in people because many veterinarians say that 80 percent of all house cats and nearly 100 percent of all hunting cats carry Bartonella microbes. Fleas bite cats and infect them with the Bartonella-like organisms, which are then transmitted to humans when they get bitten by the flea. Bartonella and BLO infections are therefore probably the most common of the vector-borne Lyme disease co-infections.

People who have active Bartonella symptoms have much more pain than people who are manifesting

“Many people with Bartonella infections are misdiagnosed as having bi-polar disorder due to their fluctuating moods; they can easily go from being angry and irritable to being depressed.”

predominantly Babesia-related symptoms. The first thing out of their mouths is usually, “You have to help me with my pain.” They have pain in their joints and the connective tissue around their joints. This joint pain will migrate to other areas of the body. So for instance, patients with active Bartonella might have knee pain, but just when they are about to go to the doctor for the pain, the pain will migrate to the left elbow. The hallmark symptom of Bartonella is

sensitivity and tenderness on the bottom of the feet, especially the soles.

Generalized pain in the body, or pain that is sharp and severe, is often related to Bartonella. Bartonella can also cause headaches and ice pick-like pain. Both Babesia and Bartonella cause headaches, but Bartonella headaches are worse. A Babesia headache produces more weird sensations in the head and pressure in the head. People with active Babesia infections will say, “I



A microscopic view of the Bartonella bacteria.

don't know if I'd really call what I have a headache. It's more like a pressure in the head.” Babesia can cause migraines as can Bartonella, but Babesia migraines are generally less severe. Bartonella prefers the occipital areas of the head; the back of the head and neck are generally painful. So pain is a dominant characteristic of Bartonella.

All of these slow-growing intracellular infections affect the brain but create different symptom patterns, according to which infection is dominant or most active. I see more depression in people with active Babesia but less variability of mood, whereas people with active Bartonella may be irritable and anxious but then “flip over” into depression. Many people with Bartonella infections are misdiagnosed as having bi-polar disorder due to their fluctuating moods; they can easily go from being angry and irritable to being depressed.

Bartonella-like organisms can also stay on the surface of the organs and tissues and cause a wide array of symptoms. One such symptom is gastritis. In fact, most cases of gastritis that aren't caused by Helicobacter pylori infections are often caused by Bartonella, which is the second-most common cause of this condition. It can irritate the stomach so that people lose their appetite and/or get heartburn.

Many people with Bartonella infections are misdiagnosed as having bi-polar disorder due to their fluctuating moods; they can easily go from being angry and irritable to being depressed.

Bartonella can cause a low-level, relapsing sore throat. People with active infections will periodically awaken with sore throats and wonder if they are coming down with a cold, but then the sore throat will

go away.

Bartonella irritates the bladder and can cause frequent urination, interstitial cystitis, or other chronic inflammatory conditions of the urinary system.

Bartonella can also cause fevers, but for patients to be able to run a fever, they need to have a relatively functional immune system, so not everyone who has a *Bartonella* infection will get a fever. Yet people will often feel hot, as if they have a fever, but their body temperature may be below normal.

Bartonella can affect the eyes and cause conjunctivitis, or inflammation of the outermost layer of the eye, which results in irritated, dry red eyes, as well as other eye problems.

Bartonella causes more skin-related problems than the other infections. Red bands or stretch marks on the skin called striae are common, as are acne and other skin problems.

Bartonella lives in the liver and spleen where it inflames these organs and compromises their functioning. When the liver and spleen are inflamed, the filtering capacity of the blood is affected, resulting in thick blood. People with *Bartonella* may have slightly elevated liver enzymes on lab tests. For instance, the alanine aminotransferase (ALT) test score may be just outside of the normal range and high only intermittently. The inflammation that *Bartonella* causes in the liver and spleen can compromise the body's detoxification system in a major way. When the spleen is compromised, the lymph glands may also become swollen, which then causes the lymph flow to become thick, sludgy and slow.

Borrelia Symptom Patterns

Borrelia symptom patterns are a bit harder to define because this organism isn't as aggressive as the others. The distinguishing symptom that it causes is fatigue; people who have active *Borrelia* symptoms tend to have more fatigue than those whose predominant symptoms are due to *Bartonella* or *Babesia*. People with active *Babesia* and *Bartonella* are much more restless than those with active *Borrelia* infections. All of the infections cause exhaustion; that is ubiquitous within the entire family of neurotoxin infections, but *Babesia* and *Bartonella* cause more restlessness, whereas people who are primarily manifesting *Borrelia* symptoms are often more tired. Feeling "wired and tired" is common with all the



Borrelia bacteria in the blood.

neurotoxin diseases, so I am really just focusing on the shades of gray here.

Borrelia causes pain, but the pain is much more diffuse and spread throughout the body. It also can be muscle-related and fibromyalgia-like, rather than primarily in the joints, as with *Bartonella*. However, doctors and patients need to keep an open mind when it comes to diagnosis and not over-generalize about symptom patterns. For instance, there is a subset of *Borrelia* patients who have arthritic-like symptoms and lots of inflammation in their joints, although I see this maybe less than 10 percent of the time.

The symptoms of *Borrelia* can be a mixture of a little of what's found in all of the other Lyme-related infections.

Borrelia affects the nervous system, but it's a bit more "ghost-like" in the symptoms that it causes, so it's not as defined or specific. If patients have been adequately treated for *Babesia* and *Bartonella* infections and have only 20 percent of their symptoms remaining, such as a bit of fatigue, achiness and brain fog, I might suspect that they still have some *Borrelia* microbes that need to be addressed.

Lyme microbes are smart and are looking for hiding places in the body; they want to be invisible and disguise themselves from the immune system. This means that they don't stay in the blood for long and quickly go to areas of poor circulation, to avoid being attacked by the immune system. Their goal is to lull the intracellular environment into complacency. For instance, *Borrelia* is able to change its form and alternate between the spirochete, cell-wall deficient and cyst forms as a way of confusing and hiding from the immune system.

Mycoplasma Symptom Patterns

Mycoplasma is an interesting organism that is also found in nearly everyone with Lyme disease. It's very small, like a virus, and some researchers believe that it is really a cross between a virus and bacteria. It can accumulate on the endothelial lining (which is comprised of cells that line the blood and lymphatic vessels) and cause inflammation and pain.

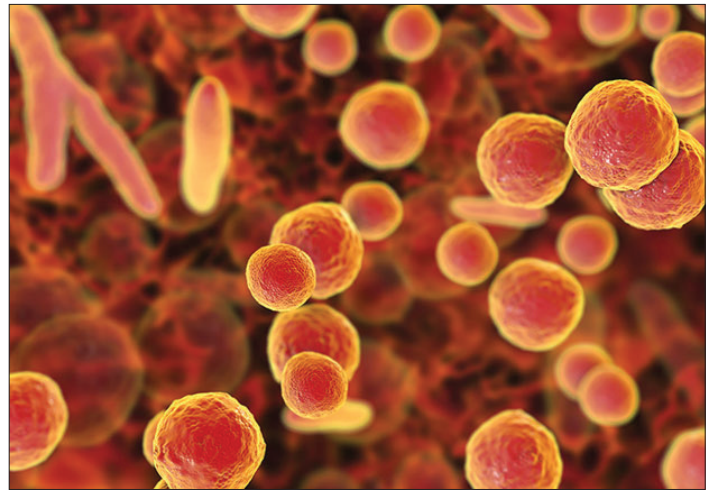
This means that people with dominant Mycoplasma infections can get migraine headaches because the infections irritate the vascular system in the brain. Or, people might have inflammatory gut or lung issues because the microbes are active on the endothelial lining of the gut and lungs. They can also be prominent in the bladder. Interstitial cystitis, or bladder inflammation is caused more often by Mycoplasma, but can also be caused by Bartonella.

Mycoplasma can cause a minor cough when it is in the lungs; not the more extreme cough that's caused by a cold or flu, but the kind of cough that occurs whenever a person takes a deep breath or laughs. People with Mycoplasma feel a little winded and may have mild inflammation in their chest. Mycoplasma can irritate the throat and cause a low-level sore throat. It also goes deep into the body and can affect the joints, connective tissue and cartilage. A rare and aggressive form of Mycoplasma can cause symptoms of rheumatoid arthritis and result in severe joint swelling and deformity.

Some German researchers believe that Mycoplasma exists in everyone in a benign form, and that it's one of trillions of bacteria that colonize the body. However, when the immune system becomes compromised, and the body's "compost heap" gets too full, then the Mycoplasma mutates into a pathogenic form and harms the body. So instead of living in harmony with us, it begins to inflame us and feed on us. I mentioned that *Borrelia* causes fatigue, but Mycoplasma is the most fatigue-causing Lyme disease-related pathogen there is.

I have found that if I have already treated my patients for all of the dominant Lyme disease co-infections, and they are even more tired than before, and their joints are all of a sudden stiff and achy, then this means that they may have a dominant Mycoplasma infection that is currently causing their symptoms.

As I mentioned earlier, the immune system prioritizes and focuses on the microbe that it currently



A microscopic view of Mycoplasma.

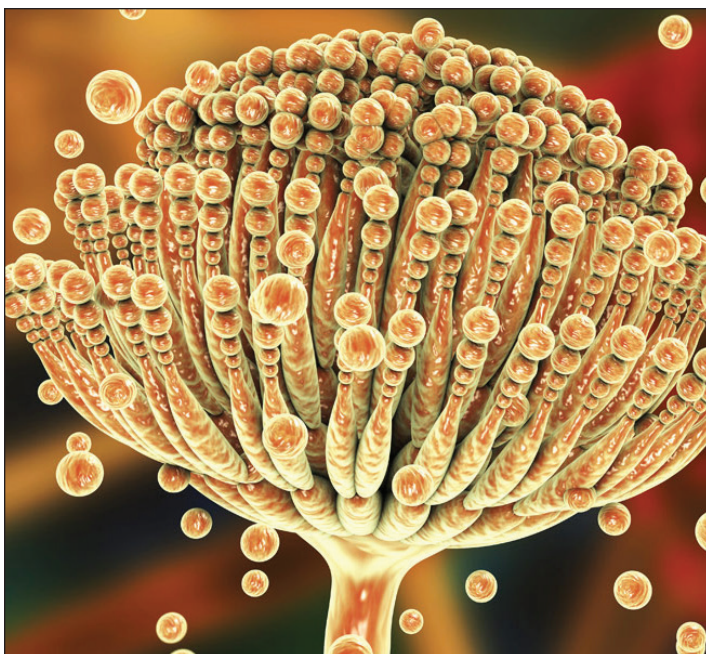
perceives to be most dangerous to the body. This means that it will often bring out Mycoplasma-like symptoms after some of the other infections, since Mycoplasma does not inflame the brain and nervous system as much as the other infections. The immune system will always protect the brain at all costs, and simplistically speaking, it does not perceive Mycoplasma to be as dangerous as some of the other co-infections; therefore, it is usually a deeper layer of infection that the immune system focuses on later in the treatment process.

Since it inflames the brain less than the other infections, people with active Mycoplasma also don't have as many cognitive problems as people with active *Babesia* or *Bartonella* or as much mood instability. Mycoplasma likes to live in the fascia layer of the skin, which is directly beneath the top layer of the skin. So people with Mycoplasma might have a crawling feeling under their skin or their skin might feel sensitive to the touch. In addition, they might have a variety of unusual rashes. Because patients with active Mycoplasma have sensitive skin, they may not like to be massaged.

Mold Symptom Patterns

Mold illness is a common co-condition in people with Lyme disease, but the medical community has generally underappreciated its effects upon the brain and immune system. Mold affects the body in the same way as the bacterial infections that I have so far described, in that its toxins stick to the surface of the cells and are absorbed into the cells, where they cause inflammation and cellular dysfunction.

The organs and systems that are most affected by mold are the self-regulating systems of the brain



A representation of mold spores.

and nervous system, as well as the endocrine, gastrointestinal and immune systems. Lyme and mold affect the immune system in the same way, and when one of these conditions is present in the body, the body becomes more susceptible to the other. In addition, 23 percent of all people have a genetic susceptibility to mold illness that can be determined by doing certain lab tests (more on this later).

Mold toxicity is important for people with Lyme and their doctors to understand because it can cause serious illness and compromise recovery from Lyme.

People who have been exposed to mold will be affected by the mold in a couple of different ways. Some lucky people, whenever they are exposed to a moldy environment, will have an immediate immune reaction; they will feel dizzy and spacey and quickly learn that they need to get out of the moldy environment. A second group of people will be less aware that they have been exposed to mold, and the spores that they inhale will stick to the mucus membranes in their sinuses, lungs and gut and colonize there. If this latter group has a genetic susceptibility to mold, they will have a greater chance of getting symptoms from mold exposure.

Mold and biotoxin expert Ritchie Shoemaker, MD, has established a set of criteria that doctors can use to determine their patients' susceptibility to mold illness. One of these involves evaluating a certain HLA DRB gene pattern, the testing for which is done by Lab Corp.

Mold toxicity is important for people with Lyme and their doctors to understand because it can cause serious illness and compromise recovery from Lyme.

A healthy immune system and body that are not genetically susceptible to mold are designed to “zap” the mold upon its entry into the body so that it cannot colonize there, but in certain immune-compromised people, it is able to colonize. Once this happens, it's very hard to dislodge. Once it's in the body, it produces toxins, called mycotoxins, which inflame the body.

Over time, the mold takes over increasingly greater areas of mucous membrane in the body and always ends up finding its way to the bowel. The bowel is dark, moist and nutrient-rich, making it a hospitable place for mold to grow. And the more compromised and damaged the good bacterial community (microbiome) on the endothelial lining of the bowel is from Lyme and other factors, the easier it will be for the mold to expand its territory there.

Anytime the mucus membranes of the body are inflamed – whether in the nose and sinuses, gut, lung, bladder lining, skin, or the vagina – mold colonization should be suspected. The person who is unlucky enough to have high mold toxin levels will have symptoms that can be difficult to differentiate from those of Lyme disease. Like Lyme toxins, mold toxins stick to the cell membranes and then ooze into the cells, where they accumulate and add to the body's cellular compost heap.

Mold organisms cannot live just anywhere in the body though; they are confined to the mucous membrane surfaces, and it is their waste products, or the mycotoxins, that enter the bloodstream and cause systemic symptoms. Consequently, the symptoms of mold toxicity are not as dynamic and variable as the symptoms caused by the adaptive Lyme microbes. Instead, they are more dull and flat. So if patients have seesaw symptoms; meaning, they get better for a while, then get worse, or have two or three good days, followed by three weeks of feeling terrible, then their symptoms are less likely to be mold-related.

In people who are predominantly battling mold toxicity, every day is the same; they struggle to get through the day and have low energy and a mild amount of brain fog. This pattern is fairly consistent. Mold also affects the brain and nervous system, so people with mold illness will have specific neurological symptoms. Neuropathies (damage or problems with the nerves) are common. Symptoms may include numbness or tingling in the hands and feet. Mold toxicity also causes a lot of depression, so when people

have a Herxheimer reaction from mold detox (removing cellular mold with toxin binders and other therapies), depression may intensify along with other mold symptoms.

Mold symptom patterns can vary and are always worse during wet or humid seasons when mold thrives. Remember, the effects of neurotoxins are additive and cumulative. So, when brain fog or another mold symptom is added to the brain fog caused by Babesia, Bartonella, heavy metals, petrochemicals or Borrelia, the effects of each organism or toxin may compound those of the others. So, people with significant brain fog probably have more than one factor or infection causing that symptom.

Rickettsia Symptom Patterns

Rickettsia is another class of common Lyme disease co-infection that has been largely underestimated or unappreciated by the medical community and which I still have not understood fully myself. Ehrlichia is a type of Rickettsia infection that most Lyme doctors are familiar with, but most of us are not familiar with the hundreds of other types of Rickettsia that can cause disease. We got lucky with Ehrlichia since there are just two species of this organism that we know of, and there is a lab test that can identify both of them.

Yet, there are many other families or species of Rickettsia that are quite harmful and for which tests do not exist. The one that we know about is Rocky Mountain spotted fever (RMSF). The infectious disease community believes that RMSF is limited to specific regions of the United States. Lyme-literate doctors didn't worry much about it initially. However, more recent evidence has shown that there are probably over 1,000 Rickettsia species, and that Rickettsia infections are more common and less regional than we had previously believed.

There can be an overall congested feeling in the body.

Rickettsial organisms are simpler than the dynamically changing Borrelia. They don't seem to have multiple growth stages or as many forms as Borrelia; there are no cell-wall deficient forms, for instance. Therefore, they may be easier to treat, but we Lyme disease practitioners need to have a higher index of suspicion about their presence before we can learn how to adequately treat them all.

I'm still honing in on the specific symptoms

that Rickettsia causes and distinguishing those from the symptoms of the other infections. I have some preliminary impressions about them, though. For instance, I've observed that people with Rickettsia can have a variety of skin and scalp rashes, the hallmark symptom being a rash on the palms and soles.

Rickettsia also causes stagnant, thick blood and congested circulation, which causes the blood vessels to become inflamed and results in blotchy and mottled skin. There can be an overall congested feeling in the body. Edema is common: people who have puffiness in their ankles or puffy faces and/or eyes when they awaken may have congested circulation due to Rickettsia.

Rickettsia commonly causes headaches. Cognitive problems, such as trouble focusing and concentrating, are generally not as common in people with active Rickettsia as in patients who are manifesting other Lyme co-infections such as Babesia and Bartonella. All of these infections can cause a bit of forgetfulness, but a person with Rickettsia will not think they have Alzheimer's like a person with Babesia and won't tend to get lost while driving home.

Rickettsia causes injected (red) blood vessels on the surface of the eye, unlike Bartonella, which causes a uniform redness. Some people have difficulty focusing their eyes and a blurriness described as "feeling like they are under water."

However, the most prominent symptom of Rickettsia is musculoskeletal problems. People with these infections have lots of numbness, tingling and joint pain in addition to achy muscles. Therefore, when patients' symptoms are vascular, musculoskeletal and less brain-related, then their doctors should suspect that they have a Rickettsia-like symptom presentation.

In Rickettsia, the lymphatic system is also more congested, as evidenced by areas of puffiness in the skin. This is because when the blood is "mucked up," the lymphatic system will try to clean it. So, picture for a moment, that the lymph is like a drainage ditch on the side of the road and that the blood is the road. If you get a hard rain, the road will drain water into the drainage ditch. Similarly, the body will dump any "gunk" from the bloodstream that is not being adequately filtered by the liver into the lymph system to try to keep the blood as clean as possible.

New Paradigms in Lyme Disease Treatment, is published by BioMed Publishing Group, LLC; www.Lymebook.com.



Bartonellosis:

An Emerging Infectious Disease of Zoonotic Importance to Animals and Humans

By Edward B. Breitschwerdt, DVM

Over the past three decades, substantial scientific evidence has begun to elucidate the emerging biomedical importance of the genus *Bartonella* and the disease bartonellosis. Our team of comparative infectious disease researchers at the North Carolina State University Intracellular Pathogens Research Laboratory has generated scientific publications related to bartonellosis in cats,

cows, dogs, dolphins, horses, human beings, river otters, sea turtles, sheep, whales, and other wildlife species. The evolving research findings from around the world have left me with the following question:

Is Bartonellosis a modern-day hidden epidemic?

If so, how could a disease of epidemic proportions involving both animals and human patients be missed

or remain hidden from diagnosticians, other scientists, physicians, and veterinarians for more than 100 years or perhaps an even a much longer period of medical history?

How much pain and suffering could have been avoided if the “hidden epidemic” called bartonellosis had been discovered sooner?

What has been the emotional, medical, occupational, and financial impact of historically undiscovered *Bartonella* species (now 38 named or candidatus species have been characterized) infections among patients with bartonellosis throughout the world?

How can an epidemic be hidden?

Hiding an epidemic caused by a genus of bacteria may be easier than one might think. First you would start with a bacterial genus that was essentially not known to exist prior to the 1990s (with the exception of two historically important *Bartonella* species, *Bartonella bacilliformis* and *Bartonella quintana*, the cause of Carrion’s Disease and Trench Fever, respectively). Next, the bacteria in question would have evolved effective mechanisms to avoid immune recognition and thereby behave as a stealth pathogen (i.e., bacteria that can fly under the radar like a stealth bomber).

In addition, Mother Nature might “design” this stealth bacterium with inherent attributes that facilitate effective maintenance of a persistent but relapsing intravascular infection (an infection involving erythrocytes, the immune cells that circulate within the blood, and the cells called endothelium that line the blood vessels), as well as long-standing dermal infections that facilitate transmission to new blood-seeking vectors.

Over time (perhaps tens of thousands of years), these stealth bacteria would differentiate genetically to selectively evolve and preferentially infect a large number of very specific animal reservoir hosts in nature.

Importantly, during evolution, these stealth bacteria would use a broad variety of insects and arthropods to facilitate transmission among the various animal populations.

Opportunistically, those arthropods (flea, sand fly, and tick bites, as examples) would periodically transmit the bacteria directly to humans and other non-

“How much pain and suffering could have been avoided if the “hidden epidemic” called bartonellosis had been discovered sooner?”

reservoir-adapted animals. Finally, to progress from periodic and infrequent infections to an epidemic, you would modify human behaviors to facilitate closer contact among the vector, the reservoir hosts, and human beings. As this epidemic has likely been ongoing throughout the history of mankind, minimal changes in human behaviors were needed to facilitate epidemic numbers of unrecognized infections with various *Bartonella* species.

From a microbiological perspective, the ideal stealth organism would have very specialized growth requirements and a very long dividing time (slow bacterial replication), which would greatly contribute to a historical inability to isolate these bacteria in microbiology laboratories throughout the world, especially when using well-established and standardized diagnostic isolation techniques. Finally, these stealth bacteria would not induce a consistent or predictable pattern of illness in animals or human patients, thereby avoiding discovery because doctors would not appreciate a defined disease pattern indicative of infection with a specific disease-causing agent. By the very nature and derivation of the word, epidemics are generally recognized when a substantial number of individuals within a defined population develop a similar disease pattern.

In many instances, the onset of illness occurs within a relatively short period after acquiring the infectious agent (for example, influenza), thereby facilitating rapid recognition of a definable disease pattern. One way to miss an epidemic is to have the offending infectious agent induce variable disease

symptomatology months to years after transmission, which would interfere with a clinician's ability to use pattern recognition (as is typically done by infectious disease physicians and veterinarians) in an effort to correlate disease symptoms with a specific infectious agent.

Most pathogenic organisms (estimates include 60-75% of all known or emerging pathogens) are zoonotic, meaning the same organism can infect or induce disease in an animal and a human being. In some instances, the animal serves as a reservoir (a healthy animal that carries the organism in the blood, intestinal tract, skin, or urinary system, often for extended periods of time) for human infection, but, in many instances, the pathogen is opportunistic (i.e., takes advantage of low immune defenses) and induces disease of similar severity in animals and people. As a reservoir host for vector-borne organisms, animals maintain organisms primarily within the blood and the dermis (skin), and in most instances these organisms, which can be very prevalent in nature, do not induce disease in the animal reservoir host.

These same organisms (bacteria, protozoa, rickettsiae, viruses) can be mildly to highly pathogenic when introduced into a non-reservoir host.

Examples include children whose immune systems have not completely developed, the elderly who experience immune senescence (a natural progressive deterioration of immune function with advanced age), or other individuals within modern-day society who are immunocompromised due to HIV, alcoholism, or therapeutically to treat an immune-mediated disease (e.g., systemic lupus erythematosus, multiple sclerosis, rheumatoid arthritis). Thus, stealth organisms of low pathogenicity (low disease-causing potential) can induce chronic and insidious, or acute, serious and potentially fatal illnesses.

Because of improved science and diagnostic testing modalities, bartonellosis is now being documented in transplant recipients and in people and animals historically treated for autoimmune conditions with immunosuppressive drugs. Previously, these conditions were not accurately diagnosed as an infectious disease, as bacterial members of the genus *Bartonella* were not known to exist throughout North America and much of the world prior to the AIDS epidemic in 1990, another epidemic that was also not initially recognized or acknowledged as such. In conclusion, *Bartonella*

“ “ These same organisms (bacteria, protozoa, rickettsiae, viruses) can be mildly to highly pathogenic when introduced into a non-reservoir host.

species have evolved a stealth pathogen strategy over thousands of years, which may well have given rise to a hidden epidemic.

To learn more about *Bartonella*:

- Understanding *Bartonella* medical webinar (FREE; <https://www.galaxydx.com/video-library/>)
- Bartonellosis, One Health Perspectives for an Emerging Infectious Disease
- Wolf, L.A., Cherry, N.A., Maggi, R.G., and Breitschwerdt, E.B., 2014. In pursuit of a stealth pathogen: Laboratory diagnosis of Bartonellosis. *Clinical Microbiology Newsletter*, 36(5), pp.33-39.

Dr. Breitschwerdt is an internist and professor of medicine and infectious diseases at North Carolina State University's College of Veterinary Medicine. He is a co-director of the Vector Borne Disease Diagnostic Laboratory which has been testing animals for vector borne infections, including Bartonella since 1984 and Chief Scientific Officer at Galaxy Diagnostics.



Zoonotic Diseases Spread from Animals to People

Members of pet-owning households have a greater risk of tick bites than those without pets.

By Lonnie Marcum, PT

What do the following recent news stories have in common? Child who visited county fair is Michigan's first swine flu case of 2017. Hantavirus confirmed in Reno, Nevada. Rabies found in dead raccoon in North Carolina. Lyme disease risk remains high into fall and winter in Connecticut.

They all have to do with zoonotic diseases—those that are spread from animals to people. In fact, according

to the CDC, zoonotic diseases account for over 60% of all communicable diseases causing illness in humans.

Animal-to-Human Transmission

Some zoonotic diseases, like rabies, are transmitted by the bite of an infected animal. The rabies vaccine for pets has greatly reduced the number of cases of the disease in the US. However, the CDC estimates that 40,000 people per year require rabies treatment, primarily after exposure to bats and other wildlife.

Other zoonotic diseases come from direct contact with an infected animal. For instance, you might get salmonella from handling a baby chick, chicken, duck, turtle, or snake.

Another mode of transmission is through contact with animal droppings, saliva, or urine. Hikers and campers may be at risk of hantavirus from rodent exposure in recreation areas, especially in the Southwest.

Animal-to-Bug-to-Human Transmission

Insects and arthropods (like ticks) provide another route of transmission for zoonoses. The infections they carry are known as vector-borne diseases. Lyme disease is currently the most common vector-borne disease in the US, affecting more than 300,000 people annually.

The Lyme bacterium is spread when a tick (the vector) feeds on an infected animal like a mouse or a squirrel and then later transfers the illness to a human. According to the CDC, 94% of all vector-borne diseases in the US come from tick bites.

Mosquitoes also transmit zoonotic diseases. The World Health Organization (WHO) estimates that mosquitoes infect more than 700 million people per year, causing in excess of a million deaths—with nearly half of those fatalities caused by malaria. While malaria was eliminated from the US in the 1950s, there are still 1,700 cases reported annually, almost all due to recent travel outside the US.

Occupational Risks

Farmers, ranchers, and veterinarians are at an increased risk for zoonotic infections due to their proximity to animals and outdoor areas where ticks and mosquitoes thrive. Examples of diseases associated with animal husbandry are leptospirosis from horses, anthrax from cattle, Q fever from sheep, brucellosis from goats, cysticercosis from pigs, and influenza A from chickens.

Veterinarians are at an obvious risk because they treat sick animals. Bartonella is particularly easy to catch as it can be transmitted from fleas, ticks, or the scratch of a cat. Cat bites are also common in veterinary practice and can result in abscess, septic arthritis, meningitis, even death.

Leptospirosis, one of the most widespread zoonotic diseases in the world, can infect a wide range of animals including rodents, dogs, and cats. It can be easily transferred to humans by contact with urine, saliva, or feces.

Food Handling and Consumption

Zoonotic disease can also be transmitted through consumption of undercooked foods. Examples of this are Ebola from bushmeat (non-domesticated animals), trichinosis from pork, E. coli from beef,

“One Health”
is a concept
that promotes
collaboration among
scientists

salmonella from poultry, Listeria from cheese, and tuberculosis from unpasteurized milk.

Food preparation can be another mode of exposure. The flesh-eating Vibrio bacteria can be acquired from cleaning fish or shellfish. It affects nearly 80,000 people, resulting in about 100 deaths per year in the US

Risk for Pet Owners

Pet owners are also at an increased risk for zoonotic diseases. For instance, giardia can be transmitted by touching contaminated dog feces, pet rats can infect their owners with hantavirus, turtles can carry salmonella, chlamydia is common with pet birds, and many small animals carry ringworm.

A recent outbreak of Campylobacter, linked to puppies sold through Petland, sickened 55 people in 12 different states and hospitalized 13.

Due to proximity to animals and the outdoors, pet owners are also at increased risk for vector-borne diseases. A recent study demonstrated that when compared to households without pets, pet-owning households had nearly twice the risk for finding crawling ticks, and 1.5 times the risk of finding ticks attached to family members.

The “One Health” Approach

“One Health” is a concept that promotes collaboration among scientists from many different specialties to achieve the best health for people, animals, and the environment.

The One Health approach recognizes that animals and humans are part of a global community. Proximity to animals, travel, and changing climate are all factors that affect the prevalence of disease.

For this reason, One Health teams include physicians, veterinarians, ecologists, and many others acting on regional, national, and global levels to achieve optimum health.

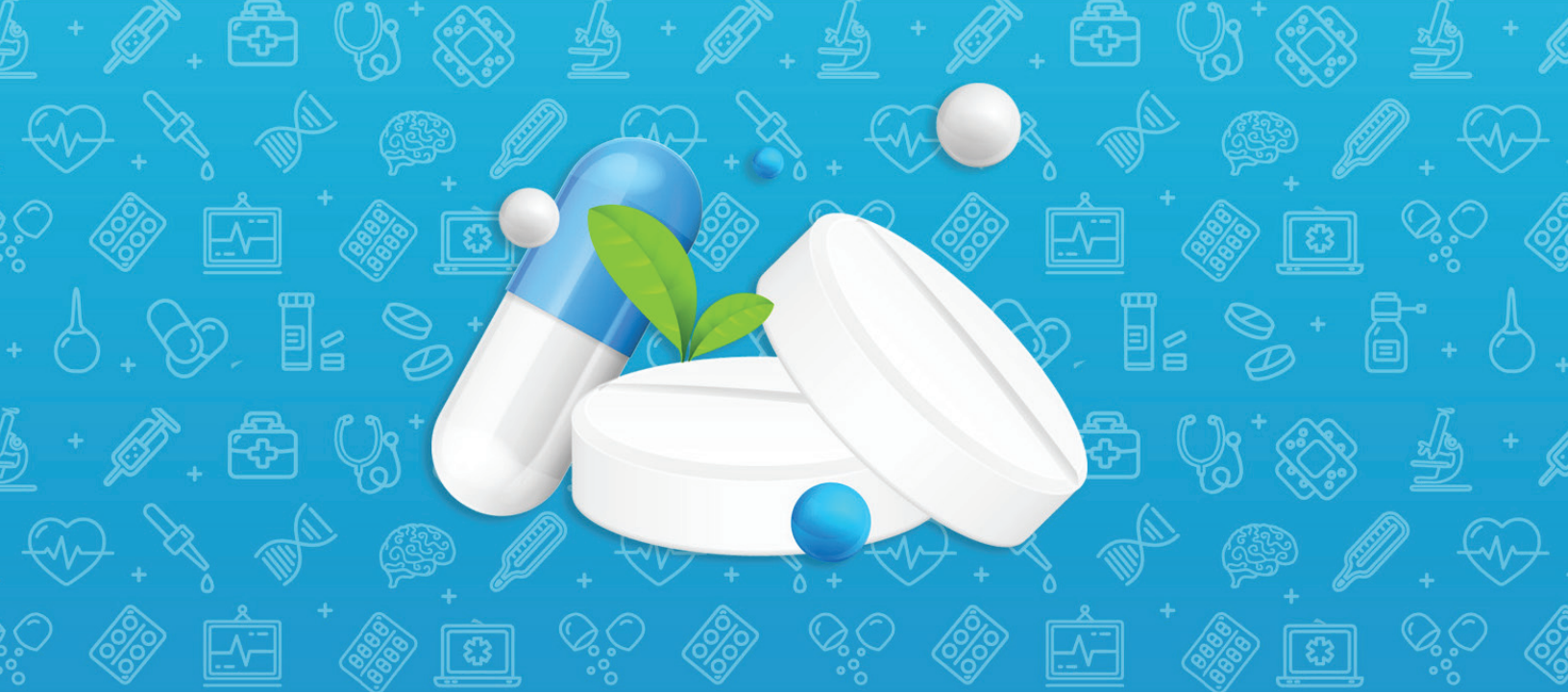
Examples of this include when veterinary records are used to predict Lyme disease, or when health officials successfully reduced the transmission of Rocky Mountain spotted fever on Native American reservations by putting flea/tick collars on stray dogs.

Prevention

As with all disease, prevention is key. The best method for preventing infection is to avoid exposure. However, if you own pets, or live, work or travel in an environment where you are exposed, there are several steps you can take to reduce your chances of becoming infected.

- Always use safe drinking water
- Protect yourself from ticks and biting insects
- Keep pets healthy and vaccinated
- Use flea/tick repellent on pets year round
- Vaccinate against preventable illnesses
- Wash hands and surfaces after handling raw food
- Wash your hands after touching animals

Lonnie Marcum is a licensed physical therapist and mother of a daughter with Lyme. Follow her on Twitter: @LonnieRhea. Email her at lmarcum@lymedisease.org.



Treating Bartonella-like Organisms

There may be as many as 30 distinct pathogenic species of Bartonella-like organisms, most of which have never been clinically defined.

By Joseph Burrascano, Jr., MD

It has been said that Bartonella is the most common of all tick-borne pathogens. Indeed, there seems to be a fairly distinct clinical syndrome when this type of organism is present in the chronic Lyme patient. However, several aspects of this infection seem to indicate that these tick-associated strains of

Bartonella are different from that described as “cat scratch disease.”

For example, in patients who fit the clinical picture, standard Bartonella blood testing is commonly non-reactive.

Furthermore, the usual Bartonella medications do not work for this—they suppress the symptoms but do not permanently clear them. Recently, thanks to advanced genotyping, it has been discovered that there may be as many as 30 distinct pathogenic species of this organism, most of which have never been clinically defined, and drug treatment studies, if they exist at all, are often misleading because for this intracellular organism, in vitro results rarely reflect in vivo efficacy. For these reasons, I like to refer to this group collectively as “Bartonella-like organisms” (BLOs).

Indicators of BLO infection include symptoms involving the central nervous system (CNS) that are out of proportion to the other systemic symptoms of disseminated Lyme disease. There seems to be an increased irritability to the CNS, with agitation,

anxiety, insomnia, twitches, tremors, and even seizures, plus symptoms of encephalitis, such as cognitive deficits and confusion. In addition, aggressive, antisocial, and inappropriate behavior has been observed, especially in young adults.

Other key symptoms may include ocular inflammation, gastritis, lower abdominal pain (mesenteric adenitis), sore soles, especially in the morning, tender subcutaneous nodules along the extensor tendons of the extremities, and red rashes.

Bartonella Rash

These rashes may have the appearance of red streaks like stretch marks that do not follow skin planes, spider veins, and/or red papular eruptions. Lymph nodes may be enlarged and the throat can be sore. Unlike borreliosis, which often causes a low-grade fever in the afternoon and a subnormal temperature in the morning, BLO infections cause an early-morning temperature elevation, mild enough that it often is missed by the patient. Keeping temperature

Treat for at least one month, and four months or longer is often needed for the more ill patients.

diaries can be very useful in this instance.

Because standard Bartonella testing, either by serology or PCR, is very insensitive, the diagnosis is a clinical one, based on the above points. Also, suspect infection with BLOs in extensively

treated Lyme patients who still are encephalitic and who never had been treated with a significant course of treatment known to be effective for BLOs.

Treating BLOs can be difficult, as drug resistance can rapidly develop to macrolides and fluoroquinolones when used as a single agent and solo courses of tetracyclines are ineffective. Cell wall drugs by themselves inhibit BLOs but do not eradicate them, but will synergize with intracellular agents. Consider adding gentamicin, as clinical studies have shown this to be essential in the most severe cases. Bottom line is that for advanced disease, as in borreliosis, drug combinations usually are needed for synergism and to



The Bartonella rash is often streaky.

decrease the risk of drug resistance.

The drug of choice to treat BLOs is levofloxacin and related advanced fluoroquinolones. Levofloxacin is usually never used for Lyme or Babesia. Thus many patients who have tick-borne diseases, who have been treated for them but remain ill may in fact be infected with BLOs. Unfortunately, levofloxacin and drugs in this family cannot be given in pregnancy or to those under the age of 18, so other alternatives, such as azithromycin and/or Rifampin, are used in these cases.

Another subtlety is that certain antibiotic combinations seem to inhibit the action of fluoroquinolones, while others seem to be neutral or additive. I advise against combining a fluoroquinolone with an erythromycin-like drug, as clinically such patients do poorly. On the other hand, combinations with cephalosporins and penicillins enhance recovery. Alternatives to levofloxacin include combinations that include Rifampin, azithromycin, gentamicin, and possibly streptomycin.

Treat for at least one month, and four months or longer is often needed for the more ill patients.

Complimentary therapies are frequently added to the treatment regimen. Supplemental arginine can reverse the epigenetic changes in the host that are caused by BLO infection, and transfer factors specific to this infection appear to be clinically helpful.

Incidentally, animal studies show that Bartonella may be transmitted across the placenta in some species, and in humans, a single case report did outline suspected maternal-fetal transmission of both *B. henselae* and *B. vinsonii subsp. berkooffii*.

BABESIA

In the US Blood Supply

By Lonnie Marcum, PT

In December 2016, the American Red Cross published the results of a two-year study into the US blood supply. They were specifically looking for an infectious parasite known as Babesia in donated blood, and they found it in 335 of the samples they tested.

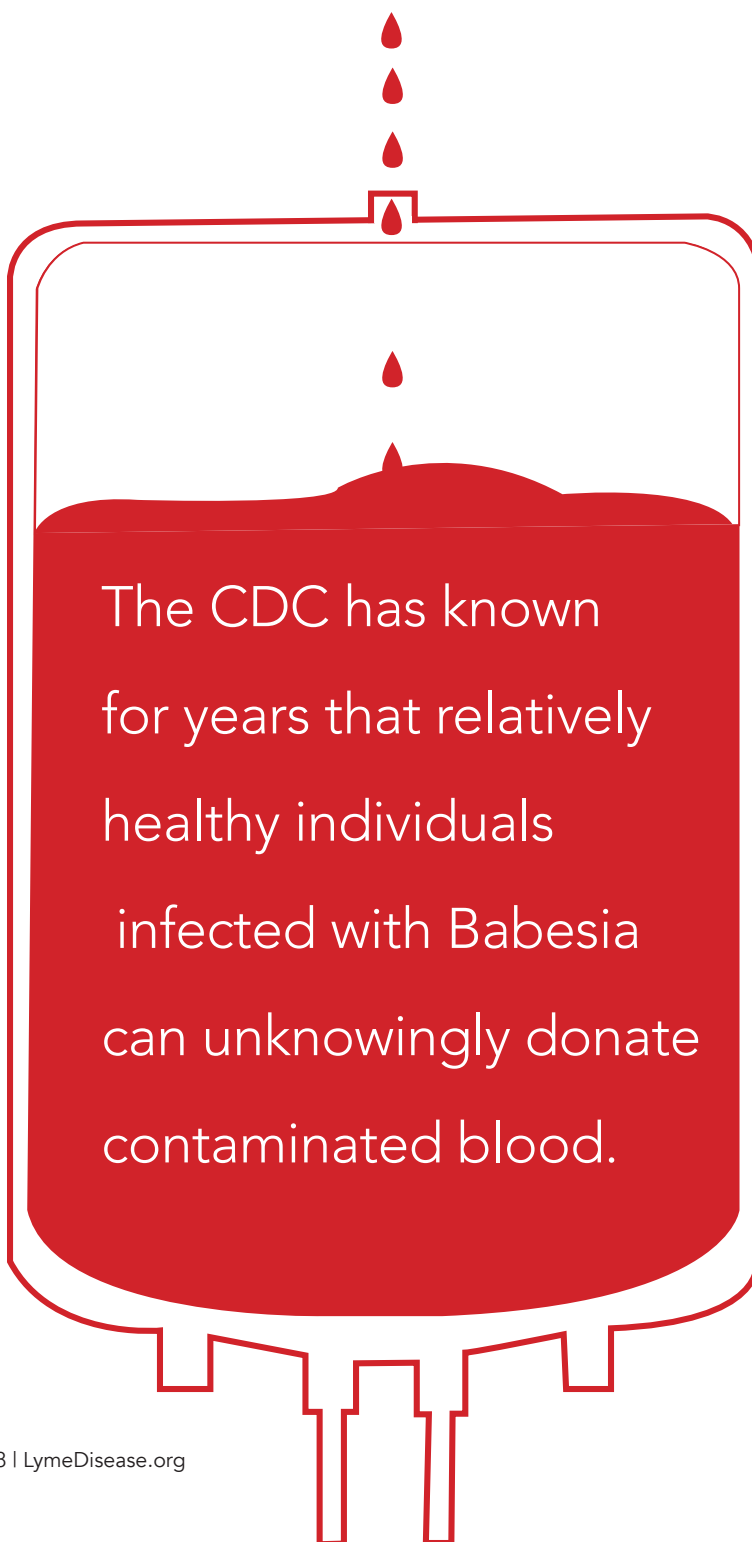
Since then, the CDC has published “Babesiosis and the US Blood Supply” and is letting the public know you can be infected

- by the bite of an infected tick (most common)
- by getting a blood transfusion from an infected donor of blood products, or
- by congenital transmission—from an infected mother to her baby (during pregnancy or delivery).

The CDC has known since 1979 that Babesia causes transfusion-transmitted infection in the United States. The FDA estimates 11% of transfusion-related deaths are caused by microbial contaminated blood, with up to 38% of the fatalities linked to Babesia.

What Is Babesia?

Babesia is a protozoan parasite that



The CDC has known for years that relatively healthy individuals infected with Babesia can unknowingly donate contaminated blood.

infects red blood cells. It is primarily transmitted to humans by Ixodes ticks—the same blacklegged ticks that carry Lyme disease. Ticks carrying the Babesia parasite have been steadily increasing over the past 30 years. Over the same time period, ticks carrying Borrelia burgdorferi (the bacteria that causes Lyme disease) have also increased as much as 500% in some areas of the US

Babesia is currently the most common co-infection associated with Lyme disease and is regarded as the foremost infectious risk to the US blood supply.

Symptoms of Babesiosis

Signs of infection may begin anywhere from one to nine weeks from the date of exposure, and may include fever, headache, fatigue, loss of appetite, anemia, day/night sweats, depression, and a feeling of “air hunger” or shortness of breath.

Many people with Babesia infection show no symptoms at all, while for others, the disease can be severe and even fatal. Patients without spleens, patients who are immunocompromised, infants, and people over the age of 50 have a higher risk for complications. Sadly, the former first lady of New Jersey, Jean Bryne, died of babesiosis in August of 2015.

How Does Babesia Get into the Blood Supply?

When screening blood donors, the American Red Cross does not ask whether donors have ever been bitten by a tick or had Lyme disease. It does state “those who have had infections with Chagas Disease, Babesiosis or Leishmaniasis are not eligible to donate.” The problem is many people with babesiosis are asymptomatic or had an infection that wasn’t diagnosed because they were never tested or they were not tested properly.

The CDC has known for years that relatively healthy individuals infected with Babesia can unknowingly donate contaminated blood. However, it wasn’t until 2011 that the CDC set a standard for surveillance and made babesiosis a reportable illness.

Unfortunately, only 31 states have implemented a system for reporting Babesia infections. Also in 2011,

the CDC published a retrospective study showing 159 cases of babesiosis contracted by blood transfusions, with 70% of those infections occurring after the year 2000, resulting in at least 12 deaths.

How Did They Find the Contaminated Blood?

Shortly after the 2011 CDC report, the American Red Cross launched a study in partnership with IMUGEN, Inc., to investigate the blood supply from four states for the presence of Babesia microti. From 2012-2014, they screened 89,153 blood-donation samples from Connecticut, Massachusetts, Minnesota, and Wisconsin and found 335 donations to be infected with Babesia microti.

Limitations of the Study

The first known case of babesiosis in the US occurred in 1966, after a resident of San Francisco became extremely ill with malaria-like symptoms that were later identified as a Babesia infection. Since then, scientists have identified hundreds of species of Babesia, with several known to infect humans.

Babesia microti is the primary cause of babesiosis in the United States. There are, however, at least five other strains of Babesia known to infect humans in the US: B. divergens, B. CA1, B. MO1, B. duncani (WA1), and a newly discovered species from Tennessee, B. TN1. However, people who travel out of the country could be exposed to several other species of Babesia.

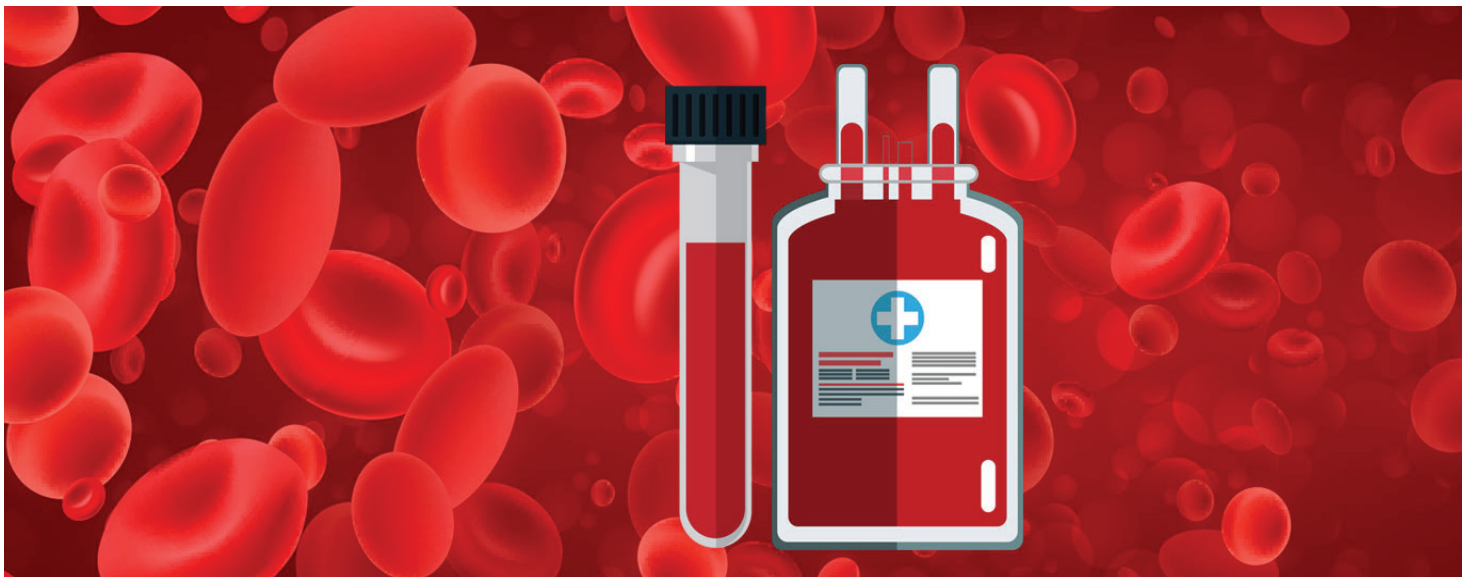
Because the Red Cross study only looked for B. microti, it is likely the actual number of cases of Babesia contamination is much higher than stated.

What Happens If You Are Given Contaminated Blood?

The researchers were able to confirm in the laboratory that Babesia-contaminated blood resulted in positive transmission 50% of the time in healthy animals. Unfortunately, most people who need blood transfusions have severe injury, infection, organ failure, cancer, or are immunocompromised.

Where Do We Go from Here?

We know that the most frequent tick-borne



pathogens in the United States, *B. burgdorferi* (Lyme disease), *B. microti* (babesiosis), and *A. phagocytophilum* (the causative agent of human granulocytic anaplasmosis), are all transmitted by Ixodes ticks. Thus, anywhere you have Ixodes ticks in the world you will also have a risk of tick-borne diseases.

With Lyme disease being reported in nearly half of all US counties and with Babesia following a similar pattern, the best thing for patients would be a universal blood screening for all tick-borne diseases. Because a universal test has not been developed, a reasonable starting point would be to begin nationwide year-round antibody screening for Babesia, as recommended by the FDA in 2015.

At this point, the best we may get is a compromise of screening blood donations from the five states

where the incidence of babesiosis is highest—Connecticut, Massachusetts, New Jersey, New York, and Rhode Island. The FDA estimates this will reduce the risk of transfusion-transmitted *Babesia microti* in the blood supply by 95%. However, this will do nothing to mitigate the risk of contracting other species of Babesia.

Recently, the Rhode Island Chapter of the American Red Cross began screening blood donations for Babesia for the state of Massachusetts as a pilot program. They will be sharing data with the FDA as they move toward a larger program. It's a start.

For more information on how to diagnose and treat babesiosis watch Dr. Richard Horowitz on babesiosis—NorVect 2014.

References: *Screening for Babesia microti in the US Blood Supply* | *Babesiosis and the US Blood Supply* | *Transfusion-Associated Babesiosis in the United States: A Description of Cases* | *Fatalities Reported to FDA Following Blood Collection and Transfusion: Annual Summary for Fiscal Year 2012* | *Geographic Distribution and Expansion of Human Lyme Disease, United States* | *Geographic Expansion of Lyme Disease in Michigan, 2000–2014* | *Centers for Disease Control and Prevention: Babesiosis CSTE Position Statement* | *American Red Cross Participating in an Investigational Study to Test the Blood Supply for a Tick-Borne Parasite in Donated Blood* | *A Case of Babesiosis in Man in the United States* | *Coinfection by Ixodes Tick-Borne Pathogens: Ecological, Epidemiological, and Clinical Consequences* | *Survey of Ixodes Pacificus Ticks in California Reveals a Diversity of Microorganisms and a Novel and Widespread Anaplasmatidae Species* | *Natural History of Zoonotic Babesia: Role of Wildlife Reservoirs* | *Ixodes Ricinus and Its Transmitted Pathogens in Urban and Peri-urban Areas in Europe: New Hazards and Relevance for Public Health* | *Cost-Effectiveness of Blood Donor Screening for Babesia Microti in Endemic Regions of the United States* | *Cost, Consequence and Cost-Effectiveness of Strategies for Donor Screening of the US Blood Supply* | *Clinical Presentation and Treatment of Transfusion-Associated Babesiosis in Premature Infants* | *Screening Begins for Babesiosis in Donated Blood*



Anaplasmosis,

*the “anti-freeze”
co-infection*

Anaplasma has been detected from coast to coast in the United States.

By Lonnie Marcum, PT

The blacklegged tick—*Ixodes scapularis* on the East Coast and *Ixodes pacificus* in the West—is the primary vector for Lyme disease in the United States. It can also transmit several other

pathogens, commonly known as co-infections. One of those co-infections is called anaplasmosis, which, according to a large survey conducted by LymeDisease.org, occurs in about 5% of patients with Lyme disease (see my other article on co-infections on page 11).

Human Granulocytic Anaplasmosis

Anaplasmosis, also known as human granulocytic anaplasmosis (HGA), is caused by the *Anaplasma phagocytophilum* bacterium (previously known as *Ehrlichia phagocytophila* or *Ehrlichia equi*). It belongs to a larger group of bacteria known as *Rickettsia*, which infect white blood cells.

Anaplasma phagocytophilum is commonly found in rodents and small mammals, and can be transmitted to humans by the bite of an infected tick.

The number of reported cases of HGA has been steadily increasing in recent years, with 2800 confirmed cases in 2014. However, these numbers are likely to be low for several reasons. Many cases go undiagnosed or are not confirmed with laboratory testing, and not all states require physicians to officially report the illness.

Geographic Distribution

The geographic distribution for HGA is very similar to Lyme, because both diseases share the same primary hosts and primary vectors. The six states with the highest incidence for HGA are Rhode Island, Minnesota, Connecticut, Wisconsin, New York, and Maryland.

The incidence of anaplasmosis is largely underreported, based on several recent studies.

Mr. Ostfeld feels that the incidence of anaplasmosis is largely underreported, based on several recent studies. In one two-year study, 45% of wild white-footed mice tested positive for Lyme disease, *Babesia*, and *Anaplasma*, suggesting high exposure rates to ticks that feed on them. Another study suggested that *Anaplasma* may act as a type of anti-freeze that helps ticks survive freezing temperatures.

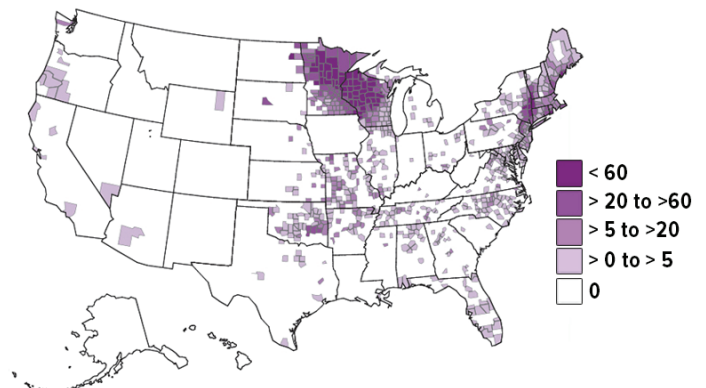
Overall, the infection rate of *Anaplasma* within questing nymphal ticks varies greatly by state, but has been detected from coast to coast.

Signs and Symptoms

The symptoms of HGA usually appear 5-14 days after the tick bite and typically include the following:

- Fever (92-100%)
- Headache (82%)
- Fatigue (97%)

Incidence of Anaplasmosis Reported to CDC by County 2000-2013*



* As reported through national surveillance, per 1,000,000 persons per year. Cases are reported by county of residence, which is not always where the infection was acquired.

*NOTE: The majority of cases are not reported to the CDC

- Muscle pain (77%)
- Shaking/chills (77%)
- Rash (fewer than 10%)
- Gastro-intestinal symptoms (rare)
- Neurological symptoms (rare)

Clinical Course

The majority of HGA cases are mild and self-limiting. Infrequently, however, complications like respiratory failure, peripheral neuropathies, bleeding/coagulation problems, pancreatitis, and kidney failure may occur. Rarely, HGA can be fatal.

A delay in treatment can result in severe symptoms that may initially resemble toxic shock syndrome—a complication that sometimes arises from certain bacterial infections.

Other serious viral or fungal infections can occur during the course of infection while the immune system is compromised. Some HGA patients may need to be hospitalized.

Co-infection with other diseases transmitted by *Ixodes* ticks (Lyme disease, *Borrelia miyamotoi*, *Babesia*, or Powassan virus) can complicate the course of HGA. If a patient has a delayed response to Lyme treatment and a low white blood cell count, it should raise suspicion for possible co-infection with *Anaplasma*.

Summary of Human granulocytic anaplasmosis

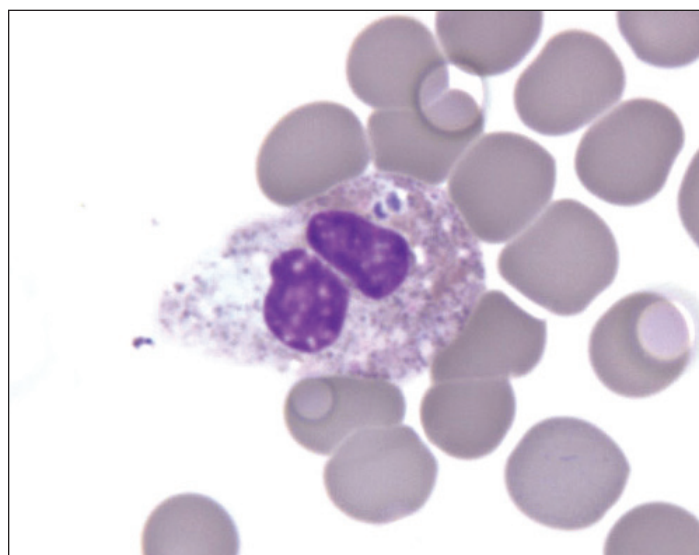
Disease	Incubation period	Initial signs and symptoms	Cutaneous signs (skin)	Laboratory findings	Estimated case fatality rate
Human granulocytic anaplasmosis (HGA)	5-21 days	Fever, headache, chills, malaise, myalgia, chills	Rash rare, in less than 10%	Thrombocytopenia, leukopenia, mild anemia, increased hepatic transaminase, increased immature neutrophils	less than 1%

Treatment

Doxycycline is the first line treatment. The CDC states: “Doxycycline is the first line treatment for adults and children of all ages and should be initiated immediately whenever anaplasmosis is suspected. Use of antibiotics other than doxycycline or other tetracyclines has been associated with a higher risk of fatal outcome for some rickettsial infections.”

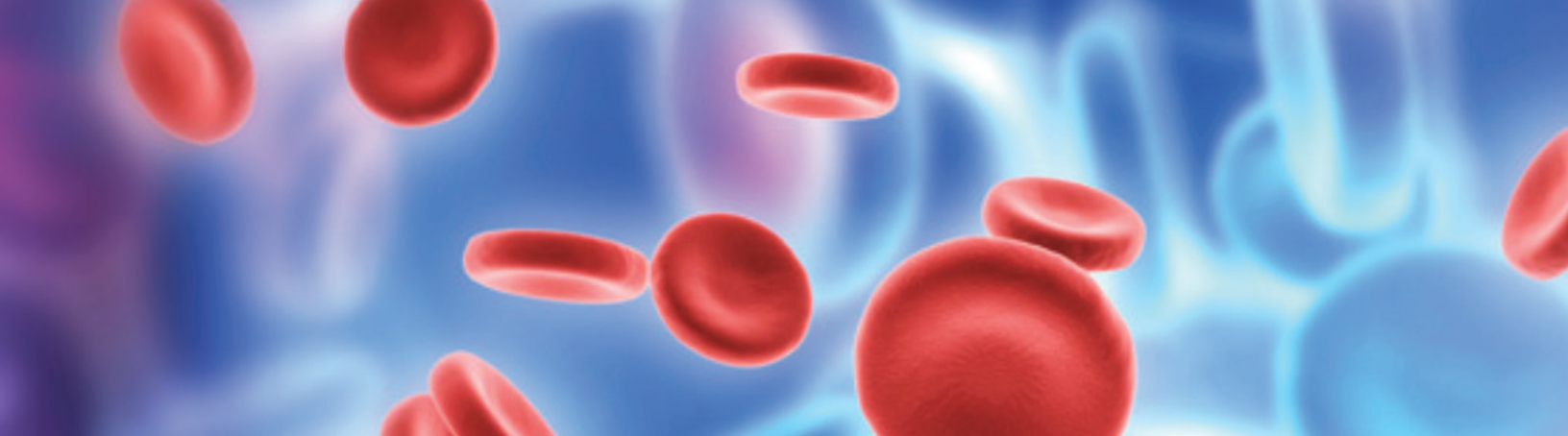
In addition, “If the patient is treated within the first five days of the disease, fever generally subsides within 24-72 hours... Severely ill patients may require longer periods before their fever resolves.”

Lonnie Marcum is a licensed physical therapist and mother of a daughter with Lyme. Follow her on Twitter: @LonnieRhea. Email her at lmarcum@lymedisease.org.



A closer look at the anaplasmosis bacteria.

References: Forbidding Forecast for Lyme Disease in the Northeast CDC MMWR | Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis — United States CDC | Emerging Tickborne Diseases | Public Health Grand Rounds, March 2017 | Serum Antibodies to Borrelia burgdorferi, Anaplasma phagocytophilum, and Babesia microti in Recaptured White-Footed Mice | Co-Infection of Blacklegged Ticks with Babesia microti and Borrelia burgdorferi is Higher than Expected and Acquired from Small Mammal Hosts | Epidemiology and Genetic Diversity of Anaplasma phagocytophilum in the San Francisco Bay Area, California | Anaplasma phagocytophilum Induces Ixodes scapularis Ticks to Express an Antifreeze Glycoprotein Gene that Enhances their Survival in the Cold.



Is Persistent Lyme Disease Caused by Another Organism Identified by Dr. Willy Burgdorfer over 35 Years Ago?

Why hasn't anyone looked into it?

By Lorraine Johnson, JD, MBA

A recent article from STAT, an affiliate of the Boston Globe, raises serious questions about the original publication of the discovery of Lyme disease by Dr. Willy Burgdorfer 35 years ago. The STAT article is based on a review of Burgdorfer's research notes and papers uncovered in his garage shortly before his death. These papers suggest that another pathogen found in patients' blood during this period, *Rickettsia helvetica*, may play a significant role in Lyme disease.

Burgdorfer referred to this pathogen, which he first discovered in Switzerland in 1978, as the "Swiss Agent." *Rickettsia helvetica* is a member of the spotted fever group *Rickettsia*.

Burgdorfer's research with Allen Steere, who first described Lyme disease, found the Swiss Agent present alongside *Borrelia* in US patient samples. However, the article Burgdorfer and his co-author Jorge Benach published on the cause of Lyme disease in 1982 neglects to mention the Swiss Agent entirely.

This omission has meant that research for the past 35 years has excluded any potential role the Swiss Agent may play in the persistence of Lyme disease in the US.

For example, patients infected may have symptoms similar to Lyme disease: a rash (although typically smaller spots), fever, muscle pain, or headache. But these patients would test negative for Lyme disease. Patients may also have an eschar type of rash (blackened or crusted skin).

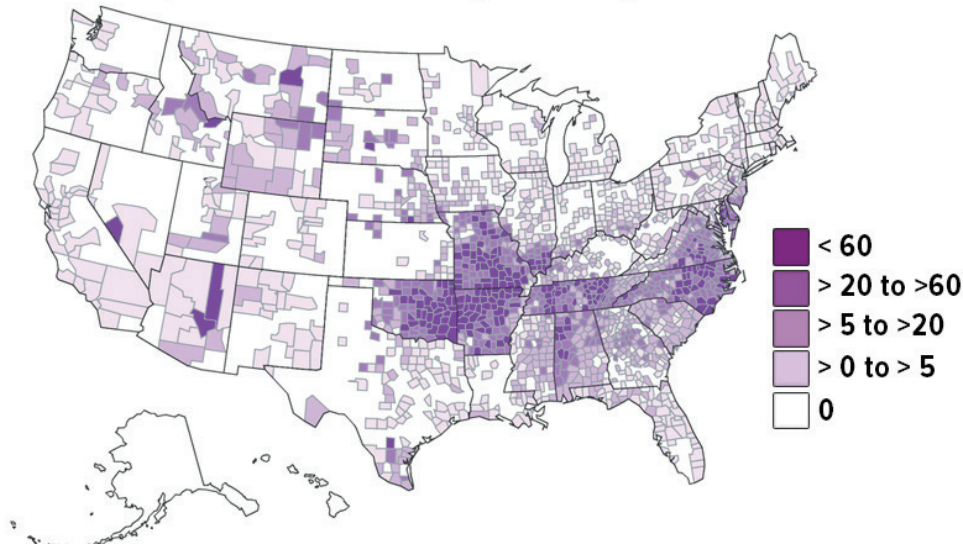
The first such cases documenting human illness in Europe in 1999 involved the sudden unexpected cardiac death of two Swedish men during exercise. Another case, published in 2009, involved a Swedish patient with meningitis. Today, the Centers for Disease Control and Prevention includes *Rickettsia helvetica* broadly in the grouping spotted fever group *Rickettsia* (SFGR) but confines its territorial range to central and northern Europe.

The CDC notes that severity of *Rickettsia* diseases vary by species and says: "Prompt treatment with doxycycline is recommended if tick-borne SFGR is suspected and should never be delayed pending the outcome of diagnostic tests." The CDC refers to disease caused by *Rickettsia helvetica* as *Aneruptive fever*.

Treatment of the Swiss Agent may involve different antibiotics or durations of treatment. The two pathogens may also exist side-by-side as co-infections increasing the severity of illness. Although Burgdorfer developed a test for the Swiss Agent that is used in Europe, it is not available in the US because it was not thought to be needed. This means that US patients cannot be tested for the specific pathogen. In addition,

Incidence of Rickettsiosis

Reported to CDC by County 2000-2013*



* As reported through national surveillance, per 1,000,000 persons per year. Cases are reported by county of residence, which is not always where the infection was acquired.

* Includes Rocky Mountain spotted fever (RMSF) and other spotted fever group rickettsioses. In 2010, the name of the reporting group changed from RMSF to spotted fever rickettsiosis.

the CDC maps of Rickettsia distribution show that it is widely distributed, even in states the CDC consider non-endemic for Lyme disease.

Rickettsiosis in the USA 2000-2013

The STAT article reports that both Jorge Benach and Allen Steere now say it is time to take a closer look at Rickettsia helvetica's role in Lyme disease.

Benach says the research "should be done" because public health concerns warrant a closer look.

For patients, looking into pathogenic factors related to persistence in tick-borne disease is long overdue. The failure to note the existence of the Swiss Agent along with Borrelia burgdorferi as bacteria in the initial publication about Lyme disease may have set back progress in understanding the pathogenicity of Lyme disease decades.

STAT is a highly regarded internet publication that prides itself on delivering "fast, deep, and tough-minded journalism." You may want to leave comments on the STAT website—this was a terrific article! You can read the entire article here: <https://www.statnews.com/2016/10/12/swiss-agent-lyme-disease-mystery/>



Inoculation eschars associated with the site of tick attachment in a patient infected with *R. parkeri*. (Photo courtesy of CDC)

[com/2016/10/12/swiss-agent-lyme-disease-mystery/](https://www.statnews.com/2016/10/12/swiss-agent-lyme-disease-mystery/)

Lorraine Johnson, JD, MBA, is the Chief Executive Officer of LymeDisease.org. You can contact her at lbjohnson@lymedisease.org. On Twitter, follow her @lymepolicywonk.



Tick-Borne Powassan Virus Can Be Deadly

Many of the patients who develop symptoms need to be hospitalized.

By Lonnie Marcum, PT

Tick-borne Powassan virus has been gaining attention after sending former North Carolina Senator Kay Hagan into a 43-day coma this past year.

Powassan virus

After being hospitalized for eight months, Senator

Hagan was released and was said to be recovering.

Unfortunately, others were not so lucky. Powassan has reportedly caused at least three deaths in late 2016.

While Powassan virus (POWV) was discovered nearly 60 years ago, many people are learning of it for the first time. Of special concern: it can be transmitted in as little as 15 minutes by the same tick that carries Lyme disease.

Because POWV has been considered so rare, with

only 75 cases reported in the United States over the past 10 years, very little has been known about it—until now.

A recent study conducted by the Marshfield Clinic in Wisconsin demonstrates that POWV may be much more prevalent than previously thought. Of 95 patients tested for suspected tick-borne disease, 66% showed evidence of current or prior Lyme infection.

Of those patients who tested positive for Lyme disease, 17% had serologic evidence of acute POWV infection. Considering there are an estimated 300,000 cases of Lyme disease per year, POWV may affect more patients than we know.

Durland Fish, PhD, a professor of epidemiology at Yale School of Medicine who specializes in vector-borne diseases, warned of POWV in 2015. He says one of the biggest concerns is that POWV jumped to the deer tick within the last 30 years and “cases are being reported in areas where they have never occurred before.”

Dr. Fish goes on to say, “As more ticks become infected with Powassan virus and more people become exposed to them, Powassan could become epidemic like Lyme disease. Because it can be a serious disease causing fatalities, and there is no treatment for it, Powassan has the potential to become a greater public health threat than Lyme disease.” After the 2017 death of two men in Cape Cod, many people are learning for the first time that ticks can carry viruses too, not just bacteria like Lyme disease. And that such tick-borne viruses can pose a significant threat to public health.

Powassan virus (POWV) is considered an “emerging infectious disease,” though it is not new. In fact, the first case was discovered in 1958 in the small town of Powassan, located in Ontario, Canada.

A Massachusetts case had a better outcome. Tucker Lane contracted Powassan in 2014 and considers himself lucky to be alive.

“[I] woke up sweating, cold, shaking... felt like I was going to puke,” he told CBS Boston. A few days later, he fell into a week-long coma. “They kind of told my parents there’s nothing more we can really do.” Eventually, however, he came out of it.

Three years later, Lane says his health is fine and he reports no lingering symptoms or damage to his brain. “I knew I got lucky in a very unlucky situation,” Lane said.



Powassan brain.

Symptoms

For those who become ill, the symptoms of POWV develop anywhere from 8-34 days after the tick bite. The initial symptoms are flu-like with a fever.

If the infection spreads to the brain, severe neurological symptoms can develop, including strong headache, mental confusion, paralysis, seizures, and unconsciousness. About 60% of patients who survive the infection are left with permanent neurological dysfunction including partial paralysis, headaches, memory impairment, and paralysis of the eye muscles. Nearly 10% of Powassan cases are fatal.

No Cure

Currently, there is no cure for POWV. Many of the patients who develop symptoms need to be hospitalized. The treatment consists of IV fluids, anti-inflammatories, and, in some cases, breathing and life support.

Powassan is a flavivirus that is related to Zika, Dengue, West Nile, and tick-borne encephalitis virus (TBEV). These are named Flava (which means yellow in Latin) after the Yellow Fever virus, which causes yellowing of the skin. Flaviviridae are a family of viruses that can cause brain swelling.

Emerging Infectious Diseases

Powassan and many other tick-borne diseases are considered emerging because the number of cases has increased significantly over recent years.

There is some debate over whether increased



North Carolina Senator Kay Hagan

geographic spread or better detection techniques have led to the increased number of reported cases. I suspect both factors play a role. (See Ehrlichia, another emerging infectious diseases.)

One way to determine whether POWV is spreading is through tick studies. There seems to be great variation from year to year but studies show anywhere from 1% to 10% of ticks in endemic states test positive for POWV compared to 20%-50% for Lyme.

Two Types of Powassan in North America

There are two types of Powassan in North America. Lineage 1 POWV is associated with both woodchucks and Ixodes cookei ticks; or squirrels and Ixodes marxi ticks. Lineage 2, sometimes called deer tick virus (DTV), is associated with the white-footed mouse and Ixodes scapularis ticks.

Because I. cookei and I. marxi do not climb up blades of grass in wait for a suitable host (a behavior known as questing), they are not thought to play a major role in the transmission of POWV.

The blacklegged or “deer tick” (Ixodes scapularis) on the other hand, has developed multiple strategies for questing. Deer ticks are also aggressive biters, making them much more competent in transmitting diseases like POWV to humans.

Add Powassan to the Tick Toxic Soup

While many tick species are known to carry POWV, the blacklegged tick (I. scapularis) is the

primary vector. Blacklegged ticks can carry many pathogens and can transmit more than one infection in a single bite. While we should be very concerned about POWV, the risk of contracting Lyme or Babesia is currently much greater.

No Grace Period

A tick becomes infected with POWV after feeding on a small mammal carrying the virus. When the infected tick bites a human, transmission can occur in as little as 15 minutes. Since ticks are so small and POWV transmission so rapid, very few patients with Powassan encephalitis will recall the tick bite.

If you get bitten by a tick while out hiking or playing, you could be infected with Powassan without even realizing anything has happened.

Hidden Epidemic?

Most Powassan virus infections are thought to be asymptomatic. This assumption is based, in part, on reviewing the results of human blood tests. Two studies found that 0.7% of New Yorkers and 3% of Canadians from Ontario carry antibodies to POWV—meaning they were infected at some point.

Rough math says 0.7% of New Yorkers would make 500,000 cases of POWV in that state alone, when in fact, only 16 cases were reported in New York from 2006 to 2015. This suggests that the majority of cases are asymptomatic, and that POWV is underrecognized as an infectious disease.

Unrecognized POWV may also contribute to the high number of Lyme disease patients who remain ill after treatment, because viruses do not respond to antibiotics. Some experts theorize that POWV and other viruses may also play a part in other chronic neurologic diseases, like lupus, multiple sclerosis, ALS, Parkinson’s, chronic fatigue syndrome, or myalgic encephalomyelitis. But this is still under investigation.

Geographic Distribution

The underdiagnosis of POWV contributes to the lack of understanding of the geographic distribution. From 2006 to 2015, there were only 68 cases of POWV reported to the CDC with eight (12%) fatalities.

After the sudden death of a woman in Maine in 2013, that state conducted its own tick study on the Powassan virus. The researchers tested a total of

Timeline of symptoms

1 to 5 week incubation period	Early symptoms approximately 1 week	Acute illness weeks to months	Chronic symptoms years
No symptoms	Fever, headache, sore throat, nausea, drowsiness, disorientation. May include: gastrointestinal issues, muscle weakness.	Fever, vomiting, respiratory distress, difficulty with speech, paralysis, loss of consciousness. May include seizures.	Memory problems, paralysis on one side of the body, muscle weakness, muscle wasting, severe headache.

1,729 *I. scapularis* ticks from 30 different locations statewide and the results were astonishing.

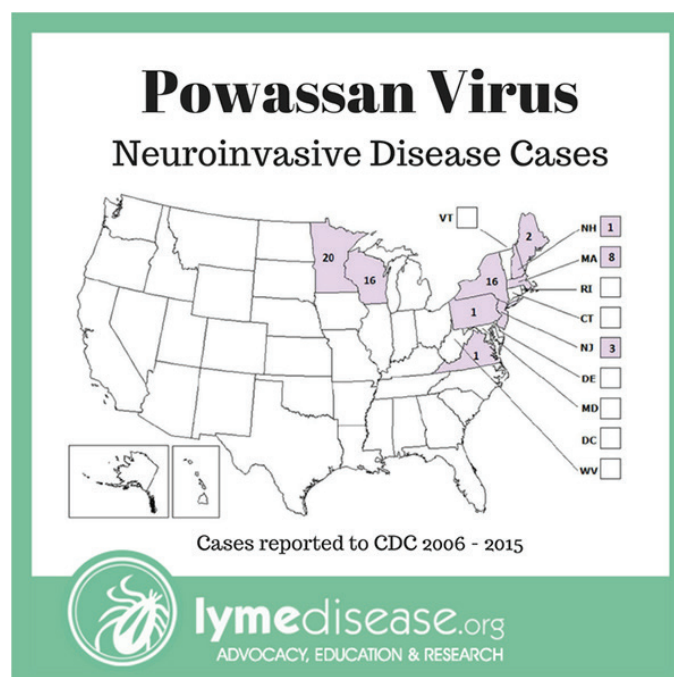
The rate of infection throughout Maine ranged from a low of 0% to a high of 16% (average 7% adult, 9% nymphs). “We were kind of surprised that we found as much as we did,” said Chuck Lubelczyk, the project director.

POWV has been established along the East Coast from Virginia to Nova Scotia, throughout New York, Pennsylvania, Michigan, Wisconsin and Minnesota, broadly throughout Canada, and in rare instances has been detected in Colorado and California.

There several other tick-borne viruses found in the US, including Heartland virus, Bourbon virus and Colorado tick fever, which will be addressed separately.

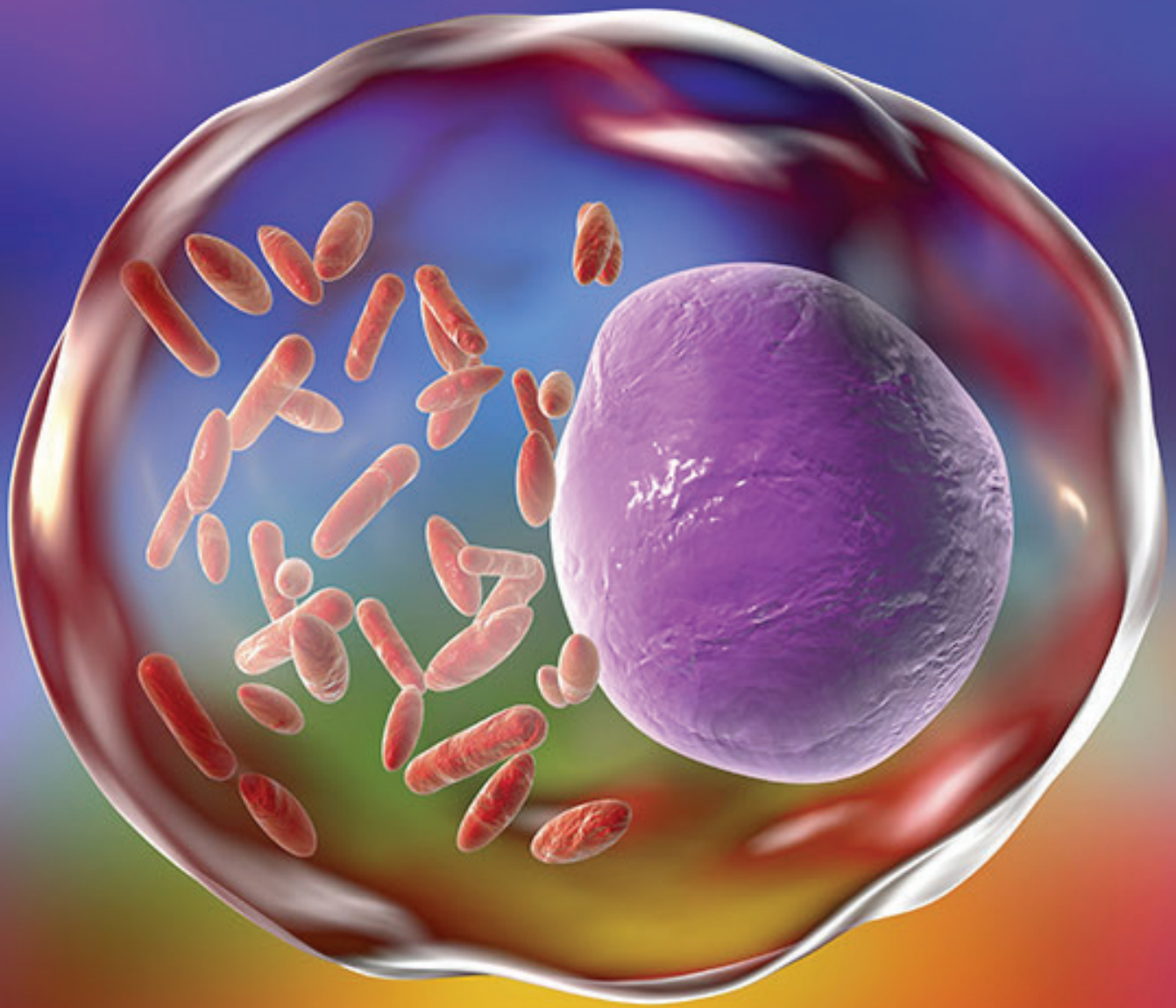
As with all tick-borne diseases, prevention is key. Click here for more information about protecting yourself, your family and your pets.

LymeSci is written by Lonnie Marcum, a Licensed Physical Therapist and mother of a daughter with



Lyme. Follow her on Twitter: @LonnieRhea. Email her at: lmarcum@lymedisease.org.

References: Centers for Disease Control (CDC) Powassan Virus Powassan Virus: An Emerging Arbovirus of Public Health Concern in North America | Powassan virus disease cases and deaths reported to CDC by year and clinical presentation, 2006-2015| Four emerging arboviral diseases in North America: Jamestown Canyon, Powassan, chikungunya, and Zika virus diseases | Changing epidemiology of Powassan encephalitis in North America suggests the emergence of the deer tick virus subtype | Emerging Causes of Arbovirus Encephalitis in North America: Powassan, Chikungunya, and Zika Viruses | Thomas LA, Kennedy RC, Ecklund CM. Isolation of a virus closely related to Powassan virus from *Dermacentor andersonii* collected along north Cache la Poudre River, Colo. *Proc Soc Exp Biol Med* 1960; 104:355–359 | Johnson HN. Isolation of Powassan virus from a spotted skunk in California. *J Wildl Dis* 1987; 23:152–153 | Powassan Encephalitis Virus in Deer Ticks (*Ixodes scapularis*) in Maine (2015-2016). Main Department of Agriculture, Conservation and Forestry.



A Closer Look at Rickettsial Infections

What you need to know

By Lonnie Marcum, PT

Millions of Americans are likely to be bitten by ticks this year. Some of them may know enough to be concerned about Lyme disease. However, the public at large—and many medical professionals—are often oblivious to other dangers posed by ticks.

Some particularly troublesome bacteria belong

to a group called Rickettsia. Although they can also be found in lice, fleas, mites, and chiggers, in the US, most rickettsial infections are thought to be transmitted by ticks.

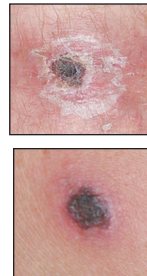
Rickettsia includes two different groups: the spotted fever group (which consists of rickettsiae and ehrlichia) and the typhus group. This post will focus on spotted fever group rickettsiae (SFGR), which includes:

Distinctive Rashes of Rickettsial Diseases

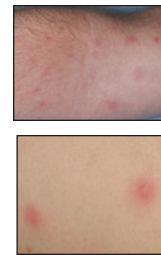
RMSF



Eschar



***R. parkeri*
rickettsiosis**



: Health Grand Rounds | Emerging Tickborne Diseases, Tuesday, March 21, 2017 at 1:00 p.m. ET

- *Rickettsia rickettsii*, also known as Rocky Mountain spotted fever (RMSF)
- *Rickettsia parkeri*
- *Rickettsia philipii*, (previously 364D) the cause of Pacific Coast tick fever
- *Rickettsia helvetica** (which may be found in the US) Rocky Mountain Spotted Fever

Rocky Mountain spotted fever (RMSF) is the most common rickettsial infection in the US. It can range from a mild illness to a fatal one.

Initial symptoms typically include high fever, severe headache, abdominal pain (with or without vomiting), and muscle pain. It often—though not always—includes a spotted rash that begins at the wrist and/or ankles, and spreads outward from there.

According to the CDC website: “RMSF is a serious illness that can be fatal in the first eight days of symptoms if not treated correctly, even in previously healthy people. The progression of the disease varies greatly. Patients who are treated early may recover quickly on outpatient medication, while those who experience a more severe course may require intravenous antibiotics, prolonged hospitalization or intensive care.”

RMSF weakens small blood vessels throughout the body, giving rise to its characteristic rash. This widespread damage to the blood vessels allows the bacteria to spread to the heart and brain—and can quickly lead to death in those under age 4, over

the age of 60, or those whose immune systems are compromised.

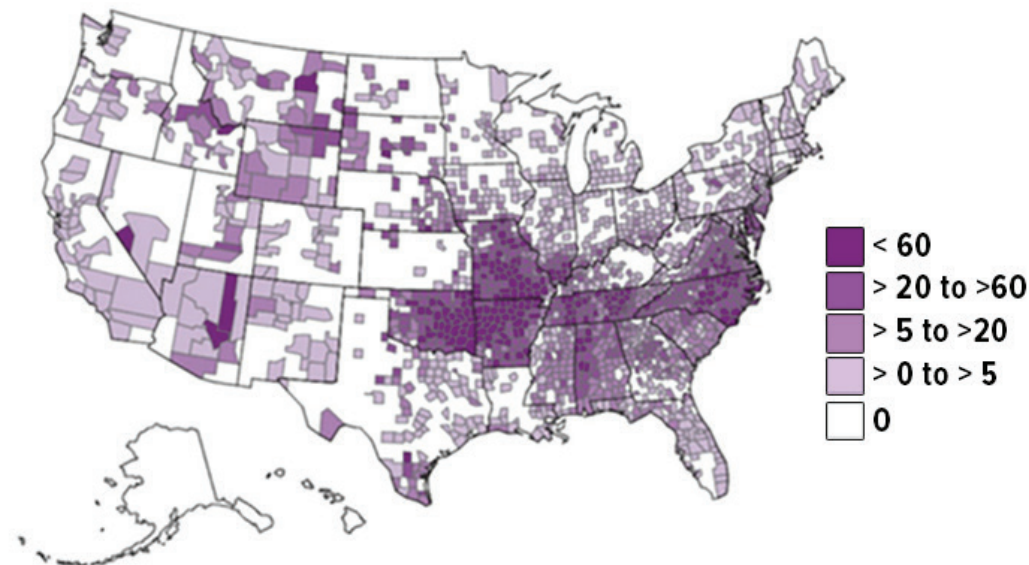
RMSF can also result in permanent nerve/organ damage or amputation. In one tragic case, an Oklahoma woman’s infection went unrecognized until it was too late. To save her life, doctors had to amputate both arms and both legs.

Prior to the use of antibiotics, RMSF had a fatality rate of up to 80%. In the US today, the fatality rate is 5%-10%. However, in neighboring Mexico, fatality rates from RMSF in recent years have been as high as 30%.

An interesting case study occurred in eastern Arizona, where there are no known American dog ticks (the primary vector of RMSF). Beginning in 2003, there were outbreaks of RMSF on several Indian reservations, with the rate of infection reaching 150 times the national average, including 19 fatalities. This was later attributed to the large population of free-roaming dogs. Unexpectedly, a different vector was identified as the culprit in these cases, the brown dog tick.

Community leaders and public health officials dramatically reduced the rate of RMSF by treating the yards of 500 homes with acaricide (pesticides that target ticks) and placing long-acting tick collars on over 1000 dogs. Afterward, ticks were only found on 1% of the dogs with collars versus 64% of the untreated dogs. These collaborative efforts helped reduce RMSF by 43% on the reservations.

Incidence of Spotted Fever Rickettsiosis Reported to CDC by County 2000-2013



* As reported through national surveillance, per 1,000,000 persons per year. Cases are reported by county of residence, which is not always where the infection was acquired.

*Includes Rocky Mountain spotted fever (RMSF) and other spotted fever group rickettsioses. In 2010, the name of the reporting category changed from RMSF to spotted fever rickettsiosis.

Other Types of Rickettsiosis

occidentalis)

Rickettsia parkerii, found along the Gulf Coast, and *R. phillipii*, from the West Coast, cause a milder form of rickettsiosis. The spotted rash is not as common but both will frequently cause an eschar (scab) or necrotic area about one centimeter across at the site of the tick bite. These other types of Rickettsiosis usually result in a mild illness that may go undiagnosed. Thus, the actual number of infections may be higher than we know.

Transmission

In the United States, Rickettsiosis is primarily transmitted by the following ticks:

- American dog tick (*Dermacentor variabilis*)
- Rocky Mountain wood tick (*Dermacentor andersoni*)
- Brown dog tick (*Rhipicephalus sanguineus*)
- Gulf Coast tick (*Amblyomma maculatum*)
- Pacific Coast ticks (*Dermacentor*

Distribution

According to the CDC, rickettsial diseases have been reported in every state except Alaska and Hawaii. In those two states, officials are not required to keep track of rickettsial diseases, so nobody knows how many cases may be there.

Incidence

In 2009, the reporting definition for RMSF was changed to include the more broad “Spotted Fever Rickettsiosis” (SFR) which includes RMSF. Using the new criteria, there were 4,470 reported cases of spotted fever rickettsiosis in 2012, the majority of which were presumed to be RMSF. In general, the number of cases of SFR are increasing—from 1.7 cases per million in 2000 to an all-time high of 14.2 cases per million in 2012.

Summary of Spotted Fever Rickettsiosis Found in the US

Disease	Incubation period	Initial signs and symptoms	Cutaneous signs (skin)	Laboratory findings	Estimated case fatality rate
Rocky Mountain potted fever	3-12 days	Fever, headache, chills, malaise, myalgia, nausea, vomiting, abdominal pain, photophobia, anorexia	Maculopapular rash 2-4 days after onset in most, might become petechial and involve palms and soles of feet	Thrombocytopenia, slight hepatic transaminase levels, normal or slight increase white blood cell count with increase neutrophils, hyponatremia	5-10%
Rickettsia parkeri rickettsiosis	2-10 days	Fever, myalgia, headache	Eschar, sparse maculopapular or vesiculopapular rash that might involve the palms and soles	Mild thrombocytopenia, mild leukopenia, increased hepatic transaminase levels	not known
Rickettsia philipii	not known	Fever, myalgia, headache	Eschar or ulcerative lesion with regional lymphadenopathy	not known	not known

Risk Factors

People who spend time outdoors, American Indians who live on reservations, and dog owners are at higher risk for contracting rickettsiosis. In a large survey conducted by LymeDisease.org, 26% of respondents reported having a rickettsial co-infection, with 6% having RMSF.

Conclusion

If you've been exposed to ticks and come down with a flu-like illness, be aware that you may have been infected with a tick-borne disease separate from

or in addition to Lyme disease. Mainstream doctors typically do not test for co-infections. Knowing the signs and making your physician aware of the appropriate treatment for SFGR may save your life or that of a loved one.

**Rickettsia helvetica was discovered by Dr. Willy Burgdorfer in 1978 and widely thought to be found only in Europe. However, it was recently uncovered in Burgdorfer's 35-year-old archives that he had seen a bacterium that highly resembled R. helvetica inside the samples of blood containing Borrelia (the bacteria that causes Lyme disease). He called this microbe the "Swiss Agent." (You can read more about that discovery [here](#).)*

Ehrlichiosis

the Tick-borne Disease No One has Heard of



While some cases of ehrlichiosis are mild, the disease can be severe or fatal if not treated correctly, even in previously healthy people.

By Lonnie Marcum, PT

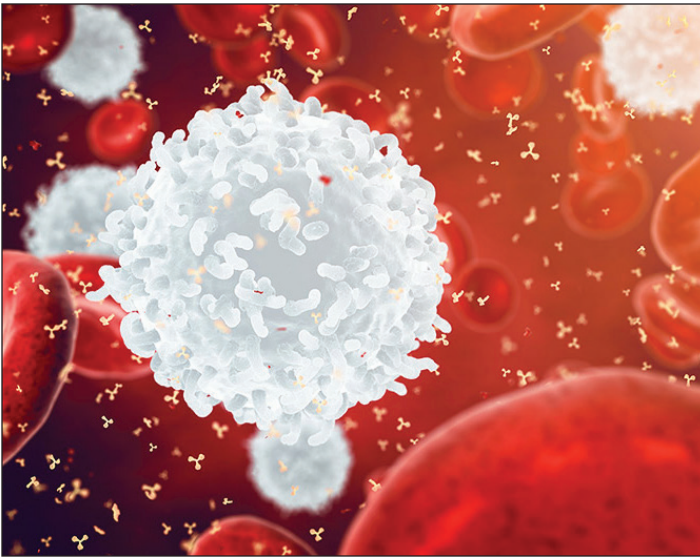
According to the experts, ticks and the diseases they carry are expanding into new geographic areas. While the majority of Americans have heard of Lyme disease, fewer than 2% have any knowledge of another tick-borne disease called ehrlichiosis.^{1,2}

As a matter of fact, my own child was CDC-positive for an ehrlichial infection (amongst other

things), and when I took her to the Emergency Room for an irregular heartbeat that developed during treatment, the ER doctor told me he had never heard of “*Ehrlichia chaffeensis*.” True story!

Warning!

In May 2017, an article in the CDC’s Emerging Infectious Diseases Journal warns that ehrlichiosis infections are being “grossly underreported” in the US, with as many as 97-99% of infections going



Ehrlichia infecting white blood cells.

unrecognized. They are projecting that the actual number of annual cases could go as high as 50% the number of Lyme disease cases—which would mean we may already have over 150,000 cases of ehrlichiosis annually.³

There are several factors causing the underreporting:

- Lack of public education/knowledge — doctors aren't testing for or diagnosing ehrlichiosis.
- Some cases are mild enough that patients do not seek medical care or a diagnosis.
- Insensitive or inaccurate testing methods may result in false-negative diagnoses.
- Reporting is voluntary and the criteria are restrictive.

Ehrlichiosis

Ehrlichiosis is the name for several tick-borne diseases that are caused by a group of bacteria known as Ehrlichia. Ehrlichia belong to a larger order of bacterium known as Rickettsiales.⁴

Rickettsiae and Ehrlichia belong to a broad group of bacteria that can be spread by a tick bite. These infections can be transmitted alone or at the same time as Lyme disease and are commonly known as co-infections.

The Ehrlichia (E) group includes:^{5,6,7,8}

- chaffeensis: the cause of human monocytic
- ehrlichiosis (HME),
- ewingii, and
- muris-like (EML).

Symptoms

While some cases of ehrlichiosis are mild, the disease can be severe or fatal if not treated correctly, even in previously healthy people.

Severe symptoms of ehrlichiosis may include difficulty breathing, respiratory failure, bleeding disorders, and kidney or heart failure.

Ehrlichia infect white blood cellsBecause Ehrlichia infect white blood cells (the cells that fight infection) and mitochondria (the powerhouse of the human cell), the consequences of untreated infection may have long-lasting effects.⁹ I often wonder if undiagnosed Ehrlichiosis isn't responsible for some portion of the millions of people with the mysterious illness known as myalgic encephalomyelitis, or "chronic fatigue syndrome."

Other symptoms of ehrlichiosis can include:

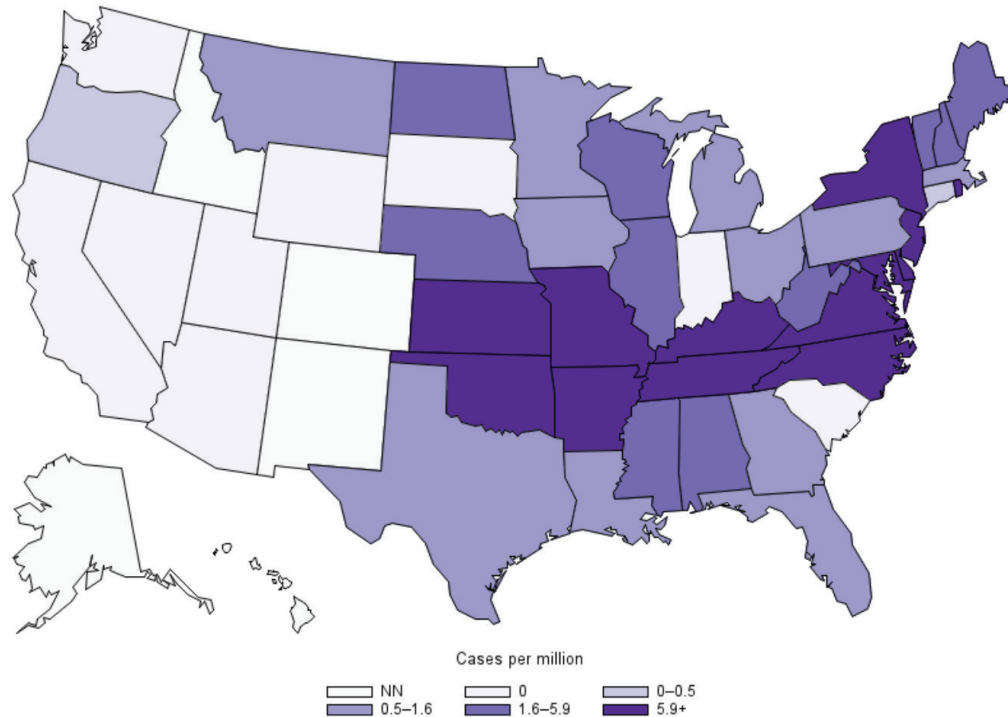
- Fever/chills and headache (majority of cases),
- Fatigue/malaise (over two-thirds of cases),
- Muscle/joint pain (25%–50%),
- Nausea, vomiting, and/or diarrhea (25% – 50%),
- Cough (25%–50%),
- Confusion or brain fog (50% of children; less common in adults),
- Lymphadenopathy (47%–56% of children; less common in adults),
- Red eyes (occasionally), and
- Rash (approximately 60% of children and 30% of adults).

Diagnosis and Treatment

Like other tick-borne diseases, diagnostic blood tests will frequently be false-negative during the first weeks of illness. And like other tick-borne diseases, treatment is most effective if started early. For this reason, healthcare providers must use their best clinical judgment and treat patients based upon early symptoms alone.

According to the CDC website: The diagnosis of ehrlichiosis must be made based on clinical signs

Figure 3 – Annual reported incidence (per million population) for *E. chaffeensis* in the United States for 2017. (NN= Not notifiable)



and symptoms, and can later be confirmed using specialized confirmatory laboratory tests. Treatment should never be delayed pending the receipt of laboratory test results, or be withheld on the basis of an initial negative laboratory result.

The CDC goes on to say: Doxycycline is the first line treatment for adults and children of all ages and should be initiated immediately whenever ehrlichiosis is suspected.¹⁰

Patients who are treated early may recover quickly on outpatient medication, while those who experience a more severe illness may require intravenous antibiotics, prolonged hospitalization, or intensive care.

Transmission

The Lone star tick (*Amblyomma americanum*) is the primary vector of *E. chaffeensis* (HME) and *E. ewingii*, with rates of infection ranging from 0 to 27 percent. In the past decade, the Lone star tick has expanded into geographic areas where it did not

previously occur. This is particularly concerning because the Lone star tick is an aggressive biter.

While there is some geographic overlap, in general these ticks are found in the following areas:

- Lone star tick: east of the Rockies,
- Gulf Coast tick (Gulf and Southern states),
- American dog tick (east of the Mississippi),
- black-legged or “deer” tick (east of the Rockies), and
- western black-legged tick (west of the Rockies).

Other Modes of Transmission

Ehrlichia chaffeensis has been shown to survive for over a week in refrigerated blood. Therefore these bacteria may present a risk for transmission through blood transfusion and organ donation. It has also been suggested that ehrlichiosis can be transmitted from mother to child, and through direct contact with slaughtered deer.^{14, 15}

Summary of Ehrlichiosis

Disease	Incubation period	Initial signs and symptoms	Cutaneous signs (skin)	Laboratory findings	Estimated case fatality rate
Ehrlichia chaffeensis (HME)	5-14 days	Fever, headache, malaise, myalgia, nausea, vomiting, diarrhea	Rash in approx. 30% of adults and 60% of children, variable rash pattern that may involve the palms and soles, appears approx. 5 days after illness onset.	Leukopenia, thrombocytopenia, increased hepatic transaminase levels, hyponatremia, anemia	3%
Ehrlichia ewingii ehrlichiosis	not known	Fever, myalgia, malaise, headache	Rash rare	Leukopenia, thrombocytopenia, increased hepatic transaminase levels	not known
Rickettsia parkeri rickettsiosis	not known	Fever, myalgia, malaise, headache	Rash approx. 12%	Lymphopenia, leukopenia, thrombocytopenia, increased hepatic transaminase levels, hyponatremia, anemia	not known

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