NATURAL TREATMENTS FOR LYME COINFECTIONS

ANAPLASMA, BABESIA, AND EHRLICHIA

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Healing Arts Press
Rochester, Vermont • Toronto, Canada

Contents

How to Use This Book and Who It Is For

In the spring of 2009, I was the 217th person ever to be diagnosed with anti-NMDA-receptor immune encephalitis. Just a year later that figure had doubled. Now the number is in the thousands. Yet Dr. Bailey, considered one of the best neurologists in the country, had never heard of it. When we live in a time when the rate of misdiagnoses has shown no improvement since the 1930s, the lesson here is that it's important to always get a second opinion. . . . While he may be an excellent doctor in many respects, Dr. Bailey is also, in some ways, a perfect example of what is wrong with medicine. I was just a number to him (and if he saw thirty-five patients a day, as he told me, that means I was one of a very large number). He is a by-product of a defective system that forces neurologists to spend five minutes with X number of patients a day to maintain their bottom line. It's a bad system. Dr. Bailey is not the exception to the rule. He is the rule.

Susannah Cahalan,
Brain on Fire: My Month of Madness

I did as much research as I could and I took ownership of this illness, because if you don't take care of your body, where are you going to live?

Karen Duffy,
Model Patient: My Life As an Incurable Wise-Ass

Illness and death are not optional. Patients have a right to determine how they approach them.

Marcia Angell, M.D.

Illness is the doctor to whom we pay most heed.

Marcel Proust

My first published exploration of Lyme disease and its coinfections occurred with the appearance of *Healing Lyme* (Raven Press) in 2005. In the years since that early work my increasing exposure to this group of emerging diseases, and the people who suffer from them, has significantly deepened my understanding of both Lyme and its coinfections. In consequence, mid-2013 saw the publication of an in-depth look at two crucial Lyme coinfections: mycoplasma and bartonella (Healing Arts Press). With the publication of this volume on babesia, ehrlichia, and anaplasma the five major coinfectious organisms of Lyme now have their own in-depth analysis and natural treatment protocols. (There are other, less common coinfections that may become more common in the future; Rocky Mountain spotted fever and various chlamydias are also [sometimes] spread by ticks.)

As with the earlier book on mycoplasma and bartonella, this book is meant to be used by specific groups of people, i.e., those who are suffering from a difficult-to-treat *Babesia* spp., *Ehrlichia* spp., or *Anaplasma* spp. infection, and/or clinicians who themselves treat those who are infected with any of these organisms.

IF YOU ARE INFECTED WITH *BABESIA, EHRLICHIA,* OR *ANAPLASMA*

This book is designed to help you understand the infectious organisms as well as some of the approaches that can be used to treat the diseases and the symptoms they cause.

Please understand that some of the book is fairly technical. That is for the clinicians (or for you if you want to delve that deeply into it). You can skip the really technical bits if you want. They are not necessary in order for you to treat either of these conditions effectively. However, I do think, if you are up for it, you will find the overview chapters on these infections useful. I have found that once someone understands what the bacteria do in the body, it tends to lessen the fear that these diseases engender. Understanding what the organisms do during infection also makes it easier to understand the treatment regimens I recommend, i.e., just why they help to turn the conditions around. Still, that being said, the deeper technical look at the cytokine cascade and the minutiae of what the organisms do in the body are not really necessary if you just want a cursory overview of the diseases and how to treat them.

This book also explores just how widespread these kinds of infections are. And, as usual, the real figures are very different than those indicated by Centers for Disease Control (CDC)—generally by a factor of anywhere from 100 to 1,000. During research for the previous coinfection book (*Bartonella* and *Mycoplasma* spp.) I found that scores of research articles, easily located in peer-reviewed journals, continually reported mycoplasma and bartonella infections to be *very* common throughout the world. In fact it turns out that between one-tenth and one-third of the United States population (as an example) is asymptomatically infected with at least one of those organisms. *Babesia, Ehrlichia,* and *Anaplasma* infections are apparently less widespread but research still finds them to be far more common than the CDC reports. Technological medical treatment for these latter three conditions is

often difficult and, as with Lyme, bartonella, and mycoplasma, many physicians don't understand how to treat or diagnose them very well. Thus, as an aid to physicians and their patients, in addition to natural protocols, this book also examines which antibiotics (and tests) research has found useful (and which ones are not).

Again, this book contains an extensive look at the natural protocols that are effective for each of the diseases. Please note: *These protocols are designed to be used along with antibiotics if you wish to do so.* I don't think you necessarily have to give up either pharmaceuticals *or* natural medicines to find health. However, if you have tried antibiotics and they have failed to help you, the protocols in this book can be used by themselves to treat all three infections.

Also, a note: *The herbs and supplements in this book are* ***not*** *the only ones in the world that will help.* Please use the protocols outlined herein *only* as a starting place, a guideline. Add anything that you feel will help you and delete anything that you feel is not useful. Microorganisms, when they enter a human body, find a very unique ecosystem in that particular person. Thus the disease is always slightly different every time it occurs. That means that a pharmaceutical or herb that works for one person may not work or work as well for another. *There is no one-size-fits-all treatment for these particular organisms.*

Again . . . there is no one-size-fits-all treatment for Lyme or *any* of its coinfections.

Anyone who says there is, is either trying to sell you something or doesn't really understand this group of infectious organisms. *There is no one way to health such that in all times and in all places and with all people it will always work.* Life, and disease, and the journey to wellness are much more complex and sophisticated than that. So, trust your own feeling sense and pay attention to what your body is telling you. *You* are the best judge of whether something is working for you or not, whether you need to add something else or not, whether you are getting better . . . or not.

Now, a comment on dosages: I will often suggest a *range* of dosages for the herbs and supplements that can help these conditions. If you have a very healthy immune system, you will probably need smaller doses; if your immune system is severely depleted, you may need to use larger doses. If you are *very* sensitive to outside substances, as some people with Lyme and these coinfections are, then you might need to use very tiny doses, that is, from one to five drops of tincture at a time. (This is true for about 1 percent of the people with these infections.) I have seen six-foot-five, 280-pound men be unable to take more than five drops of a tincture and a tiny, 95-pound woman need a tablespoon at a time. *Dosages need to be adjusted for each person's individual ecology.*

Again . . . dosages need to be adjusted for each person's individual ecology.

And . . . *please be conscious of how you respond to the medicines you are taking. If something disagrees with you, if you feel something is not right in how you are responding to a medicine,* **stop taking it.** Remember: you will always know yourself better than any outside physician. And, just a tiny rant here . . .

Tiny Rant

People Get Sick, Not Stupid

I have been told by a number of clinicians, both herbal and medical, that the majority of people with Lyme and/or its coinfections are too uneducated to understand this series of books, that they are not intelligent enough to determine which herbs to use and which herbs not to use (and, in fact, that many herbs should be discussed or dispensed *only* by properly trained and credentialed herbalists—and yes, they mean that most community herbalists and all those who are ill should not), that people with this group of diseases cannot in fact be trusted to be in

charge of their own health and journey to wellness, and that I am remiss, even foolish (i.e., stupid, silly, idiotic, witless, brainless, vacuous, mindless, unintelligent, thoughtless, half-baked, harebrained, imprudent, incautious, injudicious, unwise), in supporting members of the Lyme community in their self-empowerment. My feelings about that kind of thinking (and the people who promulgate it—you know who you are and yes, I still know where you live) can be captured in a number of common one-syllable words normally not used in polite company. (Please insert your own favorites here.)

Thus, while it *can* help to have a sophisticated clinician to aid in the journey to welless, it is not always necessary. Further, the truth is, for many people, finding such a person is sometimes impossible, hence taking charge of their own journey to wellness is the *only* option. That is most likely why the Lyme community is as potently informed as they are (much to the dismay of many physicians and paternalistic medical herbalists and naturopaths).

I do not agree with those clinicians who think you are too stupid to orchestrate your own journey to wellness, that you are too unintelligent or uneducated to understand these books, that you should not be allowed to engage in your own healing without some licensed person overseeing your regimen. In fact, I disagree with that kind of condescending attitude quite strongly. If you do feel you need a health professional to help you, then by all means find one. If you do not feel that you need someone, or that your past efforts with professionals have been unsatisfactory, then again, trust yourself to find what works for you and what does not. In fact, even if you do work with a health professional, I highly recommend that you trust yourself to determine what you are willing to take as medicine and what you are not, to determine for yourself if something is working or if it is not, to engage

in self-determination on your journey to wellness. Or as Paul Krugman once put it . . .

> When everyone—tout le monde, as Tom Wolfe used to put it, meaning a relative handful of people, but everyone who supposedly matters—is saying something it takes a real effort to step outside and say, wait a minute, how do we know that? It's especially hard if you spend your time hanging out with other Very Serious People. . . . This is what you need to know: important people have no special monopoly on wisdom; and in times like these, when the usual rules . . . don't apply, they are often deeply foolish, because the power of conventional wisdom prevents them from talking sense about a deeply unconventional situation. (Krugman, 2010)

IF YOU ARE A CLINICIAN

I have gone into these organisms in depth so that you can begin to understand just how complex their actions in the body are. It is my hope that Western herbal medicine can begin to emerge as a highly sophisticated form of healing, one *understood* to be highly sophisticated, and one that can deal with the kinds of complexities that are now commonly found in emerging infections. To that end I have introduced the idea of thinking about the synergies that exist between coinfections as well as the concept of examining the kind of cytokine cascades bacteria create during infection. Cytokines are messenger molecules that act as intercellular mediators during the body's immune responses. Each stealth pathogen, during infection, releases certain cytokines to facilitate its infection of the body and, further, to stimulate the breakdown of specific tissues to gain nutrients. Each pathogen decreases the activity of certain parts of the human immune system (interfering with an effective immune response) and activates others (stimulating

inflammation and cellular breakdown). So while some parts of the immune system become less functional, others become overactive. The overactivity comes from an organism-initiated cascade (think "domino effect") of inflammatory cytokines. Each stealth pathogen creates a different kind of cascade; that is, they stimulate certain kinds of inflammation in the body through using the body's immune response for their own ends. This is why infection with these organisms often mimics an autoimmune disease dynamic. This is important to understand when designing any kind of elegant, interventive treatment strategy. If you *know* what is happening in the body you don't have to guess what to do—you *know* what to do.

And while I don't go into it in any depth in this book, the idea of the complex synergies that exist between herbal medicines is crucial, as is the understanding of herbal synergists. These concepts are developed in more depth in the revised and expanded second edition of my book *Herbal Antibiotics* (Storey Publishing, 2012). If you wish to look deeper into plant synergists and herbal synergies, I think you will find that book useful. As well, time and space limitations made the inclusion of *in-depth* monographs on many of these herbs impossible to include in this volume. I have developed in-depth monographs on many of these herbs elsewhere . . . the only ones included in this book are those not included in other books I have written. If you would like to see them they can be found in *Healing Lyme, Herbal Antibiotics* (second edition), *Herbal Antivirals,* and *Healing Lyme Disease Coinfections: Complementary and Holistic Treatments for Bartonella and Mycoplasma*. (For specifics, see chapter 9.)

Please note that along with *Babesia, Anaplasma, Ehrlichia, Bartonella,* and *Mycoplasma* there are a number of other coinfections that are sometimes encountered, generally with less frequency (at least for now). One, tick-borne encephalitis or TBE, is dealt with in some depth in *Herbal Antivirals*. Others such as Rocky Mountain spotted fever will be covered in the revised edition of *Healing Lyme*, due out, hopefully, not too long after this book.

HOW I ARRIVED AT THE HERBAL PROTOCOLS IN THIS BOOK

The protocols in this book were developed by exploring the dynamics of the diseases themselves, their impacts in people, the experience of clinicians treating them, protocols that those with the diseases have successfully used, many hundreds of journal papers, a look at the plants' history of usage around the world for treating these and similar conditions, and my own experience with plant medicines over a nearly 30-year period. But please note . . .

The plants herein are just guidelines. The protocols themselves are just guidelines. The dosages are just guidelines. Again: there is *no* one-size-fits-all way to treat these diseases. The intent of this book is to give those who wish one an understanding of the diseases so that they can be treated more effectively and with greater sophistication. This is just a beginning, a starting place so we no longer have to grope along in the dark.

Feel free to alter, add, delete, innovate, think outside the box, argue, insist, and never settle for less than being healthy in the way that you understand it.

And remember: *all* plants are useful as medicinals.

Again, *all* plants are useful as medicinals.

The secret, as always, is in the dose, the timing, and the combination that is used. Just because a plant is not mentioned in this book does not mean it is not useful.

One of the things I have learned from the ill people I have worked with since 1986 (especially those in the Lyme community) is that when a lot of people with a lot of motivation begin looking around themselves, searching for answers, they come up with some truly amazing things. If you lock people in a room with only four ways out, someone will find a fifth way out. *Always*.

Trust yourself, and remember, only *you* know what health is for you.

1

Emerging Diseases and Coinfections

The New Epidemics

Hosts that are coinfected by multiple parasite species seem to be the rule rather than the exception in natural systems.

A. L. Graham, I. M. Cattadori, J. O. Lloyd-Smith, et al., "Transmission Consequences of Coinfection: Cytokines Writ Large?"

Patients with immunocompromised systems are at greater risk for a more prolonged and severe course of illness, especially with multiple infectious etiologies, illustrated here with Lyme disease and babesia. In these patients, reasoning to the single most likely cause of illness may not be the best approach to diagnosis and empiric treatment. Familiarity with tick-borne diseases is important and

may become more so as the habitats of humans and ticks increasingly intersect.

Y. Abrams,
"Complications of Coinfection with Babesia and Lyme Disease after Splenectomy"

Coinfections could, thus, increase vulnerability to the emergence of new parasites by facilitating species jumps, if the coinfected portion of a population provides favourable conditions for an emerging parasite to adapt to a new host species.

A. Graham, I. M. Cattadori,
J. O. Lloyd-Smith, et al.,
"Transmission Consequences of Coinfection:
Cytokines Writ Large?"

I first became interested in bacterial diseases in the early 1990s after reading about the emergence of resistant bacteria in hospitals. Having studied mathematics, I well understood what an exponential growth curve meant. I could see as well as anyone that we had only a short period of time in which to begin to address the problem.

As I studied more deeply, I began to be aware not only of resistant bacteria, the majority of which flow from hospital settings (and large, commercial farms) into the general community, but also of diseases emerging in the human population due to overpopulation and the environmental disruption that causes. Lyme was among the earliest of the emerging diseases that caught my attention and, as time went on, the coinfections that accompany Lyme (initially thought to be extremely uncommon) did so as well.

It became clear, the more I learned, that many of these emerging diseases were difficult to treat with conventional technological medicine, that the diagnostic tests were often unreliable, and that many of the

organisms did not respond well to antibiotics. As well, and most regrettably, it slowly became obvious that many physicians had little knowledge of, or much interest in, these diseases.

I have been deeply immersed in the study of emerging and resistant bacteria for over two decades now. It is clear that while technological medicine still has a role to play, sometimes an important one, evolutionary changes are occurring that make many of our assumptions about such diseases and their treatment obsolete.

I was born in 1952 into an extended family that included many physicians, among them a surgeon general of the United States. For my family, "modern" medicine was *the* way to approach disease—the *only* way. Penicillin had become widely available in 1946, just after World War II, and new antibiotics were being discovered (seemingly) every day. Vaccines, too, were making history. The year I was born there were 58,000 new cases of polio, more than 3,000 of those infected with the disease died, and many of the others were permanently disabled—some terribly so. The next year, Jonas Salk announced the successful testing of his vaccine against polio. Then, in 1962, Albert Sabin introduced his oral vaccine, something that made mass vaccination easily possible. I still remember that long walk to the lunch room in elementary school, the long wait in line, and the sugar cube in the tiny, white paper cup.

The excitement of those days is very hard to explain to newer generations, but for people then, it seemed as if infectious diseases were going to be permanently eradicated. In fact, many researchers and physicians in the late 1950s and early 1960s, including my great-uncle Lee Burney, then surgeon general of the United States, and my grandfather David Cox, president of the Kentucky Medical Association, went so far as to loudly proclaim that the end of all infectious disease was upon us. A 1963 statement by the Australian physician Sir F. Macfarlane Burnet, a Nobel laureate, is typical. By the end of the twentieth century, he said, humanity would see the "virtual elimination of infectious disease as a significant factor in societal life" (Levy 1992, 3). And in 1970, one of

my great-uncle's successors, Surgeon General William Stewart, testified to Congress that "it was time to close the book on infectious diseases" (Levy 1992, 3). With satisfaction, physician David Moreau observed in a 1976 article in *Vogue* magazine that "the chemotherapeutic revolution has reduced nearly all non-viral disease to the significance of a bad cold" (Griggs 1991, 261).

They were wrong, of course, the victims of their own hubris and a deep lack of understanding of the natural world, most especially of bacteria. By the time Moreau's comments appeared resistant bacterial diseases were already on the rise. A short 30 years later, with infectious diseases from resistant bacterial strains become rampant, the world came to face the specter of epidemic disease outbreaks more dangerous than any known in history. As bacterial resistance researcher and physician David Livermore recently put it, "It is naive to think we can win" (Bosley 2010).

There are two factors that have stimulated the emergence of potent bacterial disease organisms. The first is the tremendous overuse of antibiotics over the past 70 years. The second is the severe ecological disruption that increasing human population is causing.

In an extremely short period of geologic time the earth has been saturated with hundreds of millions of tons of nonbiodegradable, often biologically unique pharmaceuticals designed to kill bacteria. Many antibiotics (whose name literally means "against life") do not discriminate in their activity but kill broad groups of diverse bacteria whenever they are used. The worldwide environmental dumping, over the past 65 years, of huge quantities of synthetic antibiotics has initiated the most pervasive impacts on the earth's bacterial underpinnings since oxygen-generating bacteria supplanted methanogens 2.5 billion years ago. It has, according to medical researcher and physician Stuart Levy, "stimulated evolutionary changes that are unparalleled in recorded biologic history" (Levy 1992, 75). Bacteria *had* to evolve resistance. If not, due to their crucial role in the ecological functioning of this planet (and our own bodies), all life, including the human species, would already have been killed off by those very same antibiotics.

Ecological disruption has also played an extensive role. For example, the damage to wild landscapes, intrusions into forest ecosystems, the cutting of those same forests to make way for suburbs, and the damage to plant diversity and its crucial homeodynamic functions by suburban and agricultural intrusions have all had a place in stimulating the emergence of new disease groups. A study from the State University of New York is representative:

> This study examined 11 years of surveillance data in New York State to measure the relationship between forest fragmentation and the incidence of human babesiosis. Adjusted Poisson models showed that increasing edges of contact between forested land and developed land, as measured by their shared parameters, was associated with a higher incidence of babesiosis cases, even after controlling for the total developed land area and forest density, and temperature and precipitation. Each 10-km increase in perimeter contact between forested land and developed land per county was associated with a 1.5% increase in babesiosis risk. Higher temperature was also strongly associated with increasing babesiosis risk, wherein each degree Celsius increase was associated with an 18% increase in babesiosis risk. (Walsh, 2013)

Human movement into previously unoccupied forest lands significantly increases the risk of infections, from both the ecological pressure put on the infectious organisms and the increasing numbers of people in that habitat. For example, studies of forest ticks in southern Poland have found that 77 percent carry *Anaplasma*, 60 percent *Babesia*, and only 3 percent *Borrelia*. Coinfection with *Anaplasma* and *Babesia* was found in 50 percent of the ticks. The more that such locations are inhabited by people, the more likely it is that they will get bitten and develop disease. Too, the unique grouping of the infectious organisms in that ecological zone determines the kinds of coinfection complex people will develop. Thus in that part of Poland there is a much higher

chance of becoming infected with *Babesia* and *Anaplasma* than Lyme. This is something that physicians should understand: they live in a particular ecological habitat and the grouping of disease organisms in that habitat's ticks is always going to be unique—as is the immune health of that region's people.

Also crucial to the emergence of these coinfections is the reduction of wild predator populations (not only of mountain lions, for example, but of the bird species that eat insects and mice). This creates subsequent increases in the deer, mice, and insect populations that carry those bacterial pathogens, which in itself increases the movement of disease into human populations.

And finally, the reduction of large, wild mammal populations in undisturbed forest habitats plays its own important role. As fewer and fewer wild animal populations are available as hosts for the bacterial diseases that once were (mostly) limited to those populations, the bacteria have had no choice: they have had to jump species in order to find hosts in which to live. Because human beings now live in the habitat formerly occupied by those animals, many of the bacteria have moved into us. We are *not* inadvertent hosts. We are becoming primary reservoirs for many of these emerging diseases.

Unfortunately, bacterial resistance and ecological disruption can't help but intersect—with, of course, terrible ramifications. Many of the primary coinfections of Lyme are closely related to some of the most potent resistant bacterial organisms known. They are all members of the Proteobacteria phylum, a large and closely related group of bacteria.

One branch of the Proteobacteria includes *Bartonella* spp., and another includes *Ehrlichia* spp., *Anaplasma* spp., Rocky Mountain spotted fever, and the other rickettsia—all of which are coinfections of Lyme. A different but closely related branch includes *Klebsiella* spp., *E. coli*, cholera organisms, *Pseudomonas* spp., *Salmonella* spp. (including *Salmonella enterica*, the cause of typhoid fever), and *Shigella* spp.—all now resistant to many antibiotics. It also includes *Yersinia*, the organism responsible for the plague, a bacteria transmitted by fleas much

as *Bartonella* is. Still another branch includes the bacteria responsible for gonorrhea infections (also resistant), and another includes both *Helicobacter* and *Campylobacter* organisms.

There is strong evidence that both resistance and virulence factors are being shared among all members of this phylum. In other words, the various bacteria are teaching each other how to resist antibiotics and how to more easily infect people, thus making them sicker. They do this, usually, through sharing segments of DNA that have within them resistance and virulence information. *Bartonella* organisms, as an example, are often coinfective with many of the bacteria in this phylum and, in many instances, these kinds of multiple infections show a remarkable synergy during the disease process. In other words, the bacteria work together to reduce the effectiveness of the immune response and thus enable long-term infection.

In practical terms what all this means is that a great many more diseases are emerging out of the ecological matrix of the planet and infecting human beings. As well, many of them possess, or soon acquire, resistance to the majority of antibiotics that people use to treat bacterial diseases. And what they do together in the body is a great deal more complex than what any one of them does alone. The unique nature of the Lyme group of emerging infections, for example, is causing many researchers to refer to them not only as stealth pathogens but as second-generation pathogens. That is, they are very different than the bacteria (first-generation pathogens) for which antibiotics were created in the latter half of the twentieth century.

One of the most important understandings now facing us is accepting the limits of pharmaceuticals in the treatment of many of these emerging diseases. While antibiotics do still have a role, sometimes a very important one, they can no longer be relied on to provide the *sole* response to these kinds of infections as they spread through the human population. We have to approach treatment with a more sophisticated eye.

There are two important aspects to this. The first is realizing that single-treatment approaches, most of which were developed out of an

inaccurate nineteenth- and early-twentieth-century bacterial paradigm and were based on identifying the bacterial pathogen involved and killing it (i.e., monotherapy), are going to have to be abandoned as the primary method of treating these kinds of diseases. (Something that newer generations of physicians, especially in countries other than the United States, are beginning to understand.) The second is coming to understand just *what* the bacteria do in the body and then designing a treatment protocol that is *specific* in counteracting what the organisms do. In essence this means designing treatment protocols that address bacterial cytokine cascades, the particular health or non-health of the person's immune system, and the specific symptom picture that is reducing the quality of the person's life. Combined with antibacterials, of whatever sort, this creates the most sophisticated basic approach to the treatment of bacterial diseases. (If you add to that approach sophisticated human-to-human interactions oriented around deep caring and personal presence, something most physicians do not understand, you have the core of the most elegant and potent paradigm of healing disease that can occur.)

Some additional sophistications can occur for those who wish to go even deeper. Among them are the synergy that occurs among the healing agents that are used *and* the synergy that exists between the different bacteria. The use of healing agents (pharmaceuticals *or* herbs) always involves synergy between the agents used—though this is rarely addressed in a positive light. It's usually the side effects of a drug combination or drug/herb combination that are highlighted. However, herbs are synergistic with each other and can be synergistic with pharmaceuticals. For example, Chinese skullcap (*Scutellaria baicalensis*) root and licorice (*Glycyrrhiza* spp.) are synergists; they enhance the action of other herbs with which they are combined. They can, as well, enhance the action of pharmaceuticals. For example, Japanese knotweed (*Polygonum cuspidatum*) root, when used along with formerly ineffective antibiotics, can enhance the drugs' actions enough to make them effective.

As well, the microbial pathogens are often synergistic with each other. That is, when an infection involves two or more Lyme-group

organisms, the impacts on the body are often more severe. And this increase in severity is not additive, it is synergistic. This means that a simple linear approach will not give you an understanding of what the pathogens are doing in the body. As Telfer et al. (2010) comment:

> Most hosts, including humans, are simultaneously or sequentially infected with several parasites. . . . Indeed, effects are typically of greater magnitude, and explain more variation in infection risk, than the effects associated with host and environmental factors more commonly considered in disease studies. We highlight the danger of mistaken inference when considering parasite species in isolation rather than parasite communities. . . . Single parasite studies may yield incorrect or incomplete conclusions. Nonetheless, most epidemiological studies, in animals and humans, still focus on single species.

COINFECTION DYNAMICS

To generate sophisticated, reliable inverventions with these second-generation bacteria, there are a number of important dynamics to understand. The primary ones are understandings of the specific cytokine cascades that occur, the immune health (and preexisting conditions) in the host, the synergy between the various microorganisms, and their synergy with the vector of transmission.

Cytokines

The past several decades have seen a shift in the way many researchers (but regrettably few physicians) are approaching disease, nowhere more so than with the stealth pathogens that, due to their nature, often cause a wide range of symptoms. Researchers Ian Clark et al., for example, have done some marvelous work on the dynamics of cytokines specific to various disease conditions, especially malaria and its close relative babesiosis. They note:

> It is our view that focusing on malaria [and babesiosis and Lyme] in isolation will never provide the insights required to understand the pathogenesis of this disease. How can the illnesses caused by a spirochete and a virus be so clinically identical: typhoid readily diagnosed as malaria and malaria in returning travelers so commonly dismissed as influenza? . . . Understanding why these clinical confusions occur entails appreciating the sequence of events that led up to the cytokine revolution that has transformed the field over the last 15 years. (Clark et al., 2004)

Again, cytokines are small cell-signaling molecules released by cells that are damaged, cells of the immune system, and glial cells of the nervous system that are important in intercellular communications in the body. As it turns out, many disease organisms have learned to use cytokines for their own purposes.

In practical terms: When bacterium touches a cell, the cell gives off a signal, a cytokine, that tells the immune system what is happening and what that cell needs. This calls on the immune system to respond (initially, the innate immune system), which then sends specific immune cells to that location to deal with the problem. Stealth pathogens utilize this process to enable their successful infection of the body. Instead of waiting for the host's cells to release a cytokine, the microorganism does it as soon as it enters the body.

As the microorganism enters the body an initial, and very powerful, cytokine (for example, tumor necrosis factor, a.k.a. TNF) is released into the body. That initial cytokine stimulates the production of others, and those generate still others—all of which have potent impacts on the body. Thus a *cascade* of cytokines occurs. This cascade (and any subsequent immune response) is carefully modulated by the pathogen to produce the exact effects it needs to facilitate its spread in the body and its sequestration inside our body's cells (thus hiding it from the immune system), to break apart particular cells in order to get nutrients, and to shut down the parts of our immune response that can effectively deal

with the infection. It is this cascade of carefully modulated cytokines that, in fact, creates most of the symptoms that people experience when they become ill.

The cytokine cascade dynamics and its impacts alter depending on the animal host and its immune health. Clark et al. found that parasite load—that is, the numbers of organisms in the body—counterintuitively, did not correlate to severity of illness, something that plays havoc with older bacterial theories of disease. They comment:

> Since *P. falciparum* and *Babesia microti,* another hemoprotozoan protozoan, infect both humans and another host (the owl monkey, *Aotus* sp., and the mouse, respectively), it was possible to establish that the relationship [between severity of illness and parasite density] depended on a characteristic of the host, not the parasite species. This provided, for the first time, a plausible explanation for the long-standing puzzle that, although very low parasite densities cause onset of illness in first infections of human malaria and babesiosis and bovine babesiosis, mice withstand high parasite densities of several species of either causative genus before onset of illness. In other words, previously unexposed humans become ill after exposure to very few hemoprotozoan parasites whereas mice do not become ill until exposed to many organisms. Similarly inexplicable had been the observation that incredibly high malaria parasite densities (sometimes reaching a peak of 35,000 parasites per 10,000 red blood cells) do not cause illness in reptiles. (Clark et al., 2004)

And in fact, very low densities of babesial (and ehrlichial and anaplasmal) organisms in people can (and do) cause serious disease. (This is also why diagnosis is sometimes so difficult; there are so few organisms they just can't be found.) In some people high densities occur but they remain asymptomatic; in others low densities exist along with multiorgan failure, coma, and death. The belief that a high density of infectious organisms is correlated with severity of disease turns out to be

inaccurate. The thought that very few organisms could cause death did not, in older models of disease (and still for many physicians), compute. Instead of parasite density, something else is involved in the development and seriousness of the disease and its symptoms. And that something is cytokines. Clark et al. (2004) note:

> The long-postulated malaria toxin did not cause illness directly, as had been assumed since the late 19th century, but did so through inducing the host to release a shower of LPS-inducible cytokines that, at lower concentrations, are an essential part of the host immune response.

They continue . . .

> Serum TNF level in East African and West African children at time of admission correlated with the severity of disease and mortality, even though serum TNF levels varied greatly. . . . Patients with complicated malaria (combined organ dysfunction, hypotension, thrombocytopenia, and the highest parasite densities) and the longest durations between onset of clinical symptoms and diagnosis had significantly higher TNF levels than those in whom malaria ran a more benign course.

Cytokine researchers have found that even tiny alterations in existing cytokine profiles will cause significant shifts in disease symptoms. Clark et al. (2004) comment, "In one IL-2 [interleukin-2] study, 15 of 44 patients developed behavioral changes sufficiently severe to warrant acute intervention and 22 had severe cognitive defects."

Although the news has not yet reached most medical doctors, many researchers are insisting that the most important thing is not the microbial source of infection but rather the cytokine cascade that is generated. This is especially true during coinfections with multiple stealth pathogens. One of the better articles on this is "Transmission consequences

of coinfection: Cytokines writ large?" by Andrea Graham et al. (2007). The authors comment, "When the taxonomic identities of parasites are replaced with their cytokine signatures, for example, it becomes possible to predict the within-host consequences of coinfection for microparasite replication" as well as symptom picture, treatment approaches, and treatment outcomes.

(This, by the way, is the approach I use when exploring how best to treat the complex of Lyme-group coinfections. After more than a decade of experience, it turns out that interrupting the cytokine cascade these organisms initiate does in fact reduce or even eliminate both symptoms and infection.)

Immune Health and Preexisting Conditions

Lyme-group parasites, like many stealth pathogens, utilize the immune responses of whatever mammal they infect as part of their infection strategy. As Graham et al. (2007) note: "The influence of cytokines on effector responses is so powerful that many parasites manipulate host-cytokine pathways for their own benefit," as is indeed the case with *Babesia, Ehrlichia*, and *Anaplasma*. Most crucially, they continue, "the magnitude and type of cytokine response influence host susceptibility and infectiousness. Susceptibility to a given parasite will be affected by cytokine responses that are ongoing at the time of exposure, including responses to pre-existing infections." In other words, the parasites utilize inflammatory processes that are already occurring in the body (e.g., if you have preexisting arthritis) to facilitate successful infection.

But equally important is the overall *immune health* of the infected person. Telfer et al. (2008) comment:

> There is mounting evidence from experimental studies that the outcome of interactions during co-infections (for either the host or the parasite) is context dependent, potentially varying with different host or parasite genotypes or environmental conditions. Perhaps most critically, outcome can depend on the timing and sequence of

> infections. . . . Susceptibility is a property of an individual host at a given time. . . . The ability of a parasite to establish an infection successfully will depend on the initial immune response of the exposed host. On entry into the host, a parasite will experience an "immunoenvironment" potentially determined by both previous and current infections, as well as intrinsic factors such as sex, age, nutritional status and genotype. The immediate immuno-effectors in a naive host will be dominated by cells and molecules that comprise the innate immune response, and thus the efficiency of this arm of host immunity at reducing and clearing an infection will be influential in determining susceptibility.

Resto-Ruiz et al. (2003) emphasize this as well, as do so many other researchers. They note that people with "intact" immune function who become infected with *B. henselae* usually do not experience severe symptoms. However, they continue, "the reduced ability of the host's immune response to control bacterial infection apparently results in a bacteremia of longer duration." In other words, the immune status of someone with coinfections *must be* addressed as part of any treatment protocol. Due to the synergistic nature of coinfections an inescapable truth exists: the weaker or more compromised the immune system, the more likely someone is to become infected and the more likely they are to have a debilitating course of illness.

Improving the immune status of those with chronic coinfections allows the immune system, refined over very long evolutionary time, to do what it does best, which is to use very elegant mechanisms to control and clear infection. Eventually, the healthy immune system begins to identify the outer membrane proteins of the bacteria and create antibodies to them. Due to the sophistication of the bacteria's subversion of the host immune system during coinfections, this can take anywhere from four to eight months. In those whose immune systems are very compromised it may take longer; how long is directly proportional to the health of the immune system. Once the immune system creates the

proper antigens, the bacteria are then eliminated fairly rapidly from the body. Reinfection is difficult as the antibodies remain in the body for some time.

Immune system health is a crucial element in the treatment of coinfections and it is one that technological medicine is generally unable to address. It is most definitely *not* a subject in which most physicians are trained.

Parasite Synergy

Symptoms, length of illness, and its severity are all generally worse if infection occurs by more than one organism. The research of Graham et al. (2007) confirmed that, as the researchers put it, "coinfection increases the reproductive number for the incoming parasite species and facilitates its transmission through the host population." In other words, while the immune system is often compromised by the cytokine dynamics initiated by one type of bacteria, multiple, simultaneously initiated cascades are more potent in their impacts; infection is much more easily accomplished. This is, as Graham et al. comment, more common than otherwise: "Hosts that are coinfected by multiple parasite species seem to be the rule rather than the exception in natural systems and some of the most devastating human diseases are associated with coinfections that challenge immune response efficacy."

Another very fine paper on this, by S. Telfer et al. (2008), echoes Graham et al., with its authors noting, "In natural populations 'concomitant' or 'mixed' infections by more than one parasite species or genotype are common. Consequently, interactions between different parasite genotypes or species frequently occur. These interactions may be synergistic or antagonistic with potential fitness implications for both the host (morbidity and/or mortality) and parasite (transmission potential)." In other words, if you want to successfully treat someone who is infected with a vector-borne infection you need to realize up front that it is usually the case that coinfection has occurred and you have to look at the interactive picture, not merely single infectious agents. We can no

longer assume that bacterial organisms exist in a vacuum. They can't be studied in isolation.

Telfer and his associates, in another paper, explored the interactions and infection risks between cowpox virus, *Babesia microti*, *Bartonella* spp., and *Anaplasma phagocytophilum*. They note:

> We found that this community of parasites represents not four independent infections but an interconnected web of interactions: Effects of other infections on infection risk were strong and widespread, and connectance within the parasite community was exceptionally high, with evidence detected for all possible pair-wide interactions. (Telfer et al. 2010)

They found, as they note, that "the sizes of the effects of other parasites on infection risk were also similar to, and frequently greater than, other factors." Specifically here, seasonal effects. That is, infection with Lyme-group coinfections is generally higher in certain months, e.g., three times higher for anaplasmal infections and 15 times higher for babesial. However, this is matched by the synergistic effects of multiple coinfections on host susceptibility. As they comment, "The most likely explanation for these effects is that interactions between these microparasites with individual hosts have a large impact on host susceptibility."

The synergistic effects also contribute to symptom picture. If *Bartonella* is a coinfection with Lyme, for example, what you then get is assault on and resultant degradation of the collagen systems of the body by the Lyme spirochetes while a simultaneous assault on red blood cells occurs with a concomitant subversion and abnormalization of endothelial cells and their functions. So, the infected person is battling not only Lyme arthritis or neurological Lyme (both caused by collagen degradation) but a red blood cell infection (with potential anemia and lowered oxygen availability in the blood) and abnormal endothelial cell growth in the blood vessels themselves.

But the *Bartonella* bacteria also use what the Lyme bacteria are

doing for their own purposes. This, as Telfer et al. (2010) noted, also affects host susceptibility. Once Lyme spirochetes damage collagen tissues, for instance in the joints of the knee, the body sends CD34+ cells to that site to help repair the damage. This is a normal part of the healing process when collagen is damaged. But *Bartonella* typically invade CD34+ cells, so some of those CD34+ cells will be infected and the *Bartonella* will take advantage of the local inflammation to establish a colony of their own in that location. The existing inflammation actually facilitates their growth. Once established, the *Bartonella* bacteria will begin their own cytokine cascade, which will itself contribute to even more collagen degradation at that location.

The more coinfections, the more stress on the immune system. As Telfer et al. (2008) comment, "Attempts by the immune system to simultaneously counter the multiple parasite species involved in a coinfection can lead to immunopathological disease and pathology that are more than the simple additive pathogenic effects of the different parasite species." This is a crucial point. *The impact of multiple coinfectious organisms is* ***not*** *additive.* They are synergistic. They create effects that are more than the sum of the parts.

For example, infections with both *Babesia* and *Bartonella* are synergistically impactful on red blood cells and can reduce red blood cell counts up to 25 percent, leading to anemia, fatigue, breathlessness, and general weakness. In the immune-competent, neither parasite will normally create this severe an impact by themselves. (One positive note: Because both parasites are competing for red blood cells, longer studies have found that the *Babesia*, over time, tends to clear the *Bartonella* infection by outcompeting the latter organisms. Also: If someone is already infected by *Bartonella*, they are less likely to be infected with *Babesia*, and vice versa. Nevertheless, during infection with both, in the initial stages, the impact on red blood cells is immense.)

Babesia species sequester themselves in the capillary networks of the spleen and liver. *Bartonella* species sequester themselves in the endothelial cells of the capillary networks of the spleen and liver. Both then

seed the bloodstream from those locations at regular intervals. The impacts of infection with both parasites on the spleen and liver are much greater than either alone and this has to be taken into account in any treatment approach. In other words, you have to design spleen- and liver-supportive interventions that are tightly focused on normalizing functioning in those organs. This protects them from cytokine damage *and* begins to reduce habitat for the parasites, thus reducing bacterial/protozoal load and presence in the body.

Studies of coinfection with *Anaplasma* and *Borrelia* species have found that the deleterious impacts on immune function from such a double infection enhance the pathogenicity of the Lyme spirochetes and long-term infection. Researchers note, "These effects may have a significant impact on the persistence of *B. burgdorferi* and the immunologic selective pressure it is subjected to" (Moro et al. 2002). Coinfection with Lyme spirochetes and anaplasmal bacteria produces synergistic effects on cytokine expression. Interleukin-12 (IL-12), interferon-gamma (IFN-γ), and tumor necrosis factor alpha (TNF-α) are more inhibited during early infection than with either bacteria alone; IL-6 levels are higher. Coinfection with these two organisms also produces more significant impacts in the brain and on brain function. There is a synergistically increased production and release of matrix metalloproteinases (MMPs) in the brain, specifically MMP-1, -3, -7, -8, and -9. IL-10 levels (which reduce effective innate immune responses and which are induced by the bacteria during initial infection) are significantly higher, and IL-8 and MIP-1α (macrophage inflammatory protein 1-alpha) levels increase. Along with the MMPs, this leads to increased vascular permeability in the brain and central nervous system. This produces more inflammation deeper in the brain, with increased brain dysfunction and more serious neurocognitive defects. There is an increased bacterial burden throughout the body; the symptom picture is generally worse.

Coinfection with *Borrelia* spirochetes and *Babesia microti* shows similar impacts and results in both increased severity of Lyme arthritis and longer duration.

Telfer et al. (2010) also found that infection with *Anaplasma* (for example) made subsequent infection by *Babesia* much easier—in fact, twice as likely. Reversing the order of infection found the same rate of increase—each organism paves the road for the other. Telfer et al. also found that animals infected with one *Bartonella* species who were also infected by other *Bartonella* species were much more likely to have long-term infections—that is, a chronic illness.

An *Ehrlichia* infection, when combined with *Bartonella* (or *Babesia* or a hemoplasma), is often much more severe in its impacts than would be expected by looking at either alone. In this situation, both white and red blood cells are infected. Specifically, *Ehrlichia* infect neutrophils, the most abundant form of white blood cell in the body and an essential element of the innate immune system. Thus the immune system is fighting not only bacteria in the red blood cells and vascular tissues but bacteria inside its own immune cells. To make it worse, the bacteria cross-talk and engage in mutual support of each other, actually enhancing each other's impacts on the host and their resistance to antibiotics.

During coinfection with both *Mycoplasma* and *Bartonella*, there are going to be severe effects on the endothelial cells, the red blood cells, and the brain and central nervous system that are out of proportion to infection by either organism alone. Thus the cytokine impacts on those areas of the body are going to be stronger, synergistic, and more debilitating; treatment regimens must be designed to reverse much stronger effects than would occur by either alone. This often calls for larger doses, longer treatment duration, and more sophisticated intervention for symptom management. As only one example, such a double infection *may* simultaneously cause a form of regular epileptic seizures *and* periodic bouts of homicidal rage. Herbs that reduce the cytokine cascades involved *and* are specific for these types of seizures *and* are particularly calming to the nervous system, thus reducing extreme rage events, need to be used and the doses need to be largish, continual, and very focused. (Chinese skullcap is a specific example, and it tends to be synergistic with several others such as motherwort and pasqueflower

that are also specific for these kinds of conditions, although in slightly different ways.)

Vector of Transmission

The vector of transmission—that is, the tick, flea, mosquito, and so on in which the bacteria live before they are injected through a bite into a human being—plays a crucial part in the disease as well.

Bacteria have learned to take advantage of the biologically active components in their vector's saliva in order to facilitate avoidance of the immune system. For example, tick saliva itself contains highly active compounds that reduce nerve signaling, thus allowing the tick to remain embedded for long periods. The saliva also reduces swelling at the bite location and inactivates immune responses, again allowing the tick to feed for longer periods. Similar though unique dynamics occur for every insect vector in this group. The Lyme group of bacteria take advantage of this in order to more successfully infect a new host. There is in fact a synergy between the vector's inactivation of the immune system and the bacterial inactivation of immune responses. This makes penetration of the host and long-term infection much easier. Studies have consistently shown that infection through a vector of transmission produces longer and more serious infections than direct infection, that is, through hypodermic injection (by researchers). This kind of synergy is not limited, it appears, to saliva.

Although little research has occurred on louse and flea feces, two main routes of infection for *Bartonella*, researchers comment that a similar dynamic might be playing out here as well: "It is also quite likely that under natural conditions components of the flea feces other than *B. henselae* may enhance the development of *Bartonella*-induced lymphadenopathy and thus enable the onset of disease at a lower dose of infection in humans" (Kunz et al., 2008) Given the very long evolutionary relationship between ticks and Lyme or fleas and *Bartonella*, it is not surprising that the bacteria have learned to utilize both to assist their infection of new hosts.

PRACTITIONER ORIENTATION AND APPROACH TO TREATMENT

In my experience, the technological medical community tends to downplay both the impact and occurrence of coinfections in the people they see while the natural medicine community tends to exaggerate them. Oddly, despite their training, most physicians don't really understand bacterial organisms very well, nor how to treat them. They tend to look in textbooks (or drug company brochures) for a pharmaceutical that is active for the bacteria in question and apply it, a fairly superficial approach that is increasingly failing in practice. If they have not definitively *identified* the bacterial cause of the condition they will generally prescribe a broad-spectrum antibiotic that will, as often as it helps, do more harm than good (the literature is full of such blunders). They are also very poor at developing a broad, synergistic, and human view of the people they treat, the disease conditions that occur, and the pharmaceutical interventions they commonly use. Most of them stopped *reasoning* a long time ago and simply act as if the worldview they were trained in, in school, really is an accurate map of the world around them—despite current events and research clearly showing it is not.

The natural medicine community, on the other hand, often tends to be somewhat hysterical about resistant or emerging infections, commonly fails at rigor of analysis, and too often lacks the focus, and courage, needed to confront deadly or life-debilitating infections. Both communities (often) make too much money off people's suffering—though, in fairness, most (not all) of the alternative community tends to make much less; I just don't see that many herbalists with their own private airplanes. (Nevertheless, overall, the natural medicine community is much safer—and less expensive, irrespective of their level of training—and they very rarely kill their patients. *Properly* prescribed pharmaceuticals are the fourth leading cause of death in the United States.)

When approaching the treatment of coinfections, the approach should be depth based with rigor of analysis. The bacterial infections

need to be identified (muscle testing is not reliable enough, and no, ELISA is not either—neither should be relied upon as diagnostically definitive).

Once a diagnosis is achieved, a treatment protocol should be initiated. This seems obvious but in the actual world, not the theoretical one in people's heads or in books, most people are not diagnosed competently, or accurately. Many physicians and herbalists (including most naturopaths) simply look at the symptoms and *guess* at the underlying condition. In acute conditions where something must be done immediately this is a legitimate approach but *at the same time,* in the background, there needs to be a concerted effort to correctly diagnose. Physicians, counterintuitively, are often not very good at this—as a number of the case studies in this volume make clear. For many of them the problem lies in their internalized paradigms about disease, the structure of their practice, and, frankly, tremendous hubris. Those of us concerned with Lyme and its coinfections have heard scores of stories about physicians insisting that Lyme could not be the cause of a person's symptoms simply because Lyme isn't endemic in that location (so the physician refused to test for it), or that the person had already used antibiotics so the disease was cured and all the symptoms must now be in that person's head, or that the physician just did not have time for the kind of neediness that the Lyme-infected often present. Most physicians are not in the healing business but the pharmaceutical-dispensing business—these are not the same things.

Still, it is clear that in some cases antibiotics are very effective and with diseases as debilitating as Lyme and its coinfections they should be considered. However, if that kind of superficial approach fails, then an in-depth understanding of the cytokine cascades and the likely interactions between the coninfections should be developed and a treatment protocol initiated that addresses all that in depth. The most important thing in treating coinfections is to reduce the inflammatory processes the bacteria initiate, basically by counteracting the cytokine cascade they initiate. That stops pretty much all the symptoms right there, especially

if treatment protocols are also begun that are designed to protect the areas of the body that are affected. And again, the immune system must be strengthened. As Telfer et al. (2010) observe, "An immune response that effectively cleared the infection from endothelial cells would therefore ultimately control an infection [by *Bartonella*]." Importantly, this observation applies as well to *any* intervention that will protect endothelial tissue from the bacteria, not just immune response. So if you use Japanese knotweed (*Polygonum cuspidatum*) or epigallocatechin gallate (EGCG) as an interventive, abnormal endothelial cell inflammation would cease. The bacteria *can't* survive if they are not able to initiate their particular form of inflammation in the body; it is how they make habitat and scavenge food. If you simultaneously enhance immune function, the body is then able to deal with the infection on its own. The addition of protocols to reduce acute symptoms and help restore quality of life are also very helpful. Not only does this help support the body's health at that particular location but the quality of life of the infected person is enhanced. The importance of this on outcomes cannot be stressed enough.

And finally, the *human* response of the healer toward the patient is essential. People who are ill *need* deep, caring contact with another human being. It is an essential aspect of healing. Physicians (and herbalists, including naturopaths) who don't take the time for this are, in my opinion, engaging in malpractice of the most egregious sort and, in effect, betraying their duty to their patients. I have continually seen, and numerous studies have found, that this one thing, in and of itself, contributes significantly to the successful resolution of illness. Genuine caring *is* medicine and it is time, more than time, that we, as a culture, recognize that. We absolutely *have to abandon* the paradigm that insists we not touch our patients, that we not love them, that we not spend time with them, that we not act as guides for them on their journey through illness. We must abandon the training, and the teacher, that tells us that we should *not* care, that somehow, as healers, we must keep our emotional distance from those who come to us.

Antibacterials *can* help but comprehensive treatment protocols must be more complex than that simple, monotherapeutic approach. Relying on a "kill the invaders" approach is becoming increasingly ineffective. Soon, if the world's major epidemiologists and researchers are to be believed, it won't work at all.

The bacteria are *evolving.* We should, too.