ADVANCED TOPICS IN LYME DISEASE

DIAGNOSTIC HINTS AND TREATMENT GUIDELINES FOR LYME AND OTHER TICK BORNE ILLNESSES

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Fifteenth Edition
2005

Welcome to the fifteenth edition of the “Guidelines”. Since the last edition, enough new information has become available to justify this revision. New insights regarding co-infections, test refinements, and new treatment regimens are included.

I once again extend my best wishes to the many patients and caregivers who deal with Lyme, and a sincere thank you to my colleagues whose endless contributions have helped me shape my approach to tick borne illnesses. I hope that my new edition proves to be useful. Happy reading!

BACKGROUND INFORMATION

In general, you can think of Lyme as having three categories: acute, early disseminated, and chronic. The sooner treatment is begun after the start of the infection, the higher the success rate. However, since it is easiest to cure early disease, this category of Lyme must be taken seriously. Undertreated infections will inevitably resurface, usually as chronic Lyme, with its tremendous problems of morbidity and difficulty with diagnosis and treatment. So, while the bulk of this document focuses of the more problematic chronic patient, strong emphasis is also placed on earlier stages of this illness.

A very important issue is the definition of “Chronic Lyme Disease”. Based on my clinical data and the latest published information, I offer the following definition. To be said to have chronic Lyme, these three criteria must be present:

1. Illness present for at least one year
2. Have persistent major neurologic involvement (such as encephalitis/encephalopathy, meningitis, etc.) or active arthritic manifestations (active synovitis).
3. Still have active infection with B. burgdorferi (Bb), regardless of prior antibiotic therapy (if any).

Chronic Lyme is an altogether different illness than earlier types, mainly because of the inhibitory effect on the immune system (Bb has been demonstrated *in vitro* to both inhibit and kill B- and T-cells, and will decrease the count of the CD-57 subset of the natural killer cells). As a result, not only is the infection with Bb perpetuated, but the entire issue of co-infections arises. Ticks may contain and transmit to the host a multitude of potential pathogens. The clinical presentation of Lyme therefore reflects which pathogens are present and in what proportion. Apparently, in early infections, before extensive damage to the immune system has occurred, if the germ load of the co-infectors is low, and the Lyme is treated, many of the other tick-transmitted microbes can be contained and eliminated by the immune system. However, in the chronic patient, invariably the illness reflects a mixed infection, the individual components of which are now active enough that they too must be treated. In addition, many latent infections which may have pre-dated the tick bite, for example herpes viruses, can reactivate, thus adding to the illness.

An unfortunate corollary is that serologic tests can become *less* sensitive as the infections progress, obviously because of the decreased immune response upon which these tests are based. Not surprisingly the seronegative patient will convert to seropositive 36% of the time after antibiotic treatment is begun and a recovery is underway.

The severity of the clinical illness is directly proportional to the spirochete load, the duration of infection, and the presence of co-infections. These factors also are proportional to the intensity and duration of treatment needed for recovery. More severe illness also results from other causes of weakened defenses, such as from severe stress, immunosuppressant medications, and severe intercurrent illnesses. This is why steroids and other immunosuppressive medications are contraindicated in Lyme.

Many collateral conditions result in those who have been chronically ill so it is not surprising that damage to virtually all bodily systems can result. Therefore to fully recover not only do all of the active infections have to be treated, but all of these other issues must be addressed in a thorough and systematic manner. No single treatment or medication will result in full recovery of the more ill patient. Only by addressing all of these issues and engineering treatments and solutions for all of them will we be able to restore full health to our patients.

It is clear that in the great majority of patients, chronic Lyme is a disease affecting predominantly the nervous system. Thus, careful evaluation often includes neuropsychiatric testing, SPECT and MRI brain scans, CSF analysis when appropriate, regular input from Lyme-aware neurologists and psychiatrists, pain clinics, and occasionally specialists in psychopharmacology.

As an extension of the effect of chronic Lyme Disease on the central nervous system, there often is a deleterious effect on the hypothalamic-pituitary axis. Varying degrees of pituitary insufficiency are being seen in these patients, the correction of which has resulted in restoration of energy, stamina and libido, and resolution of persistent hypotension. Unfortunately, not all specialists recognize pituitary insufficiency, partly because of the difficulty in making the laboratory diagnosis. However, the potential benefits of diagnosing and treating this justify the effort needed for full evaluation. Interestingly, in a significant number of these patients, successful treatment of the infections can result in a reversal of the hormonal dysfunction, and hormone replacement therapies can be tapered off!

The concept of a "therapeutic alliance" between the caregiver and patient must again be emphasized. This means that the patient has to work with and become part of the medical team, and must take responsibility for complying with the recommendations given, maintaining the best possible health status, reporting promptly any problems or new symptoms, and especially in realizing that despite all our best efforts, success in diagnosis and treatment is never assured. The medical team must make great efforts to listen carefully to the patient and not be too quick to dismiss seemingly bizarre or illogical complaints.

CO-INFECTION

A huge body of research and clinical experience has demonstrated the nearly universal phenomenon in Lyme patients of co-infection with multiple tick-borne pathogens. Significant numbers of Lyme patients have been shown to also carry Babesia species, Ehrlichias, Anaplasmas, Mycoplasmas, Bartonellas and viruses. Rarely, yeast forms have been seen in peripheral blood. Studies have shown that co-infection results in a more severe clinical presentation, with more organ damage, and the pathogens become more difficult to eradicate. It is known that Babesia infections, like Lyme Borreliosis, are immunosuppressive. There are changes in the clinical presentation compared to when each infection is present individually, with different symptoms, and atypical signs. There may be decreased reliability of standard diagnostic tests, and most importantly, there is recognition that chronic, persistent forms of each of these infections do indeed exist. As time goes by, I am convinced that even more pathogens will be found.

Therefore, real, clinical Lyme as we have come to know it, especially the later and more severe presentations, probably represents a mixed infection. I will leave to the reader the implications of how this may explain the discrepancy between laboratory study of pure Borrelia infections, and what front line physicians have been seeing for years in real patients.

Because of this, I have a loose definition of “Lyme Disease”: I see it as more than an infection with Borrelia burgdorferi, I see it as the illness that results from the bite of an infected tick, thus incorporating all the pathogens and corollary conditions. I again emphasize this because all of these infections and conditions must be addressed and treated if a full recovery is to occur.

The evaluation of a Lyme patient must begin with testing for all currently known tick borne pathogens. Serological studies for Borrelia, Babesia, Bartonella and Ehrlichia should be combined where appropriate with direct antigen assays. Antigen detection tests (antigen capture and PCR) are especially helpful in evaluating the seronegative patient and those still ill or relapsing after therapy. Unfortunately, over a dozen protozoans other than Babesia microti can be found in ticks, yet commercial tests for only B. microti and WA-1 are available at this time, so as in Borrelia, clinical assessment is the primary diagnostic tool. In Ehrlichiosis, test for both the monocytic and granulocytic forms. Many presently uncharacterized Ehrlichia-like organisms can be found in ticks and may not be picked up by currently available assays, so in this illness too, serologies are only an adjunct in making the diagnosis.

COLLATERAL CONDITIONS

Experience has shown that collateral conditions exist in those who have been ill a long time. The

evaluation should include testing both for differential diagnosis and for uncovering other subtle abnormalities that may coexist.

Test **B12 levels**, and be prepared to aggressively treat with parenteral formulations. If neurologic involvement is severe, then consideration should be given to treatment with methylcobalamin (as outlined below in the section on nutritional support).

Magnesium deficiency is very often present and quite severe. Hyperreflexia, muscle twitches, myocardial irritability, poor stamina and recurrent tight muscle spasms are clues to this deficiency. Magnesium is predominantly an intracellular ion, so blood level testing is of little value. Oral preparations are acceptable for maintenance, but most need additional, parenteral dosing: 1 gram IV or IM at least once a week until neuromuscular irritability has cleared.

Pituitary and other endocrine abnormalities are far more common than generally realized. Evaluate fully, including growth hormone levels. When testing the thyroid, measure free T3 and free T4 levels and TSH. Nuclear scanning and testing for autoantibodies may be necessary. Quite often, a full battery of provocative tests is in order to fully define the problem.

Activation of the **inflammatory cascade** has been implicated in blockade of cellular hormone receptors. One example of this is insulin resistance, which may partly account for the dyslipidemia and weight gain that is noted in 80% of chronic Lyme patients. Clinical hypothyroidism can result from receptor blockade and thus hypothyroidism can exist despite normal serum hormone levels. In addition to measuring free T3 and T4 levels, check basal A.M. body temperatures. If hypothyroidism is found, you may need to treat with both T3 and T4 preparations until blood levels of both are normalized.

Neurally mediated hypotension (NMH) is not uncommon, and is diagnosed by tilt table testing. Symptoms can include palpitations lightheadedness and shakiness especially after exertion and prolonged standing, heat intolerance, dizziness, and fainting (or near fainting). NMH can result from autonomic neuropathy and endocrine dyscrasias. If NMH is present, treatment can dramatically lessen fatigue, palpitations and wooziness, and increase stamina. This test should be done by a cardiologist and include Isuprel challenge. This will demonstrate not only if NMH is present, but also the relative contributions of hypovolemia and sympathetic dysfunction. Immediate supportive therapy is based on blood volume expansion (increased sodium and fluid intake and possibly Florinef plus potassium). If not sufficient, beta blockade may be added based on response to the Isuprel challenge. The long term solution involves restoring proper hormone levels and treating the Lyme to address this and the autonomic dysfunction.

SPECT scanning of the brain- Unlike MRI and CT scans, which show structure, SPECT scans show function. So SPECT scans give us information unattainable through X-rays, CT scans, MRI's, or even spinal taps. In majority of chronic Lyme Borreliosis patients, these scans are abnormal. Although not diagnostic of Lyme specifically, if the scan is abnormal, the scan can not only quantify the abnormalities, but the pattern can help to differentiate medical from psychiatric causes of these changes. Furthermore, repeat scans after a course of treatment can be used to assess treatment efficacy. Note that improvement in scans lag behind clinical improvement by many months.

If done by knowledgeable radiologists using high-resolution equipment, scanning will show characteristic abnormalities in Lyme encephalopathy- global hypoperfusion (may be homogenous or heterogeneous). What these scans demonstrate is neuronal dysfunction and/or varying degrees of cerebral vasculitis. To assess the relative contributions of these two processes, the SPECT scan is done before and after acetazolamide. If the post acetazolamide scan shows significant reversibility of the abnormalities, then vasoconstriction is present, and can be treated with vasodilators, which may clear some cognitive symptoms. Therapy can include acetazolamide, serotonin agonists and even Ginkgo biloba. Therapeutic trials of these may be needed.

Under certain circumstances, two SPECT scans are done. The second must be done on a different day, after IV administration of Diamox (acetazolamide). This medication, also used for glaucoma, can actually augment blood flow in the brain. This technique can help to differentiate whether an abnormal scan is the result of poor blood flow, or poor neuron health.

You should not be given Diamox if you have:

- severe kidney/liver disease
- electrolyte abnormalities
- pregnancy
- sulfa allergy
- recent stroke
- high dose aspirin treatment

The most frequent side effects after Diamox administration are numbness of the face or arms, ears ringing, nausea, and drowsiness. If present, these symptoms can last several hours or even extend into the next day. The patient should not go to the test alone due to these possible side effects.

Two different researchers have provided evidence that B. burgdorferi, like many other pathogenic bacteria, can produce **neurotoxins**. Clinical trials aimed at removing these toxins have proven helpful in a small subset of pateints. I will discuss this in more detail in a later section.

LYME BORRELIOSIS

DIAGNOSTIC HINTS

Lyme is diagnosed clinically, as no currently available test, no matter the source or type, is definitive in ruling in or ruling out infection with these pathogens, or whether these infections are responsible for the patient's symptoms. The entire clinical picture must be taken into account, including a search for concurrent conditions and alternate diagnoses, and other reasons for some of the presenting complaints. Often, much of the diagnostic process in late, disseminated Lyme involves ruling out other illnesses and defining the extent of damage that might require separate evaluation and treatment.

Consideration should be given to tick exposure, rashes (even atypical ones), evolution of typical symptoms in a previously asymptomatic individual, and results of tests for tick-borne pathogens. Another very important factor is response to treatment- presence or absence of Jarisch Herxheimer-like reactions, the classic four-week cycle of waxing and waning of symptoms, and improvement with therapy.

ERYTHEMA MIGRANS

Erythema migrans (EM) is diagnostic of Bb infection, but is present in *fewer than half*. Even if present, it may go unnoticed by the patient. It is an erythematous, centrifugally expanding lesion that is raised and warm. Sometimes there is mild stinging or pruritus. The EM rash will begin four days to several weeks after the bite, and may be associated with constitutional symptoms. Multiple lesions are present less than 10% of the time, but do represent disseminated disease. Some lesions have an atypical appearance and skin biopsy specimens may be helpful. When an ulcerated or vesicular center is seen, this may represent a mixed infection, involving other organisms besides B. burgdorferi.

After a tick bite, serologic tests (ELISA. IFA, western blots, etc.) are not expected to become positive until several weeks have passed. Therefore, if EM is present, treatment must begin immediately, and one should not wait for results of Borrelia tests. You should not miss the chance to treat early disease, for this

is when the success rate is the highest. Indeed, many knowledgeable clinicians will not even order a Borrelia test in this circumstance.

DIAGNOSING LATER DISEASE

When reactive, serologies indicate exposure only and do not directly indicate whether the spirochete is now currently present. Because Bb serologies often give inconsistent results, test at more than one laboratory using, if possible, different methods. The suggestion that two-tiered testing, utilizing an ELISA as a screening tool, followed, if positive, by a confirmatory western blot, is illogical in this illness. The ELISA is not sensitive enough to serve as an adequate screen, and there are many patients with Lyme who test negative by ELISA yet have fully diagnostic western blots. I therefore recommend against using the ELISA. Order IgM and IgG western blots- but be aware that in late disease there may be repeatedly peaking IgM's and therefore a reactive IgM may not differentiate early from late disease, but it does suggest an active infection. When late cases of LB are seronegative, 36% will transiently become seropositive at the completion of successful therapy.

Western blots are reported by showing which bands are reactive. 41KD bands appear the earliest but can cross react with other spirochetes. The 18KD, 23-25KD (Osp C), 31KD (Osp A), 34KD (Osp B), 37KD, 39KD, 83KD and the 93KD bands are the most specific but appear later or may not appear at all. You need to see at least the 41KD and one of the specific bands. 55KD, 60KD, 66KD, and 73KD are nonspecific and nondiagnostic.

PCR tests are now available, and although they are very specific, sensitivity remains poor, possibly less than 30%. This is because Bb causes a deep tissue infection and is only transiently found in body humors. Therefore, just as in routine blood culturing, multiple specimens must be collected to increase yield; a negative result does not rule out infection, but a positive one is significant. You can test whole blood, buffy coat, serum, urine, spinal and other body fluids, and tissue biopsies. Several blood PCRs can be done, or you can run PCRs on whole blood, serum and urine simultaneously at a time of active symptoms. The patient should be antibiotic free for at least six weeks before testing to obtain the highest yield.

Antigen capture is becoming more widely available, and can be done on urine, CSF, and synovial fluid. Sensitivity is still low, but specificity is high.

Spinal taps are not routinely recommended, as a negative tap does not rule out Lyme. Antibodies to Bb most commonly are found in Lyme meningitis, but are rarely seen in non-meningitic CNS infection, including even advanced encephalopathy. Even in meningitis, antibodies are detected in the CSF in less than 20% of patients with late disease. Therefore, spinal taps are only performed on patients with pronounced neurological manifestations in whom the diagnosis is uncertain, if they are seronegative, or are still significantly symptomatic after completion of treatment. When done, the goal is to rule out other conditions, and to determine if Bb antigens or nucleic acids are present. It is especially important to look for elevated protein and mononuclear cells, which would dictate the need for more aggressive therapy, as well as the opening pressure, which can be elevated and add to headaches, especially in children.

I strongly urge you to biopsy all unexplained skin lesions/rashes and perform PCR and careful histology. You will need to alert the pathologist to look for spirochetes.

LYME DISEASE AND PREGNANCY

It is well known that B. burgdorferi, the agent of Lyme, can cross the placenta and infect the fetus. In addition, breast milk from infected mothers has been shown to harbor spirochetes that can be detected by PCR and grown in culture.

The Lyme Disease Foundation in Hartford, CT had kept a pregnancy registry since the late 1980s. They

found that if patients were maintained on adequate doses of antibiotic therapy during gestation, then no babies were born with Lyme. My own experience over the last ten years agrees with this.

Lyme literate pediatricians have treated literally hundreds of babies born with Lyme Disease, having contracted it as an intrauterine infection. He treats these children with antibiotics and finds that they generally do well, provided that treatment is aggressive and of adequate duration. Occasionally, he has to retreat these patients as Lyme infections are chronic and can tend to recur.

The options for treating the mother include oral, intramuscular, and intravenous therapy.

Oral regimens include amoxicillin, 1000 mg every 6 hours, and cefuroxime axetil (Ceftin), 1000 mg every 12 hours with food. We always document peak and trough serum levels at the start of gestation and at least once more during treatment. We like to see a peak level above 10, with a trough at least 3. These levels apply for either medication.

For patients who are very ill, or in those who cannot tolerate oral medications or achieve adequate levels, then parenteral therapy is given. Choices include benzathine penicillin (Bicillin LA), 1.2 million units IM three times per week. Intravenous can include ceftriaxone, 2g IV daily, or cefotaxime, 6g daily either as a continuous infusion or as 2g IV q8h.

During pregnancy, symptoms generally are mild as the hormonal changes seem to mask many symptoms. However, post-partum, mothers have a rough time, with a sudden return of all their Lyme symptoms including profound fatigue. We advise against breast feeding for obvious reasons as mentioned above, and we always advise help in the home for at least the first month, so adequate rest and time for needed treatments are assured.

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The Lyme Disease Foundation in Hartford, CT had kept a pregnancy registry since the late 1980s. They found that if patients were maintained on adequate doses of antibiotic therapy during gestation, then no babies were born with Lyme. My own experience over the last ten years agrees with this. The Lyme Foundation can be contacted at (860) 525-2000.
A Dr. Charles Ray Jones, a pediatrician who practices in Connecticut, has treated and kept records on literally hundreds of babies born with Lyme Disease, having contracted it as an intrauterine infection. He may be contacted at his office at (203) 772-1123.
The choices for treating the mother include amoxicillin, 1000 po q6h, and cefuroxime axetil (Ceftin), 1000 mg q12 h with food. We always document peak and trough serum levels at the start of gestation and at least once more during treatment. We like to see a peak level in or above the mid-teens, with a trough no less than 3 (5 preferred). These levels apply for either medication.
For patients who are very ill, or in those who cannot tolerate oral medications or achieve adequate levels, then therapy is given with ceftriaxone, 2g IV daily, or cefotaxime, 6g daily either as a continuous infusion or as 2g IV q8h.
We also advise against breast feeding for obvious reasons as mentioned above.

TEST GRID FOR TICK-BORNE INFECTIONS

TEST	WHERE	INTERPRETATION	VALUE	EXPENSE	COMMENTS
CD-57	Lab Corp New Jersey	Want to be >60 Normal is ~ 200	Screening test Follow progress Endpoint of Rx	$100 covered	Must be correct lab branch
ELISA (Lyme)	Anywhere	See lab slip	Useless! Too many false negatives (50%) and some false +	$100 covered	I do not order these
Western Blots (Lyme)	#1- Igenex #2- Stony Brook	Specific bands- 23-25, 31, 34, 39 Spirochetal band- 41 Neurol strain- 18, 83, 93	Shows exposure, not current disease activity Do not rely on strict CDC criteria	$300+ Igenex not covered Stony Brook is covered	
PCR (Lyme)	#1- Igenex #2- MDL	Any positive is significant for current infection Negative does not rule out infection	Positive means infection and is confirmatory Need multiple samples	$150+ each	Poor sensitivity but very specific Igenex tests both plasmid and genomic DNA (higher yield)
Bowen RIBB (Lyme)	Bowen research	Serial dilutions- higher ratio implies higher spirochete load	Totally unknown	$250 “donation”	ALL Bowen RIBBs have been positive!
Babesia smear	Anywhere	Positive confirms active infection	Useful only if infection , 2 weeks old	cheap	Treat if + Can reflect any species
Babesia serology	Igenex and MDL	See lab slip	Positive serologies generally reflect active infection	$150?	B. microti only All tests insensitive for chronic infection, but any positive is significant. Do all tests and treat if + and supported clinically
Babesia FISH	Only offered by Igenex	Positive indicates active infection	Low yield	$150?	
Babesia PCR	Igenex & MDL	Positive indicates active infection	Low yield	$150+	
Bowen smear (Babesia)	Bowen research Institute	Positive indicates active infection	More sensitive than standard smear	$250 “donation”	Will identify all species
Bartonella Serology	Anywhere	See lab slip	Low yield	Varies	Commercial assays may not detect the tick-associated strain
Bartonella PCR	#1 MDL #2 Igenex	Positive indicates active infection	Low yield	$150	

DIAGNOSTIC CHECKLIST

To aid the clinician, a workable set of diagnostic criteria were developed with the input of dozens of front line physicians. The resultant document has proven to be extremely useful not only to the clinician, but it also can help clarify the diagnosis for third party payers and utilization review committees. It is important to note that the CDC's published reporting criteria are for surveillance only, not for diagnosis

LYME BORRELIOSIS DIAGNOSTIC CRITERIA RELATIVE VALUE

Tick exposure in an endemic region 1
Historical facts and evolution of symptoms consistent with Lyme.. 2
Systemic signs & symptoms consistent with Bb infection (other potential diagnoses excluded):
Single system, e.g., monoarthritis 1
Two or more systems, e.g., monoarthritis and facial palsy 2
Erythema migrans, physician confirmed 7
Acrodermatitis Chronica Atrophicans, biopsy confirmed... 7
Seropositivity 3
Seroconversion on paired sera 4
Tissue microscopy, silver stain 3
Tissue microscopy, monoclonal immunofluorescence..... 4
Culture positivity 4
B. burgdorferi antigen recovery 4
B. burgdorferi DNA/RNA recovery 4

DIAGNOSIS

Lyme Borreliosis Highly Likely..... 7 or above
Lyme Borreliosis Possible..... 5-6
Lyme Borreliosis Unlikely..... 4 or below

I suggest that when using these criteria, you state Lyme Borreliosis is “unlikely”, “possible”, or “highly likely” based upon the following criteria"- then list the criteria.

Have you had any of the following in relation to this illness? (CIRCLE “NO” OR “YES”)

Tick bite	**N Y**	**“EM” rash (discrete circle)**	**N Y**
Spotted rash over large area	**N Y**	**Linear, red streaks**	**N Y**

	CURRENT SEVERITY				FREQUENCY				
SYMPTOM OR SIGN	**NONE**	**MILD**	**MODERATE**	**SEVERE**		NEVER	**OCCASIONAL**	OFTEN	**CONSTANT**
Persistent swollen glands									
Sore throat									
Fevers									
Sore soles, especially in the AM									
Joint pain									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									
Joint swelling									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									
Unexplained back pain									
Stiffness of the joints or back									
Muscle pain or cramps									

Obvious muscle weakness									
Twitching of the face or other muscles									
Confusion, difficulty thinking									
Difficulty with concentration, reading, problem absorbing new information									
Word search, name block									
Forgetfulness, poor short term memory, poor attention									
Disorientation: getting lost, going to wrong places									
Speech errors- wrong word, misspeaking									
Mood swings, irritability, depression									
Anxiety, panic attacks									
Psychosis (hallucinations, delusions, paranoia, bipolar)									
Tremor									
Seizures									
Headache									
Light sensitivity									
Sound sensitivity									
Vision: double, blurry, floaters									
Ear pain									
	CURRENT SEVERITY				**FREQUENCY**				
SYMPTOM OR SIGN	**NONE**	**MILD**	**MODERATE**	**SEVERE**	**NA**	**NEVER**	**OCCASIONAL**	**OFTEN**	**CONSTAN**
Hearing: buzzing, ringing, decreased hearing									
Increased motion sickness, vertigo, spinning									
Off balance, “tippy” feeling									
Lightheadedness, wooziness, unavoidable need to sit or lie									
Tingling, numbness, burning or stabbing sensations, shooting pains, skin hypersensitivity									
Facial paralysis-Bell's Palsy									
Neck creaks and cracks, stiffness, neck pain									
Fatigue, tired, poor stamina									
Insomnia, fractionated sleep, early awakening									
Excessive night time sleep									
Napping during the day									
Unexplained weight gain									
Unexplained weight loss									
Unexplained hair loss									
Pain in genital area									
Unexplained menstrual									

irregularity									
Unexplained milk production; breast pain									
Irritable bladder or bladder dysfunction									
Erectile dysfunction									
Loss of libido									
Queasy stomach or nausea									
Heartburn, stomach pain									
Constipation									
Diarrhea									
Low abdominal pain, cramps									
Heart murmur or valve prolapse?									
Heart palpitations, pulse skips									
"Heart block" on EKG									
Chest wall pain or ribs sore									
Head congestion									
Breathlessness, "air hunger", unexplained chronic cough									
Night sweats									
Exaggerated symptoms or worse hangover from alcohol									
Symptom flares every four weeks									
Degree of disability									

Since your last visit here, has there been any of the following (CIRCLE "NO" OR "YES")

New tick bite **N Y** **New "EM" rash (discrete circle)** **N Y**

New spotted rash over large area **N Y** **New linear, red streaks** **N Y**

DATE OF YOUR LAST TEST FOR LYME AND OTHER TICK-BORNE DISEASES

_____

	CURRENT SEVERITY				**CHANGE SINCE LAST VISIT**				
SYMPTOM OR SIGN	**NONE**	**MILD**	**MODERATE**	**SEVERE**	**NA**	**GONE**	**IMPROVED**	NO CHANGE	**WORSE**
Persistent swollen glands									
Sore throat									
Fevers									
Sore soles, especially in AM									
Joint pain									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									
Joint swelling									
Fingers, toes									
Ankles, wrists									
Knees, elbows									
Hips, shoulders									

Unexplained back pain									
Stiffness of the joints or back									
Muscle pain or cramps									
Obvious muscle weakness									
Twitching of the face or other muscles									
Confusion, difficulty thinking									
Difficulty with concentration, reading, problem absorbing new information									
Word search, name block									
Forgetfulness, poor short term memory, poor attention									
Disorientation: getting lost, going to wrong places									
Speech errors- wrong word, misspeaking									
Mood swings, irritability, depression									
Anxiety, panic attacks									
Psychosis (hallucinations, delusions, paranoia, bipolar)									
Tremor									
Seizures									
Headache									
Light sensitivity									
Sound sensitivity									
Vision: double, blurry, floaters									
Ear pain									
	CURRENT SEVERITY				**CHANGE SINCE LAST VISIT**				
SYMPTOM OR SIGN	**NONE**	**MILD**	**MODERATE**	**SEVERE**	**NA**	**GONE**	**IMPROVED**	**NO CHANGE**	**WORSE**
Hearing: buzzing, ringing, decreased hearing									
Increased motion sickness, vertigo, spinning									
Off balance, “tippy” feeling									
Lightheadedness, wooziness, unavoidable need to sit or lie									
Tingling, numbness, burning or stabbing sensations, shooting pains, skin hypersensitivity									
Facial paralysis-Bell's Palsy									
Neck creaks and cracks, stiffness, neck pain									
Fatigue, tired, poor stamina									
Insomnia, fractionated sleep, early awakening									
Excessive night time sleep									
Napping during the day									

Unexplained weight gain									
Unexplained weight loss									
Unexplained hair loss									
Pain in genital area									
Unexplained menstrual irregularity									
Unexplained milk production; breast pain									
Irritable bladder or bladder dysfunction									
Erectile dysfunction									
Loss of libido									
Queasy stomach or nausea									
Heartburn, stomach pain									
Constipation									
Diarrhea									
Low abdominal pain, cramps									
Heart murmur or valve prolapse									
Heart palpitations, pulse skips									
"Heart block" on EKG									
Chest wall pain or ribs sore									
Head congestion									
Breathlessness, "air hunger", unexplained chronic cough									
Night sweats									
Exaggerated symptoms or worse hangover from alcohol									
Symptom flares every four weeks									
Degree of disability									

SYMPTOM CHECK LIST

This is not meant to be used as a diagnostic scheme, but is provided to streamline the office interview. Note the format- complaints referable to specific organ systems are clustered to better display multisystem involvement.

NAME_____DATE_____

RISK PROFILE (*PLEASE CHECK*)

Tick infested area__ Frequent outdoor activities__ Hiking__ Fishing__ Camping__
Gardening__ Hunting__ Ticks noted on pets__ Other household members with Lyme__

Do you remember being bitten by a tick?..... No__ Yes__ when_____
Do you remember having the "bull's eye rash"? ..No__ Yes__
Any other rash?..... No__ Yes__

Have you had any of the following? CIRCLE ALL YES ANSWERS

1.Unexplained fevers, sweats, chills, or flushing
2.Unexplained weight change- (loss or gain- circle one)
3.Fatigue, tiredness, poor stamina
4.Unexplained hair loss
5.Swollen glands: list areas_____

6.Sore throat
7.Testicular pain/pelvic pain
8.Unexplained menstrual irregularity
9.Unexplained milk production; breast pain
10.Irritable bladder or bladder dysfunction
11.Sexual dysfunction or loss of libido
12.Upset stomach or abdominal pain
13.Change in bowel function- (constipation, diarrhea)
14.Chest pain or rib soreness
15.Shortness of breath, cough
16.Heart palpitations, pulse skips, heart block
17.Any history of a heart murmur or valve prolapse?
18.Joint pain or swelling: list joints_____
19.Stiffness of the joints or back
20.Muscle pain or cramps
21.Twitching of the face or other muscles
22.Headache
23.Neck creaks and cracks, neck stiffness, neck pain
24.Tingling, numbness, burning or stabbing sensations, shooting pains, skin hypersensitivity
25.Facial paralysis (Bell's Palsy)
26.Eyes/Vision: double, blurry, increased floaters, light sensitivity
27.Ears/Hearing: buzzing, ringing, ear pain, sound sensitivity
28.Increased motion sickness, vertigo, poor balance
29.Lightheadedness, wooziness, unavoidable need to sit or lie down
30.Tremor
31.Confusion, difficulty in thinking
32.Difficulty with concentration, reading
33.Forgetfulness, poor short term memory, poor attention, problem absorbing new information
34.Disorientation: getting lost, going to wrong places
35.Difficulty with speech or writing; word or name block
36.Mood swings, irritability, depression
37.Disturbed sleep- too much, too little, fractionated, early awakening
38.Exaggerated symptoms or worse hangover from alcohol

LYME DISEASE TREATMENT GUIDELINES

LYME BORRELIOSIS:

GENERAL INFORMATION

After a tick bite, Bb undergoes rapid hematogenous dissemination, and for example, can be found within the central nervous system as soon as *twelve hours* after entering the bloodstream. This is why even early infections require full dose antibiotic therapy with an agent able to penetrate all tissues in concentrations known to be bactericidal to the organism.

It has been shown that the longer a patient had been ill with Bb prior to first definitive therapy, the longer the duration of treatment must be, and the need for more aggressive treatment increases.

More evidence has accumulated indicating the severe detrimental effects of immunosuppressants including steroids in the patient with active B. burgdorferi infection. Never give steroids or any other immunosuppressant to any patient who may even remotely be suffering from Lyme, or serious, permanent damage may result, especially if given for anything greater than a short course. If immunosuppressive therapy is absolutely necessary, then potent antibiotic treatment should begin at least 48 hours prior to the immunosuppressants.

TREATMENT RESISTANCE

Bb contains beta lactamases, which, with some strains, may confer resistance to cephalosporins and penicillins. This is apparently a slowly acting enzyme system, and may be overcome by higher or more continuous drug levels especially when maintained by continuous infusions (cefotaxime) and by depot preparations (benzathine penicillin). Nevertheless, some penicillin and cephalosporin treatment failures do occur and have responded to sulbactam/ampicillin, imipenim, and vancomycin, which act through different cell wall mechanisms than penicillin and the cephalosporins.

There is evidence that B. burgdorferi can remain viable within cells, such as macrophages, lymphocytes, endothelial cells, neurons, and fibroblasts. Bb has been shown to evade the effects of beta lactam antibiotics *in vitro* by sequestering in these intracellular niches. In addition, Bb can coat itself with host cell membranes, and it secretes a glycoprotein that can encapsulate the organism (an "S-layer"). Because this glycoprotein binds host IgM, it is possible that host protein as well as cell membrane hide Borrelial antigens. In theory at least, these coatings interfere with immune recognition, thus affecting the clearing of Bb, and also cause seronegativity.

There are multiple strains of *Borrelia burgdorferi* and they vary in their antigen profile and antibiotic susceptibilities. It has also been recognized that B. burgdorferi can exist in at least three different morphologic forms: spirochetal, spheroplast (or l-form), and the recently discovered cystic form. L-forms and cystic forms do not contain cell walls, and thus beta lactam antibiotics will not affect them. Spheroplasts seem to be susceptible to tetracyclines and some erythromycins, yet the cyst has so far only been proven to be susceptible to metronidazole. Apparently, Bb can shift among the three forms during the course of the infection and cause the varying serologic responses seen over time, including seronegativity. Because of this, it may be necessary to change antibiotic or even prescribe a combination of agents.

Vegetative endocarditis has been associated with Borrelia burgdorferi, but the vegetations may be too small to detect with echocardiography. Keep this in mind when evaluating patients with murmurs, as this may explain why some patients seem to continually relapse after even long courses of antibiotics.

THE CD-57 TEST

Our ability to measure CD-57 counts represents a breakthrough in Lyme Disease treatment. It can be used to help determine how active the infection is, how well the treatment is working, and whether, after treatment ends, a relapse is likely to occur!

This is how it works:

Chronic Lyme infections are known to suppress the immune system. The Lyme spirochete can affect all major cell types of the immune system, but it most clearly can impact a specific subset of the natural killer cells. This is called the CD-57 subset.

Just as in HIV infection, which suppresses T-cell counts, Lyme suppresses killer cell counts. As in HIV infection, where abnormally low T-cell counts are routinely used as a marker of how active the infection is, in Lyme we can use the CD-57 count to indicate how active the Lyme infection is.

When Lyme is active, the CD-57 count is suppressed. We currently are having our tests run by LabCorp (a specific California branch of LabCorp runs this test). At this lab, the expected range for the CD 57 count is above 60. In my experience, those who do not have Lyme, or those who are cured of their infection, typically have counts above 180. However, in the chronic Lyme patient, CD-57 counts are usually well below 60.

This test can be run at the start of therapy, then every several months to document the effectiveness of treatment. One hopes to see a rising trend over time. When antibiotic therapy is finally at an end, if the CD-57 count is not in the normal range, then a Lyme relapse is more likely to occur.

Because at this point we believe that only Borrelia will affect the CD-57 this way, a sick patient with a high CD-57 is probably ill with something other than Lyme, such as a co-infection.

Before you have a CD-57 test run, be sure it will be sent to the proper branch of LabCorp. Otherwise, they probably will do the wrong test, wasting your money and time.

BORRELIA NEUROTOXIN (With thanks to Dr. Shoemaker)

Two groups have reported evidence that Borrelia, like several other bacteria, produce neurotoxins. These compounds reportedly can cause many of the symptoms of encephalopathy, cause an ongoing inflammatory reaction manifested as some of the virus-like symptoms common in late Lyme, and also potentially interfere with hormone action by blocking hormone receptors. At this time, there is no assay available to detect whether this compound is present, nor can the amount of toxin be quantified. Indirect measures are currently employed, such as measures of cytokine activation and hormone resistance. A visual contrast sensitivity test (VCS test) reportedly is quite useful in documenting CNS effects of the neurotoxin, and to follow effects of treatment. This test is available at some centers and on the internet.

It has been said that the longer one is ill with Lyme, the more neurotoxin is present in the body. It probably is stored in fatty tissues, and once present, persists for a very long time. This may be because of enterohepatic circulation, where the toxin is excreted via the bile into the intestinal tract, but then is reabsorbed from the intestinal tract back into the blood stream. This forms the basis for treatment.

Synthetic fiber agents, available by prescription for the treatment of high cholesterol, have the ability to bind some bacterial toxins. When take orally in generous amounts, the neurotoxin, present in the intestinal tract, binds to the resin, is trapped, and then excreted. Thus, over several weeks, the level of neurotoxin is depleted and clinical improvement can be seen. Current experience is that improvement is first seen in three weeks, and treatment continues for two to four months. Retreatment is always possible.

Two prescription medications that can bind these toxins include cholestyramine resin (Questran), and Welchol pills. These medications may bind not only toxins but also many drugs and vitamin supplements.

Therefore no other oral medications or supplements should be taken from one hour before, to three hours after a dose of one of these fiber agents.

Cholestyramine must be taken four times daily, and Welchol is prescribed at three pills twice daily. While the latter is obviously much simpler to use, it is less effective than cholestyramine. The main side effects are bloating and constipation, best handled with increased fluid intake and gentle laxatives.

COURSE DURING THERAPY

As the spirochete has a very long generation time (12 to 24 hours *in vitro* and possibly much longer in living systems) and may have periods of dormancy, during which time antibiotics will not kill the organism, treatment has to be continued for a long period of time to eradicate all the active symptoms and prevent a relapse, especially in late infections. If treatment is discontinued before all symptoms of active infection have cleared, the patient will remain ill and possibly relapse further. In general, early disseminated LB is treated for four to six weeks, and late LB usually requires a minimum of four to six months of continuous treatment. All patients respond differently and therapy must be individualized. It is not uncommon for a patient who has been ill for many years to require open ended treatment regimens; indeed, some patients will require ongoing maintenance therapy to remain well.

Several days after the onset of appropriate antibiotic therapy, symptoms often flare due to lysis of the spirochetes with release of increased amount of antigenic material and possibly bacterial toxins. This is referred to as a Jarish Herxheimer-like reaction. Because it takes 48 to 72 hours of therapy to initiate bacterial killing, the Herxheimer reaction is therefore delayed. This is unlike syphilis, in which these reactions can occur within hours.

It has been observed that symptoms will flare in cycles every four weeks. It is thought that this reflects the organism's cell cycle, with the growth phase occurring once per month (intermittent growth is common in Borrelia species). As antibiotics will only kill bacteria during their growth phase, therapy is designed to bracket at least one whole generation cycle. This is why the minimum treatment duration should be at least four weeks. If the antibiotics are working, over time these flares will lessen in severity and duration. The very occurrence of ongoing monthly cycles indicates that living organisms are still present and that antibiotics should be continued.

With treatment, these monthly symptom flares are exaggerated and presumably represent recurrent Herxheimer-like reactions as Bb enters its vulnerable growth phase then are lysed. For unknown reasons, the worst occurs at the fourth week of treatment. Observation suggest that the more severe this reaction, the higher the germ load, and the more ill the patient. In those with long-standing highly symptomatic disease who are on I.V. therapy, the week-four flare can be very severe, similar to a serum sickness reaction, and be associated with transient leucopenia and/or elevations in liver enzymes. If this happens, decrease the dose temporarily, or interrupt treatment for several days, then resume with a lower dose. If you are able to continue or resume therapy, then patients continue to improve. Those whose treatment is stopped and not restarted at this point usually will need retreatment in the future due to ongoing or recurrent symptoms because the infection was not eradicated. Patients on I.V. therapy who have a strong reaction at the fourth week will need to continue parenteral antibiotics for several months, for when this monthly reaction finally lessens in severity, then oral or IM medications can be substituted. Indeed, it is just this observation that guides the clinician in determining the endpoint of I.V. treatment. In general, I.V. therapy is given until there is a clear positive response, then treatment is changed to IM or po until free of signs of active infection for 4 to 8 weeks. Some patients, however, will not respond to IM or po treatment and I.V. therapy will have to be used throughout. As mentioned earlier, leucopenia may be a sign of persistent Ehrlichiosis, so be sure to look into this.

Repeated treatment failures should alert the clinician to the possibility of an otherwise inapparent immune deficiency, and a workup for this may be advised. Obviously, evaluation for co-infection should be performed, and a search for other or concurrent diagnoses needs to be entertained.

There are three things that will predict treatment failure regardless of which regimen is chosen: Non-compliance, alcohol use on a regular basis, and failure of the patient to obtain proper rest. Advise them to take a break when (or ideally before) the inevitable mid afternoon fatigue sets in.

All patients must keep a carefully detailed daily diary of their symptoms to help us judge the effects of treatment, the presence of the classic four week cycle, and treatment endpoint. One must follow such diaries, temperature readings in late afternoon, physical findings, notes from physical therapists, and cognitive testing to best judge when to change or end antibiotics.

Remember- there currently is no test for cure, so this clinical follow-up assumes a major role in Lyme Disease care.

LYME DISEASE TREATMENT INFORMATION

There is no universally effective antibiotic for treating LB. The choice of medication used and the dosage prescribed will vary for different people based on multiple factors. These include duration and severity of illness, presence of co-infections, immune deficiencies, prior significant immunosuppressant use while infected, age, weight, gastrointestinal function, blood levels achieved, and patient tolerance. Doses found to be effective clinically are often higher than those recommended in older texts. This is due to deep tissue penetration by Bb, it's presence in the CNS including the eye, within cells, within tendons, and because very few of the many strains of this organism now known to exist have been studied for antibiotic susceptibility. In addition, all animal studies of susceptibility to date have only addressed early disease in models that behave differently than human hosts. Therefore, begin with a regimen appropriate to the setting, and if necessary, modify it over time based upon response.

ANTIBIOTICS

There are several types of antibiotics in general use for Bb treatment. The tetracyclines, including doxycycline and minocycline, are bacteriostatic unless given in high doses. If high blood levels are not attained, treatment failures in early and late disease are common. However, these high doses can be difficult to tolerate. For example, doxycycline can be very effective but only if adequate blood levels are achieved either by high oral doses (300 to 600 mg daily) or by parenteral administration.

Penicillins are bactericidal. As would be expected in managing an infection with a gram negative organism such as Bb, amoxicillin has been shown to be more effective than oral penicillin V. Because of its short half-life and need for high levels, amoxicillin is usually administered along with probenecid. Since blood levels are extremely variable they should be measured.

Cephalosporins must be of advanced generation: first generation drugs are rarely effective, and second generation drugs are comparable to amoxicillin and doxycycline both in-vitro and in-vivo. Third generation agents are currently the most effective of the cephalosporins because of their very low MBC's (0.06 for ceftriaxone) and they have been shown to be effective in penicillin and tetracycline failures. Cefuroxime axetil (Ceftin), a second generation agent, is also effective against staph and thus is useful in treating atypical erythema migrans that may represent a mixed infection, containing some of the more common skin pathogens in addition to Bb.

When choosing a third generation cephalosporin, there are several points to remember: Ceftriaxone has 95% biliary excretion and can crystallize in the biliary tree with resultant colic and possible cholecystitis. GI excretion results in a large impact on gut flora. Biliary and superinfection problems with ceftriaxone can be lessened if this drug is given in interrupted courses, such as three to five days in a row each week. More recently, chenodeoxycholic acid, used to dissolve gallstones, is being prescribed along with ceftriaxone as prophylaxis. Cefotaxime is less convenient to administer because of the need for either multiple daily doses or continuous infusions, but as it has only 5% biliary excretion, it never causes biliary concretions, and may have less impact on gut flora. It is the experience of some clinicians that cefotaxime can be even

more efficacious if given as a continuous infusion, rather than in interrupted doses.

Erythromycin has been shown to be almost ineffective as monotherapy. The advanced macrolides and azalides such as azithromycin and clarithromycin can be difficult to tolerate orally due to their tendency to promote yeast overgrowth and poor GI tolerance at the high doses needed. As they have impressively low MBCs and do concentrate in tissues and penetrate cells, they theoretically should be ideal agents. However, initial clinical results were disappointing, especially with oral azithromycin. It has been suggested that when Bb is within a cell, it is held within a vacuole and bathed in fluid of low pH, and this acidity may inactivate this class of antibiotics. Therefore, they are administered concurrently with hydroxychloroquine or amantadine, which raise vacuolar pH, rendering these antibiotics more effective. It is not known whether this same technique will make erythromycin a more effective antibiotic in LB. Another alternative is to administer azithromycin parenterally. Results are excellent, but expect to see abrupt Jarisch-Herxheimer reactions.

Metronidazole (Flagyl) is commonly used in select patients with treatment resistant, chronic Lyme. When present in a hostile environment, such as growth medium lacking some nutrients, or spinal fluid, or serum with certain antibiotics added, Bb will change into a cystic form. This cyst seems to be able to remain dormant, but when placed into an environment more favorable to its growth, the cyst can open, and an intact spirochete emerges. The conventional antibiotics used for Lyme, such as the penicillins, cephalosporins, etc. do not kill the cystic form of Bb. Furthermore, the cyst lacks the usual surface antigens found on the spirochete (these are the markers detected by ELISAs and western blots). This may be another reason for the chronically sick Lyme patient remaining seronegative.

There is evidence that metronidazole will kill the cystic form. This fits with the now well known clinical observations that metronidazole can be remarkably effective for many chronic Lyme patients. However, this medication apparently has no effect on intact spirochetes. Therefore, the trend now is to treat the chronically infected patient who has resistant disease by combining metronidazole, which has minimal effect on B. burgdorferi, with one or two other antibiotics to target all forms of Bb. Because there is laboratory evidence that tetracyclines may inhibit the effect of metronidazole, this class of medication may not be as useful as others in these two- and three-drug regimens. There have been some recent reports that Bb does not contain genes that would confer susceptibility to metronidazole. However, this clearly does not fit with *in vitro* and a large body of clinical data, which have demonstrated the usefulness of this agent in the Lyme patient. Perhaps we do not have all the genetic information needed to dismiss the use of this agent. Once again, real world experience is one step ahead of bench research.

Important precautions:
1. Pregnancy while on metronidazole is not advised, as there is a risk of birth defects.
2. No alcohol consumption! A severe, "antabuse" reaction will occur, consisting of severe nausea, flushing, headache, and other unpleasant symptoms.
3. Metronidazole is potentially neurotoxic. Peripheral neuropathy may result. Therefore, breaks in treatment are commonly prescribed, such as using this agent every other week.
4. Yeast overgrowth is especially common. A strict anti-yeast regimen must be followed.
5. VERY severe Herxheimer-like reactions are seen in the more ill patient during the first week of therapy, and again four weeks later.

COMBINATION THERAPY

This consists of using two or more dissimilar antibiotics simultaneously. Combinations should utilize dissimilar antibiotics for antibiotic synergism, to better compensate for differing killing profiles and sites of action of the individual medications, and to cover the three known morphologic forms of Bb. The idea is to work in body fluids and in deep tissues, outside and within cells, and effect killing by different mechanisms for synergism. Clinically useful examples include amoxicillin plus clarithromycin, ceftriaxone plus azithromycin, benzathine penicillin plus metronidazole, etc. Note how complimentary these are for treating infection with Bb. GI intolerance and yeast superinfections are the biggest drawbacks to this type of treatment. However, these complications can often be prevented or easily treated, and the clinically

observed benefits of this type of regimen clearly have outweighed these problems in selected patients.

PULSE THERAPY

This consists of administering antibiotics (usually parenteral ones) two to three days in a row per week. The efficacy of this regimen is based on the fact that it takes 48 to 72 hours of continuous bactericidal antibiotic levels to kill the spirochete, yet it will take longer than the four to five days between pulses for the spirochetes to recover. This allows for several advantages:

- Dosages are doubled (ie: cefotaxime, 12 g daily), increasing efficacy
- More toxic medications can be used with increased safety (ie: vancomycin)
- May be effective when conventional, daily regimens have failed.
- IV access may be easier or more tolerable
- More agreeable lifestyle for the patient
- Often less costly than daily regimens

Note that this type of treatment is expected to continue for a minimum of ten weeks, and often must continue beyond twenty weeks. As with all Lyme treatments, specific dosing and scheduling must be tailored to the individual patient's clinical picture based upon the treating physician's best clinical judgment.

MONITORING THERAPY

Drug levels are measured, where possible, to confirm adequate dosing. The regimen may have to be modified to optimize the dose, and again at any time major changes in the treatment regimen occur. With parenteral therapy, CBC and chem/liver panels are done at least twice each month, especially during symptom flares, with urinalysis and pro- time monitored monthly.

INDICATORS FOR PARENTERAL THERAPY

The following are guidelines only and are not meant to be absolute. It is based on retrospective study of over 600 patients with late Lyme disease.

- Illness for greater than one year
- Prior immunosuppressive therapy
- Major neurological involvement
- Active synovitis with high sedimentation rate
- Elevated protein or cells in the CSF

KETEK (telithromycin)

Ketek is now being used in treatment regimens for a variety of tick-borne diseases. Ketek is an antibiotic related to erythromycin. It has several advantages over erythromycin, azithromycin (Zithromax), and clarithromycin (Biaxin), and may replace these medications in the treatment of some tick-borne diseases:

- In the test tube ("*in vitro*") telithromycin is the most effective antibiotic ever studied against B. burgdorferi, the agent for Lyme disease.

- Is also somewhat effective for Bartonella and Babesia.

- Is stable in the acid environment in our cells where chronic Borrelia hide- thus may be very effective, and may not need to be given with Plaquenil or Amantadine.

- Has been engineered to prevent drug resistance.

- Has almost no negative impact on intestinal germs, hopefully minimizing the risk for diarrhea.
- Can be taken with or without food.

Disadvantages:

- May interact with a wide variety of medications (see reverse side of this flier). You may need to change the dose of other medications you take, or may have to stop some of them. PLEASE notify all your other care givers if you are taking Ketek, and keep this flier with you at all times, as medications given in an emergency may also react with Ketek. Do not take if you are on Propulcid (cisapride) or Orap (pimozide), or if you have a congenital heart condition that includes a "long QT interval".
- Can cause blurry vision and even double vision, so be careful with hazardous activities, including driving.
- Liver enzymes may become elevated. Blood tests should be done regularly to monitor this.
- The usual precautions of any antibiotic also still apply- risk for allergy, stomach upset, Herxheimer reactions, etc. Notify your local MD or us immediately if you experience any adverse reactions.

DRUGS TO AVOID WHILE ON KETEK (partial listing):
Cholesterol drugs- Lipitor, Mevacor, Zocor and Crestor
NOTE: Pravastatin (Pravochol) and fluvastatin (Lescol) are OK, as are ezetimibe (Zetia), colesevelam (Welchol) and cholestyramine (Questran).
Anti-arrhythmic heart drugs- Class 1A (quinidine, procainamide, etc.), Class III (dofetilide, etc.)
Cisapride (Propulcid), pimozide (Orap)
Antifungals- itraconazole (Sporanox), ketoconazole (Nizoral), voriconazole (Vfend).
Ergot alkaloids for Migraine
DRUGS WHICH MAY REQUIRE DOSAGE ADJUSTMENTS (partial listing):
Levels of these drugs go up: Sedatives and anesthetics-Midazolam (Versed), triazolam (Halcion)
Heart drugs-sotalol (Betapace), metoprolol (Lopressor, Toprol), digoxin (Lanoxin)
HIV drugs- rionavir (Norvir), sirolimus (Rapamune); anti-rejection drug tacrolimus (Prograf), cyclosporine
phenytoin (Dilantin), phenobarbital
These drugs lower Ketek levels: rifampin, phenytoin (Dilantin), tegretol, phenobarbital

QTc INTERVAL

- Measure the precordial lead that has the best T wave (usually V-2 or V-5)
- Measure from the start of the Q wave to the end of the T wave
- QT interval is inversely related to the heart rate (slow pulse results in a longer QT)
- QTc is the QT corrected for heart rate
- QTc = QT $\div \sqrt{}$ RR interval
- Normals: Females <450 ms, Males < 470 ms
- Want K+ > 4.0, Mg++ > 2.0; avoid hypocalcemia
- Check EKG at baseline, then, if there is still concern, repeat the EKG at least 5 half-lives after medication is begun

FLAGYL

There has been a lot of discussion and excitement about the drug Flagyl (metronidzole). Here's the scoop: When present in a hostile environment, such as growth medium lacking some nutrients, or spinal fluid, or serum with certain antibiotics added, the Lyme spirochete, Borrelia burgdorferi (Bb) will change into a cyst form. This cyst seems to be able to remain dormant, but when placed into an environment more favorable to its growth, the cyst can open, and an intact spirochete emerges. A recent article has demonstrated that the cystic Borrelia burgdorferi, when injected into a mouse, can result in a spirochetal infection. . However, this information is *VERY* preliminary, and is based on laboratory work that may not reflect what happens in people.,

The conventional antibiotics used for Lyme, such as the penicillins, cephalosporins, etc do not kill the cystic form of Bb. Furthermore, the cyst lacks the usual surface markers found on the spirochete (these are the markers detected by ELISAs and western blots). This may be another reason for seronegativity, especially in the chronically sick patient.

There is evidence that Flagyl will kill the cystic form. This fits with the now well-known clinical observations that Flagyl can be remarkably effective for many chronic Lyme patients. However, this medication apparently has no effect on intact spirochetes. Therefore, the trend now is to treat the chronically infected patient who has resistant disease by combining Flagyl with one or two other antibiotics to target all forms of Bb. Because there is laboratory evidence that tetracyclines may inhibit the effect of Flagyl, this class of medication should not be used in these two- and three-drug regimens.

Important precautions:

1. Pregnancy while on Flagyl is not advised, as there is a risk of birth defects.
2. No alcohol consumption! A severe, "antabuse" reaction will occur, consisting of severe nausea, flushing, headache, and other nasty symptoms.
3. Yeast overgrowth is especially common. A strict anti-yeast regimen must be followed.
4. Flagyl can be irritative to the nervous system- in the short term, it may cause irritability, "spacey" feelings, etc. Longer term, it can affect the peripheral nerves, causing tingles, numbness, etc. If you develop this nerve irritation, call us. If mild, a change in dose may be required. Often, extra vitamin B can clear these symptoms. If the nerve symptoms persist or are strong, then Flagyl must be discontinued.
5. Strong Herxheimer-like reactions are seen in almost everyone during the first week, and again four weeks later. My advice is to try to push through these if at all possible, but seek medical attention with any symptom flare, because the flare-up may not be a Herxheimer. It could reflect another illness that must receive medical attention and treatment. I have seen Lyme patients think they were having a Herxheimer, when in fact they had other infections, including infected IV lines, bladder infections, pneumonia, etc.

RIFAMPIN

Rifampin is a well-known antibiotic that has been in use for many decades. It is primarily used to treat Tuberculosis, but also has been used in other conditions, such as prevention of meningitis in those exposed, for treating resistant Staph, etc.

Recently, much excitement in Lyme circles has been generated about this medication, because of its many potential uses in those infected with tick-borne illnesses.

Potentially, rifampin may be effective in treating Bartonella, Ehrlichia, Mycoplasma, and Borrelia (Lyme). There are as yet no formal clinical studies on the use of this medication in these illnesses, but many patients have been treated with rifampin and have had favorable results.

Rifampin is not considered a first choice for treating these illnesses, because although it is simple to take and inexpensive, rifampin in rare circumstances has caused abnormalities in blood counts and liver tests. Therefore, when used, regular blood tests are usually performed to monitor for side effects. Rifampin can

also discolor urine, tears and sweat (brownish-orange) so do not be alarmed if you see this. It may also stain some types of water-permeable contact lenses.

If you are taking rifampin and you develop new or worse symptoms, or a new infection appears such as a severe sore throat, high fever, etc., stop the medication and call the office right away, as these may be signs of drug-related side effects.

Taking rifampin when pregnant is not advised. Do not take this if you are or may become pregnant. If you are on rifampin and do become pregnant, stop this drug immediately and contact your MD.

Please keep a symptom diary while you're on this medication so your progress can be tabulated.

ANTIBIOTIC CHOICES

ORAL THERAPY: Always check blood levels when using agents marked with an *, and adjust dose to achieve a peak level in the mid- teens and a trough greater than five. Because of this, the doses listed below may have to be raised. Consider Doxycycline first due to concern for Ehrlichia.

*Amoxicillin- Adults: 1g q8h plus probenecid 500mg q8h; doses up to 6 grams daily are often needed
Pregnancy: 1g q6h and adjust.
Children: 50 mg/kg/day divided into q8h doses.

*Doxycycline- Adults: 100 mg qid with food; doses of up to 600 mg daily are often needed, as doxycycline is only effective at high blood levels. Not for children or in pregnancy.
If levels are too low at tolerated doses, give parenterally.

*Cefuroxime axetil- Oral alternative that may be effective in amoxicillin and doxycycline failures. Useful in EM rashes co-infected with common skin pathogens.
Adults and pregnancy: 1g q12h and adjust. Children: 125 to 500 mg q12h based on weight.

Tetracycline- Adults only, and not in pregnancy. 500 mg tid to qid

Erythromycin- Poor response and not recommended.

Clarithromycin- Adults: 500 to 1000 mg q12h. Add hydroxychloroquine, 200-400 mg/d or amantadine 100-200 mg/d. Cannot be used in pregnancy or in younger children

Azithromycin- Adults: 500 to 1200 mg/d. Adolescents: 250 to 500 mg/d.
Add hydroxychloroquine, 200-400 mg/d, or amantadine 100-200 mg/d
Cannot be used in pregnancy. Oral azithromycin is not as effective as clarithromycin.

Augmentin- Cannot exceed three tablets daily due to the clavulanate, thus is given with amoxicillin. This combination can be effective when Bb beta lactamase is felt to be present.

Chloramphenicol- Not recommended as not proven and potentially toxic.

Metronidazole (see text): 500 to 1500 mg daily in divided doses. Adults only.

PARENTERAL THERAPY

Ceftriaxone- Risk of biliary sludging can be minimized with intermittent breaks in therapy (ie: infuse five or less days in a row per week).
Adults and pregnancy: 2g q12h, four days in a row each week.
Children: 75 mg/kg/day up to 2g/day

Cefotaxime- Comparable efficacy to ceftriaxone; no biliary complications.
Adults and pregnancy: 2g q8h; may dose as high as 12g daily. Suggest a continuous infusion.
Children: 90 to 180 mg/kg/day dosed q6h (preferred) or q8h, not to exceed 12 g daily.

*Doxycycline- Requires central line as is caustic.
Surprisingly effective, probably because higher overall, and spiked blood levels when given parenterally.
Always measure blood levels.
Adults: 400 mg q24h and adjust based on levels.
Cannot be used in pregnancy or in younger children.

Azithromycin- Requires central line as is caustic.
Dose: 500 to 1000 mg daily in adolescents and adults.

Penicillin G- IV penicillin G is minimally effective and not recommended.

Benzathine penicillin- Surprisingly effective IM alternative to oral therapy. May need to begin at lower

doses as strong, prolonged (6 or more week) Herxheimer-like reactions have been observed.
Adults: 1.2 million U three times per week (higher doses with large body habitus)
Adolescents: 300,000 to 2.4 million U weekly.
May be used in pregnancy.

Poorly studied but anecdotally effective

Vancomycin- observed to be one of the best drugs in treating Lyme, but potential toxicity limits its use. It is a perfect candidate for pulse therapy to minimize these concerns. Use standard doses and confirm levels.

Imipenim and Unisyn- similar in efficacy to cefotaxime, but often works when cephalosporins have failed.
Must be given q6 to q8 hours.

Cefuroxime- useful but not demonstrably better than ceftriaxone or cefotaxime.

Ampicillin IV- more effective than penicillin G. Must be given q6 hours.

TREATMENT CATEGORIES

PROPHYLAXIS of high risk groups- education and preventive measures. Antibiotics are not given.

TICK BITES - Embedded Deer Tick With No Signs or Symptoms of Lyme (see appendix):

Decide to treat based on the type of tick, whether it came from an endemic area and percent infected, how it was removed, and length of attachment (nymphs: at least one day; adults: anecdotally, as little as four hours). The risk of transmission is greater if the tick is engorged, or of it was removed improperly allowing the tick's contents to spill into the bite wound. High risk bites are treated as follows (remember the possibility of coinfection!):

1) Adults: Oral therapy for 21 days.
2) Pregnancy: Amoxicillin 1000 mg q6h for 6 weeks. Test for Babesia, Bartonella and Ehrlichia.
   Alternative: Cefuroxime axetil 1000 mg q12h for 6 weeks.
3) Young Children: Oral therapy for 21 days.

EARLY LOCALIZED - Single erythema migrans with no constitutional symptoms:

1) Adults: oral therapy for 6 weeks.
2) Pregnancy: 1st and 2nd trimesters: I.V. X 21 days then oral X 6 weeks
   3rd trimester: Oral therapy X 6 weeks.
   Any trimester- test for Babesia, Bartonella, and Ehrlichia
3) Children: oral therapy for 6 weeks.

DISSEMINATED DISEASE - Multiple lesions, constitutional symptoms, lymphadenopathy, or any other manifestations of dissemination.

EARLY DISSEMINATED: Milder symptoms present for less than one year and not complicated by immune deficiency or prior immunosuppressive treatment:

1) Adults: oral therapy until no active disease for 4 weeks (4-6 months typical)
2) Pregnancy: As in localized disease, but duration as above. Treat throughout pregnancy, and do not breast feed.
3) Children: Oral therapy with duration based upon clinical response.

PARENTERAL ALTERNATIVES for more ill patients and those unresponsive to or intolerant of oral medications:

1) Adults and children: I.V. therapy for at least 6 weeks (until clearly improved). Follow with oral therapy or IM benzathine penicillin until no active disease for 6-8 weeks. I.V. may have to be resumed if oral or IM therapy fails.
2) Pregnancy: IV then oral therapy as above.

LATE DISSEMINATED: Present greater than one year, more severely ill patients, and those with prior

significant steroid therapy or any other cause of impaired immunity:

1) Adults and pregnancy: extended I.V. therapy (10 or more weeks), then oral or IM, if effective, to same endpoint.
2) Children: IV therapy for 6 or more weeks, then oral or IM follow up as above.

LONG TERM TREATMENT OF CHRONIC LYME DISEASE WITH BENZATHINE PENICILLIN

Late stage infections with Borrelia burgdorferi, the agent of Lyme Disease, often require aggressive therapy. Comparative studies published by Fallon et. al. at Columbia University have shown that parenteral therapy is superior to oral therapy in this group of patients. Options include intramuscular long acting penicillin G (benzathine penicillin, or “Bicillin-LA”) or intravenous antibiotics.

For an antibiotic in the penicillin class to be effective, time-killing curves show that significant levels of antibiotic must be sustained for 72 hours. Bicillin LA is an oil-based formulation that meets these criteria.

Published studies in children and adults, combined with over a decade of experience with this therapy by front line, Lyme-treating physicians have established the efficacy, safety and usefulness of this medication. In many patients it is more effective than oral antibiotics for treating Lyme, and compares closely to intravenous therapy in terms of efficacy.

It is usually administered three times weekly for six to twelve months. It has the advantage of being relatively inexpensive, free of gastrointestinal side effects, unlikely to promote the overgrowth of yeast, and has an excellent safety record spanning many decades.

Finally, an added plus is that family members can be trained to administer this treatment at home.

CEFTRIAXONE TREATMENT FOR CHRONIC LYME DISEASE

A subset of patients who have severe, longstanding illness due to Borrelia burgdorferi carry persistent infection despite having previously received antibiotic treatments which have eliminated the disease in less ill individuals. The mechanism for such persistence has been the subject of many peer reviewed articles. They include persistence of B. burgdorferi in protective niches, inhibition and lysis of lymphocytes, survival in phagocytic vacuoles, antigenic shifts, slow growth, and dormancy and latency.

One successful approach in the more ill patient, published in the early 1990s, is to use higher doses of ceftriaxone in a pulsed-dose regimen. Since then, clinical experience has expanded upon this concept, and at the MLDA Lyme Congress in September, 2002, Cichon presented data and a pulsed high dose regimen which supports and refines this concept.

Treatment with ceftriaxone is dosed at 4 grams daily- given either as 2 grams IV twice daily, or 4 grams slowly once a day, four days in a row each week, usually for 12 or more weeks. Such a regimen is not only more effective in the Chronic Lyme patient, but regular interruptions in treatment lessen the potential complications of intensive antibiotic therapy with ceftriaxone, such as biliary sludging and colitis. Hence a more effective, safer regimen that by virtue of the treatment breaks, is less costly and affords the patient a more acceptable lifestyle.

CHRONIC LYME DISEASE (PERSISTENT/RECURRENT INFECTION)

By definition, this category consists of patients with active infection, of a more prolonged duration, who are more likely have higher spirochete loads, weaker defense mechanisms, possibly more virulent or resistant

strains, and probably are significantly co-infected. Neurotoxins may also be significant in these patients. Search for and treat for all of these, and search for concurrent infections including viruses, chlamydias, and mycoplasmas. These patients require a full evaluation for all of these problems, and each abnormality must be addressed.
This group will most likely need parenteral therapy, especially high dose, pulsed therapy, and antibiotic combinations, including metronidazole. Antibiotic therapy will need to continue for many months, and the antibiotics may have to be changed periodically to break plateaus in recovery. Be vigilant for treatment-related problems such as antibiotic-associated colitis, yeast overgrowth, intravenous catheter complications, and abnormalities in blood counts and chemistries.

If treatment can be continued long term, then a remarkable degree of recovery is possible. However, attention must be paid to all treatment modalities for such a recovery- not only antibiotics, but rehab and exercise programs, nutritional supplements, enforced rest, low carbohydrate, high fiber diets, attention to food sensitivities, avoidance of stress, abstinence from caffeine and alcohol, and absolutely no immunosuppressants, even local doses of steroids (intra articular injections, for example).

Unfortunately, not all patients with chronic Lyme disease will fully recover and treatment may not eradicate the active Borrelia infection. Such individuals may have to be maintained on open-ended, ongoing antibiotic therapy, for they repeatedly relapse after antibiotics are stopped. Maintenance antibiotic therapy is thus mandatory.

In patients who have chronic Lyme, who do not fully respond to antibiotics, one must search for an explanation. In many cases, these patients are found to have pituitary insufficiency of varying degrees. The abnormalities may be extremely subtle, and provocative testing must be done for full diagnosis. Persistent fatigue, limited stamina, hypotension, and loss of libido suggest this possibility.

Similarly, a small but significant number of these patients harbor toxic levels of heavy metals. Challenge testing by knowledgeable, experienced clinicians is necessary for evaluation. Treatment must be directed toward correcting the specific abnormalities found, and post-treatment retesting to assess efficacy of treatment and endpoint of therapy should be done. Suspect this when poor immune responsiveness and persistent neuropathic signs and symptoms are present.

SAFETY

Nearly two decades of experience in treating thousands of patients with Lyme has proven that therapy as described above, although intense, is generally well tolerated. The most common adverse reaction seen is allergy to probenecid. In addition, yeast superinfections are seen, but these are generally easily recognized and managed. The induction of Clostridium difficile toxin production is seen most commonly with ceftriaxone, but can occur with any of the antibiotic regimens mentioned in this document. However, pulsed dose therapy and regular use of the lactobacillus preparations seems to be helpful in controlling yeast and antibiotic related colitis, as the number of cases of C. difficile in Lyme patients is low when these guidelines are followed.

When using central intravenous lines including PICC lines (peripherally inserted central catheters), if ANY line problems arise, it is recommended that the line be pulled for patient safety. Salvage attempts (urokinase, repairing holes) are often ineffective and may not be safe.

Please advise all patients who take the tetracyclines of skin and eye sensitivity to sunlight and the proper precautions, and advise birth control if appropriate. When doxycycline is given parenterally, do not refreeze the solution prior to use!

Remember, years of experience with chronic antibiotic therapy in other conditions, including rheumatic fever, acne, gingivitis, recurrent otitis, recurrent cystitis, COPD, bronchiectasis, and others have not revealed any consistent dire consequences as a result of such medication use. Indeed, the very real consequences of untreated, chronic persistent infection by B. burgdorferi can be far worse than the

potential consequences of this treatment.

METHYLCOBALAMIN

(Methyl B12)

Methylcobalamin is a prescription drug derived from vitamin B12. This can help to heal problems with the central and peripheral nervous system, improve depressed immune function, and help to restore more normal sleeping patterns. Many patients note improved energy as well.

Because the oral form is not absorbed when swallowed or dissolved under the tongue, Methyl B12 must be taken by injection.

Long term studies have never demonstrated any side effects from this drug. However, do expect the urine to turn red shortly after each dose. This is expected- if the urine is not red, let us know. You may need a higher dose or your present supply may have lost potency.

Dose:
This is based on body weight, but generally is 25 mg. (1 c.c.) as a daily injection, for 3 to 6 months.

Always keep vials in the refrigerator, even if unopened.

The injectible form of this is not available in regular drug stores. It must be manufactured (compounded) by specialty pharmacies on order. We will fax or mail the prescription to the pharmacy and they will express mail the medication to you when it is ready-this takes approximately 3 days.

CO-INFECTIONS IN LYME

PIROPLASMOSIS (Babesiosis)

TREATING BABESIOSIS

Babesia infection is becoming more commonly recognized, especially in patients who already have Lyme Disease. It has been published that as many as 66% of Lyme patients show evidence of co-infection with Babesia. It has also been reported that Babesial infections can range in severity from mild, subclinical infection, to fulminant, potentially life threatening illness. Subclinical infection is often missed because the symptoms are incorrectly ascribed to Lyme. Babesial infections, even mild ones, may recur even after treatment and cause severe illness. This phenomenon has been reported to occur at any time, including up to several years after the initial infection! Furthermore, such Babesia carriers pose a risk to the blood supply as this infection has been reported to be passed on by blood transfusion.

Treating Babesia infections had always been difficult, because the therapy that had been recommended until 1998 consisted of a combination of clindamycin plus quinine. Published reports and clinical experience have shown this regimen to be unacceptable, as nearly half of patients so treated have had to abandon treatment due to serious side effects, many of which were disabling. Furthermore, even in patients who could tolerate these drugs, there was a failure rate approaching 50%.

Because of these dismal statistics, the current regimen of choice for Babesiosis is the combination of atovaquone (Mepron, Malarone) plus an erythromycin-type drug, such as azithromycin (Zithromax), clarithromycin (Biaxin), or telithromycin (Ketek). This combination was initially studied in animals, and then applied to Humans with good success. Fewer than 5% of patients have to halt treatment due to side effects, and the success rate is clearly better than that of clindamycin plus quinine. When a prolonged

course of therapy is prescribed, blood counts and chemistries are checked every three weeks to assure safety and tolerability of this regimen.

The duration of treatment with atovaquone combinations for Babesiosis varies depending on the degree of infection, duration of illness before diagnosis, the health and immune status of the patient, and whether the patient is co-infected with Borrelia burgdorferi. Typically, a three-week course is prescribed for acute cases, while chronic, longstanding infections with significant morbidity and co-infection will require a minimum of four months of therapy. Relapsed have occurred, and retreatment is occasionally needed
GENERAL INFORMATION
Piroplasms are not bacteria, they are protozoans. Therefore, they will not be eradicated by any of the currently used Lyme treatment regimens. Therein lies the significance of co-infections- if a Lyme patient has been extensively treated yet is still ill, suspect a co-infection.

Babesia infection is becoming more commonly recognized, especially in patients who already have Lyme Disease. It has been published that as many as 66% of Lyme patients show evidence of co-infection with Babesia. It has also been reported that Babesial infections can range in severity from mild, subclinical infection, to fulminant, potentially life-threatening illness. The more severe presentations are more likely to be seen in immunocompromised and elderly patients. Milder infections are often missed because the symptoms are incorrectly ascribed to Lyme. Babesial infections, even mild ones, may recrudesce and cause severe illness. This phenomenon has been reported to occur at any time, even up to several years after the initial infection. Furthermore, asymptomatic carriers pose risks: to the blood supply as this infection has been reported to be passed on by blood transfusion, and to the unborn child from an infected mother as it can be transmitted *in utero*. Some quotes from the literature:

Krause, PJ. Spielman, A, Telford, SR et.al.. *Persistent parasitemia after acute Babesiosis* N Engl J Med 1998. 339:160

“The clinical spectrum of human Babesiosis ranges from an apparently silent infection to a fulminant malaria-like disease.”
“When left untreated, silent Babesial infection may persist for months to years.”
“Silent infections, which occur in about a third of infected people, may recrudesce.”
“Babesial infection may recrudesce after many months of asymptomatic parasitemia.”
“Although parasites were initially detected microscopically in the blood of two of the untreated subjects, and all of the treated subjects, none could be found a week after the onset of illness.”
“Persistent symptoms of Babesiosis accompanied persistent blood-borne Babesial DNA”
“The persistence of seroreactivity increasingly correlated with the persistence of Babesial DNA.”
”In those with only subtle symptoms, Babesiosis often remains undiagnosed.”
“Furthermore, physicians tend not to recognize Babesial infection in those who are co-infected with the agent of Lyme Disease, because Babesial symptoms tend to be ascribed to Lyme Disease.”
“Physicians caring for patients with moderate to severe Lyme disease should consider obtaining diagnostic
tests for Babesiosis and possibly other tick-borne pathogens… especially in patients experiencing “atypical Lyme disease” or patients in whom the response to antibiotic treatment is delayed or absent.”

Krause, PJ, Telford, SR, Spielman, A, et.al. *Concurrent Lyme disease and Babesiosis*. JAMA 1996. 275(21):1657

“Subjects with evidence of both infections reported a greater array of symptoms than those infected by the spirochete or piroplasm alone.”
“Co-infection generally results in more intense acute illness and a more prolonged convalescence than accompany either infection alone.”
“Spirochete DNA was evident more often and remained in the circulation longer in co-infected subjects than in those experiencing either infection alone.”
“Co-infection might also synergize spirochete-induced lesions in human joints, heart and nerves.”
“Babesial infections may impair human host defense mechanisms…”

“The possibility of concomitant Babesial infection should be considered when moderate to severe Lyme Disease has been diagnosed.”

SYMPTOMS
In milder forms, symptoms may include a vague sense of imbalance without true vertigo, headache, mild encephalopathy, fatigue, sweats, air hunger and occasionally cough. When present as a co-infection with Lyme, initial symptoms of the illness are often more acute and severe. Suggestions of co-infection include the above symptoms, but the headaches are more severe, and encephalopathy is out of proportion to the other Borrelia symptoms. The fulminant presentations include high fevers, shaking chills and hemolysis, and can be fatal.

DIAGNOSTIC TESTS
Diagnostic tests are insensitive and problematic. There are at least thirteen Babesial forms found in ticks, yet we can currently only test for B. microti and WA-1 with our serologic and nuclear tests. Standard blood smears reportedly are reliable for only the first two weeks of infection, thus are not useful for diagnosing later infections and milder ones including carrier states where the germ load is too low to be detected.

Krause, PJ, Telford, SR, Spielman, A, et.al. *Concurrent Lyme disease and Babesiosis*. JAMA 1996. 275(21):1660
“As is common in the case of Babesial infections, parasites frequently cannot be seen in blood films.”

Therefore, multiple diagnostic test methods are available and each have their own benefits and limitations and often several tests must be done. Be prepared to treat based on clinical presentation, even with negative tests.

SEROLOGY
Unlike Lyme, Babesia titers can reflect infection status. Thus, persistently positive titers or western blots suggest persistent infection.

PCR
This is more sensitive than smears for B. microti, but will not detect other species.

ENHANCED SMEAR
This utilizes buffy coat, prolonged scanning (up to three hours per sample!) and digital photography through custom-made microscopes. Although more sensitive than standard smears, infections can still be missed. The big advantage is that it will display multiple species, not just B. microti.

FLUORESCENT IN-SITU HYBRIDIZATION ASSAY (FISH)
This technique is also a form of blood smear. It is said to be 100-fold more sensitive than standard smears for B. microti, because instead of utilizing standard, ink-based stains, it uses a fluorescent-linked RNA probe and ultraviolet light. The Babesial organisms are then much easier to spot when the slides are scanned. The disadvantage is that currently only B. microti is detected.

TREATMENT
Treating Babesia infections had always been difficult, because the therapy that had been recommended until 1998 consisted of a combination of clindamycin plus quinine. Published reports and clinical experience have shown this regimen to be unacceptable, as nearly half of patients so treated have had to abandon treatment due to serious side effects, many of which were disabling. Furthermore, even in patients who could tolerate these drugs, there was a failure rate approaching 50%.

Krause, PJ. Spielman, A, Telford, SR et.al.. *Persistent parasitemia after acute Babesiosis* N Engl J Med 1998. 339:162

“Of the treated subjects, almost half had symptoms that were consistent with reactions to quinine, including hearing loss, tinnitus, hypotension, and such gastrointestinal symptoms as anorexia, vomiting, and diarrhea”
“Although treatment with clindamycin and quinine reduces the duration of parasitemia, infection may persist and recrudesce and side effects are common.”

Because of these dismal statistics, the current regimen of choice for Babesiosis is the combination of atovaquone plus azithromycin. This combination was initially studied in animals, and then applied to Humans with good success, because when atovaquone was used alone, resistance developed in 20% of cases, but reportedly did not occur when azithromycin was added. Fewer than 5% of patients have to halt treatment due to side effects, and the success rate is clearly better than that of clindamycin plus quinine.

The duration of treatment with atovaquone plus azithromycin for Babesiosis varies depending on the degree of infection, duration of illness before diagnosis, the health and immune status of the patient, and whether the patient is co-infected with Borrelia burgdorferi. Typically, a three-week course is prescribed for acute cases, while chronic, longstanding infections with significant morbidity and co-infection will require several months of therapy. Relapses have occurred, and retreatment is occasionally needed.

Problems during therapy include diarrhea, mild nausea, the expense of atovaquone (over $600.00 per bottle- enough for three weeks of treatment), and rarely, a temporary yellowish discoloration of the vision. Regular blood counts, liver panels and amylase levels are recommended during any prolonged course of therapy. Patients who are not cured with this regimen can be retreated but with higher doses, as this has proven effective in many of my patients. Artemesia (a non-prescription herb) may be added, but is not effective when used alone. Metronidazole can also be added to increase efficacy, but there is minimal clinical data on how much more effective this regimen is.

EHRLICHIOSIS

GENERAL INFORMATION

While it is true that this illness can have a fulminant presentation, and may even become fatal if not treated, milder forms do exist, as does chronic low-grade infection, especially when other tick-borne organisms are present. The potential transmission of Ehrlichia during tick bites is the main reason why doxycycline is now the first choice in treating tick bites and early Lyme, before serologies can become positive. When present alone or co-infecting with B. burgdorferi, persistent leukopenia is an important clue. Thrombocytopenia and elevated liver enzymes are less common, but likewise should not be ignored. Headaches, myalgias, and ongoing fatigue seem to relate to this illness, but are extremely difficult to separate from symptoms caused by Bb.

DIAGNOSTIC TESTING

Testing is problematic with Ehrlichia, similar to the situation with Babesiosis. More species are known to be present in ticks than can be tested for with clinically available serologies and PCRs. In addition, serologies and PCRs are of unknown sensitivity and specificity. Standard blood smears for direct visualization of organisms in leukocytes are of low yield. Enhanced smears using buffy coats significantly raises sensitivity and will indicate a wider variety of species. Despite this, infection can be missed, so clinical diagnosis remains the primary diagnostic tool. Again, consider this diagnosis in a Lyme Borreliosis (LB) patient not responding well to therapy.

TREATMENT

Standard treatment consists of Doxycycline, 200 mg daily for two to four weeks. Higher doses, parenteral therapy, and longer treatment durations may be needed based on the duration and severity of illness, and whether immune defects or extreme age is present. However, there are reports of treatment failure even when higher doses and long duration treatment with doxycycline is given. In such cases, consideration may be given for adding rifampin, 600 mg daily, to the regimen.

BARTONELLA
BARTONELLA

Bartonella has become an important topic of discussion among Lyme patients.

Bartonella has been newly found to be the most prevalent of all the tick-borne pathogens, even more so than Borrelia! The strain of Bartonella being seen seems to be a new one- it is not usually picked up on standard Bartonella blood testing, and the usual Bartonella medications do not work for this. Lyme and Babesia medications don't treat this either.

Symptoms may include encephalitis, cognitive deficits, confusion, seizures, occasionally anxiety, peripheral neuropathies, fatigue, gastritis, sore soles, especially in the AM, tender subcutaneous nodules, and red rashes. Lymph nodes may be enlarged.

Because standard Bartonella testing, either by serology or PCR, may not pick up all strains of this organism, the blood test is very insensitive. Therefore, the diagnosis is a clinical one, based on the above points.

The drug of choice to treat this is Levaquin (levofloxacin). Levaquin is usually never used for Lyme or Babesia, so many patients who have tick-borne diseases, and who have been treated for them but remain ill, may in fact still be infected with Bartonella. It has been suggested that Levaquin may be more effective in treating this infection if a type of antacid prescription called a "proton pump inhibitor" is added. Examples include Nexium, Protonix, Prevacid, etc. Drugs like Pepcid and Zantac are not proton pump inhibitors and will not be helpful.

Levaquin is generally well tolerated, with almost no stomach upset. Very rarely, it can cause confusion- this may be relieved by lowering the dose. There is, however, one side effect that would require you to stop taking this drug: it may cause a painful tendonitis, usually of the largest tendons. If this happens, then the Levaquin must be stopped or tendon rupture may occur. Unfortunately, Levaquin and drugs in this family cannot be given to those under the age of 18, so other alternatives are used in children.

Incidentally, animal studies show that Bartonella may be transmitted across the placenta. No human studies have been done.

Bartonella henselae, the agent of cat scratch disease, has been found in Ixodid ticks and as a co-infection in patients with Lyme Disease. With co-infection, symptoms of Bartonella are almost impossible to distinguish from Lyme, but may include lymphadenopathy, splenomegaly, hepatomegaly, headache, encephalopathy, somnolence, flu-like malaise, weight loss, sore throat, and a papular or angiomatous rash. In acute cases, there can be hemolysis with anemia, high fever, weakened immune response, jaundice, abnormal liver enzymes, and myalgias. Endocarditis and myocarditis have been reported. More severe infections are associated with immune deficiency and possibly occurrence of opportunistic infections. As in Lyme Disease and Babesiosis, Bartonella may be transmitted to the fetus in the infected pregnant patient.

Diagnostic tests include serology, blood and CSF PCR, and biopsy of skin lesions and lymph nodes.

In the co-infected Lyme patient, eradication may be difficult. Many antibiotic agents have been reported to be effective, including cephalosporins, fluoroquinolones, erythromycins, gentamicin, rifampin and streptomycin. In practice, these patients seem to do best with a combination regimen that utilizes agents that can penetrate cells. Typical combinations include an erythromycin, plus a fluoroquinolone or rifampin. Treatment progress is most commonly assessed by PCR post treatment and serial titers.

NUTRITIONAL SUPPLEMENTS IN DISSEMINATED LYME DISEASE
EAST END MEDICAL ASSOCIATES, P.C. J.J. Burrascano Jr., M.D.
RECOMMENDED NUTRIONAL SUPPLEMENTS
Scientifically Validated Nutritional Support

Studies on patients with chronic illnesses such as Lyme and Chronic Fatigue have demonstrated that some of the late symptoms are related to cellular damage and deficiencies in certain essential nutrients. Double blinded, placebo controlled studies, and in one case direct assay of biopsy specimens have proven the value of some of the supplements listed. Some are required, while others are optional -see below. They are listed in order of importance.

I have found that the quality of supplements used is often more important than the dose. In fact, I do not recommend "mega doses". Instead, seek out, if possible, pharmaceutical grade products, especially if USP certified. I recommend Pharmanex products because they fit these criteria. In the list below, it is indicated whether the products should be gotten from Pharmanex, or whether a different source, or even a generic substitute is OK. To order Pharmanex products, call 1-800-487-1000 and give the following U.S. reference number: 9256681-R.

BASIC DAILY REGIMEN
ACIDOPHILUS (required when on antibiotics)
Essential to maintain the normal balance of intestinal flora; the best kinds are frozen or refrigerated to ensure potency. Take two with each meal. Plan to mix together several different brands to broaden the spectrum. You can get acidophilus from most vitamin stores. An alternative that does not need refrigeration and can be taken only once a day is a high potency, patented product called "Pro Bio" from Pharmanex. In addition drink "Kefir", 2 to 4 ounces a day on occasion, and have 4 ounces of yogurt daily if possible.

MULTI-VITAMIN (required)
I recommend the Life Pack family of multivitamins. These are unique supplements-Pharmaceutical grade and USP certified, they are the only products clinically proven in double blinded, placebo controlled crossover studies to quench free radicals and raise antioxidant levels in the blood and lipids. Choose LifePak for males under 40,
LifePak Women for hormonally active women, and LifePak Prime for postmenopausal women and for men over 40. They are available through Pharmanex. Continue long term.

CO-Q10- *required, but do not use if you are taking the prescription drug atovaquone (Mepron, Malarone).*
Deficiencies have been related to poor function of the heart, limitations of stamina, gum disease, and poor resistance to infections. Heart biopsy studies in Lyme patients indicated that they should take between 200 and 300mg daily of standard CoQ 10, or 90 mg (three caplets) of the well absorbed, highly purified, crystalline CoQ 10 product sold by Pharmanex, (surprisingly, the Pharmanex brand is far less expensive than the generic!).

VITAMIN B (required).
Clinical studies demonstrated the need for supplement vitamin B in infections with Borrelia, to help clear neurological symptoms. Take one 50 mg B-complex capsule daily. If neuropathy is severe, an additional 50 mg of B-6 can be added. Generics are OK.

MAGNESIUM (required)
Magnesium supplementation is very helpful for the tremors, twitches, cramps, muscle soreness, heart skips and weakness. It may also help in energy level and cognition. The best source is magnesium L-lactate dehydrate
("Mag-tab SR", sold by Niche Pharmaceuticals: 1-800-677-0355, and available at Wal-Mart). DO NOT rely on "cal-mag", calcium plus magnesium combination tablets, as they are not well absorbed. Take at

least one tablet twice daily. Higher doses may cause diarrhea, and you should check with your physician before using more than this. In some extreme cases, injections or intravenous doses may be necessary.

ESSENTIAL FATTY ACIDS: (required)
Studies show that when EFAs are taken regularly, statistically significant improvements in fatigue, aches weakness, vertigo, dizziness, memory, concentration and depression are likely. There are two broad classes: GLA (omega-6 oils) and EPA (omega-3 oils), derived respectively from plant and fish oils. This is what to take:
Plant Oil: Use “Barlean’s Omega Twin”- This is a refrigerated product obtained from the local health food store. Take one to two tablespoons daily. May be mixed with food, put on salads, etc.
Fish Oil: Use “Marine Omega” by Pharmanex. Use four daily, taken on a full stomach.

OPTIONAL SUPPLEMENTS FOR SPECIAL CIRCUMSTANCES

FOR NEUROLOGIC SYMPTOMS
ACETYL-L-CARNITINE this is taken along with SAM-E. This combination can result in noticeable gains in short term memory, mood and cognition. The Acetyl Carnitine also is said to help heart and muscle function. Doses: Acetyl-L-carnitine- 1500 mg daily on empty stomach. SAM-e- 400 mg daily with the acetyl carnitine. Available in most vitamin stores. Positive results may appear as early as 3 weeks; use for 3+ months.
METHYLCOBALAMIN (Methyl B12)
This is a prescription drug made from vitamin B12 that helps to heal damage to the nervous system. Must injected into the muscle, as it will not be effective if used under the tongue, or swallowed. Use 25 mg daily.
FOR INCREASED ANTIOXIDANTS
GREEN TEA
Green, but not black tea contains some of the most potent antioxidants around (80-100 times more effective than vitamin C), plus EGCGs, which may have inhibitory effects on cancer! Demographic studies performed in China revealed that at least four cups daily are need to reap this benefit. I can see using this when cancer risks are a concern, and if ultra high potency antioxidants are desired. I strongly suggest you get only caffeine-free tea. “TeGreen “ capsules by Pharmanex contain 97% pure tea polyphenols and each capsule is the equivalent of four to seven cups of decaffeinated green tea. This is a nice alternative when you get tired of drinking so much tea.
CORDYMAX
Cordyceps is a well-known herb from Tibet and has been shown in clinical studies to improve stamina, fatigue, and enhance lung and antioxidant function. It also raises superoxide dismutase levels, important to prevent lesions in the central nervous system (brain and spinal cord). The positive effects can be dramatic; can be used long term. Available from Pharmanex as "CordyMax".
FOR IMMUNE SUPPORT
REISHI MAX
This enhanced extract from cracked spores of the reishi mushroom has been shown in clinical studies to augment function of the Natural Killer Cells- the part of the immune system that combats certain infectious agents and serves in cancer surveillance. Take four a day. Available from Pharmanex.
ECHINACEA
May be helpful in fighting acute and chronic viral illnesses. Choose a pharmaceutical grade brand ("Immune Formula" by Pharmanex), and do not use the liquid form as this contains alcohol. Do not take daily on a long-term basis, as the benefit may wear off. Therefore, use four a day for three weeks per month.
FOR FATIGUE
ALPHA LIPOIC ACID

FOR JOINT SYMPTOMS
GLUCOSAMINE
Can be of long term benefit to the joints. Do not be mislead into buying a product that also contains chondriotin, as this chemical does not add anything, but it can make the product more expensive. Look for a product that contains the herb Boswellia serrata- this is a non-irritative anti-inflammatory. Although many

generic exist, the Pharmanex product, "Cartilage Formula" has the right ingredients and is of proven efficacy. Expect improvement only over time (several weeks), but plan to use this indefinitely to maintain joint health.

FLEX CREAM

An amazing product that really works and has a money back guarantee. Use for any type of body pain- spread on a thick layer and do not rub in. Takes 30 to 60 minutes to work, then lasts many hours. A Pharmanex exclusive.

OTHER OPTIONAL SUPPLEMENTS

CREATINE (optional)

Creatine has been shown to be of benefit in neuromuscular degenerative diseases such as Lou Gherig's Disease (ALS) and can be very helpful in supporting low blood pressure, as in NMH. It may also benefit strength, stamina, and heart function. Important: To use this safely, you must have an adequate fluid intake. The creatine product should contain taurine, an amino acid needed to enhance creatine absorption, plus some carbohydrate to aid creatine entry into muscle. You will need a 20 gram loading dose for the first five days, then 4 to 10 grams daily maintenance. Try "Cell Tech" from the Vitamin Shop, and follow label directions.

MILK THISTLE (optional)

Useful to support liver function. Take 175 mg three times daily- use an 80% Silymarin extract. Available from many vitamin stores. A more potent product, available from Pharmanex, is called "Detox Formula".

LYME DISEASE REHABILITATION

Despite Lyme treatments, you will NOT return to normal unless you exercise!

Those with longstanding Lyme and associated tick-borne diseases end up in poor physical condition. In late stage disease, many negative effects to the body are occurring: the muscles are shrinking, weakening, and are being replaced by scar tissue and fat. To some degree, the heart muscle also suffers. The lungs, ribs, and muscles of respiration are also affected, as are the joints, nerves, liver, etc.

Besides these physical effects, chemical changes occur. The per cent fat content of the body as a whole rises, the cholesterol rises, and the balance between the "good" and "bad" cholesterols (HDL and LDL, respectively) becomes less favorable. Also, in at least 80% of the patients, significant weight gain occurs.

To make matters worse, because of the extreme fatigue and body pain, many patients end up spending inordinate amounts of time in bed, and get far less exercise than they had before they became ill.

As a result of all this, they are stiff, weak, tired, have poor stamina, and are at increased risk for cardiovascular disease and diabetes.

Therefore, a vital part of any plan for recovery must include various forms of physical therapy, the extent of which depends on an individual patient's condition, followed by an exercise program.

The physical therapy should involve massage, heat packs and pads, and simple range of motion exercises to relieve discomfort, promote better sleep and flexibility. This then evolves into an exercise program that starts with stretching and mild muscular strengthening, to lessen joint pain and increase mobility and stamina. Finally the program must include a specific program of *non-aerobic* conditioning to reverse the negative effects on the heart, lungs, and circulation, and to help with correcting the chemical imbalances described above.

Diet also plays an important role. This is the time for the very best of health habits. I recommend light, low fat food, with high quality nutritional value, absolute abstention from alcohol, elimination of caffeine, a decrease in sugar and starch intake, and if applicable, a serious commitment to weight loss. Smoking is completely out!!!

Professional guidance will be needed, from therapists of various types and from dietary counselors. Written orders for therapy are attached as page 3 of this handout.

It is indeed a difficult task to regain your health after a serious bout with Lyme Disease. By following this advice, your physical and emotional well being will dramatically improve. After what you've been through, you deserve nothing less.

EXERCISES AS A FORM OF THERAPY FOR LYME DISEASE

I encourage all Lyme patients to go through a formal rehabilitation program. Generally, this involves progressing from simple physical therapy modalities, then to stretching and mobility training, and finally to formal strengthening exercises supervised either by the physical therapist, or by a qualified, credentialed exercise coach.

A surprising thing happened which none of us expected- when Lyme patients went further with their rehab, to include a whole-body conditioning program, the Lyme seemed to go away!

I have seen this occur repeatedly, including in some patients who did not even go on antibiotics!

Although the scientific basis for this is not known, there are several reasonable theories. It is known that the Lyme spirochete, Borrelia burgdorferi, will die if exposed to all but the tiniest oxygen concentrations. If an aggressive exercise program can increase tissue perfusion and oxygen levels, then this may play a role in what is being seen. Also, during aggressive exercise, the core body temperature can rise above 102 degrees; it is known that B. burgdorferi is very heat sensitive. Perhaps it is the added tissue oxygenation, or higher body temperature, or the combination, that weakens the Lyme Borrelia, and allows the antibiotics and our defenses to be more effective. In addition, there is now evidence that a carefully structured exercise program may benefit T-cell function in the immune system, an obvious potential benefit in an illness like Lyme that is known to weaken immune responses.

As you progress through rehab, you must make it your goal to participate in a one-hour aggressive exercise class every other day (three times per week). BUT- you must be patient! It takes at least six weeks of regular physical therapy to be able to join a light conditioning and stretching program, and six more weeks are usually needed before heavier exercises can begin. Finally, only after several weeks of this level of physical training will you be able to say that you have made a major dent in your illness. Please note that the program consists of conditioning and strengthening, and NOT aerobics.

Because high body temperatures may play a role in this phenomenon, I advise against using swimming as the chosen exercise.

A final few words of caution: do not jump into an aggressive program until you are ready for it and your physical therapist agrees. Do not try any *aerobics* until your Lyme is no longer active, and your physician okays it. You may need a cardiac stress test first to ensure safety. And finally, please join a program run by a trained professional with proper credentials.

Best wishes and good luck working out your Lyme!

LYME REHAB-PHYSICAL THERAPY PRESCRIPTION

NAME_____
D.O.B._____ DATE_____

Please enroll this patient in a program of therapy to rehabilitate him/her from the effects of chronic tick-borne diseases. If necessary, begin with classic physical therapy, then progress when appropriate to a whole body conditioning program.

THERAPEUTIC GOALS (to be achieved in order as the patient's ability allows):

PHYSICAL THERAPY (if needed):
1. The role of physical therapy here is to prepare the patient for the required, preferably gym-based exercise program outlined below.
2. Relieve pain and muscle spasms utilizing multiple modalities as available and as indicated: massage, heat, ultrasound, and passive and active range of motion. DO NOT use ice or electrical stim unless specifically ordered by our office.
3. Increase mobility, tone and strength while protecting damaged and weakened joints, tendons, and ligaments, and teach these techniques to the patient. Use light weights/minimal resistance but a lot of repetitions in any exercises prescribed. Aerobics are not permitted. Transition the patient to the gym-based program outlined below.
4. Please see the patient two days per week- but do not schedule two days in a row!

EXERCISE Begin with a private trainer for careful direction and education.

PATIENT EDUCATION AND MANAGEMENT (to be done during the initial one-on-one sessions and reinforced at all visits thereafter):
1. Instruct patients on correct exercise technique, including proper warm-up, breathing, joint protection, proper body positioning during the exercise, and how to cool-down and stretch afterwards.
2. Please work one muscle group at a time and perform extensive and extended stretching to each muscle group immediately after each one is exercised, before moving on to the next muscle group.
3. A careful interview should be performed at the start of each session to make apparent the effects, both good and bad, from the prior visit's therapy, and adjust therapy accordingly.

PROGRAM:
1. Aerobic exercises are NOT allowed, not even low impact variety, until your stamina improves.
2. Conditioning: work to improve strength and reverse the poor conditioning that results from Lyme, through a whole-body exercise program, consisting of light calisthenics and weight lifting, using small weights and many repetitions. This can be accomplished in exercise classes called "stretch and tone", or "body sculpture", or can be achieved with exercise machines, or carefully with free weights.
3. Each session should last one hour. If the patient is unable to continue for the whole hour, then modify the program to decrease the intensity to allow him/her to do so.
4. Exercise no more often than every other day. You may need to start by exercise every 4^{th} or 5^{th} day initially, and as your abilities improve, work out more often, but NEVER two days in a row. The days you do not exercise should be spent resting.
5. This whole-body conditioning program is what is required to achieve wellness. Simply placing the patient on a treadmill or an exercise bike is not acceptable (except briefly, as part of a warm-up), nor is a simple walking program.

PHYSICIAN'S SIGNATURE_____

MANAGING YEAST OVERGROWTH

Many patients with weakened defenses, such as from chronic illnesses, including Lyme Disease, develop an overgrowth of yeast. This begins in the mouth and then spreads to the intestinal tract. Therefore the primary line of defense is careful oral hygiene plus the eating of foods that replenish the beneficial bacteria and crowd out the yeast (such as yogurt and Kefir, and taking acidophilus).

MOUTH: A tongue with a sticky beige coating, bad breath, and a bad taste in the mouth are signs of oral yeast, also known as "thrush". You will need to follow the protocol below, and use the special products that are listed.

CLEANSING
Brush your teeth, tongue, gums, inner cheeks and palate first with toothpaste, then again for 30 seconds while holding an antiseptic mouthwash in your mouth Then, rinse by scrubbing while holding plain water in your mouth.

TOOTHPASTE
Use “AP-24” toothpaste, sold by NuSkin Enterprises. Unlike conventional toothpastes that may contain alcohols, formaldehydes and abrasives, this product cleans in a unique way. It contains two “surfactants” (detergent-like cleansers) that are very effective without being harsh. This product is available in two forms- regular and whitening (both contain fluoride). Choose either one. In addition, get from them their patented toothbrush that is designed to work with this toothpaste. It cleans better and is far gentler than regular or electric toothbrushes.

Order AP-24 products by calling 1-800-487-1000. The U.S. reference # is 9256681-R

MOUTHWASHES
Use an antiseptic mouthwashe (Scope, Listerine, etc.), and brush your teeth, tongue, gums, cheeks and the roof of your mouth while holding the mouthwash in the mouth. Do this for 30 seconds, then rinse repeatedly with water.

For especially thick or resistant thrush, the most effective (and drastic) treatment, employed as a last resort, consists of using "Dakin's Solution" as a mouth rinse. Make this by mixing one teaspoon of household liquid bleach (Clorox) in four ounces of water. A small amount is held in the mouth while brushing, then spit out, and repeated until the thrush has cleared. This is usually a one-time treatment, but may have to be repeated every few weeks.

After using an antiseptic, it is necessary to immediately eat yogurt or chew an acidophilus capsule to replenish the beneficial flora in the mouth. Because the germ count, both harmful and beneficial, will be artificially reduced after such a cleaning, and because yeasts are opportunists, the yeast infection will come back. By having the yogurt or acidophilus then, the yeast will be crowded out and a more normal oral flora will result.

INTESTINAL TRACT: An overgrowth of yeast here will ferment dietary sugars and starches, forming acids, gas, and alcohols. Symptoms include gas, bloat, heartburn and/or pain in the stomach area, and because of the alcohol, there can be headaches, dizziness, lightheadedness, wooziness and post-meal fatigue. To clear intestinal yeast, first the tongue and mouth must be cleared so yeast does not reenter the system with every swallow. Next, since yeast germs feed on sugars and starches, avoid simple carbohydrates including sugars, starches, and fruits. See the diet outlined on the next page. Finally, to replenish the normal, beneficial microbes, eat PLAIN yogurt daily, drink Kefir, 4 ounces daily, or take acidophilus, 2 capsules three times daily after meals.

J.J. BURRASCANO JR., M.D.

YEAST CONTROL DIET
Restricted carbohydrate regimen

FOODS ALLOWED
All protein foods, such as meat, fish, fowl, cheese, eggs, dairy, tofu

FRUITS
Fruits may be a problem because they contain a large amount of sugars. However, if the fruit contains a lot of fiber, this may make up for the sugars to some degree. Thus:

- Only high fiber fruits are allowed
- Only very small amounts!
- Fruits are only allowed at the end of a meal, and never on an empty stomach

ALLOWED
Grapefruit, lemons, limes, tomatoes, avocado
SMALL AMOUNTS ONLY! (The high fiber content in these hard, crunchy fruits makes up for the carbohydrates)
Pears, apples, strawberries, cantaloupe, etc.
NOT ALLOWED (These soft fruits do not have enough fiber)
Oranges, watermelons, bananas, grapes, etc.
No fruit juices either!

VEGETABLES
Green vegetables and salads are O.K. Avoid or limit starchy vegetables (potato, rice, beans, etc.) and avoid pasta.

STARCHES
None!! If it is made from flour- any kind of flour- it is not allowed. (No breads, cereals, cake, etc.)

SWEETENERS
NOT ALLOWED
No sugars at all, and no fructose or corn syrup
ALLOWED (if tolerated)
Stevia (safest), honey, Splenda, Aspartame (NutraSweet, Equal)
Saccharin products are not recommended

DRINKS
ALLOWED
Water, seltzer, caffeine-free diet sodas, coffee and tea without sugar or caffeine, vegetable juices
NOT ALLOWED
Fruit juices, regular sodas, and any drinks sweetened with sugars or syrups

PATIENT INSTRUCTIONS ON BITE PREVENTION AND TICK REMOVAL

HOW TO PROTECT YOURSELF FROM TICK BITES

PROPERTY Remove wood piles, rock walls, and bird feeders as these attract tick-carrying small animals and can increase the risk of acquiring Lyme.
INSECTICIDES: Property should be treated with a product called "Damminix". This consists of cardboard tubes containing cotton balls that have been dipped in insecticide. These tubes are placed around the property in the wooded areas and below shrubs. Mice, which are a key link in the propagation of Lyme disease, find the cotton and bring it back to their burrows to be used as nesting material, with the result being a big decrease in the number of ticks in the area. Unfortunately, after two years tick populations may rise again as other small animals that do not gather cotton become hosts to the ticks. Therefore, Damminix alone is not sufficient. Use this product in conjunction with liquid or granular insecticides.
LIQUID & GRANULAR PESTICIDES: Products meant for widespread application such as permethrin and its derivatives are preferred. They are available as a liquid concentrate and as granules. If liquid insecticides are used, application should be by fogging, not by coarse sprays. Apply these products in a strip a few feet wide at the perimeter of the lawn at any areas adjacent to woods and underbrush. Also treat any ornamental shrubs near the house that may serve as a habitat for small animals. The best time to apply these products is in late Spring and early Fall.

CLOTHING When wearing long pants, tuck the cuffs into the socks so any ticks that get on shoes or socks will crawl on the outside of the pants and be less likely to bite. Also, light colored clothing should be worn so the ticks will be easier to spot. Smooth materials such as windbreakers are harder for ticks to grab onto and are preferable to knits, etc.

Tick repellents that contain "permethrin" (Permanone, Permakill) are meant to be sprayed onto clothing. Spray the clothes before they're put on, and let them dry first. Do not apply this chemical directly to the skin.

Ticks are very intolerant of being dried out. After being outdoors in an infested area, place clothes in the dryer for a few minutes to kill any ticks that may still be present.

SKIN: Insect repellents that contain "DEET" are somewhat effective when applied to the arms, legs, and around the neck. Do not use any repellent over wide areas of the body as they can be absorbed causing toxicity. Also, it is inadvisable to use a product that contains more than 50% DEET, and 25% concentrations are preferred. Use repellents cautiously on small children, as they are more susceptible to their toxic effects. Be aware that this repellent evaporates quickly and must be reapplied frequently.

Check carefully for ticks not only when home but frequently while still outside!

HOW TO REMOVE AN ATTACHED TICK
Using a tweezer (not fingers!), grasp the tick as close to the skin as possible and pull straight out. Then apply an antiseptic. Do not try to irritate them with heat or chemicals, or grasp them by the body, as this may cause the tick to inject more germs into your skin. Tape the tick to a card and record the date and location of the bite. Remember, the sooner the tick is removed, the less likely an infection will result.

APPENDIX

RATIONALE FOR TREATING TICK BITES

Prophylactic antibiotic treatment upon a known tick bite is recommended for those who fit the following categories:

1. People at higher health risk bitten by an unknown type of tick or tick capable of transmitting Borrelia

burgdorferi, e.g., pregnant women, babies and young children, people with serious health problems, and those who are immunodeficient.

2. Persons bitten in an area highly endemic for Lyme Borreliosis by an unidentified tick or tick capable of transmitting B. burgdorferi.

3. Persons bitten by a tick capable of transmitting B. burgdorferi, where the tick is engorged, or the attachment duration of the tick is greater than four hours, and/or the tick was improperly removed. This means when the body of the tick is squeezed upon removal, irritated with toxic chemicals in an effort to get it to back out, or disrupted in such a way that its contents were allowed to contact the bite wound. Such practices increase the risk of disease transmission.

4. A patient, when bitten by a known tick, clearly requests oral prophylaxis and understands the risks. This is a case-by-case decision.

The physician cannot rely on a laboratory test or clinical finding at the time of the bite to definitely rule in or rule out Lyme Disease infection, so must use clinical judgment as to whether to use antibiotic prophylaxis. Testing the tick itself for the presence of the spirochete, even with PCR technology, is not reliable enough to guide your decision to treat, as false positives and false negatives occur.

An established infection by B. burgdorferi can have serious, long-standing or permanent, and painful medical consequences, and be expensive to treat. Since the likelihood of harm arising from prophylactically applied spirochetal antibiotics is low, and since treatment is inexpensive and painless, it follows that the risk benefit ratio favors tick bite prophylaxis.