

## ACIDS

# Australian Chronic Infectious Disease Society Guidelines Version 1.51

Australian Chronic Infectious Disease Society Limited

Guidelines for the management of borreliosis, babesiosis, bartonellosis, theileriosis and associated diseases.

Copyright notice: This document is the copyright of

**Australian Chronic Infectious Disease Society Limited**  
**Suite 603, 6th Floor**  
**379-383 Pitt St**  
**Sydney NSW 2000**

### Disclaimer

These guidelines for diagnosis and management of borreliosis (Lyme disease) and the associated co-infection diseases of babesiosis and bartonellosis are intended for the sole use of medical practitioners with an interest in the treatment of borreliosis. Concurrent persistent infection with other pathogens needs to also be considered by the practitioner. These guidelines are not meant to be comprehensive, nor are they meant to be strict guidelines for managing the disease. Guidelines should serve as a framework to assist practitioners in achieving desirable health outcomes for patients blending practitioner knowledge with informed patient consent. In no case are these guidelines intended to replace the individual clinical judgement of the medical practitioner involved. In these diseases informed consent is of paramount importance as will be explained in treatment.

### Aim:

1. The guidelines are for the diagnosis and management of borreliosis and its co-infections in Australia. To our current knowledge this is mainly tick borne disease though other arthropods are implicated on a small scale.
2. To form a collective of knowledgeable doctors able to offer advice in this emerging field.
3. Education and research into these diseases in Australia.
4. There are many experienced practitioners who have trod the path of managing these infections. For the practitioner new to this illness, find a mentor; for the experienced colleague, it is an expected component that our profession teach and assist colleagues.

## Borreliosis

Borreliosis, otherwise known as Lyme disease in the USA and UK but borreliosis elsewhere in the world, is an infectious illness caused by the spirochaete *Borrelia burgdorferi* (Bb) and related species particularly *B. afzelii* and *B. garinii*. In most cases borreliosis is an illness that forms as a result of a bite from an infected tick. The borreliosis infection can result in acute phase generalised illness but often disseminate slowly and can lead to a more chronic and more disabling form of disease. This chronic form of borreliosis frequently leads to severe dysfunction in the immune system with associated opportunistic infections and co-infections leading to production of biologic toxins, metabolic and hormonal imbalances and a form of severe chronic fatigue. Recognition and early treatment of borreliosis leads to a higher success rate of cure. Chronic borreliosis is associated with severe morbidity and in some cases significant mortality, especially in cases of neuroborreliosis. *Borrelia* can

invade every tissue in the body and in this respect has earned the moniker “the second great imitator” – after syphilis. It can produce profoundly differing sets of symptoms from one individual to another.

The following *Borrelia* genotypes have been found in Australia to date, on sequencing by a NATA accredited laboratory Australian Genome Research Facility (AGRF) Sydney:

- *B. burgdorferi* with multiple strains but principally N40, CA382 and ZS7
- *B. afzelii*
- *B. garinii*
- *B. valaisiana*

And by immunoblot (Mikrogen)

- *b. bavariensis*

## The *Borrelia* Associated Co-infections

Co-infections are often transmitted at the same time, a result of multiple pathogens harboured by the tick, or indeed from separate multiple tick bites. The following are often found associated with borreliosis in Australia and believed to be tick borne:

- Anaplasma species (former name human granulocytic anaplasmosis)
- Babesia species
- Bartonella species
- Ehrlichia chaffeensis species (former name human monocytic ehrlichiosis)
- Rickettsiae species (which are also known to have other vectors besides ticks, eg midges)
- Theileria species

## Babesiosis

Babesiosis is likened to malaria and is often mistaken in the third world for that condition. It is an intracellular erythrocyte piroplasm at about one tenth the size of the malarial piroplasm. It is difficult to find with microscopy of Giemsa stained thin films and must be sought manually not by automation. Proper analysis should take of the order of 25 to 30 mins and for this reason serology and PCR analysis will create a better level of diagnostic accuracy. Acute babesiosis in the immune compromised or splenectomised patient is described well in the literature and involves a rapid intensive care management involving IV antibiotics and often exchange transfusion. In borreliosis which is an immune suppressive disease we see a different presentation. The patient can present with marked neurological disorder including brain fog and disordered mentation and thrombotic and embolic events including CVA (stroke) and these symptoms can last as long as their disease state. These patients will describe severe night sweats, bad enough to saturate clothing and sheets. As well they will often have chest wall and or sternal pain. These patients characteristically present to an emergency department for suspect myocardial infarction or pulmonary embolus. But these will be tested negative and the patient sent home advised that nothing serious has been found. The Society's advice to every medical practitioner is that these patients must be investigated in an emergency department at the very least once for the aforementioned life threatening states.

In Australia we are finding *B. duncani*. We have suspicion of other strains.

## Theileriosis

This is the new name for the infection that used to be classified as *Babesia microti*. DNA studies showed it to be a sister genus to the babesias but belonging to the theileria genus. Clinically we cannot distinguish a difference on presentation to that of *Babesia duncani*. It is however easier to treat.

## Bartonellosis

This is classically understood to be cat scratch disease in paediatrics and caused by *Bartonella henselae*. However it can also be transmitted by ticks. In a publication still in-press 17 genera of *Bartonella* are described that cause human infection [Angelakis]. The key immediate features suggesting *Bartonella* infection are endocarditis, lymphadenopathy, neuroretinitis, angiomas, fever within days of tick bite, osteomyelitis and arthropathy. It is very important to recognise that it is an immune suppressive disease. In the presence of Lyme disease bartonellosis can also take a lower grade persistent course and clues to the diagnosis are severe balance problems or linear red streaking marks looking like striae or parallel cat scratch lines or angiomas of varying size, or pain in the soles of the feet for the first few steps getting out of bed or electric shock feelings in limbs more than the trunk or ice-pick headaches. Finally severe neurological disease and in particular encephalopathy with convulsions gives a high index of suspicion for this infection. We have one such case of borreliosis plus bartonellosis due to ticks from the grey kangaroo in a New Zealander visiting on holidays.

The known worldwide species that can be expected to be in Australia are *B. henselae*, *B. claridgeiae* and *B. quintana*. However the species *B. australis*, *B. cooperi*, *B. queenslandensis*, *B. rattiaustraliensis* and *B. antechini* are found in Australia in the Grey kangaroo, mottled tail rat, grassland melomys, Tunney's rat and finally fleas and ticks. Given the numbers of clinical *Bartonella* patients seen but tested negative for *B. henselae*, it would seem some of these are causing undocumented human infection and tentatively we suspect the first and the last for transmission to humans.

## Anaplasmosis

This is an infectious disease caused by *Anaplasma phagocytophilum*, a member of the rickettsiales genus. It is an infection of granulocytic blood cells and was formerly known as human granulocytic ehrlichiosis. It causes profound illness with a low white cell count. Immediate treatment is imperative on suspicion before laboratory proof is available because this infection can be fatal. In the immune suppression caused by Lyme disease infection can be protracted.

## Ehrlichiosis

This is an infectious disease caused by *Ehrlichia chaffeensis*, a member of the rickettsiales genus. It is an infection of the monocyte line of blood cells and was formerly known as human monocytic ehrlichiosis. It again causes profound illness with a low white cell count. Immediate treatment is imperative on suspicion before laboratory proof is available because this infection can be fatal. In the immune suppression caused by borreliosis, infection can be protracted.

## Rickettsial infections

These are infectious disease transmitted to humans by ticks and fleas principally. They fall into three taxonomic groups:

- Spotted fever group rickettsia with 6 types
- Typhus group rickettsia with 2 types
- Scrub typhus group rickettsia with 4 types

We recommend testing at Australian Rickettsial Reference Laboratory Geelong to confirm any positive serological finding from a standard laboratory

### Concurrent Infections

The following are problematic infections/pathogens associated with borreliosis worldwide. There is suggestion that these may also be transmitted by ticks:

- Mycoplasma species including fermentans
- Chlamydomphila species (formerly Chlamydia pneumonia)
- Brucellosis
- Q-fever (coxiella burnettii)
- Toxoplasmosis
- Histoplasmosis
- Leptosirosis
- Yersiniosis

Chronic viral infections including HIV, HHV-6, parvovirus B19, CMV and in particular EBV.

### Incidence

Tentative projection of 102,000 in Australia with chronic borrelial infection

### Prevalence table

Data shortly to be published by one of our members shows

	Percentage Positive	N	Sample size
Never left Australia	17	83	492
Female	62	311	500
Report a tick bite ever	71	240	340
Describe a rash consistent with EM	78	108	139
Illness length average	7.4		343
Illness time median	3		343
Illness time SD	9.49		343
Illness time min	0.2	1	343
Illness time max	49	1	343
Laboratory proven borrelial infection Aust Biologics	55	127	216
Laboratory proven borrelial infection Igenex	58	146	252
Proven borrelia with elimination of dual testing	50	251	500
Laboratory proven bartonella infection	19	23	122
Laboratory proven duncani infection	27	33	123
Laboratory proven theileria infection	11	13	123
Clinically suspected borrelia infection	74	371	500
Clinically suspected bart bab or theileria infection	61	307	500
Patients with neither proven or clinically suspicious disease	10	50	500

## Removing a tick:

Given that the predominant mode of vector transmission centres on tick bite, a brief discussion regarding the appropriate method of arthropod removal should be discussed. Ticks utilise a specialised organ known as a hypostome which has barb-like structures and 'salivary' cement to hook the parasite in place. There are many suggestions regarding the 'safe' removal of ticks. Initial attachment is now known to be involved in disease transmission by the tick saliva as well as the later regurgitation of gut contents.

1. Do not poison or attempt to kill the tick; try to remove the tick alive and intact.
2. Using a tick removal device, or fine pair of quality tweezers grasp the tick near head at the level of the skin.
3. Pulling gently, firmly and perpendicular to the skin remove the tick carefully so as to not disrupt the body.
4. If mouth parts are retained they should be removed by excision and a 2mm punch biopsy is perfect. This also provides a good sample for PCR analysis if desired.

## Immediate after care of a tick bite

Don't apply cortisone cream or administer cortisone orally or parenterally. This is because cortisone worsens the outcome of borreliosis infection in the long term and makes it harder to treat. Many descriptions of tick allergy in Australia do not describe an urticarial eruption. An urticarial eruption lasts a maximum of 24 hours though it can recycle.

## Tick anaphylaxis

Pure tick anaphylaxis does exist and is equally as severe as bee bite anaphylaxis. For the above reason do not consider cortisone, which would take 6 hours to work, but use adrenalin 1/1000 at a dose of 0.5ml at first in an adult. Be prepared to repeat this before the patient settles. These patients who are potentially subject to exposure should consider auto-injector delivery of adrenalin.

## Vectors

The most common vector for borreliosis in Australia is ticks. One proven species is the paralysis tick *Ixodes holocyclus*. This is about to be published and is peer reviewed. It is important to note the distribution of this tick is the entire eastern coastline right up into the ranges and in the south spreading back up across Melbourne and into central western Victoria. Many patients report having no knowledge of tick attachments, but the nymphal form is very small and hard to find.

## Other methods of disease transmission

### Sexual transmission

The incidence of sexually transmitted Lyme is currently unknown however there is definitive evidence that this does exist.

### Pregnancy

Direct transmission via the placenta to the unborn child has been seen in numerous families for both borreliosis and bartonellosis. There are literature reports.

## Blood Transfusion

Blood transfusion is highly likely to transmit borreliosis, and has been shown to transmit babesiosis. This is of serious concern, due to the under diagnosis of these diseases in Australia.

## Symptoms of Borelliosis

In a classic presentation of borreliosis a rash may develop in association with the tick bite. This rash is commonly known as Erythema Migrans (EM), a macular rash greater than 5 cm diameter, which is diagnostic of borrelial infection. It occurs in fewer than half of the patients. EM rashes can more rarely appear like a bullseye rash. EM begins formation within four days of the tick bite, however it may present several weeks after the bite, and then in association with constitutional symptoms. Multiple lesions may appear over the body and this is suggestive of multiple bites rather than haematogenous spread to skin. Occasionally a macular or haemorrhagic rash may appear and generally these rashes are only slightly irritating or pruritic. This indicates co-infection. Common symptoms of acute borreliosis are mild temperature elevation, headache (meningitic), retro-orbital pain and flu like symptoms or general malaise. Joint pains in Australia indicate co-infection as might glandular swelling, sweats and fever. Borreliosis is principally a neurological disease on this continent. There seems to be a total absence of the described North American single or pauci migratory arthritis with gross swelling, which is reminiscent of rheumatic fever.

Chronic borreliosis can present as a multi-system disorder with almost any brain and body symptom. See the attached assessment tool. In worst-case scenarios of chronic borreliosis there have been prior diagnoses of severe autoimmune disease, particularly rheumatoid arthritis, multiple sclerosis, sarcoidosis, motor neurone disease and ALS. There are often appellations of chronic fatigue syndrome and fibromyalgia. Borreliosis is also associated with psychological disorders, including panic lasting more than 30 minutes, severe depression, chronic anxiety, obsessive compulsive disorder and schizophrenia. Learning difficulties in children are also observed, as well as ADD, ADHD and autistic spectrum disorder.

## Diagnostic Tests

The diagnoses of borreliosis and its co-infections are often initially clinical due to the lack of confirmatory pathology results. The gold standard for diagnosis is a history of tick exposure and development of classical symptoms, medically confirmed EM, positive sero conversion, IgG and IgM positive, a positive microscopy for spirochaetes, a positive Western Blot and positive PCR test. In an ideal world this would categorically diagnose borreliosis in Australia. Unfortunately the above situation is not very common. The following is a list of initial tests that could be considered in a patient presenting with symptoms that may indicate chronic infection of borreliosis and can be concurrent infection:

- FBC, ESR, CRP, UEC LFT'S, CD57+ (CD3-) subset
- Serology for Rickettsia, Mycoplasma, Chlamydia Pneumoniae IgA,G,M, EBV, CMV, parvovirus B19 ,HHV6, Brucellosis, Q fever sero, Toxoplasmosis sero, Histoplasmosis, leptospirosis, HIV, Syphilis.

Chronic borreliosis infections are known to suppress the immune system and can decrease the quantity of CD57 subset of the natural killer cells. Sick patients with high CD57 may be ill with something more than borreliosis, such as a co-infection. Babesiosis can cause a marked elevation.

- If a patient has arthritic issues you may need to consider testing:  
ANA, ENA's, ANCA, Rheumatoid factor, CCP antibody, CK, ASOT, Anti-DNase, Ross River Virus and Barmah Forest Virus.
- Some patients may have indications for testing:  
ACE, Coeliac Disease, Anti-gliaden antibodies, IgG, IgA, Tissue Transglutamase and Coeliac Disease genetic test, TSH, T4, T3, Reverse T3, thyroid antibodies, insulin. GTT, other hormonal studies, vitamin D (25 and 125 OH), urinary kryptopyrroles and lastly visual contrast sensitivity testing.

## Specific Borrelia Testing

1. Polymerase Chain Reaction (PCR) testing on blood, urine and serum for borrelia, Elispot for borreliosis, Mikrogen immunoblot for borreliosis. These tests are performed by Australian Biologics, Pitt St Sydney. Blood is cultured for 3 weeks in preparation for testing. As well they offer PCR testing on blood for mycoplasma including fermentans, chlamydia trachomatis and chlamydophila. By far Australian Biologics is currently the most effective diagnostic lab in Australia for the diagnosis of borreliosis and its associated infections.
2. Palms Laboratory is a hospital based pathology lab associated with Royal North Hospital in Sydney. They perform Elisa tests, IgG and IgM for borreliosis and if positive will perform Western Blot testing. The incidence of positive results from this laboratory remains low when the same patients' blood is tested simultaneously elsewhere in Australia, USA or Germany. We understand their primers are from Dublin and also test band 30 not band 31 on western blot. Band 31 is known to be the key band found in neurological Lyme disease.
3. The Australian Rickettsia Reference Laboratory in Geelong Victoria is particularly useful for testing Rickettsia infections in full and to a high standard. It has just started doing borrelial PCR. They have offered anaplasma and ehrlichia testing but no ACIDS doctor has seen a positive to date.
4. Sullivan Nicolaidis Pathology in Queensland is now performing bartonella PCR on skin, and will also do a non NATA Bartonella henselae and quintana on blood with PCR if requested.
5. IgeneX in the USA is a dedicated TBD laboratory highly successful at testing for Elisa, western blot and PCR testing for borreliosis and all the co-infections. Unfortunately there is considerable expense with this testing.
6. Infectolab in Augsburg Germany is also a valuable resource for testing, as is
7. Redlab in Belgium.
8. Advanced labs USA – 1 week cultured borrelia testing
9. Galaxy labs in USA – good for bartonella henselae and quintana testing

## Management of Borreliosis and Co-infections

There is an importance to understand that antibiotic and similar anti-infectives are essential in returning a patient to good health. There are two fallacies believed by some patients in Australia, firstly that herbal medicines is all the treatment that is needed, the second at the other extreme is that they must have intravenous antibiotics. Only 10% of patients presenting with these infections have pure borreliosis infection. There is no co-infection requirement for intravenous treatment with rare exception so 90% of patients will respond to orals for co-infection.

Golden rules of treatment:

Rule 1 - you must treat babesia, theileria and bartonella infection before borreliosis

Rule 2 - when using parenteral antibiotics for borrelia, cell wall + intracellular antibiotic + cystic form treatment is required – simultaneously

Rule 3 - when using oral cell wall antibiotics for borrelia, cell wall + intracellular antibiotic treatment is required – simultaneously

## Education

There should be dissemination of information about borreliosis to the patient, carers and family as well as to the general practitioner involved in their medical treatment. It is essential for all involved to be fully informed about the symptoms, possible reactions to treatment, particularly the Herxheimer reaction, and the long term nature of treatment required to assist the patient in regaining their health. This extends to education of the community, dissemination of information through local councils, state government agencies and federal government health services so that all assistance is given without difficulty.

## Advice to the Patient and GP

### *Patient habitat*

The patients living environment is very important. Patients often require reduced noise, reduced light, and easy access to bathroom and living areas. A mould free, warm, dry home/living space is required.

### *Diet*

Diets free of gluten, wheat, dairy and soya products and low in fructose are necessary to reduce stress on the small bowel which is the great majority of the adult immune system. Fresh food that is adequately washed and freshly prepared will maximise nutritional benefit. Green juices made from a variety of vegetables also assist greatly. Sugars must be avoided if taking antibiotics long term to reduce candidiasis problems, particularly in females. Fructose, sugars and starches also provide food for chronic infection organisms.

### *Sleep*

Many patients with borreliosis suffer from disturbed sleep patterns usually with difficulty going to sleep, wakefulness and Circadian Dysrhythmias. Sleep when tired, and sleep regular hours at night in a dark quiet bedroom. Melatonin 3-10mg taken around 7-8pm each night may help regulate sleep. Level 4 sleep is a deep recuperative sleep that lasts only several minutes but is only attained after two dream sessions in the one sleep interval. This is about 3.5 hours or a fraction longer. It is essential to get to this level on a majority of nights. The only drugs that can achieve this are tricyclic antidepressants, usually at doses of 50mg or 75mg, and quetiapine 25mg nocte. You may consider compounding this to as low as 10mg.

### *Exercise every second day*

Patients with borreliosis should be encouraged to be as active as possible within the limits of the disease. Aim to build up to 45 mins in the long term. This can be divided on that day. It is stressed that anaerobic exercise not aerobic exercise is required and that it should be every second day. This is because any exercise suppresses the immune system for 24 hours. Some patients will be severely de-conditioned and the help of physiotherapy and exercise physiologist will be beneficial.

### *Emotional Health*

Unfortunately borreliosis patients have often been psychologically damaged by family, friends, the community and the medical profession due to the failure to diagnose the condition correctly and institute appropriate management. Many patients in Australia have been wrongly diagnosed with Conversion Disorder and other harmful labels including Munchausen's. This situation will only change

when every general practitioner, physician and allied health professional is fully informed and has significant enough insight to make the correct diagnosis. Psychologists and counsellors are extremely beneficial in assisting patients with borreliosis. , as living with long term organic chronic illness often needs supportive psychotherapy. Obtaining family and friends support once the diagnosis has been made is essential to the patients' health. Mixed with pharmacotherapy where appropriate there is no reason for these patients to suffer emotionally. They have a tough time as it is physically. Support groups are available around the country to reduce the incidence of social isolation.

## Treatment of borreliosis with antibiotics

Once the diagnosis of borreliosis has been made treatment with antibiotics is essential. BUT co-infections must be treated first. The treatment will vary depending on whether the borreliosis is acute or chronic. Children should be treated differently to adults, pregnant women will require appropriate treatment and finally the very unwell patient with serious complicated borreliosis and co-infections will require extensive specialised management.

### Acute borreliosis

Acute borreliosis usually occurs after an initial tick bite with symptoms of flu like illness and possibly an EM rash. It takes many days after the bite for constitutional symptoms to occur. If you see immediate illness within 1-2 days then bartonella infection is likely. Usually diagnostic tests are not performed unless a patient is extremely ill as generally most tests will be negative for any of the borreliosis or co-infections at this stage. Elisa and western blot take 6 weeks to become positive. Central tissue biopsy of the tick attachment site for PCR analysis is the only early diagnostic step that can be taken. At the 10 day mark the Elispot LTT starts to become positive.

### Adult Antibiotics

For adults doxycycline 200mg – 400mg, always taken with food, for 6 weeks for erythema migrans. If the patient is extremely unwell which signifies disseminated disease with fevers and night sweats 400mg daily is advisable. That is the standard dose some Lyme doctors use. Side effects include benign intracranial hypertension and severe photosensitivity. Warn that the sun must be avoided at these doses. Severe reflux can be avoided by taking the chloride form of doxycycline immediately at the beginning of the main meal and avoid lying down for one hour. Low body weight women often need the dose divided bd. Note that doxycycline at 400mg is bactericidal.

### Children 7 Years or Less

Amoxycillin 20-30 mg per kilogram per day given in equally divided doses every 8 hours for 6-8 weeks.

### Children 8 Years and Older

The dosage is doxycycline 50mg two daily always taken with food for 6-8 weeks. The doxycycline can be compounded or crushed and mixed with food. If there is a penicillin allergy, cefuroxime axetil as an oral suspension 10-15mg per kilogram per dose twice daily can be given for 6-8 weeks.

### General note

All these medications can be acquired under the PBS authority system at the above recommended doses. Probiotics should be given twice daily taken well away from the antibiotics. The refrigerated forms are superior. Ten billion units a day are required in adults, adjust according to body weight.

## Chronic Borreliosis

We define Chronic borreliosis as an illness that has persisted for greater than three months involving multiple body systems such as neurological involvement, severe joint inflammation, marked gastrointestinal symptoms, cardiac involvement with or without POTS (Postural Orthostatic

Tachycardia Syndrome), arrhythmias and myocarditis. Many patients with borreliosis often present with other diagnoses but really do have multi systemic borreliosis. Accurate clinical assessment and diagnosis is essential for the correct management and specific treatments. Borreliosis is a very unusual infective disease presenting as the cell wall spirochaete, intracellular and then cystic form simultaneously. The borrelia often involve intracellular infection within any cell group within the body. The cystic form is highly resistant to treatment. The cell wall form is usually treated with penicillins and cephalosporins. Intracellular forms are treated with tetracyclines particularly doxycycline, minocycline and the macrolides including clarithromycin, azithromycin, clindamycin and lincomycin. Be aware the macrolides do not enter the CNS very well when treating neurologic disease. Cystic forms are treated with metronidazole or tinidazole or hydroxychloroquine (Plaquenil). These antibiotics are usually given orally and some are given by intramuscular injection. Some can be given intravenously by daily cannulation or the use of a PICC Line. There is also a biofilm form of the borrelia and this is discussed below. A biofilm example is dental plaque which is not borrelial.

The patient will often arrive highly self-educated about the disease and its treatment options.

The following is a list of well recognised antibiotic protocols that are used in Australia by experienced borreliosis treating doctors. Sharing of information with colleagues in Europe, Asia and North America support these current Australian proposed guide lines.

### Oral Antibiotics:

#### **Rule 3 = cell wall + intracellular antibiotic is required - simultaneously**

Amoxicillin 500mg capsules (always with food), week 1: 2 tds, maximum dose: 4 tds. Probenecid 500mg 1 tds can be used to potentiate the effects of the amoxicillin.

Usually amoxicillin is commenced for a period of 1 week before other antibiotics are added due to the risk of side effects due to the Herxheimer reaction which occurs as a result of bacterial death and the associated interleukin storm to cell wall breakdown products. Often one may need to back off and build the dose up gradually.

Doxycycline 200mg per day (always with food) is usually started after 1-2 weeks. Then increase dosage each week. A minimal dose of 400mg is ultimately required as this dose is bactericidal. It is better as a single dose but may be split bd. A large person may require 500 to 600mg. If you see herxing caused by doxycycline then it will be due to a co-infection not borrelia.

Minocycline 200mg per day before food is especially useful in neurological disease and is the preferred intracellular antibiotic under 30 years of age for proven borreliosis in a supposed diagnosis of motor neurone disease. It does not cause the photosensitivity of doxycycline and is better tolerated in some people. However there are two concerns with its use, benign intracranial hypertension and development of a lupus syndrome which is why this drug has come under PBS restriction.

The cystic form is induced only by parenteral cell wall antibiotics and is discussed below.

Avoiding the sucrose molecule reduces the nutrient resource for fungi/yeasts. The duration of treatment is dependent on the severity of illness and the response of the patient to treatment. Treatment which lasts for 6-12 months for chronic borreliosis is normal and many patients will require longer. We are aiming to return the patient to good health. This does not necessarily assume 100% eradication of the spirochaete. Basic pathology tests FBC, UEC and LFT should be performed monthly at least. Three month review is recommended to check if there has been progress. One can assume that if there is no progress by this time then there is a block or treatment is incorrect. At these reviews one should always be on the lookout for the onset of prior quiescent or new symptoms

of bartonella and babesia infection. Such emergence during therapy is unfortunately all too common and thorough diagnostic elimination of these two infections at the start is essential before full scale borrelial treatment as discussed below.

### Parenteral Antibiotics

**Rule 2 = cell wall + intracellular antibiotic + cystic form treatment is required – simultaneously**

Neurological borreliosis is usually treated with parenteral therapy both in the USA and Europe. Indeed there has been a preponderance of intravenous therapy. We do not see IV as essential in the first instance. We consider it second line treatment unless there is urgent indication such as encephalopathy, convulsions, motor neurone type presentation or similar problems. The emphasis would be on the urgency to treat. However please take note of the co-infection incident rate and the necessity to treat these first. We have seen considerable harm caused by the use of IV ceftriaxone in the presence of fulminant bartonella and babesia without these being addressed first. It is the opinion of the society that treating all three at once is not practical and overwhelms the patient.

1. Benzathine penicillin 1.8 grams IMI once weekly to a maximum dose of 1.8 grams IMI twice weekly, or 3 times a week in a large person. There is a benzathine penicillin efflux pump at the BBB which can be blocked with the H2 antihistamines or statins, thus aiding spectacularly in treating neurological disease.
2. Ceftriaxone 2 grams by IVI infusion given over 20 minutes 7 days per week via cannula or PICC line. Maximum dose is 4 grams (2gm bd) on 4 days per week in more serious infections particularly neuroborreliosis. The main side-effect of this medication is biliary stasis. To prevent this, the use of ursodeoxycholic acid 250mg 1 tds is recommended (private script). The QTc needs to be watched carefully and should be measured weekly in the mornings. FBC UEC and LFT should be done weekly. Mild leucopaenia is common and not a worry, but below 3000 is an indication to suspend treatment for 1 or 2 weeks until the count has returned to normal.
3. Very rarely you may come across resistance to the above. The alternative drugs are ertapenem, beta-lactam antibiotics and vancomycin. The last is very powerful at treating borrelial infection.

Then simultaneously there is the requirement for an intracellular antibiotic as discussed above, for example doxycycline at 400mg daily.

For the cystic form the following are recommended, commencing by 4 weeks into treatment:

1. Metronidazole orally 400mg 3 daily for 2 weeks on 2 weeks off
2. Tinidazole 500mg daily 2 weeks on 2 weeks off. This drug also has activity on all three forms.
3. Hydroxychloroquine (Plaquenil) 200mg tds. This will involve retinal checks.

### Biofilm Forms

Borrelial spirochaetes are identified in biofilm forms. There is no published scientific evidence yet supporting the benefit of biofilm eradication when treating chronic Lyme disease, however, it makes logical sense that all forms of borrelia need to be eradicated. Many practitioners use biofilm therapy for complex borrelial disease. This advice then is preliminary:

It is recommended 9 cis-decanoic acid be administered as 2-3 tablespoons of coconut oil a day or Serrapeptase, one to two capsules two times per day. Other effective enzymes are lumbrokinase and nattokinase.

## Other Treatments

### Supplements

1. Probiotics 2 daily
2. Vitamin B complex 1 per day
3. Vitamin C 1000mg 1 bd
4. Zinc, 30 – 120mg elemental Zn daily. In the presence of pyrroluria add B6 and P5P as well.
5. Coenzyme Q10 100-300mg per day. One study of 50 ME/CFS patients showed 74% had a genetic SNP which prevented them converting CoEnzymeQ10 to Ubiquinol. If there is never a response to CoEnzymeQ10, it would be reasonable to substitute 100mg Ubiquinol daily for the CoEnzymeQ10, despite the extra expense.
6. Magnesium 400-800mg nocte. Important to use this with quinolones to prevent tendon injury
7. Glutathione 200-500mg bd or its precursors. , an absorbable form, e.g. Lipoceutal Glutathione, or a glutathione inducer, such as Max GXL or liposomal glutathione (n.b. Glutathione is broken down into its components in their passage through the gut wall, and not necessarily reconstituted in the blood stream. Precursors given separately are not necessarily constituted into glutathione after ingestion. Lipoceutal glutathione is absorbed intact. IV glutathione can be effective. Transdermal glutathione can be used but smells awful.)
8. alpha lipoic acid 300mg to 1200mg daily – for peripheral neuropathy or if on ciprofloxacin [Horowitz]

These supplements are advised in all patients with borreliosis due to selective malabsorption and to assist in metabolic processes.

### Medications

#### *Sleep*

1. Melatonin 3-10mg 7-8 pm
2. Tricyclic antidepressants
3. Low dose quetiapine 25mg nocte

These have been discussed above.

#### *Seizures*

1. Clonazepam 0.5 mg quarter to half mane, quarter to a half midi, quarter to two nocte can be used in preventing seizures which are non-epileptiform. These include tremors, twitches, fasciculation, faints, collapses and fit like symptoms. (n.b. Clonazepam has a tremendously long half life of over 30 hours, and more often than 12 hourly dosing is meaningless)
2. Topiramate and lamotrigine can also be used to treat seizures and to help prevent migraines in borreliosis patients.
3. Seizure like muscle spasm may be due to borrelial neurotoxin released by the spirochaete. One clue to this is reduced night vision related to visual contrast sensitivity which can be tested for. This neurotoxin is perfectly secreted by the liver in bile and equally perfectly resorbed in the gut with long term accumulation. The resorption can be blocked with cholestyramine 4gm sachets 2 daily or charcoal tablets throughout the day usually for a period of 2 months.[Chro

#### *Pain*

Many patients with borreliosis experience significant pain symptoms including headache, sinus pain, atypical facial pain and generalised body neuropathic pain. The following is a list of medications that can be used but treatment usually needs to be individualised due to the variability of severity of pain and pain tolerance.

1. Long acting paracetamol 665mg 2 bd to 2 tds. (Disadvantage – this reduces glutathione levels)
2. Tramadol 50mg to 200mg bd.
3. Pregabalin 25-300mg bd for neuropathic pain is highly useful but often is limited by its side effects.
4. Paracetamol, codeine combination drugs are also useful.
5. Oxycodone orally or as a patch can also be used in more severe cases. Be very careful in relation to risk of addiction.
6. Low dose naltrexone 1-5mg per day as a single dose has been shown to assist some patients in controlling pain and reducing neurological inflammation. The mechanism is not fully understood and this off label use of naltrexone is highly useful in some patients.
7. Fentanyl can be given as a patch. Again the same precautions are present in case of tolerance and dependence

Note on 5 and 7: Many patients have reduction in narcotic receptors and even high doses of narcotics may not be effective

### *POTS (Postural Orthostatic Tachycardia Syndrome)*

POTS is often a difficult symptom to manage in many patients with severe borreliosis. Frequent monitoring of blood pressure, regular ECGs and the assistance of a cardiologist is highly recommended. SSRI's can cause or make POTS much worse.

Strategies to deal with this are

1. The consumption of water 2-3 litres per day
2. Sodium chloride (salt) 1 teaspoon 2-3 times daily
3. The use of therapeutic short leg stocking 20-30 mmHg worn continuously from arising out of bed is very useful in maintaining the blood pressure.
4. Liquorice (*Glycyrrhiza glabra*) is an anti-inflammatory, adrenal tonic with aldosterone-like activity through the potentiation of cortisol. 100mg a day of glycyrrhizin acceptable for long-term use. Caution sodium retention and low potassium levels. Works well in combination with Hawthorn, Tienchi ginseng and Astragalus.
5. Fludrocortisone acetate 0.1mg half to two mane is often required to prevent severe hypotensive episodes.
6. Propranolol 10mg 1-2 bd often is required to prevent supraventricular tachycardia (SVT). Verapamil may also be used.
7. Mimirin nasal spray can be considered if ADH is low and osmolality high
8. Midodrine, methylphenidate, selective serotonin reuptake inhibitors, pyridostigmine, and erythropoietin, either alone or in combination were successfully used in a recent trial [Kanjwal]

### *Gastrointestinal (GIT) Support*

1. Probiotics should always be used in patients on long term antibiotics. Probiotic powder 1-2 teaspoons bd for upper GIT symptoms and capsules 2 bd for general GIT support, taken well away from antibiotics. Bioscreen research shows a large majority of CFS patients have an overgrowth of d-lactate producing bacteria – streptococci and enterococci. Therefore avoid most acidophilus containing probiotics, and concentrate on those with a preponderance of l-lactate producing lactobacilli – *L. rhamnosus* and *L. casei*, e.g. Metagenics Ultra Flora LGG, Metagenics Fembiotic, Bioceuticals ProDophilus, and add *Saccharomyces boulardii* – Bioceuticals SB Floractiv.

2. Constipation can be assisted with slippery elm capsules 2 bd, macrogol sachets 1-2 daily and magnesium oxide powder quarter to one teaspoon daily. Medium to high doses of Vitamin C, especially soluble powder, higher doses of fish oil, and Aloe vera juice can also be helpful.
3. Loperamide hydrochloride can be used to help treat diarrhoea.
4. Gut relief formulas including combinations of glutamine, n-acetyl glucosamine, marshmallow, curcumin and aloe vera may be very helpful for maintaining normal intestinal permeability.

Be aware bartonella infection of the GIT is as equal a problem as borrelial infection if not more. Bartonella therapy in this instance can cause severe Herxheimer reactions. Research into *B. henselae* infections shows it can infest the stomach and oesophageal lining resulting in severe gastro-oesophagitis and severe reflux disease. This can be mistaken for GIT complaints or mistaken for sensitivity or intolerance of the medication. It is a very tortuous path to tread. There are numerous symptoms that borreliosis patients experience due to the infection and the reactions they experience to treatment. If there is difficulty managing the severity of symptoms always seek advice from other practitioners in the field, be early to refer to a hospital if any serious or life threatening symptoms occur and be forever vigilant for the unexpected. Borreliosis is a very complex illness and as the organisms die and particularly if there are co-infections, varied and unusual symptoms can occur singly or in combination leading to a complex disease pattern. Always monitor patients regularly with weekly review of a patient initially then review once a month and finally once every three months during treatment. The response to these therapies is very variable and initially side effects to medications need to be managed and particularly Herxheimer reactions need to be recognised and managed accordingly. Often this just requires an explanation to the patient and reassurance but sometimes alteration of treatment by dosage reduction or symptom reduction therapies need to be instituted. Always seek advice or assistance from knowledgeable doctors in the field or appropriate specialists if a serious complication arises.

### Paediatric Chronic Borreliosis Treatment

Children present a therapeutic dilemma as often they have acquired this disease congenitally or have experienced a tick bite leading to the development of borreliosis. Often children have been unwell for some time before an accurate diagnosis is made and congenital borreliosis often presents with slowly mounting symptoms and is unlike adult borreliosis. There is increasing evidence that a proportion of Autistic Spectrum Disorder, failure to thrive, ADHD and behavioural and learning disorders are associated with active borreliosis. Treatment usually involves a combination of amoxicillin, co-trimoxazole, clarithromycin, tinidazole, metronidazole and cefuroxime axetil. Treatment with these medications depends on the age of the child, the severity of symptoms and the duration of the illness. As with adult patients probiotics should be given with all other antibiotic combinations. As a general rule, commencing with amoxicillin tds and clarithromycin bd in appropriate age and weight related doses constitutes an effective treatment. An alternate to amoxicillin is cefuroxime axetil 250mg. If parenteral therapy is used then rule 2 becomes mandatory with the use of metronidazole pulsed two weeks on two weeks off. This is due to cyst formation induced by this mode of treatment. Children under two require highly specialised care as the use of antibiotics damages the immune system. We suggest you contact the society for help. It is next to impossible to suspect the co-infections clinically, however the presence of convulsions is a major indicator of bartonella infection and a CVA is an indicator of babesia or theileria infection.

### Other Treatment modalities

The use of treatments such as herbal medicines, hyperbaric oxygen therapy, ozone therapy, salt with vitamin C, rifting and other modalities will be brought to the practitioners' attention by a lot of patients. Some of these treatments are without doubt helpful but certainly not curative in their own right which

their proponents often claim. The society r refrains from making any suggestions in favour or against at this juncture.

## Monitoring of the patient

### Acute Borreliosis

When a patient is diagnosed with acute borreliosis, the assessment and diagnosis is usually clinical and appropriate treatment needs to be instituted for 6-8 weeks. Sometimes 12 weeks is needed though this appears to be when babesia co-infection occurs which is important to recognise clinically early to avoid protracted infection. Generally the patient should be reviewed at the end of the treatment, and only if symptoms persist should they be investigated. Early diagnosis and treatment of borreliosis will generally prevent the development of chronic borreliosis.

### Chronic Borreliosis

The society defines chronic borreliosis when infection has been present for more than 3 months. The primary reason we choose that time interval is that experience has taught us that the infection is more difficult to treat. Review should be monthly as a general rule by the GP. If they are very unwell, review weekly or fortnightly is advisable. Pathology testing should be undertaken on a monthly basis, FBC, ESR, CRP, LFT, UEC. An ECG should be performed monthly on patients receiving ceftriaxone infusions as this drug may cause a prolonged QT interval which can lead to arrhythmic episodes. The same applies to azithromycin, clarithromycin and roxithromycin at the doses that are used. All patients should have had a CT of brain and an MRI is more preferable. Order a CT at least if not done. Where there is significant neurological disease it is worth documenting the degree of cerebral involvement with a SPECT CT of brain. Note a PET scan is not adequate and is often suggested by radiology departments. Any reported areas of reduced perfusion are highly significant. We are experiencing some units reluctant to call this neuroborreliosis.

### Duration of Treatment

Chronic borreliosis treatment usually is between 3 months and 3 years. Some patients require much longer treatments especially if they have been undiagnosed for many years, or even decades before treatment is commenced. Generally antibiotics are stopped when symptoms have ceased for 2 months, there is no Herxheimer response to the antibiotics and the CD57 has returned to normal above 120. Patients should be reviewed at 6 weeks after stopping all treatment then every 3 months for a period of 2 years. Only after this time if there has been no relapse of symptoms could the suggestion that disease has been "cured" be made. Post Lyme Syndrome is defined by the IDSA (Infectious Disease Society of America) as the persistence of any symptoms following 4 weeks of IV therapy. They promulgate that appropriate therapy from there is the use of antidepressants, analgesics and supportive measures. ACIDS does NOT subscribe to this theory.

### Pregnant Women and Borreliosis

Women who are pregnant and have developed acute borreliosis following a tick bite should be treated with amoxicillin 500mg 2 tds for 8-12 weeks. Six weeks treatment for an acute EM following a tick bite is appropriate therapy when there are no systemic or constitutional symptoms.

Where there is a diagnosis of chronic borreliosis, treatment must be aimed at the foetus only for the duration of the pregnancy. The treatment is the long acting benzathine penicillin, 1.8 gm IMI weekly from diagnosis or the known onset of pregnancy with the total withdrawal of all other treatments. Flayl 400 mg tds is added in the second and third trimester, again to treat cyst formation.

The society has no formulated opinion at this juncture on the treatment of foetal transmission of the co-infections or such possibility of transmission.

## Co-infection and concurrent infections

Borreliosis is often associated with other infections due to the complexity in number of pathogens present in the tick (nature's dirty needle). The following is a list of the prime infections that we deal with in Australia and possible antibiotics that can be introduced in combination with the borreliosis treatment.

### Mycoplasma infections

1. Doxycycline 400mg daily.
2. Mycoplasma fermentans will require ciprofloxacin 500mg bd. The literature supports 8 weeks therapy. Magnesium should be co-administered to help prevent any tendon damage. Use Magmin bd.

### Chlamydia Pneumoniae

1. Doxycycline 400mg daily with food. Yes the macrolides are equally effective but you will be treating neuroborreliosis simultaneously unless your patient has the arthritic form from the USA.
2. Rifampicin is also effective – 600mg daily
3. NAC 600mg twice a day for the elementary form of this bacterium which is analogous to a spore. Continue this until all borrelia treatments stop. In this regard it is also beneficial to hepatic detoxification pathways.

### Babesia and Theileria

These are protozoal infections and respond to the following antibiotics.

1. Artemisinin 400-500mg bd. for 3 consecutive days per week
2. Hydroxychloroquine sulphate 200mg bd. Retinal checks will be required.
3. Doxycycline 400mg daily with food.
4. Artemether, lumefantrine 20mg;120mg (Riamet and in USA literature Coartem) taken 3 days in a week. 4 bd at 7am and 3pm first day then 7am 7pm next 2 days. We recommend weekly but acknowledge that there is variable opinion on this being used weekly or fortnightly.
5. Trimethoprim working up to 450mg daily. On the continent of Australia we are finding this drug a key implement in co-infection control. See below.
6. Atovaquone 750mg in 5ml twice a day for three to six months. This must be consumed with oil/fat to obtain absorption, literally it binds to oil to be carried across the gut wall.
7. Azithromycin 500mg 1 daily. ECG monitoring at the start and monthly of the QTc is essential.
8. Malarone. This combination drug of atovaquone and proguanil can be used, and is used frequently in North America. It can't be used below 3 years of age. It has a high side effect profile and the society's practitioners try to avoid its use.
9. Clindamycin IV is used in resistant cases in the USA.

A combination (usually 3) of these medications will be required to assist in the removal of these piroplasms in borreliosis patients. Babesia is often a serious co-infection leading to very severe symptoms in affected patients, and is harder to eradicate than theileria. A good starting regime would be drugs 1 + 3 + 5.

### Bartonella

1. Doxycycline 400mg daily with food.

2. Rifampicin 600mg daily usually for 12 to 26 weeks.
3. Hydroxychloroquine sulphate 400mg daily with food. (potentiates 1 and 2 by raising the intracellular *ph*)
4. Ciprofloxacin 500mg bd is useful in resistant cases or intolerance of doxycycline or rifampicin. With ciprofloxacin, magnesium should be administered to help prevent any tendon damage.
5. Gentamicin, this drug should be given IVI twice daily in very seriously ill patients with bartonellosis in a therapeutically appropriate hospital environment. Monitoring of kidney function and peaks and troughs is essential. Recently 6mg/kg with normal renal function given over 1 hour once in 24 hours has been shown to be safe and effective for many infections.

### Combined Babesia, Bartonella and Theileria treatment

Drs Derham (clarithromycin) and Mayne (doxycycline) have developed the following protocol for combination treatment with very good success over treatment periods of 6-8 months:

- Week 1  
hydroxychloroquine (Plaquenil) 200mg tab 1 daily 5 days then 1 twice a day
- Week 2  
add Artemisinin 400mg twice a day for 3 consecutive days per week. Be prepared to ramp up to the stronger Riamet later if necessary
- Week 3  
add azithromycin 500mg tab starting at 1/4 tab daily and building up 1/4 each four days to a full tablet. Take this full dose for 2 months then reduce to one tablet 3 times per week. ECG monitoring at the start and monthly of the QTc is essential
- Week 4  
add clarithromycin 250mg three times a day or cheaper alternative roxithromycin 150mg morning and 300mg evening. ECG monitoring at the start and monthly of the QTc is essential.  
OR  
add doxycycline building up as tolerated from 100-200mg daily through to 400mg (500 mg in heavier individuals)
- Week 5  
add trimethoprim 300mg half twice a day for 2 weeks and then 1/2 morning and 1 at evening

### Rickettsia infection

1. Doxycycline 200mg daily with food.
2. Ciprofloxacin 500mg twice daily. Magnesium should be co-administered to help prevent any tendon damage.

Warning – do not use a sulphonamide in the presence of a rickettsial disease, it worsens the infection.

### Viral infections EBV

In viral infections such as acute EBV, HSV etc, start with acyclovir 800mg twice a day for 1 week, then three times a day the second week and then four times a day for 2 months. If unsure of viral infection a simple CD4 count will guide the decision.

### General notes on the co-infections

It is important to note that the treatment for borreliosis with antibiotics often covers the treatment of some of the co-infections. It is important to recognise that other co-infections may exist with borreliosis and if the patient is not improving or is developing more serious symptoms particularly skin

rashes, neuropathic pain and neurological symptoms, co-infection diagnoses need to be investigated. It is also important to understand that the co-infections of bartonella and babesia need to be treated first then later the borreliosis. This is poorly understood across the medical community and a cause of treatment programs spanning many years with no improvement. It is noted during IV treatment of borreliosis in the presence of previously undetected co-infection, that the patient gets worse and there is a flare of the co-infection of babesia or bartonella or indeed both

**Rule 1 – you must treat babesia, theileria and bartonella infection before borreliosis**

## Severe Borreliosis Disease and Co-infections

Unfortunately borreliosis and its co-infections often present late or develop serious symptoms early in the disease requiring a much more aggressive treatment protocol to reduce symptoms and hopefully successfully treat the disease. Extreme borreliosis may present with neurological symptoms like multiple sclerosis, motor neurone disease, Parkinson's disease and severe autoimmune diseases such as rheumatoid arthritis like joint diseases. Deaths from these scenarios are occurring in Australia.

Generally doctors specialising in treatment of this form of borreliosis need to be sought and currently that is mainly among the general practice community. Hospital based treatments in Australia are generally lacking due to the uncertainty of diagnosis. This situation is also paralleled in Europe and North America where the concept of chronic borreliosis and its severe manifestations are not recognised by a majority of the medical community. Treatment should be designed so that cell wall antibiotics are given intravenously, such as ceftriaxone, ertapenem or other carbapenems and even vancomycin in resistant cases, as discussed previously. The tetracycline tigecycline may be used IV when oral tetracycline is not tolerated. It is the only IV form available in Australia. A patient may individually import IV doxycycline from the USA. Metronidazole can also be administered IV.

In serious borreliosis, combinations of the antibiotics should be administered aggressively but with constant clinical and pathological monitoring. The preferred environment is obviously a hospital. Patients with very serious neurological life threatening borreliosis may well respond to aggressive treatment. Treatment should continue for up to 3 months to ascertain the effectiveness of treatment, and longer once success is evident until clinical judgement dictates that less aggressive therapy is appropriate.

## Blocks to treatment

During therapy whenever a patient's progress stalls we must review the following blocking factors [Horowitz]

1. Infections - Bacterial / Parasitic / Viral / Fungal
2. Immune dysfunction - depressed CD57
3. Tissue Inflammation - brain / joints / organs
4. Toxicity -multiple chemical sensitivity, environmental illness, heavy metals, mould and neurotoxins. Dental implants and amalgams are a focus of chronic infection. HLA DR alleles testing. One of the sickest groups of patients is those with genetic defects making them particularly susceptible to mould. This group will not improve with any treatment until the challenge is removed from their environment and this always involves checking for environmental mould remediation index, and either taking serious remediation steps for the residence if positive or moving residence. A 10-step process has been described by Dr Ritchie Shoemaker at [www.survivingmold.com](http://www.survivingmold.com) and further discussion is out of the scope of these guidelines. [Shoemaker]

5. Allergies - foods, drugs, environmental
6. Nutritional & enzyme deficiencies/ functional medicine. Abnormalities in biochemical pathways, eg pyroluria - check urine kryptopyrrole (KP) (a wide range of diseases associated with this - the disorder makes Zn and B6 unavailable for metabolism). To test use SAFE laboratories, Qld, or Nutripath, Vic. Plasma porphyrins may need checking.
7. Genetic disorders of methylation pathways – MTHFR testing
8. Mitochondrial dysfunction
9. Psychological disorder - stress, PTSD, abuse, depression, anxiety, OCD...
10. Endocrine abnormalities - thyroid, GH, adrenal, sex hormones, pituitary, vit D deficiency. GTT and insulins may need to be checked.
11. Sleep disorders - acute and chronic, medications, pain, nocturia, depression/anxiety, sleep apnoea, RLS...
12. Autonomic Nervous System Dysfunction
13. Gastrointestinal - leaky gut, candida, dysbiosis, coeliac disease, colitis, cancer...
14. Elevated LFT's - antibiotics, EtOH, hepatitis, hemochromatosis, Wilsons disease,  $\alpha$ -1AT deficiency, chemicals (carbon tetrachloride, drugs)...
15. Drug use/Addiction – particularly illicit
16. Deconditioning - need for PT/Exercise program...

### MTHFR testing

Two genetic loci are responsible for known clinical defects of methylation pathways in the liver at this juncture. They are C677T and 1298C. Patients who are homozygous for either and have these arthropod infections will have clinical delays in recovery or blocks with a failure to metabolise heavy metals, break down products, toxins etc. There are genetic tests for both ordered simply as “MTHFR testing” at any lab. You can safely ignore any heterozygous finding even if both are so, supplement only the homozygous patients.

For the C677T mutation use 5-methyltetrahydrofolic acid. Start at 400mcg a day and build up to 1200mcg daily.

For the 1298C use folinic acid 1mg (Dr Vera's 500mcg) daily

### Mould sensitivity

This is another major issue in these diseases. There are genetic factors that influence ability to handle mould. Those with defects are at a very serious disadvantage due to the inability to present biotoxins from the mould to antigen presenting cells, and the resulting inflammation due to a chaotic immune response. In susceptible individuals it is currently thought recovery is next to impossible without relocating away from a mouldy environment. Testing involves examining the HLA DQ and DRB1 genetic loci. DQ2 (often part of the 7-2-53 or 17-2-52A mould susceptible genotypes) and DQB1 03-02 (often part of the 4-3-53 multisusceptible haplotype) are deleterious. Coeliac DQ/DR testing with a Sonic Group laboratory (Sullivan & Nicolaidis, Clinipath, Douglas Hanly Moir, Melbourne Pathology and Capital Pathology) is recommended as other laboratories currently do not report the exact DQ and DRB1 alleles. We recommend using the Rosetta Stone established by Dr Ritchie Shoemaker at [www.survivingmold.com/lab-tests](http://www.survivingmold.com/lab-tests) for correctly establishing the gene type in all patients. Dr Shoemaker has established a 14-step process for overcoming biotoxin-related inflammation. This precise methodology will be covered in separate guidelines on mould-related illness.[Shoemaker]

### Discussion

Borreliosis and its co-infections are emerging illnesses in Australia. More patients are presenting each year with unexplained symptoms, and undiagnosed syndromes. In patients presenting with unusual

symptoms, Chronic Fatigue Syndrome and atypical variance of serious illnesses including autoimmune disease and neurological diseases such as multiple sclerosis and motor neurone disease, the diagnosis of borreliosis should be considered. As the diagnostic tests become available to more accurately diagnose borreliosis and its co-infections, early and effective treatment will expectantly reduce the development of more serious forms of borreliosis. The medical community has an obligation to their patients and the community at large to embrace this emerging illness, to understand its causes, its diagnosis and its treatment. Seeking advice from colleagues specialising in this area is fundamental and continuing education by attending conferences and meetings in relation to borreliosis and co-infections is beneficial to experience first hand tools for treatment. These guidelines will fill some of the gaps in the existing medical information in Australia. Further development, research and associated discussions need to take place to improve the outcome for our patients. We should always consider borreliosis and co-infections in our assessment of unusual or prolonged conditions without an obvious diagnosis. A keen observant mind is far more important than a lack of evidence in the diagnosis of borreliosis, with as always clinical acumen the superior foundation to properly delivered health care.

These guidelines are published and distributed by the newly formed Australian Chronic Infectious Disease Society Limited, and presented by all members of the board:

- Dr Catherine Morris, Chairman
- Dr Peter Dobie, Secretary
- Dr Peter Mayne, Finance Officer and Education
- Dr Hugh Derham Media inquiries and Website
- Dr Sandeep Gupta Education and IT

We are indebted in turn to our mentors and teachers, principally ILADS and the Burrascano guidelines [Burrascano] and the German Borreliose society [German Borreliose].

**Australian Chronic Infectious Disease Society Limited**  
**Suite 603, 6th Floor**  
**379-383 Pitt St**  
**Sydney NSW 2000**

**Our website is [www.acids.org.au](http://www.acids.org.au)**

## References

### *Angelakis*

Pathogenicity and treatment of Bartonella infections. Emmanouil Angelakis, Didier Raoult  
International Journal of Antimicrobial Agents  
<http://www.sciencedirect.com/science/article/pii/S0924857914001186>

### *Burrascano*

<http://www.lymenet.org/BurrGuide200810.pdf>

### *German Borreliose Society*

<http://www.borreliose-gesellschaft.de/Texte/guidelines.pdf>

*Horowitz*

Publications including "Why Can't I get Better? Solving the Mystery of Lyme and Chronic Disease"  
Richard I Horowitz MD

*Kanjwal*

Postural orthostatic tachycardia syndrome following Lyme disease. Khalil Kanjwal, Beverly Karabin,  
Yousuf Kanjwal, Blair P. Grubb  
Cardiology Journal , 2011, Vol. 18, No. 1, pp. 63–66

*Shoemaker*

see [www.survivingmold.com/lab-tests](http://www.survivingmold.com/lab-tests)

Evidence Based Guidelines for the Management of Lyme Disease. The International Lyme and  
Associated Diseases Society. Expert Rev. Anti-infect. Ther.2(1), Suppl. (2004)

Lyme Disease: Point/Counterpoint. Stricker, Raphael B. Lutin, Andrew. Burrascano, Joseph J.  
Expert Rev.  
Anti-infect. Ther, April 2005. 3(2), 155-165

An Understanding of Laboratory Testing for Lyme Disease. Harris, Nick S. J.  
Spiro. and Tick-Borne Dis. Vol 5, 1998. 16-26

Gestational Lyme Borreliosis. MacDonald, Alan B.  
Rheumatic Diseases Clinics of North America 15 (4), Nov.

1The Open Neurology Journal, 2012, 6, (Suppl 1-M10) 158-178

1874-205X/12 2012 Bentham Open

Open Access

Chronic Lyme Disease and Co-infections: Differential Diagnosis

Walter Berghoff\*989. 657-678