

## ACIDS

Australian Chronic Infectious Disease Society

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### Aim:

1. The guidelines for diagnosis and management of Lyme disease and co-infections in Australia.
2. To form a collective of doctors in this emerging field.
3. Education and research into these diseases in Australia.

### What is Lyme Disease?

Lyme Disease is an infectious illness caused by the Spirochete, *Borrelia Burgdorferi* (Bb). In most cases Lyme Disease is an illness that forms as a result of a bite from an infected tick. Co-infections are often transmitted at the same time, as a result of multiple infections harboured by the tick. Lyme disease and its co-infections can result in acute illness but often disseminate into the body leading to a more chronic form of disease. This chronic form of Lyme disease 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 Chronic Fatigue Syndrome with severe deconditioning. Recognition and early treatment of Lyme Borreliosis (LB) leads to a higher success rate of cure. Chronic Lyme Disease is associated with severe morbidity and in some cases significant mortality, especially in cases of neurological Lyme disease.

### Lyme Disease and Co-infections

The following is a list of the co-infections associated with Lyme Disease:

- *Borrelia* - Relapsing Fever
- *Borrelia Burgdorferi*, *Afzeli* and *Garnii*
- *Mycoplasma* Species
- *Chlamydia Pneumoniae*
- *Rickettsias* Species
- *Bartonella* Species

- Babesia Species
- Ehrlichia
- Anaplasmosis
- Chronic viral infections including HHV-6, CMV and EBV.

### **Vectors:**

The most common vector for Lyme Disease in Australia are ticks. Many patients report having no knowledge of receiving tick bites, but often relate being bitten by bedbugs in Indonesia and lice (birds). Theoretically any biting insect that feeds on blood is a possible carrier for Lyme Disease.

### **Other Disease Transmission:**

#### *Sexual transmission*

***The incidents of sexually transmitted Lyme are currently unknown however there is definitive evidence that this does exist. The ratio of male to female transmission occurring slightly higher than that of female to male. This is particularly true in patients with chronic Lyme Disease.***

#### *Pregnancy*

Direct Transmission via the placenta to the unborn child has been observed in numerous families. Many children infected with Lyme Disease from their mothers present as unwell at birth, but more often they become ill in childhood or adolescence.

#### *Blood Transfusion*

Blood transfusion is highly likely to transmit Lyme Disease. This is of serious concern, due to the under diagnoses of Lyme Disease in Australia.

#### *Intravenous Drug Use and Tattooing*

Intravenous drug use has been known to pass on Lyme Disease therefore theoretically non-sterile tattooing is also at risk of directly transmitting this disease.

#### *Symptoms of Lyme Disease*

In a classic presentation of Lyme Disease a rash may develop in associations with the tick bite. This rash is commonly known as Erythema Migrans, which is diagnostic in Bb infection. It occurs in fewer than half

of the patients. EM rashes can appear like a bullseye rash, often beginning formation within four days of the tick bite, however may present several weeks after the bite, in association with constitutional symptoms. Multiple lesions may appear over the body and many could have an atypical appearance. Occasionally a haemorrhagic rash may appear and generally these rashes are only slightly irritating or pruritic. The EM rash can be caused directly by the Bb infection but may result from a co-infection. Common symptoms of Acute Lyme Disease are fever, sweats, joint pain, headache, sore eyes, glandular swelling and malaise. Chronic Lyme Disease can present as a multi-system disorder with almost any brain and body symptom. See Assessment Tool as follows.

### Chronic Lyme Disease Assessment Tool

Symptoms	Mild	Moderate	Severe	Constant	Intermittent
Headache					
Brain Ache					
Migraine					
Dizziness					
Light-headedness					
Faintness					
Sore Eyes					
Red Eyes					
Dry Eyes					
Photophobia					
Blurred Vision					
Double Vision					
Earache					
Blocked Ears					
Deafness					
Tinnitus (Ringing in the ears)					
Sinus Congestion					
Sinus Pain					
Post Nasal Drip					
Runny Nose					
Blocked Nose					
Bleeding Nose					
Sore Throat					
Mouth Ulcers					
Cold Sores					
Swollen Glands					
Swollen Throat					
Swollen Thyroid					
Difficulty Swallowing					
Cough					

Wheeze					
Congestion					
Shortness of Breath at Rest					
Shortness of Breath on Exertion					
Chest Pain					
Palpitations Fast					
Palpitations Hard					
Elephant on the Chest					
Rib and Chest Pain					
Nausea					
Weight Gain					
Weight Loss					
Vomiting					
Reflux (Heartburn)					
Regurgitation of food					
Bloating					
Belching					
Flatulence Odorous					
Flatulence Non-Odorou					
Constipation					
Diarrhoea					
Explosive Diarrhoea					
Loose Motions					
Anal Itch					
Anal Bleeding					
Anal Mucus					
Stinging of Urination					
Pain of Urination					
Frequency of Urination					
Blood in Urine					
Hesitancy of Urination					
Incontinence					
Urinary Retention					
Sexual Dysfunction					
Impotence					
Painful Periods					
Heavy Periods					
Irregular Periods					
Vaginal Thrush					
Painful Intercourse					
Muscle Pain					
Muscle Weakness					

Joint Pain					
Joint Swelling					
Twitches					
Tremors					
Fasciculations					
Pins and Needles					
Numbness					
Rashes					
Skin Lumps					
Skin Lesions					
Skin Bruising					
Cold Sensitive					
Heat Sensitive					
Night Sweats					
Hot Flushes					
Cold Hands					
Cold Feet					
Poor Sleep					
Difficulty Going to Sleep					
Frequent Waking					
Unrefreshed Sleep					
Poor Exercise Tolerance					
Pain with Exercise					
Post Exertional Fatigue					
Brain Fog					
Poor Memory					
Poor Concentration					
Thought Disorder					
Loss of Words					
Inability to Read					
Inability to Write					
Inability to Spell					
Mood Swings					
Depression					
Anxiety					
Anger Outbursts					
Obsessive Compulsive Behaviour					
Agitation					
Panic Attacks					
Reactive to Foods					
Reactive to Allergens					
Reactive to Chemicals					

Reactive to Noise					
Reactive to Light					
Reactive to Movement					
Reactive to Supplements					
Reactive to Medication					
Level of Fatigue - Bedridden					
Level of Fatigue - Housebound					
Level of Fatigue – Inability to Work					
Level of Fatigue – Inability to Study					
Level of Fatigue – Inability to Go Out					
Level of Fatigue – Inability to Relate to People					

The worst-case scenarios of chronic Lyme Disease cause the development of severe autoimmune diseases, particularly severe generalised reactive Arthritis (Rhumatoid Arthritis- like), a Multiple Sclerosis- like disease, a Motor Neurone disease- like illness and severe forms of Chronic Fatigue Syndrome. Lyme Disease is also associated with psychological disorders, including severe depression, chronic anxiety, obsessive compulsive disorder and Schizophrenia. Learning difficulties in children are also observed, as well as Autistic Spectrum Disorder.

### Diagnostic Tests

The diagnosis of Lyme disease and its co-infections is often initially made clinically due to the lack of confirmatory pathology results. The gold standard for diagnosis is a history of tick exposure and development of classical symptoms confirmed EM, positive sero conversion, IgG and IgM positive, a positive tissue microscopy, a positive Western BLOT and positive PCR test. In an ideal world this would diagnosis categorically Lyme Disease in Australia. Unfortunately the above situation is not very common. The following is a list of useful tests that should be undertaken for patient presenting with symptoms that could be Chronic Lyme Disease, possibly in association with co-infections:

- FBC, ESR, CRP, MBA-20, CK.
- Iron studies, VIT B12, Plasma Zinc, Copper and red cell foliate.
- ANA, ENA, ANCA, Rheumatoid factor, CCP antibody.
- TSH, T4, T3, Reverse T3, Anti-thyroid antibodies, TRAB, insulin.
- ASOT, Anti-DNase, ACE, Coeliac Disease, Anti-gliaden antibodies, IgG, IgA, Tissue Transglutamase and Coeliac Disease genetic test, CD57, IgG Subset and IgA.
- Rickettsia, Q Fever, Borrelia, Bartonella, Mycoplasma and Chlamydia Pneumoniae antibodies.
- Ross River Virus, Barmah Forest Virus, Flavivirus, EBV, CMV and Toxoplasmosis.
- 25OH Vit D, 125DiOH Vit D.

The above tests although not exhaustive are particularly useful in determining the extent and severity of Lyme Disease and Co-infections. The 125DiOH Vit D, CD57 and CRP are all very useful in the diagnosis and management of Lyme Disease. Chronic LD 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 are probably ill with something other than Lyme Disease, such as a co-infection. 125DiOH Vit D is converted through the kidney from 25OH Vit D due to chronic inflammation and infections. It is an extremely useful tool for monitoring LD, with the 125DiOH Vit D as a biomarker representing the success or not of treatment. CRP is also extremely useful determining the extent and severity of infection and inflammation in association with LD.

### Specific Lyme Disease Tests

1. Polymase Chain Reaction, PCR testing on blood, urine and serum for Borrelia. PCR testing on blood for Mycoplasma and PCR on blood for Chlamydia, Elispot for Lyme Disease, Microgen for Lyme Disease. These tests are performed by Australian biologics, Pitt St Sydney and Chief Scientist Jenny Burke is enormously well informed in this area of testing. Her team will assist in the collecting of specimens for these tests, which usually takes between 4-6 weeks. By far Australian Biologics is currently the most effective diagnostic lab in Australia for the diagnosis of Lyme disease and its co-infections. Recently Australian Biologics has commenced testing for Babesia PCR.
2. Palms Laboratory is a hospital based pathology lab associated with Royal North Hospital in Sydney. They perform Elisa tests, IgG and IgM for Lyme Disease and if positive will perform Western Blot testing.
3. The Australian Rickettsia Reference Laboratory in Geelong Victoria is particularly useful for testing Rickettsia infections.
4. Sullivan Nicolaides Pathology in Queensland is now performing Bartonella PCR and Serology.
5. IgeneX in the USA is successful for testing Elisa, Western Plot and PCR testing for Lyme Disease and all the co-infections. They provide a series of tests specific to Australian Lyme Disease. Unfortunately there is considerable expense with this testing.
6. Infecetalab in Augsburg Germany is also a valuable lab.

### Future Testing

The University of Sydney is currently undertaking pathological studies on Lyme Disease from Australian patients. This research project headed by Dr Ann Mitrovic is using volunteers with known possible Lyme Disease and a control group to develop a standardise form of Elisa, Western Blot and PCR testing which can be used throughout Australia for diagnosis of Lyme Disease and co-infections. The hope is by 2014 when the study is completed and the findings published, the ongoing doubt about the diagnosis of Lyme Disease in Australia will cease allowing for a concerted effort to treat this emerging disease. This will be aided by accurate pathology services.

The following is a list of doctors who are constructive and helpful in understanding the diagnosis and relevance of pathology in the diagnosis of Lyme Disease:

Dr Joseph Burrascano (USA)

Dr Richard Horowitz (USA)

Dr Garth Nicolson (USA)

Dr Steven Harris (USA)

Dr Armin Schwatzbach (Germany)

Dr Carson Nicholas (Germany)

## **Management of Lyme Disease and Co-infections**

It is important to understand the diagnosis of Lyme Disease and its co-infections in Australia will have a profound effect on the patient, families, friends, the community in general inclusive of the medical profession. Unfortunately there is still considerable controversy around the diagnosis of Lyme Disease yet there is no question that Lyme Disease is present in Australia. Once diagnosed it is important that each patient be treated correctly with support for patient and families.

### **Education**

Dissemination of information about Lyme Disease 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 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.

## **Guidelines to the Patient**

### **Patient Terrain**

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

### **Diet**

Many Lyme Disease patients experience food and chemical sensitivity syndrome. Diets free of Gluten, dairy products, soya products and sugar are often necessary. Avoidance of food chemicals including colourings, preservatives and additives and a general reduction in all processed food is desirable. Fresh food that is adequately washed and freshly prepared will maximise nutritional benefit. Green juices



made from a variety of vegetables also assist in digestion. Filtered water is fundamental and avoidance of soft drinks, caffeine in coffee or tea and no alcohol is advisable.

### *Sleep*

Many patients with LD suffer from disturbed sleep patterns usually with difficulty going to sleep, wakefulness and Cicadium Dysrhythmias. Frequent napping should be avoided and regular hours of sleep in a dark quiet bedroom is desirable. Melatonin 3-6mg taken around 7-8pm each night may help regulate sleep. Amitriptyline 10-20mg at night and/or Clonazepam 0.5mg quarter to two at night can also assist in sleep. Note Clonazepam is often used in divided doses to reduce Non-Epileptiform seizures often seen in Lyme Disease patients.

### *Exercise*

Patients with LD should be encouraged to be as active as possible within the limits of the disease. This could mean just supported exercise in a bed ridden patient right through to an active exercise program using 1-2kg dumbbells for 3-5 minutes per day as well as walking from 5-10 minutes per day. Obviously as patients improve they may well be able to extent their exercise program to a more normal degree of exercise. Generally exercising one day with a rest day the next is desirable when first starting a graded exercise program.

### *Emotional Health*

Unfortunately Lyme Disease 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 due to the poor diagnostic skills of their physician. This situation still strongly exists in Australia and will only change when every general practitioner, physician and allied health professionals are fully informed and have significant enough insight to make the correct diagnosis. Psychologists and counsellors are extremely beneficial in assisting patients with Lyme Disease. Obtaining family and friends support once the diagnosis has been made is essential to the patients' health.

## **Treatment of Lyme Disease with Antibiotics**

Once the diagnosis of Lyme disease has been made treatment with antibiotics is essential. The treatment will vary depending on whether the Lyme Disease 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 Lyme Disease and co-infections will require very specialised management.

### **Acute Lyme Disease**

Acute Lyme Disease usually occurs after an initial tick bite with symptoms of a flu like illness and possibly a rash. Usually diagnostic tests are not performed unless a patient is extremely ill as generally most tests will be negative for any of the Lyme Disease or co-infections at this stage.

### **Adult Antibiotics**

Doxycycline 200mg always taken with food for 6-8 weeks. If the patient is extremely unwell with fevers and night sweats 200mg twice daily is advisable. Side effects include nausea, epigastric pain, photophobia, photo sensitivity and severe reflux (patients to take Doxycycline with food and to avoid lying down for one hour).

### **Children 7 Years or Less**

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

### **Children 8 Years and Older**

Doxycycline 50mg two daily twice daily always taken with food. The Doxycycline can be compounded or crushed and mixed with food and given again for 6-8 weeks.

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. As for all patients receiving long term antibiotics probiotics should be given twice daily either as a powder or capsule as well as Nystatin should be given twice daily to prevent an overgrowth of Candida Albicans in the bowel. Children Nystatin Suspension usually 2ml twice daily and for Adults 500000IU (two capsules) twice daily. All these medications can be acquired under the Authority System.

## **Chronic Lyme Disease**

Chronic Lyme Disease is defined 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 POTS (Postural Orthostatic Tachycardia Syndrome) and Arrhythmias. Many patients with Lyme Disease often present with other diagnoses but really do have systemic Lyme Disease. Accurate clinical assessment and diagnosis is essential for the correct management and specific treatments. Borreliosis is a very unusual infective disease. The Spirochetes often involve Intracellular infection within any cell group within the body as well as Extracellular involvement between cells in body fluids and blood and can metamorphose into a cystic form that are highly resistance to treatment. The Extracellular forms are usually treated with penicillins and Cephalosporins. Intracellular forms are treated with Tetracyclines particularly Minocycline, Doxycycline and Macrolides including Clarithromycin, Azithromycin, Clindamycin and Lincomycin. Cysts forms are treated with Metronidazole or Tinidazole. Other antibiotics used include Rifamycin, Atovaquone, Hydroxychloroquine Sulphate, Sulfamethoxazole with Trimethoprim as well as Fluconazol. These antibiotics are usually given orally and some are given by intramuscular injections and also can be given intravenously by daily cannulisation or the use of a PICC Line.

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

## Oral Antibiotics:

1. Amoxicillin 500mg capsules (always with food)
  - Week 1: 1 tds
  - Week 2 onwards: 2 tds
  - Maximum dose: 3 tds

Probenecid 500mg 1-2 tds can be used to potentiate the effects of the Amoxicillin.

Usually Amoxicillin is commenced for a period of 2-4 weeks before other antibiotics are added due to the risk of side effects but mainly due to the Herxheimer reaction which occurs as a result of bacterial death and associated immune response.

Doxycycline 200mg per day (always with food) is usually started at 2-4 weeks. A maximum dose of 200mg bd is recommended in more severely ill patients who are tolerant to this antibiotic.

Tinidazole 500mg 4 capsules taken weekly after the evening meal is usually commenced 6-8 weeks into the treatment.

The combination of Amoxicillin, Doxycycline and Tinidazole is a basic oral treatment for active Lyme Disease. Patients should also receive Nystatin 500000IU 2 bd as well as a good quality probiotic capsule 2 bd for the duration of the treatment to prevent gastrointestinal dysbiosis. The duration of treatment is dependent on the severity of illness and the response of the patient to treatment. Treatments which last for 6-12 months for Chronic Lyme Disease is normal and many patients require much longer treatments to improve their symptoms and successfully treat their disease. Basic pathology tests should always be performed monthly and if indicated more frequently.

## Other Treatments With Antibiotics

Lyme disease is a complex illness and the response to treatment is very variable. The following is a list of other alternative antibiotics that can be given as alternatives to the standard regime already mentioned.

1. Benzathine Penicillin 1.8 grams IMI once weekly to a maximum dose of 1.8 grams IMI twice weekly.
2. Ceftriaxone 2 grams by IVI infusion given over 20 minutes 5 days per week via Cannular or PICC Line. Maximum dose 4 grams 4 days per week in more serious infections particularly Neurological Lyme Disease. The main side-effect of this medication is Biliary Stasis. To prevent this, the use of Ursodeoxycholic Acid 250mg 1 bd is recommended (private script).
3. Metronidazole orally 400mg 3 daily for 3 days per week or 500mg IVI weekly to twice weekly is also highly effective in the treatment of Bb Cysts.
4. Minocycline 100-200mg per day before food is especially useful in Neurological Lyme Disease and Joint Arthritis.
5. Diflucan 100mg 1 twice weekly to 1 daily can be used to prevent Systemic Candidiasis.
6. Nystatin 500000 IU 1-2 bd to 2 tds is essential in all the antibiotic protocols to prevent gastrointestinal candidiasis.

## Co-Treatments

### Supplements

1. Probiotics 2 daily
2. Vitamin B complex 1 per day
3. Vitamin C 1000mg 1 bd
4. Zinc, 10-30mg 1 daily
5. Coenzyme Q10 100-300mg per day
6. Magnesium 400-800mg nocte
7. Glutathione 200-500mg bd

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

### Medications

#### *Sleep*

1. Melatonin 3-6mg 7-8 pm
2. Amitriptyline 10mg half to two nocte
3. Clonazepam 0.5mg quarter to two nocte

These can be used singularly or in combination to assist in the disturbed sleep pattern often experienced by LD patients.

#### *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 includes tremors, twitches, fasciculations, faints, collapses and fit like symptoms.
2. Topiramate and Lamotrigine can also be used to treat seizures and to help prevent migraines in LD patients.

#### *Pain*

Many patients with Lyme Disease 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 2 bd to 2 tds.
2. Tramadol 50mg to 200mg bd.
3. Pregabalin 25-300mg bd for neuropathic pain is highly useful but unfortunately 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 1-4.5mg 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.

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

POTS is often a difficult symptom to manage in many patients with Severe Lyme Disease. Frequent monitoring of blood pressure, regular ECGs and the assistance of a cardiologist is highly recommended. Simple strategies to deal with this include :

1. The consumption of water 2-3 litres per day
1. Sodium Chloride (salt) 1 teaspoon 2-3 times daily
2. The use of therapeutic short leg stocking 20-30 mmHg worn continuously if out of bed are very useful in maintaining the blood pressure.
3. Licorice and Panax Ginseng herbal tonic 3ml qid can also assist.
4. Fludrocortisone Acetate 0.1mg half to two mane is often required to prevent severe hypotensive episodes.
5. Propranolol 10mg 1-2 bd often is required to prevent Supraventricular Tachycardia (SVT).

### ***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.
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.
3. Loperamide Hydrochloride can be used to help treat diarrhoea.

There are numerous symptoms that LD 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. Lyme Disease is a very complex illness and as the organisms die and particularly if there are co-infections varied and unusual symptoms can occur singularly or in combination leading to a complex disease pattern. Always monitor patients regularly with weekly review of patient initially then review once a month and finally once every two month 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 or symptom reduction therapies need to be instituted. Always seek advice or assistance from other Lyme Disease literate doctors or appropriate specialists if a serious complication arises.

## **Chronic Lyme Disease Treatment of Children**

Children present a therapeutic dilemma as often they have acquired this disease congenitally or have experienced a tick bite leading to the development of Lyme Disease. Often children have been unwell for some time before and accurate diagnosis is made and congenital Lyme Disease often presents with symptoms slowly and is unlike adult Lyme Disease. There is some evidence that Autistic Spectrum Disorder, failure to thrive and behavioural and learning disorders are actually due to active Lyme Disease. Treatment usually involves a combination of Amoxicillin, 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 Nistatin and probiotics should be given with all other antibiotic combinations. As a general rule commencing with Amoxicillin tds then Metronidazole twice weekly and eventually Clarithromycin bd in appropriate age and weight related doses constitutes an effective treatment.

## **Monitoring**

### **Acute Lyme Disease**

When a patient is diagnosed with Acute Lyme Disease the assessment and diagnosis is usually clinical and appropriate treatment needs to be instituted for 6-8 weeks. 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 Lyme Disease will generally prevent the development of Chronic Lyme Disease.

### **Chronic Lyme Disease**

Patients who have Chronic Lyme Disease should be reviewed monthly as a general rule. If they are very unwell review weekly or fortnightly is advisable. Initiation of treatment with intravenous antibiotics should be undertaken within a medical environment. Pathology testing should be undertaken on a monthly basis, FBC, ESR, CRP, LFT, Urea, Electrolytes and CRT. An ECG should be performed monthly on patients receiving Ceftriaxone infusions as this drug may cause a long QT interval which can lead to arrhythmic episodes. CD57 and 125DiOH Vit D should be performed every 3 months to monitor the progress of the treatment. Specific tests including MRI of brain, Spect scan CT of brain and EEG's should be used in the diagnosis and management of Neurological Lyme Disease.

### **Duration of Treatment**

Acute Lyme Disease 6-8 weeks is usually required for complete resolution of symptoms. Chronic Lyme Disease treatment usually is between 3 months and 2 years. Some patients require much longer treatments especially if they have been undiagnosed for many years, even decades before treatment is commenced. Generally antibiotics are stopped when symptoms have been significantly reduced and there is no Herxheimer response to the antibiotics and pathology tests have returned to normal. Some patients will require a graded reduction of antibiotics if they have had Chronic Lyme Disease for a very long time. 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 due to permanent injury to tissue and organs after long standing LD. This condition is often difficult to distinguish from active LD.

## **Pregnant Women**

Women who are pregnant who have developed Acute Lyme Disease following a tick bite or have been diagnosed with Chronic Lyme Disease should be treated during their pregnancy to prevent their child from acquiring congenital Lyme Disease. Considering that the Extracellular form of Bb is the likely transmission of this bacteria through the placental barrier to the unborn foetus the use of Amoxicillin 500mg 2 tds for 6 weeks is recommended for Acute Lyme Disease and 500mg 2 tds in the third trimester is recommended for Chronic Lyme Disease to prevent transmission through the placenta barrier. Doxycycline and Tinidazole are contraindicated in pregnancy. As always probiotics and Nistatin are to be used in combination with the Amoxicillin. If patients are allergic to Penicillin Cefuroxime Axetil 500mg bd for 6 weeks is recommended.

## **Co-infections**

Lyme Disease is often associated with co-infections due to the complexity of infective organisms present in the tick (other biting insects that have caused the illness). The following is a list of co-infections and possible antibiotics that can be introduced in combination with the Lyme Disease treatment.

### ***Mycoplasma***

1. Doxycycline 200mg daily with food or Minocycline 100mg daily before food.
2. Azithromycin 500mg 1 weekly to 1 twice weekly can be added to potentiate the effect of the other antibiotics.

### ***Chlamydia Pneumoniae***

1. Doxycycline 200mg daily with food
2. Azithromycin 500mg 1 weekly to 1 twice weekly can be added to potentiate the effect of the other antibiotics.

### ***Babesia***

This is a Protozoa infection and responds to the following antibiotics.

1. Atozaquone 750mg in 5ml with a dose of 5ml db for three to six months.
2. Azithromycin 500mg 1 daily 5 days per week.
3. Artemisinin 500mg 1 bd.
4. Hydroxychloroquine Sulphate 400mg daily with food.
5. Doxycycline 200mg daily with food.
6. Cefuroxime Axetil 500mg bd.

A combination of these antibiotics will be required to assist in the removal of this Protozoa in LD patients. Babesia is often a very serious co-infection leading to very severe symptoms in affected patients.

### ***Bartonella***

1. Doxycycline 200mg daily with food.
2. Hydroxychloroquine Sulphate 400mg daily with food.

3. Rifampicin 300mg 1 bd usually for 6-12 weeks.
4. Gentamicin, this drug should be given IVI twice daily in very seriously ill patients with Bartonella in a therapeutic appropriate environment. Monitoring of kidney function is essential.

### ***Rickettsia***

1. Doxycycline 200mg daily with food.
2. Azithromycin 500mg 1 weekly to 1 twice weekly.

It is important to note that the treatment for Lyme Disease with antibiotics often covers the treatment of the co-infections. It is important to recognise that other co-infections may exist with Lyme Disease 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.

### **Extreme Lyme Disease and Co-infections**

Unfortunately Lyme Disease 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 Lyme Disease will present with Neurological Symptoms like Multiple Sclerosis, Motor Neuron Disease, Parkinson's Disease and severe autoimmune disease such as Rheumatoid Arthritis like joint diseases.

Generally doctors specialising in this form of Lyme Disease 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 and a possible political agenda by the infectious diseases community. This situation is also paralleled in Europe and North America where the concept of Chronic Lyme Disease and its severe manifestations are not recognised by all of the medical community.

Treatment should be generally include that all antibiotics be given intravenously.

1. Clindomycin 600mg daily IVI or Lincomycin 600mg bd IVI or Vancomycin 500mg bd IVI or Doxycycline 200-400mg IVI. These antibiotics are used in the treatment of Intracellular Bb infection.
2. Metronidazole 500mg IVI weekly to 500mg IVI daily for Cystic form.
3. Amoxicyllin 4 grams IVI daily or Ceftriaxone 4 grams IVI 4 days per week or Ticarcillin 3.1 grams IVI daily for Extracellular form.
4. Fluconazole 100mg IVI daily to prevent Candida Albicans overgrowth.
5. Nistatin 500000 IU to 2 tds. Probiotic capsules 2 bd.

In serious Lyme Disease combinations of the antibiotics should be administered aggressively but with constant clinical and pathological monitoring. Patients with very serious neurological life threatening Lyme Disease may well respond to aggressive treatment. Treatment should continue for at least 4-6 weeks and usually up to 3 months to ascertain the effectiveness of treatment.



## Discussion

Lyme Disease and its co-infections is an emerging illness in Australia. More patients are presenting each year with unexplained symptoms, and undiagnosed syndromes. There appears to be a questionable lack of support from the medical community in general. 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 Neuron Disease, the diagnosis of Lyme Disease should be considered. The days of diagnosing unexplained illnesses as conversion reaction or other psychological illnesses must be at an end. As the diagnostic tests become available to more accurately diagnosis Lyme Disease and its co-infections, early and effective treatment will expectantly reduce the development of more serious forms of Lyme Disease. 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 Lyme Disease and co-infections is beneficial to experience first the hand tools for treatment. These introductory 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 Lyme disease 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 Lyme Disease.

“CHANCE FAVOURS THE PREPARED MIND” Louis Pasteur

These guidelines follow an initial meeting of Dr Peter Maine, Dr Andrew Ladham and Dr Richard Schloeffel on the 27<sup>th</sup> of July 2013. The guidelines were prepared by Dr Richard Schloeffel on the 4<sup>th</sup> of August 2013 with the assistance of Morgan George, medical assistant.