BORRELIOSIS IN MID NORTH COAST OF NEW SOUTH WALES, WITHOUT OVERSEAS TRAVEL.

Introduction

The tick borne bacterial infections called Borreliosis, with their wide range of systemic presentations, are recognised on all continents except Australia and Antarctica. The debate about indigenous Borrelia species distracts doctors from including this infection in their differential, despite Australians visiting endemic areas, many international visitors, potential feral reservoirs, and the frequency of tick bites.

We report 2 cases of Borrelia burgdorferi infection in the Mid North Coast region of New South Wales.

HSG case study

An 18 year old woman presented (with her mother) in January 2012 for case review and a new opinion after multiple unsuccessful treatments for abdominal pain, over the previous 5 years.

She reported fluctuant, but recurrent, severe lower and RIF **abdominal pain** with fatigue, nausea, vomiting, headaches since ~2007. The initial episode was acute and severe requiring presentation to the Base hospital ED. That occasion had no associated symptoms, and it resolved without explanation. She was briefly well, but within months there was recurrence with associated odd symptoms. These included: Episodic tight band around chest ("iron bar") – corset like, but no cough; palpitations; pyuria, (but multiple negative MSUs); episodic temporary mild paresis – migratory, R eye tremor, in 2010 sharp disabling pain in L arm and leg - spreading to upper and lower limbs, jaw and scalp, with no dysaesthesias - briefly improving with Fe replacement and a speculative course of prednisolone (CNS reported normal on examination by a very thorough general physician); through 2011- tingling in cheeks for 1-2 hours at a time, fortnightly; episodic cognitive slowing with expressive dysphasia and trouble with word finding, maths and spelling; an overarching sense of fatigue; mood changes with 'derealisation' sensations (Sleep was OK); multiple sore throats and 'flu like' illnesses with multiple unsuccessful cultures; chronic cold hands and feet, with frequent unexplained episodes of shivers and fevers.

In 2009 the pain and disparate symptoms were markedly worse with an intercurrent EBV infection and a finding of helicobacter gastritis. She lost weight to 49kg in 2011. At one ED attendance noted were rigors and temperature to 39^{o}, but no cause was identified and surprisingly the CRP was only 5. She also described other pain - migrating though large joints, with stiff hands and neck, while her fatigue deteriorated though 2011, and mastalgia. She had a bizarre reticular rash on the abdomen (it was attributed to the use of a hot water bottle).

Treatment from multiple paradigms rendered a little improvement then relapse. Diagnoses raised included Chronic Fatigue syndrome, "abdominal migraine", biliary akinesia, and she had been on domperidone and omeprazole for "rotting teeth" caused by "nocturnal reflux". Incidentally Mother reported that the patient had many tick bites over the years, though could not recall an Erythema Migrans type rash.

Social and Family Hx

Living with parents, in school year 12. Denies alcohol, smoking or other drugs.
Mother - hypertension, sibling - depression.
Allergies – erythromycin = vomiting

PMHx - EBV hepatitis, possible shingles, mycoplasma pneumonia 1997, mild scoliosis. Multiple episodes of pharyngitis.

Surgical treatments that had been attempted for the pain had included – Laparotomy and Appendicectomy, Gastroscopy, Cholecystectomy. Specialists seen included a Paediatrician, Paediatric Gastroenterologist, Paediatric Neurologist, Physician, Colorectal Surgeon – all very competent and senior doctors. Extensive investigation had already been done.

On examination she was well grown and intelligent, congruent, sporting a fair "Irish" complexion. The rash on her belly was spectacular, purple/brown, reticular with broad fuzzy borders. It was not tender nor pruritic. There was not apparent lymphadenopathy. Abdomen was soft, - no masses. There was vague tenderness on R side and flank. The rest of the examination was unremarkable.

While history and results were collated, she was advised to trial gluten free, trial a candida clearance. She was given a referral to a specialist dietitian to assess and if necessary guide her through consideration of occult food reaction – eg Amine intolerance, as well as referral to a physiotherapist to reconsider the scoliosis as a cause for referred pain.

Normal results – over 4 years:
Imaging
Abdominal Ultrasound x3, pelvic U/S x2
MRI x2 and MRA brain (for headaches, vomiting and 1 episode photophobia)
Biliary HIDA scan –"NORMAL BILLIARY FLOW" but some pain with the contraction. = "Uncertain significance".

General pathology – normal or negatives:
B12, folate, Ca++, Fasting BSL
CRP – throughout, Serum HCG x4 – quant and qual,
U/E/C, LFT, lipase, Cholesterol and TGs –fasting, CK, Alpha1 antitrypsin
TSH, Cortisol– AM and PM, FSH, LH, oestrogen, progesterone, prolactin, DHEAS
FBC, Lymphocyte surface markers, Serum protein studies – except IgG4 , Cryoglubulins
TTgA (x4) and IgA , ANA, ENA, C3, C4, Liver/kidney microsomal Ab, Mitochondrial Ab, Smooth Muscle Ab - T and V, RAST to food staples,
Chlamydia trachomatis and Neisseria pcr,
Serology hepatitis B&C, Toxoplasma, Treponemes, leptospira, flavivirusses Q fever
Osmolality serum and urine, S-insulin, PTH, IGF1,
RBC Zn, RBC Mg,
Apo E genotype - 3/3, Coeliac HLA susceptibility – no DQ2 or 8
Optometrical exam NAD
ECG – normal Q-T

Abnormal results
Fe = mild low in 05/2010, and 01/12 eg ferritin 29
LFT 05/2010 albumen 52 (38-49), total protein 85 (65-81) = mild high
Esr 17@ 2010, 15@2011, 2@ 02/2012
CMV serology – neg IgM but pos IgG 01/2009 suggesting past exposure

EBV serology – pos IgM and IgG VCA 07/2009, Pos IgG VCA &NA but neg IgM 2012 & 2013 – supporting acute infection in 2009.
IgG4 low <0.01 (0.03-2.01) 02/2012 – (but it is undetectable in 10% normal)
Random Total Cholesterol 3.5 (3.9-5.5) in 11/2012
CXR -Pectus excavatum and mild thoracic scoliosis. **Low Grade bilateral bronchial wall thickening 2011**
Positive Elisa for Borrelia via S&N Pathology but subsequently only 2 bands on the Western Blot via Westmead, prompting further Borrelia serology in the US reference lab.
Rickettsia spotted fever group 02/2012 = 128 titre (but scrub typhus and typhus groups negative). **Post Rx** ELISA equivocal, Rickettsia = 1:256 for scrub typhus.

Igenex (USA) pathology: Babesia microti IgM and IgG negative
HMA and HGE negative, Bartonella neg
Babesia Duncani IgM neg, **IgG pos 80 but negative post Rx**
Spotted fever group and typhus group pos 80 titre
Borrelia IgM indeterminate on 31 and 41 bands May 2012
IgG pos 31 (highly specific) and 41 = positive to International Lyme and Associated Diseases Society (ILADS) criteria, negative surveillance CDC criteria
But post Rx = IGM pos on 18,31,34,41,58,66. IgG added39

Progress
May 2012 - in consideration of a Lyme like illness. Rx was started and blood samples sent to the Lyme Reference lab. (doxycycline 100mg bd, then up to 200mg bd)

June 2012 - Abdominal pain was all gone! Appetite had returned and eating well, regaining weight to 68kg. She described some episodes consistent with Jarisch – Herxheimer reactions[1]. She complained of a new problem of aching knees – needing crutches. She recalled that she had had similar pains in the past with intercurrent illnesses. Rx June 2012 = Ibuprofen 400mg bd prn, amoxicillin 500mg bd, Grapefruit seed extract 400mg daily, a probiotic – Ultraflora Restore, Artemesinin SOD 1 daily, glutathione 5ml daily, "Soothe and relax "capsules 2 tds, Zinc sustain1 daily, Omeprazole 20mg daily, FerroF 1 bd,
In July, doxycycline was ceased - in case it contributed to the knee pain (although this is not a recognised SFX) Then all pharmaceuticals were ceased, but cessation made no difference. A 3 day trial of a higher dose artemisinin was initiated, but was not tolerated, nor was a minocycline trial.

August 2012 = plaquenil 200mg, Ibuprofen changed to diclofenac 50mg tds prn, Amoxicillin 500mg tds, and herbal mixtures. With this regime she reported feeling really well with all symptoms gone. This happy state persisted, apart from an intercurrent UTI in September. She was able to regain concentration to do her HSC and reported by November to be feeling "95%" and the healthiest since aged 12.

By December 2012 she was well, waking refreshed, No pain.
Maintained with Amoxil 500mg tds only. She moved to Canberra for work and is functioning as a normal healthy young woman in full time work.

<u>BR case study</u>
In 2011 a 54 year old male presented with worsening arthralgia, malaise, fatigue, cognitive clouding, memory loss, large joint arthritis and bursitis.

He was working as a bush regenerator in his own business, *which involves moving through scrub, creek banks and forest cutting, spraying vegetation and replanting*

native plants. He had previously been involved with small scale beef cattle work and a bush tourism enterprise in NSW, QLD, NT.
Past Medical history: Appendicectomy as teenager. Tennis elbow 2006, multiple dental fillings, painful left shoulder in 2008 with no specific objective findings on imaging.
Family Hx: mother with breast cancer in her 70s, father with Sick Sinus Syndrome, both still living. Some atopy in the family. Cousin with "sarcoidosis"
Social history: Married with 4 well adult children. Non smoker, ETOH – 2-3 units per week, no other drugs.

Started in 2010 noting more intense reactions to tick bites, until he started using permethrin soaked clothing. Another bite would cause pain in base of skull and neck and leave him bed ridden with a "flu like" malaise for over 2 days.

Through 2011 - evolved overwhelming fatigue, with weakness and poor condition, difficulty getting out of bed, struggling to work 2 hours at a time, struggling to manage his business, night sweats – around 3am- with abdominal/epigastric pain, intermittent diarrhoea, decreased libido, nocturia; increase in tinnitus, mild vertigo with nausea from simple movements, postural dizziness –leaning to the left, sensations of buzzing, forgetful, difficulty concentrating, losing names and words, disorientation, difficulty reading and mental blocks, unable to learn new information, lack of energy, restless, insomnia, sudden increase in cramping attacks, redness and spots on fingers, hypersensitive/hyperalgic shins and teeth, cold extremities, prickling and tingling of feet, numbness around neck and shoulders; **Pain** - lower back, L & R hip, L knee, neck and base of skull, toes, R shoulder (in absence of recalled injury but progressed to frozen shoulder); a non productive cough persistant and relapsing. Later in the course he reported a universal intolerance of red meat – associated with abdominal pain but no frank urticarial or anaphylactoid Sx;

On examination there were no consistent significant or focal findings (including objective neurological) apart for the pain elicited with movement of the mentioned joints, and eventually, features consistent with frozen shoulder.

He initially had a variety of investigations for viral infections, zoonoses, allergy, lung, nutrition, tumours, immune disease, as well as physio, lifestyle interventions and vitamins. His wife recalled a rash consistent with erythema migrans around the R deltoid. In February 2012 the possibility of "lyme disease like infection" was considered.

'Normal or negative' pathology – 2011 - 2012
UEC, LFT, Ca++, BSL, cholesterol, Urate,
Fe studies, B12, folate, RBC Mg , RBC Zn, Vitamin D
CRP, Homocysteine,
TTgA, Gliadin Ab, ANA, ENA, anti DNA, C3, C4, Protein studies -IgA,IgG,IgM, Total IgE, RAST meats and milk =0, Rheumatoid Factor and CCP
CEA, PSA,
TSH, DHEAs
Heavy metals B-Cd, B-Pb, B-Hg
MTHFR = heterozygote for C677t mutation
S-A.C.E. 21 u/l (20-70)
Lymphocyte surface markers – CD57 low end – 68 x 10*6/l with CD57/3 ratio 4.1% = low, the rest normal
Faeces (via Histopath specialist pathologist) no pathogens found and no toxins. No cysts, ova parasites detected.
Occult blood x 3 negative.

Serology for: parainfluenza titre 5, influenza B titire 8, enterovirus group titre 8, adenovirus neg, BFV , Rickettsia, Bartonell hensellae, Chlamydia psittaci and C. pneumonia, Letpospira, HHV6, Q fever IgG/IgM, Syphilis, Toxoplasma, CMV, Brucella,
EBV IgM negative , IgG pos in VCA -Indicating past exposure
Local Borrelia IgM/IgG Elisa via Sullivan and Nicolaides, - negative pre & post Rx
Mycoplasma pneumonia IgM positive 6/3/12 but negative IgG, then both negative 16/7/12, Flaviviruses and Dengue.

Imaging: CXR x2 nad
Spirometry nad

Abnormal results
FBC – persistant eosinophilia 0.91- 0.64 (0-0.6) – slowly reducing to 0.64 11/2/13
Imaging: 14/9/12 u/s R shoulder – some thickening of bursa - bursitis?
Serology: RSV low titre – 15 @ 5/7/11 (when persistant cough was early symptom)
RRV equivocal IgM and pos IgG 5/7/11 – suggesting mid term past infection

USA results via Igenex Inc. 7/2/12 and 11/2/2013
Negative for - Bartonella hensellae F.I.S.H; Bartonella IFA for IgM and IgA; HGE - IFA for Igm and IgA, Anaplasma phagocytophillum, Babesia FISH; B.duncanii and B.microtti -IFA neg for IgM and IgG, PCR Borrelia burgdorferi – whole blood and serum pcr for OSPa and flagellin genes- negative
Erlichia Chafeensis – low positive titre IgM – 1:20,
IgM western blot positive for 39, 41,66,83-93 kda bands = positive for Borrelia Burgdorferi on CDC and ILADS criteria, and on post Rx -increased with highly specific 31, 34 added and 23-25 increased from "indeterminate" to positive.
IgG western blot positive for 41 and 45 kda bands => not positive to criteria, but post test added weak bands on 31,39. **Both times local serology was negative**.

Treatments
Partial relief from the increasing abdominal pain was obtained with esomeprazole 40mg daily prn, and magnesium reduced the cramps and some of the nightly foot pain. However the nightly abdominal pain only ceased when he stopped eating mammalian meat. Marsupial meat is ok.

Rx directed at Borrelia from July 2012: doxycycline 100mg bd, increasing to 200mg bd. In August 2012, after formal eye examination, Plaquenil 200mg daily, Grapefruit seed extract 400mg/day were started for the cyst form.
He had a trial of Bicillin imi 900mg weekly for 4 weeks for the spirochaetal form. Each IMI was followed by 24-36 hours of symptoms consistent with a Jarisch – Herxheimer reaction. However he reported a dramatic turnaround with more energy than for 2 years. He was able to manage a full physical working week again for the first time in a year. He still had forgetfulness and migratory joint aches, but bowel function had normalised. He reported sunburn sensitivity (doxycycline side effect). September 2012 changed to amoxicillin 500mg tds + probenicid 500mg bd, with curcumin added and probiotics. October 2012 - Restarted with cefuroxime 250mg bd. Complementary therapies: Acetyl-l-carnitine1g bd, Curcumin – cumerone 15ml tds, Combantrin for intestinal worms.

Progress
10/2012 ceased all treatments for a break, and to see if the residual abdo pain was a side effect. He still felt well for 1 week, then deteriorated with a return of most symptoms – especially pain, forgetfulness, fatigue.

In November 2012 - after restarting doxycycline, cefuroxime, plaquenil (post optometrical exam), Grapefruit seed extract, cumerone, probiotics – he felt "brilliant", working hard and physical, normal hours, no problems. No further gut symptoms. There was a residual problem with R shoulder bursitis. By December all symptoms improved. **Normal cognitive function had returned** and his employees commented on that.

Jan 2013 - Osteopathy, muscle relaxant and manipulation to R shoulder gave improvement, as physio had not helped. There was a return of some twitchiness in the feet – felt like needing to rub feet on stones- and some dizzy spells. This coincided with running out of grapefruit seed extract.

Discussion for case studies

These 2 patients presented to a rural GP clinic. However tick bites, and the possibility of tick borne infections, are an issue for outer suburban areas and communities where there are parks, and ticks. Very broad differential diagnoses had been considered and excluded[2]. As noted the young woman had undergone multiple surgical procedures over the course of her chronic relapsing illness, without lasting benefit, and each performed on a "clinical diagnosis", though with variable supporting evidence for each paradigm.

However, when the diagnosis of tick borne infection was pursued, the clinical scenario was consistent, temporally congruent, plausible, and supported - but only by serology at an international reference lab. Furthermore when treated as a "lyme like illness", the conditions responded, and these patients with chronically deteriorating disease recovered to normal functioning. Finally they both exhibited curious episodes that were consistent with Jarisch - Herxheimer reactions, but not consistent with known antibiotic side effects or allergies – supporting the argument for a microorganism killing event[1]. The diagnosis of "Lyme–like" illness was, and generally is, also a "clinical" exercise as Borrelia infections are notorious for being multisystem, variously presenting, with difficult to interpret and often unreliable serology[3,4,5].

The pathognomonic Erythema Migrans rash is variously reported to present in as little as 40% of cases[6], Eschars may be small and not recognised, the 2 phase serology system of Elisa and then dry kit Western Blot (the current Australian standard) has been reported[3] as having a sensitivity less than 50%. The microaerophillic Borrelia are reported to enter a variety of tissues (including neural and immune) and hence present a confusing panoply of syndromes that mimic other diagnostic paradigms[4]. Cases have been reported of apparent Motor neurone disease[7], atypical parkinson's syndrome, multiple sclerosis[8], psychosis[9], and of course rheumatoid arthritis[24]. It has been called the new " great imitator"[10].

Alternative explanations for these cases could be:
1 the ultimate serology was misleading as certain viruses such as the flaviviruses, EBV, HHV6, CMV, and rickettsiae can cross react with Borrelia serology
However a viral syndrome does not explain response and resolution with a Lyme disease antibiotic protocol;
2 Auto immune disease – though this was not indicated in immune serology and function and response to antibiotic regimes must raise concern over that paradigm;
3 A psychological phenomena – but that is not amenable to antibiotic treatment, not likely to cause objective fevers, and neither patient had a plausible setup;
4 Toxicity – certainly a risk for the bush regenerator but not the high school student

and the lack of renal or hepatic responses does not support such profound toxicity;
5 Allergy – but the symptoms were not consistent, there was no anaphylaxis as described in the new phenomena of tick mediated mammalian meat allergy [11,12] ;
6 a chronic infection but with some organism other than Borrelia Burgdorferi sensu lato - Indeed there is a cluster of unrelated organisms transmitted in tick bites that are frequently identified as common coinfections to Lyme ie Babesia sp, Rickettsia and Orientia sp, mycoplasma, Anaplasma/Erlichia, with challenging syndromes.
7 these patients simply had a bad run of unrelated serial conditions that are being lumped together for the diagnosis – but this is inconsistent with the serology, the consistency of the dis-ease, and the response to treatment.

Since the 1980s case reports have emerged from along the Australian Eastern Seaboard of Lyme disease or a similar syndrome [13, 14, 15, 16]. However Australian authorities have discounted the likelihood of an indigenous/endemic Borrelia (or Babesia until 2012), the authenticity of the cases, and even when accepted, assumed the patient contracted the illness overseas [17]. Further it has been argued that Lyme disease is transmitted only by North American Ixodes scapularis ticks with the white tailed deer as the sylvan host.

Emerging evidence shows an expanding repertoire of related borrelia sp in Europe, Asia, Africa, and the Americas – with an expanding range of Ixodes sp and other ticks, other arthropod vectors, and rodent, ungulate or other host[4,18]. Furthermore Australia receives and sends a vast array of tourists and goods annually, while we have an indigenous Ixodes holocyclus (the “paralysis” tick), large established populations of feral deer and other ungulates and ubiquitous rodents, with established endemicity of known coinfections such as the rickettsiae, mycoplasma and babesia.

Unfortunately, in Australia, the access to definitive testing for some tick borne diseases is limited and very expensive for the patient. Given the significant false negative rate of the 2 tier system (reinforced by these cases), samples must be sent to reference labs in the US or Europe, even if the clinician is permitted to consider it. Even then we are relying on a narrow band of reagents honed for North American serogroups. In addition, investigation here of the common co-infection of babesiosis is limited to thick and thin film with giemsa stain although locally acquired babesia is no longer in doubt.[19]

Internationally, controversy continues over the chronicity of Borrelia infections. This was fuelled by a recent study of only 17 patients[20 -] out of an estimated 30,000 infections in the USA annually. This study merely showed it is possible to be reinfected with Borrelia, but was incomprehensively extrapolated and publicised as proving there is no condition of chronic infection post short course antibiotic. Yet we have similar models of chronic infection and multiple tissue invasion requiring long treatment plans with other spirochaetes (the Treponemes and leptospira –especially once they have reached late tissue invasion stage), mycobacteria TB and leprae, Q fever, Rickettsia sp, as well as the long known Borrelia sp causing Louse borne relapsing fever, Vincent’s angina and tick borne relapsing fever.

Acute Borreliosis, if recognised, can be successfully treated with a 3 week course of antibiotic – usually a tetracycline or beta lactam. However the chronic infection needs to address the 3 phases - spirochaete, l-form, cyst - for a sufficient number of it’s slow replication cycles, as well as possible co-infections[21]. The patient is usually debilitated and needing a complex of restorative, nutritional, emotional therapy[4].
Animal studies show the propensity for a life long infection, while post mortem

studies have found active neuroborreliosis demonstrating inflammatory damage very similar to that attributed to Alzheimer's disease.[21]

CONCLUSIONS

"Lyme" disease - indigenous or not - seems to polarise health authorities and some medical practitioners in Australia. This is a distraction. There is no shortage in Australian general practice of patients with unexplainable illness who fail to be assisted by subspecialist referral, investigation and treatment, and who often are given "diagnoses of exhaustion" like chronic fatigue syndrome, idiopathic, psychogenic, hypochondriasis or "functional" disorders. In a US clinic seeing "chronic fatigue syndrome" a study found 98% of international criteria CFS patients to be carrying borrelia, and directed treatment significantly improved over 62%[22].

One of these patients with Borrelia serology (CDC criteria) positive and a clinical course consistent with Borreliosis, had never left Australia – the bush regenerator. The high school student has travelled to Pacific islands, Europe, NZ, Malaysia (though her only tick bites were in NSW). There is a semiformal network of people suffering similar illnesses along the east coast, with or without a travel history[23]. These 2 patients did not walk in clutching "lyme" as the next fashionable hypochondriac's catchbag, but were well down the track of a debilitating, otherwise inexplicable, disease and after an exhausting process of exclusion. The outcome has been very positive.

Front line clinicians need awareness and an open mind to consider the challenging arthropod borne Borreliae and associated infections, not be distracted by debates about geography. Patients need access to more advanced diagnostic testing. If not Borreliosis – indigenous or feral - then Australian research is urgently needed to clarify what it is these people with positive serology are suffering.

Authors: CheneyT[1]; HerzbergG[2]; McManus M[3]

Affiliations: 1 Rural GP, VMO for Mid North Coast Local Health District;
2 Rural GP;
3 Honorary Associate Sydney University, Pharmacology, School of Medical Sciences; Director Karl McManus foundation.

Bibliography

1 Fauci AS (et al) (Ed.). (2008). Harrison's Principles of Internal Medicine (17th Edition ed., Vol. I). USA: Mcgraw Hill.
2 Nau, R., Christen, H. J., & Eiffert, H. (2009). Lyme disease - Current State of Knowledge. Dtsch. Arztebl. Int. , 105(5), 72-82.
3 Stricker, R., & Johnson, L. (2007). Let's Tackle the Testing. BMJ , 335, 1008.1.
4 Mcmanus, M., & Herzberg, G. Lyme Borreliosis - An Australian Perspective. Jnl Integrative Medicine , 18 (2), 12-19.
5 Ang CW, e. a. (2011). Large Differences Between Test Strategies for Detection of Anti-Borrelia Antibodies are revealed by comparing eight ELISAs and five immunoblots. Eur. J. Clin, Microbiol. Infect. Dis , 30 (8), 1027-1031.
6 Burrascano , J. J. (2008). Advanced Topics in Lyme Disease. 16.
7 Harvey, W. T., & Martz, D. (2007). Motor Neurone Disease recovery associatd with IV ceftriaxone and Anti-babesia therapy. Acta. Neuol. Scand. , 115 (2), 129-131.
8 International Lyme and Associated Diseases Society. (2004). Evidence Based Guidelines for the Management of Lyme Disease. Exp. Review AntiInfective Ther. , 2 (1).
9 Fallon, B. A., & Nields, J. (1994). Lyme disease - a Neuropsychiatric Illness. American Journal of Psychiatry , 151, 1571-1583.
10 Margulis, L., & et al. (2009). Spirochete round bodies, Syphilis, Lyme disease and Aids - Reurgence of the Great Imitator. Symbiosis , 47 (1).
11 Van Nunen, S., & et al. (2007). The association between Ixodes holocyclus tickbite reactions and Red Meat allergy. Internal Medicine Journal , suppl 5, A132.
12 Commins, & et al. (2009). Delayed anaphylaxis, angio oedema and urticaria after consumption of red meat in patient with specific IgE antibodies for Galactose-alpha-1,3 galactose. Journal of Allergy and Clinical Immunology , 123 (2), 426-433.
13 Stewart, A., & et al. (1982). Lyme Arthritis in the Hunter Valley. Medical Journal of Australia , 1 (139).
14 Lawrence, R. H., Bradbury, R., & Cullen, J. S. (1986). Lyme Disease on the NSW Central Coast. Medical Journal of Australia (145), 364.
15 McCrossin, L. (1986). Lyme Disease on the NSW South Coast. Medical Journal of Australia (144), 724-725.
16 Hudson, B. J., Stewart, M., & et al. (1998). Culture-Positive Lyme Borreliosis. Medical Journal of Australia (168), 500-502.
17 NSW Government Dept of Health. (2012, July). Lyme Disease Fact Sheet. Retrieved November 2012, from www.health.nsw.gov.au/factsheets/infectious/lyme_disease.html
18 Bacon RM, K. K. (2008). Surveillance for Lyme Disease - United States 1992-2006. MMWR Surveil. Summ. , 57 (10), 1-9.
19 Sanjaya N S, e. a. (2012). First report of human babesiosis in Australia. 196, 350-352.
20 Nadelman, R. B. (2012). Differentiationof Reinfection from Relapse in Recurrent Lyme disease (Vol. 367). USA: New England Journal of Medicine.
21 Miklossy, J., & et al. (2008). and local inflammation in Lyme Borreliosis. J. Neuroinflammation , 25 (5), 40.
22 Shor, S. (2011). Retrospective analysis of a cohort of internationally case defined Chronic Fatigue Syndrome patients in a Lyme endemic area. Bulletin of the IACFS/ME , 18 (4).
23 Lyme Disease Association of Australia. (n.d.). www.lymedisease.org.au. Retrieved January 2013