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The Use of Dapsone as a Novel “Persister” Drug in the Treatment of Chronic Lyme Disease/Post Treatment Lyme Disease Syndrome

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Abstract

Dapsone (diaminodiphenyl sulfone, i.e., DDS) is commonly used to treat dermatological conditions including acne, dermatitis herpetiformis, and leprosy. *Mycobacterium leprae*, a known “persister” bacteria, requires long-term treatment with intracellular medications including rifampin and Dapsone. Other “persister” bacteria recently have been identified, including *Borrelia burgdorferi*, the agent of Lyme disease.

Objectives: We tested the efficacy of DDS in patients with chronic Lyme disease/PTLDS with tick-borne co-infections including Babesiosis, who failed commonly used antibiotic and antimalarial protocols.

Methods: 100 patients with Lyme disease, 56 of who were Babesia positive, were placed on Dapsone and folic acid in combination with either one or two other intracellular drugs, including rifampin, tetracyclines, and/or macrolide antibiotics. Several patients also took cephalosporins, and all patients were on protocols to treat cystic forms of *Borrelia* and biofilms.

Results: Patients completed a symptom severity survey before beginning treatment with Dapsone and then again after at least one month of treatment scoring their complaints from 0 indicating “none” to 4 indicating “severe” for symptoms including fatigue, joint and/or muscle pain, disturbed sleep, and cognitive difficulties. Results demonstrated that Dapsone significantly improved all patients’ clinical symptoms except for headache, where changes did not reach statistical significance. In addition, Dapsone, known to have anti-malarial effects, helped resistant Babesia symptoms of sweats, chills, and flushing. Lyme positive, Babesia positive patients also demonstrated significant changes in pain, disturbed sleep, and cognitive difficulties. Side effects included macrocytic anemia and rare cases of methemoglobinemia, which resolved by either decreasing the dose of Dapsone or increasing folic acid.

Conclusion: Dapsone is a novel and effective “persister” drug for those with PTLDS and associated tick-borne co-infections who have failed classical antibiotic protocols. Further prospective trials must determine the DDS dose, length of treatment and best combination antibiotic therapy in order to effect a long-term health benefit.

Keywords: Dapsone; Rifampin; Chronic Lyme disease; Post Treatment Lyme Disease Syndrome (PTLDS); Biofilms; Babesiosis; Tick-borne co-infections; “Persister bacteria”; Morgellons syndrome; Multisystemic infectious disease syndrome

Background

The question of whether Lyme disease persists after standard courses of antibiotic therapy has been a hotly debated topic in the medical field for the past 30 years. Patients with chronic Lyme disease (also called Post Treatment Lyme Disease Syndrome, PTLDS by some in the medical community) [1] have been shown in National Institutes of Health (NIH) double blind studies to be as sick as patients with chronic congestive heart failure, and many patients become disabled if not treated early on in the course of their illness [2]. The Centers for Disease Control (CDC) [3] reported a significant increase in the number of Lyme cases in the US from 2005-2010, with an annual incidence of approximately 329,000 cases. This led to revised estimates of over 300,000 new cases per year. In August 2015, CDC researchers revised their estimates upwards once again, showing a 320% increase

in Lyme cases in the past 20 years [4]. Part of this escalation is due to the increasing distribution of *Ixodes scapularis* and *Ixodes pacificus* ticks in the United States, where 842 counties were affected in 2015, versus 396 in 1998 [5]. Birds are known to carry ticks and spread the infection across the US [6], accounting for part of the increased numbers. The National Science Foundation has identified Lyme disease as one of several emerging pandemic disease outbreaks that threaten global public health and world economies [7]. Resolving the question of persistence and finding effective treatment solutions are increasingly important as cases continue to rise, leading to long term disability.

There is lack of scientific consensus as to why many patients after standard courses of Lyme treatment go on to develop chronic symptoms. One hypothesis is that persistent infection, apart from autoimmune phenomenon and tissue damage, is underlying chronic symptomatology [8]. Scientists at the NIH recently attempted to answer whether Lyme disease could persist by conducting studies using live, disease free ticks and allowing them to feed on either animals or humans who had been previously treated for Lyme disease using “standard” courses of antibiotics. This technique is known as

xenodiagnostics. The first xenodiagnostics study in 2014 demonstrated that the DNA from *Borrelia burgdorferi* could be found in patients previously treated for Lyme disease [9]. A second xenodiagnostic study by Hodzic et al. in 2014 [10] in mice also found evidence of persistent DNA. Although spirochetes could not be cultured from tissues, low numbers of *Borrelia* DNA were detectable up to eight months after completion of therapy. RNA transcription of genes was also seen with visualized spirochetes, proving ongoing infection. Why weren't standard antibiotics such as doxycycline or IV Rocephin able to completely eradicate the infection?

Many refractory infections are attributable to biofilm colonies [11]. Biofilms are made up of cells and extracellular polymeric substance (EPS), creating a matrix. Biofilms constitute a sheltered environment and prior work by Sapi [12,13] showed that biofilms in *Borrelia burgdorferi* protect the bacteria in chronic cutaneous borreliosis and that biofilm formation in *Borrelia* species accounts in part for inadequate killing with short-term antibiotics [14]. *Borrelia* is also known to be able to avoid immune surveillance through immune evasion by regularly changing outer surface proteins through gene recombination [15], can go deep in tissues where antibiotics don't penetrate well, has long replication times (requiring longer courses of treatment), is able to evade the complement system [16], form cysts (cell wall deficient forms) that have been shown to survive in adverse conditions [17], and hide in the intracellular compartment [18,19]. Research has shown that many persister bacteria exist as intracellular infections, like TB and leprosy [20].

Johns Hopkins researchers in 2015, [21,22] as well as researchers from Northeastern University (Kim Lewis and colleagues) [23] demonstrated that *Borrelia burgdorferi* can form persister cells. Persisters are a small fraction of quiescent bacterial cells that survive lethal antibiotics but can regrow leading to post-treatment relapse. Examples include mycobacterium, syphilis, endocarditis, and biofilm infections.

An analysis by DeLong et al. [24] concluded that prior NIH double-blind treatment trials on Lyme disease produced mixed results, with some studies showing no benefit [25] and others showing temporary benefit [26,27]. Discrepancies in the scientific literature can be explained by a failure of prior studies to address the different forms of *Borrelia* and biofilms, use long enough treatment courses, inadequately screen and treat associated co-infections like *Babesia*, which can increase symptomatology and severity of illness [28], or adequately treat associated autoimmune manifestations of Lyme. Failures may also have been due to using intracellular drugs not known to be effective in treating persister bacteria, like mycobacterial infections [29]. We chose Dapsone, diaminodiphenyl sulfone (DDS), in a preliminary clinical trial. DDS is known to be an effective treatment against slow growing, intracellular persister bacteria like leprosy [30], for treatment of Dermatitis herpetiformis [31] and has anti-inflammatory effects in autoimmune conditions like Lupus. Many Lyme patients present with autoimmune manifestations secondary to molecular mimicry [32-35]. Dapsone also is used topically for severe acne [36], and has anti-malarial properties [37], which could be useful in those co-infected with *Babesiosis*, a common tick-borne co-infection associated with Lyme disease [38].

Case Presentation

The patient was a 46-year-old white female with a past medical history significant for breast cancer with a lumpectomy (post radiation

therapy), hyperlipidemia, irritable bowel syndrome, reactive hypoglycemia, migraines, ADHD, depression, and Lyme disease. Her Lyme symptoms began three years prior to her consultation with me, with flu-like symptoms several days after being out in her garden pruning rose bushes. She did not remember getting a tick bite, but she lived in a Lyme endemic area in the Northeastern US. She began complaining of drenching night sweats with chills and flushing, interfering with her sleep. She was not yet in menopause, and she still had regular periods with a normal FSH, LH and hormone levels. She then experienced a 20-pound weight gain, severe fatigue, hair loss, swollen glands and a sore throat that would come and go, decreased libido, occasional right lower pelvic pain (with a negative gynecological exam), and an unexplained cough and shortness of breath (with negative pulmonary exams). She complained of joint pain and stiffness in her fingers, knees, and hips that would migrate and come and go, migratory muscle pains of the lower extremities, facial twitching, headaches, tingling of her nose, blurry vision with episodes of diplopia with negative eye exams, tinnitus, balance problems with dizziness, irritability, depression, insomnia, and severe memory and concentration problems. A brain MRI was suggestive of possible demyelination. She also had unexplained skin rashes, with lesions on her face, arms, legs, nose, and abdomen, and she reported filaments and fibers coming out from the lesions. These lesions were intermittently pruritic in nature and “stinging”. A dermatologist could not determine the origin of the lesions. These were subsequently determined to be a manifestation of Morgellons disease.

When I saw the patient for her initial history and physical examination, her blood pressure was 170/100 with a pulse rate of 104 BPM. She had a history of hypertension which had never been treated. Her physical exam only revealed red swollen nasal turbinates suggestive of allergies, and fibrocystic breasts (with a small scar over the right breast, post lumpectomy), with some healing lesions of her skin. Social history was positive for a pack a day for 20 years smoking history, and exposure to inks, dyes, and different chemicals from her work in a paper mill for several years before returning to the Northeastern US. She was on Neurontin 600 mg at bedtime for her neuropathy, Lunesta 2 mg for sleep, and Adderall for her ADHD. Family history was positive for MS (mother), and cardiovascular complications in her father and brother (strokes).

Significant prior laboratory results included positive markers for inflammation (ESR 51), an ANA of 1:1280, hyperlipidemia, toxoplasmosis exposure, and positive herpes virus exposure. Cancer markers were within normal limits (CEA, CA 15-3). We ordered an expanded tick-borne panel for Lyme, Ehrlichia, Anaplasma, *Babesia*, Bartonella, rickettsial infections and Tularemia, and evaluated the patient for Chlamydia and Mycoplasma exposure, viral infections (EBV, CMV, HHV-6, West Nile), and autoimmune disease (dsDNA, ssDNA, sm AB, Sjögren's antibodies, rheumatoid factor, and anticardiolipin antibodies). We also assessed vitamin levels (B12, folate, methylmalonic acid, homocysteine), mineral levels (magnesium, iodine, selenium, zinc), a food allergy panel (IgE antibodies), an anti-gliadin antibody and TTG level to rule out gluten sensitivity/ceeliac disease, a hormone panel (adrenal, thyroid, and sex hormones), Vitamin D levels, lipid peroxides (a marker of oxidative stress), immunoglobulin levels and subclasses, as well as an HbA1c, VAP lipid profile and PLAC test, to further evaluate her cardiovascular risk with untreated hypertension and a family history of strokes.

Testing confirmed the clinical diagnosis of Lyme disease and associated tick-borne co-infections. She had a positive ELISA, a

Western blot with *Borrelia* specific bands (31 and 39 kDa with no history of the LYMERix vaccine), Babesiosis (*Babesia* WA-1/duncani, 1:256 positive), Toxoplasmosis (IgG positive), Mycoplasma and Chlamydia exposure, and lab values were suggestive of Bartonella, with an elevated vascular endothelial growth factor (VEGF) at 94 (normal range 31-86). There was significant inflammation with a HS-CRP of 19.8 (normal less than 1) and an elevated 1,25/25 OH Vitamin D ratio, with a low 25 OH Vitamin D at 28 (normal greater than 30). She was antigliadin positive, TTG negative (gluten sensitive), had a mildly elevated HbA1c and lipids (suggestive of metabolic syndrome), and severe adrenal deficiency (low DHEA, low cortisol levels). Preliminary diagnoses were Lyme and Morgellons disease [39], associated tick-borne co-infections, with evidence of exposure to Babesiosis, possible exposure to Bartonellosis, inflammation with non-specific autoimmune markers, gluten sensitivity, and hormonal dysregulation.

She began a low salt, low carbohydrate, gluten-free diet and began an exercise program combined with a series of rotating antibiotic regimens and hormonal/detoxification support. Clinical improvement was seen intermittently with combinations of double or triple intracellular antibiotics, which included tetracyclines [40] macrolides [41], rifampin and quinolones. The patient also improved with Lyme and *Babesia*/Bartonella treatment, where Bicillin injections [42] and minocycline, ciprofloxacin, and Malarone were her best treatments. She kept relapsing however every time she was taken off antibiotics. This clinical picture went on for years, although her Morgellons skin lesions cleared up and never returned.

In April of 2015 we began using DDS as a “persister regimen” with resistant patients who had failed prior treatments, with some successes. The patient still complained of severe day sweats, night sweats and chills even though she was not in menopause, symptoms which were consistent with persistent Babesiosis. She had failed trials of several antiparasitic medications including Clindamycin, Coartem, Mepron and Zithromax, Malarone, Daraprim, and antimalarial herbs like Artemisinin [43,44]. She also complained of severe fatigue, migratory joint and muscle pain, anxiety, and incapacitating brain fog with memory/concentration problems despite negative neurological work-ups and prior treatment for her Lyme and associated co-infections. The patient signed an informed consent to use Dapsone for PTLDS, after receiving an explanation of possible side effects (including anemia and methemoglobinemia). She was placed on oral Plaquenil 200 mg PO BID, Nystatin tablets 500,000 units PO BID, Minocycline 100 mg PO BID, Rifampin 300 mg PO BID, DDS 100 mg PO QD, Leucovorin 5 mg PO QD, as well as Malarone 100/250 mg PO BID, for her Lyme, *Babesia*, and probable Bartonella exposure. She remained on hydrocortisone (Cortef) 10 mg in the morning for her low adrenal function with DHEA (sublingual), with high dose probiotics to prevent yeast infections and diarrhea.

The patient returned for a medical consultation after being on Dapsone for 5 weeks, and was feeling “the best she had ever felt in the past 12 years”. Her cognitive difficulties had resolved and her brain function felt almost 100% back to normal. She reported improvements in joint and muscle pain, stamina and overall energy, with improved moods and decreased depression. Her resistant *Babesia* symptoms also improved, as she reported significantly less heat intolerance, temperature dysregulation, sweats and chills. She went from 20% of normal functioning (on a scale of 0%-100%) to 75%-80% in a short period of time. She exhibited mild anemia from the Dapsone, but at a tolerable level.

Dapsone was highly effective for this patient when combined with other intracellular medications. We are in the process of evaluating different combinations of antibiotics with Dapsone, combining it with pulsed antibiotics such as cephalosporins, to find the most effective protocols for patients suffering with Lyme and tick-borne co-infections.

Research

Methodology

Published research has shown that novel persister drug regimens for Lyme disease such as using IV Daptomycin have been effective in eliminating biofilm microcolonies for *Borrelia burgdorferi* when standard drug regimens were ineffective, but Daptomycin is expensive and must be administered through IV access [45]. No human clinical trials with Daptomycin have been conducted to date. Our research is the first published pilot study of an effective oral persister drug regimen in patients failing traditional antibiotic therapies for Lyme disease. Some of our patients are also showing positive effects of Dapsone on symptoms from tick-borne co-infections including Babesiosis.

After signing informed consent forms that outlined the proposed benefits and potential risks of our pilot study, patients enrolled in a preliminary Dapsone trial at our medical center based on the drug's action on persister bacteria [46]. Each participant received detailed instructions that outlined the need for blood testing every three weeks, dietary guidelines, and the name and phone number of the medical center's head nurse if anyone had questions or medical issues.

Inclusion criteria: All 100 patients in our pilot study fit the criteria for a clinical diagnosis of Lyme disease [47] supported by a physician documented erythema migrans (EM) rash and/or positive laboratory testing, including a positive ELISA, and/or C6 ELISA [48], PCR, positive IgG/IgM Western blots and/or *Borrelia* specific bands on a Western blot [49]. Among the 100 patients in the study, 56 tested positive for Babesiosis, by either Giemsa stain, indirect immunofluorescent assay (IFA), PCR, and/or fluorescent in-situ hybridization (FISH) testing.

Exclusion criteria: Patients under the age of 18, patients having a known allergy to Dapsone or any medication used in the trial, and/or having significant laboratory abnormalities including a pre-trial anemia were excluded from our trial.

Patients were assigned to one of several different treatment groups based on their prior response to antibiotics for Lyme and associated co-infections. Patients who had significant Jarisch-Herxheimer reactions to a tetracycline, macrolide, and/or rifampin, were not given that particular drug combination. A previous positive clinical response to any or all of those medications allowed us to include them in our trial, unless there were potential adverse drug interactions. Combinations of medications used in our pilot study included Dapsone between 25 to 100 mg per day, with or without rifampin, with either a tetracycline (doxycycline, minocycline) and/or a macrolide (azithromycin, clarithromycin) and a cephalosporin (cefuroxime axetil, cefdinir, cefixime), or patients took Dapsone as a sole intracellular agent.

These regimens were chosen to include combinations of double and triple intracellular antibiotics with a persister drug (Dapsone) with antimalarial medication (Malarone) and herbs (Artemisinin,

Cryptolepis), as well as an antibiotic targeting active bacteria (cephalosporin) as per the Yin-Yang model [20]. We avoided mixing macrolides and quinolones because of potential QT interactions on the

electrocardiogram. Patients also took treatments targeting cystic forms of Borrelia such as hydroxychloroquine [50], and biofilms (serrapeptase, monolaurin, and/or stevia) [13].

Symptom		Mean	SD	t	p
Fatigue; tiredness	Pre	2.44	1.12	2.69	0.008
	Post	2.17	1.16		
Joint and/or Muscle Pain	Pre	2.02	1.05	3.83	<0.001
	Post	1.66	1.04		
Headache	Pre	1.2	1.06	1.6	0.113
	Post	1.06	1.11		
Tingling, numbness and/or burning of the extremities	Pre	1.21	1.09	2.26	0.026
	Post	1.04	1.02		
Disturbed Sleep	Pre	1.6	1.13	2.81	0.006
	Post	1.35	1.16		
Forgetfulness	Pre	1.66	1.23	5.13	<0.001
	Post	1.3	1.1		
Difficulty with speech or writing	Pre	1.45	1.2	2.83	0.006
	Post	1.23	1.16		
Day sweats, night sweats, chills, flushing	Pre	1.25	1.18	3.62	<0.001
	Post	0.92	1.01		

Table 1: Dapsone Pre v. Post Symptom Severity Scores.

Result and Discussion

One hundred patients (71 females, 29 males) completed a symptom severity survey before beginning treatment with Dapsone and again after at least one month of treatment. The duration of treatment ranged between one and four months. Patients scored their symptoms from 0 indicating “none” to 4 indicating “severe” for a list including fatigue, joint and/or muscle pain, disturbed sleep, and cognitive difficulties. The symptom severity survey came from factors identified in our own validation work on the Horowitz-MSIDS Questionnaire [51] (paper in progress) and the work of Shadick [52].

Paired-samples t-tests were conducted using SPSS comparing symptom severity from pre- and post-test scores from patients in our

DDS preliminary study. Results demonstrated that Dapsone significantly improved all patients’ clinical symptoms as measured by our survey except for headache, where scores did not reach statistical significance (see Table 1 for Means, SDs, t values and p values). In addition, Dapsone, a drug known to have anti-malarial effects [37] significantly helped resistant Babesia symptoms in this cohort of 56 Lyme patients who tested positive for Babesiosis, as demonstrated by improvement in day and night sweats $t(55)=4.078, p<0.0001$ (Table 2). These Lyme positive, Babesia positive patients demonstrated significant improvements in the following symptoms on Dapsone: joint and/or muscle pain, disturbed sleep, forgetfulness, difficulty with speech or writing, and day sweats, night sweats, chills and flushing. The 44 Lyme positive, Babesia negative patients demonstrated

significant improvements in fatigue, tiredness, joint and/or muscle pain, and forgetfulness.

It is not clear from this pilot study whether it is Dapsone alone or Dapsone interacting with one or more anti-infective agents that is responsible for the clinical improvements. Examination of the effects of drug combinations, dosages, length of treatment (less than, or greater than three months), and biofilm agents on post treatment symptom

severity via four analyses of variance calculations failed to reach statistical significance. We hypothesize that there are a number of potential explanations for this outcome, including inadequate sample size, dosage, length of treatment, and the possibility that Dapsone created a floor effect making it difficult to see differences among the other drug regimens.

	None	Mild	Moderate	Moderately Severe	Severe
Pre	30.40%	19.60%	30.40%	16.10%	3.60%
Post	35.70%	35.70%	23.20%	5.40%	0%

Table 2: Dapsone Pre v. Post Symptom Severity for Day Sweats, Night Sweats, Chills, Flushing for Lyme Positive, Babesia positive patients.

Dapsone was well tolerated in our patients, without obvious negative effect on the G.I. microbiome. Common side effects in some patients included intermittent symptom flares (Jarisch-Herxheimer reactions), as well as a macrocytic anemia, requiring higher doses of folic acid and/or a decreased dosage of Dapsone. Some patients decreased Dapsone to every other day to minimize side effects. High dose folic acid (up to 30 mg/day) helped to reduce the side effects of anemia in the majority of our patients, and the anemia generally resolved within 4-5 weeks off DDS. Two patients were also Coombs

antibody positive without evidence of frank hemolytic anemia, and two other patients had evidence of elevated levels of methemoglobin that resolved promptly off the drug or with re-introduction of Dapsone with increased antioxidant support. Despite the side effects, a majority of participants (59%) reported Dapsone was more effective than prior antibiotic regimes used to treat their resistant symptoms. Potential explanations for the improved efficacy of DDS apart from its action as a persister drug, is that Dapsone has both antibacterial and anti-malarial properties (Table 3).

Symptom	Lyme + Babesia +				Lyme + Babesia -			
	Mean	SD	t	p	Mean	SD	t	p
Fatigue; tiredness			1.22	0.228			2.20*	0.033
	Pre	2.39	1.02		Pre	2.44	1.22	
	Post	2.23	1.13		Post	2.12	1.24	
Joint and/or Muscle Pain			2.30*	0.025			2.93*	0.006
	Pre	2	0.94		Pre	2.05	1.15	
	Post	1.69	0.98		Post	1.69	1.12	
Headache			1.38	0.172			0.68	0.499
	Pre	1.16	1.09		Pre	1.26	1.04	
	Post	1	1.12		Post	1.17	1.1	
Tingling, numbness and/or burning of the extremities			1.75	0.086			1.09	0.281
	Pre	1.2	1.03		Pre	1.24	1.09	
	Post	1.02	0.99		Post	1.12	1.08	
Disturbed Sleep			3.10*	0.003			0.6	0.56
	Pre	1.6	1.18		Pre	1.59	0.99	
	Post	1.22	1.12		Post	1.51	1.14	
Forgetfulness			3.58*	0.001			3.52*	0.001
	Pre	1.7	1.18		Pre	1.6	1.24	
	Post	1.33	1.08		Post	1.28	1.14	

Difficulty with speech or writing				2.03*	0.047				1.85	0.071
	Pre	1.48	1.13			Pre	1.4	1.24		
	Post	1.28	1.14			Post	1.19	1.18		
Day sweats, night sweats, chills, flushing				4.08*	<.001				1.24	0.221
	Pre	1.43	1.19			Pre	1.05	1.15		
	Post	0.96	0.89			Post	0.86	1.15		

Table 3: Lyme positive, Babesia positive patients v. Lyme positive, Babesia negative patients paired samples t-tests for each symptom.

Prior leprosy research has demonstrated that a minimum of 12 months of treatment with Dapsone paired with rifampin is necessary to achieve clinical efficacy [53,54]. Although our study implies a role for persister drugs like Dapsone in patients failing classical antibiotic protocols, there are many unanswered questions arising from our preliminary research. What is the optimum dosage of Dapsone and length of time of treatment to prevent relapses in Lyme/PTLDS? Are two or three intracellular antibiotics sufficient for improving clinical symptoms and if so, which ones? Are active cell wall drugs (penicillins and cephalosporins) and treatments against biofilms necessary to effect long-term clinical improvement?

Prospective clinical trials with Dapsone need to be conducted, while also researching different drug combinations in the laboratory (in vitro) to determine their efficacy against *Borrelia burgdorferi*. PCR studies in chronically ill patients would also be helpful to determine which pathogens are present, since the majority of sick patients with chronic Lyme disease who come to our medical center have co-infections, as well multiple overlapping factors responsible for chronic persistent illness. The first author calls this syndrome, Lyme-MSIDS [51]. MSIDS stands for Multiple Systemic Infectious Disease Syndrome, and represents sixteen potential overlapping medical problems contributing to persistent symptoms in the Lyme patient. Ticks now contain multiple bacterial, viral, and parasitic infections that can be simultaneously transmitted with *Borrelia burgdorferi*, the agent of Lyme disease. Patients infected with Lyme disease and associated co-infections are much sicker and resistant to standard therapies [38]. This was the case with our patient, who had simultaneous evidence of Lyme, Babesia, and probable Bartonella increasing her symptomatology. Morgellons disease, an unusual but pathognomonic skin disorder recently demonstrated to be associated with Lyme disease [39], also was effectively treated in this patient using intracellular antibiotics.

In conclusion, Lyme disease is the number one spreading infectious disease in the United States, [55] and although early treatment with tetracyclines and cephalosporins may be curative in up to 75%-80% of individuals [56] many patients never see a tick bite and go on to develop chronic disabling manifestations. New and less expensive persister drugs are needed for Chronic Lyme disease/PTLDS. Recent published data on the bacteria's ability to persist, and the lack of a proven cure for those who continue to suffer, forces us to look for new answers. This case study and preliminary research on using Dapsone as a novel antibiotic for Lyme disease and associated co-infections illustrates the importance of researching established drug regimens for persister bacteria in new clinical settings.

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