Dr. Richard Horowitz reports promising results with Dapsone treatment

E arlier this year, Lorraine Johnson, Lymedisease.org's CEO, interviewed Dr. Richard Horowitz about his observational trial using Dapsone with his patients. Dr Horowitz is a board certified internist in private practice in Hyde Park, N.Y. He is medical director of the Hudson Valley Healing Arts Center, an integrative medical center which has treated over 12,000 chronic Lyme disease patients in the last 29 years. He is one of the founding members and past president of the International Lyme and Associated Diseases Society. Dr.

Horowitz is also the author of the best-selling book "Why Can't I Get Better? Solving the Mystery of Lyme and Chronic Disease."

QThe NIH trials have been criticized because they looked at a highly selective group of patients. For example, patients with co-infections might be excluded. What type of patients were in your study?

AThat's an important question. Fallon's study, if you remember, screened 3600 people to get a sample of 36. When you look at our Dapsone study, you will see that the way we did it was much more inclusive. If you had an EM rash you were in; if you had positive C6 you were in; if you had a positive IgM or IgG Western Blot you were in; if you had a positive PCR, you were included. We didn't limit the criteria to having to have five bands that were positive on an IgG Western blot. To do this kind of a clinical study when you're treating patients that are sick, you've got to do what is reasonable in a medical office—I'm still a treating clinician.Most of the people we see improve by diagnosing and treating abnormalities on the 16 point MSIDS map, yet many of the people in our Dapsone study were still very sick, even though they had been treated by us for some time.They were ill with ongoing Lyme symptoms, and many had co-infections: *Babesia*, and some clinically looked like *Bartonella*.Recently there's been some research interest in conducting animal studies—with mice for example, using medications for Lyme. But patients that come into my office don't just have Lyme. They have for example co-infections, hormone abnormalities, POTS/dysautonomia, sleep disorders, heavy metals, and food allergies. Mice are not going to have the same problems driving the inflammatory response, making them sick. So how relevant is the research?

Editor's note: MSIDS stands for Multi-Systemic Infectious Disease Syndrome, which is how Dr. Horowitz explains Lyme disease.

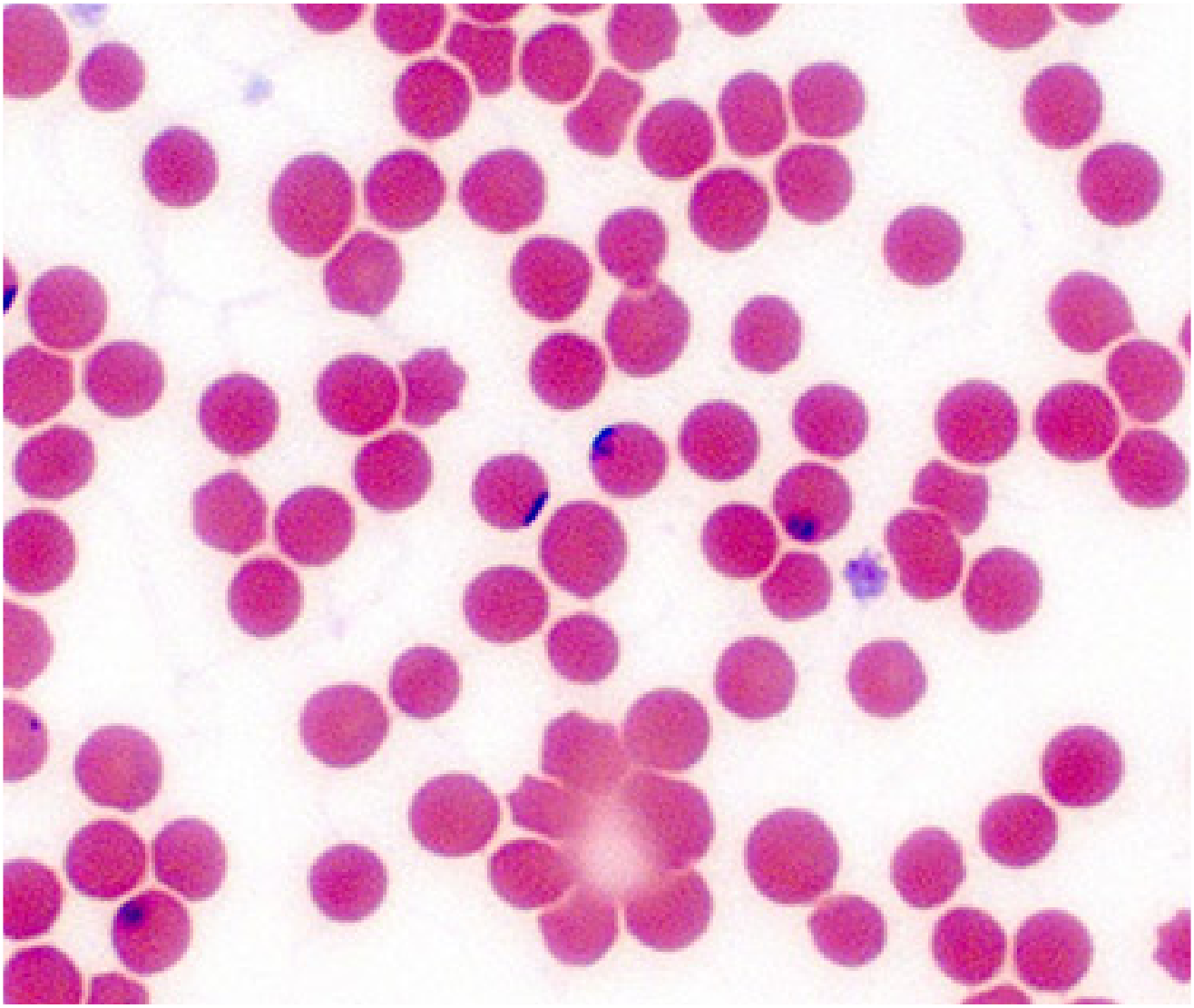
QDid your study have a control group?

ANo, it was an observational study—one where we observed how patients we were treating responded in the real world with treatments we use in our practice. The published study was on the first 100 patients. We'd like to take this study further and do randomized controlled trials in the future. It is working so well that I have applied for a grant to do a prospective study with Johns Hopkins.

QMy understanding is that you used Dapsone alone or with other antibiotics that you commonly use in your practice. What made you think to try Dapsone? Has it been used to treat Lyme disease?

ADapsone is known to be effective against persister cells in leprosy, but this is the first time

it has been tried for Lyme disease. The light just went off in my head when Dr. Ying Zhang, at Johns Hopkins, and Dr. Kim Lewis, at Northeastern University, started publishing about persister bacteria. It's funny. We all knew that *Borrelia* persisted, but once they said it's a "persister bacteria" then I looked in the medical literature and said, 'well what are all the other persister bacteria that are out there and how do we treat them?'That's the beauty of using a regimen like this—it's already been used for years for another persister bacteria, leprosy. Then I read up on the properties of the drug, and said to myself 'Wow, it also has anti-malarial properties!' They use Dapsone for toxoplasmosis and malaria prophylaxis.



These are organisms that are genetically very similar to *Babesia*, which is for many, a chronic parasitic infection keeping them ill. Dapsone just seemed to be a great candidate because so many of my patients have overlapping coinfections with bacterial and parasitic persisters. We know that *Borrelia* can persist, we know that *Babesia* can persist, and *Bartonella* also can persist. I had done studies on *Bartonella* persistence which I presented

at the international Lyme conferences years ago. We have even found persistence of *Mycoplasma* species. My thought was that we needed to create a regimen that's going to simultaneously hit all of these different intracellular bacteria causing inflammation, while also going after the cell wall forms, cystic forms and biofilms.

Q What other types of therapy were the patients on in addition to Dapsone?

A We used standard regimens we regularly use in our practice to treat the abnormalities on the MSIDS map. For Lyme infections, this includes treatments against the different forms of *borrelia*, as well as biofilms. We've also recently started to incorporate regimens based on Dr. Kim Lewis' work, where we pulse cephalosporins three days a week, to try and improve efficacy.

Q What did you find? Was it effective?

A We need to strike a tone of caution. We know that Dapsone is helping people that have failed other protocols, but we don't know the best dose, the best combination of drugs to use with it (although it seems the more intracellular medications, including rifampin, the better). We also don't know the ideal length of therapy to try and effect a cure, if it is possible. Some are on the protocol for 12 months and they are much better, but there can be significant side effects that clinicians need to know about and manage. I would never say that this would be a first line drug for someone who's never been treated. But for people who have already been through multiple regimens orally and I.V. that have failed, it is a protocol they should consider, especially if they also have babesiosis.People who responded to Dapsone were the kind of people who had already taken two or three intracellular drugs, a cyst buster and biofilm busters, as well as cell wall drugs and anti-malarial therapies, and they were still sick. Interestingly enough, we found that it was quite effective for neuro-cognitive symptoms. We had some people on Dapsone alone, without any other drugs, who had significant neuro-cognitive improvement. The only thing that didn't get better in the 100 patients in this retrospective pilot with Dapsone was headaches. But, symptoms of resistant fatigue, joint and muscle pain, tingling and numbness, disturbed sleep, as well as day sweats, night sweats, chills and flushing (from Babesia), all significantly improved.

Dapsone was useful for the majority of these symptoms. But what we don't know at this point is: what is the best combination and length of treatment? Is 50 mg of Dapsone for a year going to be enough? Is 75 mg? Is 100 mg? What is the best combo? Is a two-drug combo adequate with rifampin? Does it have to be a three-drug combo with doxy? We are hoping to have a lot more information when we do our retrospective study of 400 patients when they complete a year of treatment.

Q Some researchers say that when patients who have been ill a while respond to antibiotics, that it is due to an antihistamine effect. We know that antihistamines suppress the immune system and reduce inflammation. Do you think this treatment response is due to an antihistamine effect?

A Certainly histamine is a player, as it is definitely causing inflammatory problems in those with leaky gut and *Candida*. Also, antibiotics like tetracycline and macrolides are known to have anti-inflammatory effects. But when you see the kind of Herxheimer reactions that people have with Dapsone, then you know it's not just anti-inflammatory! It's killing bacteria. There are some individuals who have very severe herxes and need to take a break

from Dapsone for a couple of days, while alkalizing and increasing their detoxification, and then go back on it. Some find that it's better tolerated that way, and they still improve.

Q Do patients relapse when they go off the treatment? Do you know the optimal amount of time they should adhere to the protocol?

A We found that Dapsone worked in the majority of patients in the published study. What's not known is the length of time they need to stay on it. What I do know, however, is that the protocol is going to be necessary for at least one year in those who have been sick for a long time, because several of the patients who are no longer in the study, who stopped at six months, had relapses after improving. Some were positive for *Bartonella*. We need to extend it out to one year for those patients.We have continued treating after the period in the published study. I'm looking at a minimum of 12 months of treatment because that is what they are using for leprosy, using a similar combination– Rifampin/Dapsone.

Q Did you have any adverse side effects?

A The main side effect of Dapsone is Herxheimer reactions, which can be quite severe. The second most common side effect is anemia. Most get a macrocytic anemia, which can vary between mild and severe. It can be controlled with high dose folic acid, averaging around 50 mg a day.The third side effect is rashes. It's a sulphur derivative, which many can't tolerate, but these were rare cases. I think roughly four out of the 400 patients, around 1%, had a rash in our studies. Interestingly, not all people who are allergic to sulphur drugs like Bactrim get a rash with Dapsone.The fourth, and most serious side effect of Dapsone is called methemoglobinemia. This is when the hemoglobin in the blood that carries oxygen gets oxidized, and does not effectively carry oxygen. We probably saw significant elevations in about 1%, although mild elevations were seen in many, although they were asymptomatic. They didn't get any of the severe telltale manifestations of methemoglobinemia, which are blue hands and feet, blue lips, shortness of breath, and significant fatigue. In that case, Dapsone has to be stopped immediately. You also want to increase your folic acid, and increase your antioxidants, like glutathione, that reverses methemoglobin. There is a treatment that reverses it almost immediately, which can be given in severe cases. It's called methylene blue, and is administered intravenously in an emergency room.Treatments must therefore be monitored very carefully by a healthcare provider who knows how to prevent and manage these side effects. We have everyone on high doses of folic acid, which minimizes the anemia. They are generally on high doses of

antioxidants like NAC and glutathione, which helps prevent methemoglobinemia, while avoiding oxidant therapies (like ozone). We then follow methemoglobin levels in the blood, with a CBC and comprehensive metabolic profile, looking at kidney and liver functions, at least every three weeks. Before women start it, you also want to correct an iron deficiency anemia. We tell women that if they have any heavy menstrual cycles, or if they should experience any unusual heavy bleeding, to contact the office immediately, and consider stopping Dapsone while increasing their iron. You don't want overlapping sources of anemia while on the drug.

Q What about cost?

A Dapsone is generic and inexpensive. So is rifampin and most of the other drugs we are using with it. Some patients with severe *Babesia* have to use Malarone and herbs with Dapsone to increase the efficacy, which also increases the cost. When you look at the cost of Mepron at $750 a bottle however, and you look at the cost of Dapsone as a generic drug, you're talking significant savings. It could also save the health care system a lot of money, because we can avoid I.V. therapy in some because of the neuro-cognitive benefits, and its effective on some resistant symptoms – especially neuropathy – where may have failed classical drugs. They're on Lyrica, Neurontin, Cymbalta or other neuropathic drugs and they are still suffering. The Dapsone protocol might eliminate the need to use some of these symptomatic treatments because we're getting to one of the root cause of the problem, which is persistent intracellular infections.

Q So, what's next, Dr. Horowitz? Are you going to continue with this work?

A This first study was 100 patients. Unfortunately, that number of patients is not large enough to break them down into subgroups to see the efficacy of the different drug regimens. Our next study will look at approximately 400 patients. We will have statisticians look at the different groups – one group might be on Dapsone with only rifampin, another group might take minocycline and Dapsone, and other groups, triple intracellular therapies, like mino, rifampin and Dapsone. We even have some responding to four intracellular drugs, but ultimately, we have to evaluate which combinations are the most effective in clinical practice.

We are working with Dr. Eva Sapi at the University of New Haven in Connecticut to take these different combinations and place them in culture and then ask, 'Which of these combos is superior in killing *borrelia*?' and do those same combinations work in clinical practice? So far, in her preliminary work, she found that rifampin and Dapsone were decreasing biofilms and *borrelia* in culture by around 30% in 3 days' time, which is encouraging. We'll also be looking at whether patients who improve remain well after

stopping the protocol. That's the big question. This is a regimen that gives renewed hope to those suffering with persistent Lyme disease who have failed classical treatment protocols.

Q What about cost?

A Dapsone is generic and inexpensive. So is rifampin and most of the other drugs we are using with it. Some patients with severe *Babesia* have to use Malarone and herbs with Dapsone to increase the efficacy, which also increases the cost. When you look at the cost of Mepron at $750 a bottle however, and you look at the cost of Dapsone as a generic drug, you're talking significant savings.It could also save the health care system a lot of money, because we can avoid I.V. therapy in some because of the neuro-cognitive benefits, and its effective on some resistant symptoms – especially neuropathy – where may have failed classical drugs. They're on Lyrica, Neurontin, Cymbalta or other neuropathic drugs and they are still suffering. The Dapsone protocol might eliminate the need to use some of these symptomatic treatments because we're getting to one of the root cause of the problem, which is persistent intracellular infections.

Q You've already published one book and I understand that you have a couple of books coming out later this year that will include some of the information from this study as well as your other work. Tell me about them.

"Horowitz is one of the most prominent 'Lyme literate' physicians…patients wait for months to see him, and several told me that he had essentially cured them of a disease that nobody else seemed able to treat." —*The New Yorker*

RICHARD I. HOROWITZ, MD

Author of the Bestselling Why Can't I Get Better?

How Can I Get Better?

An Action Plan for

TREATING RESISTANT LYME & CHRONIC DISEASE

A"How

Can I Get Better?" is scheduled to come out in February, 2017, and it is available now as a pre-order on Amazon. It will be a simpler to read version of the first book, focused on providing clear explanations of testing and treatment protocols for the general public. It will also contain the most important scientific updates since my first book came out, with a very practical action plan so people know what do when they're sick and not getting better.I also have included updates on all aspects of the MSIDS model affecting health, with exciting new research on Alzheimer's and other chronic diseases. The addendum of the book will also contain all of the dosages of medications and supplements that I use, clearly laid out, so that health care providers have an easy to use manual for their patients. Everyone will now have access to the most effective, cutting edge protocols that we use in our practice to help our resistant cases. That's why it's called "How Can I Get Better? An Action Plan for Treating Resistant Lyme and Chronic Disease."

QRich, it's nice to see the data from clinical practice finally being gathered and analyzed.

AWell, Lorraine, somebody had to do it. You and I have been at this for a long time, looking for solutions for all these hundreds of thousands of suffering Lyme patients. I just couldn't hold back my excitement when I saw the persister research coming out of major universities. You get frustrated as a clinician when you see that even though many patients improve with your current treatments, others stay sick for so long or relapse. The intense suffering and the disability — patients deserve better. You want to do what you can to help these sick and suffering people…you want to try and make a difference in the world.

Dr. Horowitz's books can be found at: http://amzn.to/2cinJG0/ [See more at his website, http://www.cangetbetter.com/symptom-list]