

Written Transcript
July 10, 2008 Voice Chat meeting
with Dr. Mark Buchfuhrer (Dr. B)

Audio link for this transcript:

<http://video.google.com/videoplay?docid=-7766971241156535124&hl=en>

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<http://www.rlshelp.org/>

Restless Leg Syndrome: Coping with Your Sleepless Nights, co-written by Dr. Buchfuhrer:

http://www.amazon.com/Restless-Legs-Syndrome-Sleepless-Neurology/dp/1932603573/ref=pd_bbs_sr_1_s9_rk?ie=UTF8&s=books&s9r=8a02b54113481942011349a2387f0067&itemPosition=1&qid=1217182425&sr=1-1

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Q: Where are we right now, and what's on our plate right now?

Dr. B: I actually got involved with restless legs in 1991, just about the time the foundation was getting going. What happened was, a patient came to see me. Her real name is Elizabeth but she's always been called Bill. I guess her dad wanted a boy instead of a girl. She was a retired high school principal/professor, and came to see me with bad restless legs. She had augmentation from Sinemet, and she had actually done the research already and wanted me to give her Permax instead. That was a drug I had never heard of at the time. So I did a little research and found out a bit about it. Even though I was a sleep specialist I hadn't seen a heck of a lot of restless legs, as was pretty common with sleep specialists who do mostly sleep apnea. Anyway, we got her fixed up thanks to the help of Permax, and she was so grateful she started a support group. As I always like

to say, she dragged me in kicking and screaming into the support group. I wasn't very willing to start because I had at the time three little kids. I was very busy, and this was four Sundays a year, which I wasn't sure I had the time for. But it kind of worked out and I got real involved when I realized, hey, there are a ton of you patients out there, and there's a lot we can do for you, and there was a lot of needless suffering. I think I got on the RLS Foundation medical advisory board in '96. I'm sorry, '96 was when we started our website and our online support group for a local group in southern California. '99 was when I got involved in the medical advisory board of the RLS Foundation. That was until 2005. I've had a couple years off and now I'm back on the medical advisory board. We usually do two three-year terms, so I'll probably be on for the next six years. Now, that gives you a little introduction to how I got involved in restless legs, and I guess with getting the website going I did quite a bit of work. And then I got recruited to do the algorithm which we published in 2004, the restless legs algorithm in the Mayo Clinic Proceedings. Not long after that I wrote the first book that you heard before, Coping with Restless Legs, with Wayne Hening. We actually have two other books that I've written with Wayne Hening, both for doctors. And the third one is by PCI Communications and is actually a fairly good book for doctors. It's probably even a better one to suggest if doctors want some information, and I think you can probably find it on Amazon also. Now that's I guess all the introduction you guys need as far as I go.

As far as where we are with restless legs, clearly we're in a pretty good situation over the last few years where we have two drugs FDA approved, and a few drugs on the way. Unfortunately we were going to have a drug available right now, Requip CR. Most of you may know that Requip was the first drug approved in 2005 for restless legs. It's gone generic as of a few weeks ago or a month ago or so. Requip CR was supposed to come out to replace it. However, there was a little glitch and the FDA said to the Glaxo people, the GSK people, that they have to do a little more research and they decided that it just wasn't worth it, in part because they have another drug coming down the pike which will be available right around the time that this drug would have been available, the Requip CR, if they would have done the additional studies required. I can tell you a little bit more about them, but I think at this point it may be more interesting for you guys to ask me questions so that you can get your own questions answered.

Q: My question is on augmentation. Would you define that please?

Dr. B: Okay, augmentation is actually very easy to define, although it's taken doctors years to figure this out. Richard Allen at Johns Hopkins actually was the first one to describe it with a nice paper in 1996. Until then it really wasn't very well understood. What augmentation is, is actually a worsening of the restless legs due to taking a medication, typically a dopamine medication like Sinemet or Mirapex or Requip. What happens is weeks or typically months - sometimes it can be even a week or two, especially with Sinemet, but typically it takes three or four weeks with Sinemet and maybe two to three or four months, or a little longer, with the dopamine agonists Mirapex and Requip. What happens is the worsening has a few characteristic qualities. The first is that the restless legs starts to get worse and occurs earlier in the day. So let's say you only have restless legs at bedtime, 11:00 when you go to bed. You're put on Requip or

Mirapex, three or four months later you start noticing that you're getting symptoms at 7 or 8:00 in the evening, which you never had before. If you keep taking the medication, it perhaps could get even worse so it starts happening 4 or 5 in the afternoon or even earlier. Now, if that's the only manifestation of the restless legs, that it occurs earlier, usually it's not that big a deal because then what we'll do is we'll give the medication a little earlier. So instead of giving it at, let's say, 9 or 10:00 for the 11:00 bedtime we might give it at 6pm and then it might wipe out the restless legs for the entire evening and take care of that mild augmentation. However if the augmentation gets worse, let's say it keeps occurring earlier in the day and you have to start giving 2 or 3 doses, we'd better rethink what we're doing. The other thing that happens with augmentation is that the symptoms start becoming more intense. You can't sit as long, they occur sooner, and they're just more intense symptoms. The other characteristic thing is that they will start spreading to other body parts. So for example if you only had restless legs in your legs, and several months after taking the medication you're saying, gosh, they're occurring earlier in the day, they're a little more intense, and they're also in my arms, that may be augmentation also. What we feel is going on in augmentation is that the receptors, the dopamine receptors, are getting a little "not happy", they're kind of getting sensitized by the medication and they're reacting a little strangely. What's interesting about augmentation, again it's a worsening of the augmentation to where it was before you started the medication, usually several months before. We can prove that it's augmentation rather than just something else causing it to be worse. Like for example, sometimes you get a patient who's on a dopamine agonist and they start to get worse and you say oh my gosh, is it augmentation, and then you find out they've been given an antidepressant like in the Prozac family, and that may be worsening the restless legs. So it may not be the medication. You have to rule out everything else. But once you've done that, the way to prove it is if you stop the offending drug, which is usually a dopamine agonist or Sinemet, within a week or 2 or 3, usually 2 weeks, the RLS will go back to where it was at baseline. Of course, you have to be very careful because, for about a week or so the RLS may go into hyper drive and you have to treat that week or two of marked worsening until things go back to the way they were before.

Q: Dr. B, do you believe that the dopamine medication should be titrated down or stepped off of, or is it okay depending on time limits, is it okay to just cut them cold?

Dr. B: Well, I'll tell you what I do. When I get a patient with significant augmentation, what I do is I cut them off cold turkey. Because the problem is the receptor being bugged by the dopamine, so you want to end it as soon as possible. Now I know when I do this that the RLS is going to get dramatically worse for about a week or two as I just mentioned, so what I do is I supply my patient usually with a potent opioid pain medication in the codeine/Vicodin/Oxycodone/Methadone family. And I make sure they get enough of it so that they can treat the withdrawal symptoms from getting acutely off of the dopamine agonist or Sinemet or whatever it happens to be. Once that week or two is over, they just simply stop the medication, the opioids, and then we go to plan B and give them something else that will take care of their restless legs.

Q: What is the latest research on the link between iron deficiency or low ferritin levels and restless legs?

Dr. B: The question is, for those of you who may not have heard her completely, is: what is the latest research on the link between low iron or low serum ferritin levels and restless legs? Well, most of the research actually unfortunately is pretty old. It's interesting, because even way back in 1944, Karl Ekbom who discovered or in the modern day described the restless legs syndrome, even then he thought that anemia was associated with it and saw that there was a high percentage of anemic patients. So we've kind of known a little bit about this link. In the last 10 years there have been several papers that have just linked low ferritin levels with restless legs. But these are just studies where they just look at patients and they see how bad they are and what they have, and they found that when the ferritin levels were lower, patients did worse. There's been very few if any studies showing that giving iron really improves the situation. We know that a little bit anecdotally but they haven't done too much of that. So most of the data that we have is just looking at statistics on patients with restless legs and find out that they have lower ferritin (levels) than patients without restless legs. And the ones that tend to be worse are the ones with lower ferritins. Now the exception to what I have just said is the group at Johns Hopkins, which is led by Richard Allen and Chris Earley. They've been doing a lot of research on iron. In fact, that's the foremost clinical place that iron research in restless legs is being done. There's another place with John Connor and I'm just blanking which university he's associated with. He's a PhD not an MD and they're doing more theoretical research rather than the more clinical stuff that Earley and Allen are doing at Johns Hopkins. But I'll tell you some interesting data on this that is fascinating for me, and I'm sure it will be fascinating for you guys. What the Johns Hopkins guys did a few years ago is they took a bunch of fairly severe restless leg patients, they examined their serum ferritin levels. Just let me say for those of you who don't quite understand ferritin and iron and anemia and all these things, iron is important, is necessary to make the hemoglobin, which is the red stuff in the red blood cells. So when you don't have enough iron you can't make enough red cells. You can measure how anemic someone is by looking at the red cells, or what we call the hemoglobin. But that's the last thing that happens when you're low on iron. The body will fight, even when you're pretty darn low on iron, the body will fight to produce red cells. What we next did is we looked at the iron levels, and that's the next best thing to do to see if there's an iron problem after looking at the hemoglobin. Of course, you can have a normal hemoglobin and the iron levels may be a little low, but the body's still doing well. However, that still doesn't give us a good clue, because sometimes you can have a normal hemoglobin, normal iron levels in the blood, but there still may be a body deficiency of iron storage. So what we then do is we look at serum ferritin. That's how the body typically stores iron. So even in a patient with a normal hemoglobin and normal iron, you sometimes find low serum ferritins. Of course, the absolute best way to find out how well the iron stores are in the body is to do a bone marrow biopsy, which is unfortunately very painful. It is done on patients who you're really concerned about what their iron stores are. Or chemotherapy patients get this all the time to check their blood cells and iron, etc. But we don't like to do that, so the serum ferritin is the most accurate way that we doctors, and especially we restless leg doctors, like to look at the

iron status of patients. So what the team at Hopkins did is they looked at serum ferritin levels, but they even went one step further. They took what we call CSF, cerebrospinal fluid, levels of ferritin. What that requires is to do a spinal tap, put a needle right between two of the spines, usually in the lower back, and suck out a little bit of spinal fluid that runs in the spine and around the brain. It all communicates together. So by checking the levels of ferritin there you can see what the brain levels of ferritin are. And of course that's the most accurate for restless legs. What they found is that most of these patients, or most all of them, had low ferritin in the CSF around the brain and spine. Some of them even had pretty good levels in the blood but the brain was low. And that's what happens because the body will pull all the iron in the form of ferritin away from the brain and other places and suffer so that we can get enough iron into the bone marrow. Now they found these low levels and what they did is, they didn't give oral iron. Now oral iron is pretty tough to take. People get nausea and stomach upset; people get constipation; some get diarrhea. The ideal way to take it is an hour before eating on an empty stomach, of course, with some vitamin C to acidify the stomach and make it absorb better, which makes it absorb very well but increases the chance of getting some stomach upset. And even after all that, it's really tough to get the levels up. So what these guys did at Hopkins, is they bypassed that – they gave the iron intravenously, and by doing that they brought the level way up. Now typically what we say is when we check a serum ferritin level, is we want to get the level above 50. Most of the labs report normal levels as over 10 or 20. We're a little more aggressive; we want it over 50. What the guys at Hopkins did, they gave it intravenously, usually about 2 or 3 or 4 series of infusions of this iron, and they got the levels around 200. Well, lo and behold, about 80+% of the patients all of the sudden had their RLS symptoms completely vanish. They could drop all their medication, and these were severe patients for the most part. They dropped all their medications; they felt great. They said, "My RLS is cured." Anyway, very interestingly, 6 month to maybe 2 years later, these patients started calling back and saying, "My RLS is coming back, what's going on?" So they brought them back to Hopkins and rechecked their serum ferritins and their CSF ferritins, the ferritins around their brain, and lo and behold, these guys were again low on ferritin. Now typically, when we get someone with iron deficiency, anemia or not, and we tank them up full of iron, and typically this will be someone who has like a bleeding ulcer or women with heavy menstrual periods or God-knows-what, who get low on iron, once we tank them up, unless they bleed again, they're good for life. So this was very perplexing. And now what we believe is that the real defect in restless leg syndrome may in fact be a leaching out of iron faster than normal. We all lose a little iron every day but we get it back in our diet very, very easily. We feel that restless leg patients are losing it much faster, so the normal diet doesn't come close to replacing it. And at least the guys at Hopkins postulate that the genetic defect may be something to do with iron metabolism and that the RLS is only secondary to that.

Q: Can one get augmentation while on Gabapentin?

Dr. B: The answer is absolutely not, unless you're on a dopamine agonist with it. But Gabapentin has never ever been reported to cause augmentation. The only drugs that cause augmentation are so far the dopamine drugs, which are Sinemet and Mirapex and

Requip. The only exception to that rule is that Ultram, which is generically called tramadol, there's been a couple of cases reported by Richard Allen in one of the sleep journals. In fact I've seen a few patients myself with augmentation induced from tramadol or Ultram. But except for the drug I mentioned, no other drugs have ever, ever been associated with augmentation.

Q: My ferritin level is 3, but no doctors seem to want to do the IV.

Dr. B: Well, here's the story. First of all, are you anemic also?

Q: Not that I know. All my other counts were okay.

Dr. B.: Okay. Here's the dilemma we have. In this case, the serum ferritin is low, but she's managing to squeeze enough hemoglobin out of whatever iron stores she has in the ferritin, so she's not that anemic. Here's what the rule is. I've given a couple of iron infusions, but only to patients that are anemic and you can improve the anemia. The problem we have is that although there's some very rare reactions to iron infusion – we call them anaphylactic reactions, a kind of super allergic reaction which someone can even die from – although they occur very rarely, they're so serious that we don't want to give iron infusions unless there's another reason like anemia that won't respond to oral iron. Or if we're doing it experimentally. I can tell you, a lot of the kidney doctors who have a lot of anemic patients give this all the time. Really, it's much, much safer now than in the old days. Anaphylactic reaction used to occur with the older preparations. But the legacy of this fear is still here, and most doctors, I hate to say it myself included, are a little reticent to give iron infusion therapy intravenously unless we have refractory anemia or anemia that won't improve with conservative measures.

Q: People who benefit from the IV solution, how are they considered anemic? What were the tests that showed they were anemic? And for how many years have they been anemic?

Dr. B: The patients who got the iron infusion therapy at Johns Hopkins, almost none of them were anemic. They just had low serum ferritin levels, meaning under 50. But the majority of them were actually not anemic and would not have been given intravenous iron by any other doctor. The Hopkins guys were doing this on an investigative, research basis with a protocol that was approved and patients gave consent. So they're doing it with informed consent in a very different way. So really the only criteria for them to be admitted was to have a serum ferritin of under 50.

Q: I have severe restless legs. I've had it for about 3 years now. It's 24 hours a day. It never goes away. I've been put on Requip and Gabapentin was my first doses. I was up to 3mg of Requip and I can't remember the amount of Gabapentin, but when I reached 3mg of Requip I started experiencing severe stabbing pains in my calves. And I talked to my doctor, and the word that came out of his mouth was fibromyalgia. My question to you, doctor, is do you know of any relationship between fibromyalgia and the increase of the Requip?

Dr. B: Not really. In fact, I'll tell you a couple of interesting stories about this. There is a big overlap between fibromyalgia and restless legs. We don't really understand fibromyalgia that well, or how to diagnose fibromyalgia. I don't want to go into great detail, but you need a bunch of trigger points, you have to be fatigued. There's a lot of very common symptoms that occur with many disorders, so until recently many doctors did not even believe that fibromyalgia was a distinctive disorder. Anyway, what you tend to see is patients with restless legs who don't sleep well may have a lot of fibromyalgia symptoms. We tend to see quite a few. In fact, at our southern California support group meetings we often get 30 or 40, 50, 100 people, we've had a few times when we've had groups of 20 or 30 fibromyalgia patients coming. So there is this connection already. However, although we have 2 drugs recently approved for fibromyalgia – one of them is Lyrica, which we use for restless legs, so it helps both problems – recently they have approved Cymbalta, which is an antidepressant drug similar to Effexor, not too much different than the Prozac family of drugs, and that's supposed to help fibromyalgia. However, that's a drug that worsens restless legs, so there's a little difference here. However, there's a book written by a doctor in Oregon in the Portland area called The Fibromyalgia Cure. He wrote it about 4 or 5 years ago, and 2 of his miracle drugs to cure the fibromyalgia were Mirapex and Requip. So if anything, I'm not an expert in the field of fibromyalgia, but some of the previous experts actually propounded using the dopamine agonists to treat fibromyalgia. So certainly I would have to venture to say that it would be very unlikely for the dopamine agonist to cause fibromyalgia. Furthermore, I have used a zillion doses of Requip and Mirapex, and although sometimes I get paradoxical responses where the restless legs gets worse or some other funny things, there certainly has been no significant episodes of fibromyalgia coming out of the blue. Furthermore, your description of what your symptoms are don't exactly meet the criteria of fibromyalgia. So even though your doctor said fibromyalgia, I'm not sure that qualifies for a definitive diagnosis. I can tell you even in the best of hands, which is usually a rheumatologist – those are the fibro experts these days, or sometimes a neurologist – even in the best of hands, it is often difficult to establish a diagnosis of fibromyalgia.

Q: Dr. B, I'd like to ask you, since I'm one of the people who has pain with RLS, when we talk about pain with RLS or pain due to fibromyalgia, what I found was that my RLS is very predictable and in the same place every time, whereas my fibromyalgia friends with RLS, their pain moves around.

Dr. B: That's correct. The thing that kind of is the hallmark of fibromyalgia is that they have generalized achy muscles. In fact, I'm not an expert enough to tell you how many trigger points you need. What trigger points are, what the doctor does is he puts his thumb fairly hard into different muscle points, and if they hurt that's called a trigger point. You have to have so many trigger points to be diagnosed as a fibro patient. So this is more generalized, where it will be a point in the back, in the arms, in the leg, it could be all over. Whereas restless legs, all you restless leg guys know that you're getting it in one leg, both legs, sometimes alternating, sometimes arms, but as you heard before, it is very predictable where the problem occurs.

Q: I seem to have developed RLS after getting off of trazadone. Is that possible? Also, does Lexapro cause RLS?

Dr. B: Okay, coming off trazadone shouldn't really cause restless legs. Trazadone is actually a restless leg-friendly antidepressant, but it's typically a poor antidepressant. It has a sleeping quality. In fact a lot of general physicians use it as a sleeping pill because it's nonaddicting, although it tends to make people groggy. If you get the right dose to help people sleep, they get groggy the next day. But just stopping it shouldn't make restless leg worse to the best of my knowledge. I've actually never seen that happen before, but anything is possible. Perhaps it was treating some of the anxiety or depression and stopping it increased that problem. RLS often gets worse when other problems get worse.

The second part of the question was Lexapro. Lexapro is one of the SSRI drugs. These are the antidepressants in the Prozac family. In fact, I'll list off the ones in that group. Prozac was the initial one, then Paxil, Celexa. Lexapro is actually just a pure form of Celexa. Zoloft is in there also. Those are the main SSRI's. All of those tend to worsen restless legs. Now, there are patients who can take those and have little or no problem, but I would say the majority of patients will get some significant worsening of restless legs if they go on one of those SSRI's.

Q: When I take the medication for pain, such as ibuprofen, Tylenol, even Percocet, all interact with my Mirapex and cause a worsening of RLS. Any suggestions?

Dr. B: That's kind of a little strange, because typically the anti-inflammatories like Motrin, ibuprofen, etc., and aspirin and Tylenol, really have no positive or negative effect on restless legs. Now one thing I'll say, whenever I say anything general about restless legs. Patients are weird in general, and RLS patients are weirder than most, so anything I say in general will always have exceptions. So I can't explain that whatsoever. But the more unusual part of that is Percocet, which is a very strong combination of regular Tylenol and oxycodone, should actually eliminate restless legs. We use that all the time, with Percocet or pure oxycodone. It's one of the more powerful opioids that should actually improve restless legs. So you have me there. I've rarely if ever heard a patient complain that an opioid actually made restless legs worse, because 98% of them will actually get improvement with an opioid.

Q: I'm trying to get off of Mirapex because I think it makes me have impulse or obsessive behavior. I have also tried Requip with the same results. Any suggestions what to try?

Dr. B: There's unfortunately a very small percentage of patients who get this compulsive behavior, or better termed, impulsive control problems. Of course, they can manifest as gambling problems, shopping problems, or other things that are kind of impulse control issues. This usually occurs at the higher doses that the Parkinson's patients use the same dopamine agonists Mirapex and Requip for, but we now are seeing a whole bunch of restless leg patients even at the lower doses. If this occurs – by the way, sometimes this

is a dose response type of thing, where a lower dose may not cause it but a little higher dose may. Typically what I do with that, because you don't want to see people have these impulse control problems. We've had people who lose lots of money when they're on this medication because they're buying things they don't need or they gamble or God knows what. Because it can be a fairly serious problem we usually stop the medication. The alternatives that we suggest are the anticonvulsants like gabapentin, the trade name is Neurontin, or pregabalin, the trade name for that is Lyrica. The other choice would be to go on a low dose of a pain medication such as an opioid, or tramadol, which often works very well. And sometimes I'll combine them. But those are the typical alternatives for people who are having unwanted effects with the dopamine agonists.

Q: Is there something other than meds to take during the day? I now take ropinirole 3mg per night, which I just started instead of Requip. These seem to act like muscle relaxers and make me sleepy. Is there anything for while you want to be active? This person also had a second question, is there any other meds that can help? I know caffeine, etc., but any other thoughts on what can help other than what we can cut out?

Dr. B: Well, that's kind of a difficult problem, and there's two ways to look at it. If the Mirapex and Requip can easily cause sleepiness, especially when taken at reasonable doses during the daytime, which this particular patient is doing. Strangely enough, we even see the paradoxical effect. We have some patients who get insomnia with these medications, so they can do funny things in the brain, and they can be totally opposite in different patients. So, very tricky to understand. However you really have two choices here. If the medication is doing a good job on the restless legs, and you think, gosh I don't want to stop this because I don't want to go to the other classes, then you're stuck either being sleepy, or what I would do, and I've actually done this a few times, is give a drug like Provigil. Provigil, the generic on that is medafonil, and it's a drug that sleep specialists like myself use quite a lot for patients who have narcolepsy, sleep apnea, and other extra sleepy disorders, things that make people extra sleepy during the daytime. Now, just let me add, I, as a doctor, I particularly do not like adding a medication to treat the side effect of another medication. Sometimes we're stuck and we have to do that. But if I had my choice, what I would do with a patient who complains of sleepiness with Mirapex and/or Requip is change to another class of medication. Unfortunately, gabapentin, which is one of the anticonvulsants, one of the alternatives, tends to make people sleepy also. Lyrica is a little less so, but it still can make people sleepy. Often when I have trouble I go to the opioids and tramadol, and it's surprising how well a whole bunch of the patients who have trouble with the other medications still tolerate these and don't have any sleepiness. So we either change to one of the alternative I mentioned, or if we don't like doing that, we may consider adding the drug Provigil to the existing regimen. But again I'm not a big fan of treating a side effect of a drug by adding another medication.

Q: I was just wondering about wrapping my legs really tightly with an Ace bandage when nothing else seems to help, whether or not that could be harmful. I fall asleep with it, and it's like as tight as I can get it, practically.

Dr. B: Well, the answer to that is, people get really concerned with Ace bandages being wrapped tightly, and extremities, the feet turning purple. They figure, oh my god, maybe the foot's going to fall off or you're going to get gangrene overnight. No concern whatsoever. What you're cutting off when you do stuff like that typically is the venous circulation. You might get some swelling or some temporary problems, but the arterial circulation goes at a much, much higher pressure, and it would be very, very tough to really put it tight enough to cut off that circulation. When someone has a limb wound or a limb amputate, we can put a tourniquet on tight enough to do that, but trust me, if you did it at that level, you probably would not be able to fall asleep. So not much of a concern, and if that works for you, that's fine.

Q: I have severe RLS and PLMD, successfully treated with Mirapex. I recently have had severe full leg cramping at night, sometimes one leg, sometimes both legs. Is this cramping typical of RLS or PLMD?

Dr. B: No. The leg cramping is a totally separate problem. It has absolutely, positively nothing to do with RLS or PLMD. Unfortunately, we have no idea what causes leg cramps. We know some situations such as fatigue of the legs and things like that that may bring it on at times, but not always predictably. However, these are absolutely, positively separate problems. They just happen to occur in the legs, so people kind of associate them together. In the old days when you could get quinine sulfate fairly inexpensively over the counter, or even by prescription inexpensively, doctors used to prescribe or recommend that left, right, and center for every restless leg patient. Of course, what's happened over the last few years is we now can barely get quinine, which is the only treatment we know that actually helps prevent the leg cramping, but it has to be taken before. But again, these are totally separate problems.

Q: The FDA just the beginning of this year put out a warning about taking quinine without being under a doctor's consent.

Dr. B: Actually, here's what happened, because you cannot get quinine without a prescription for the last several years. But what has changed more recently is the FDA put out a warning. First of all, what they did is they got rid of all the generic quinine. They only let one company produce it, and now it's only brand name and very expensive, and it's only indicated for malaria. What happened is, most doctors, when they see the FDA put out something strong like that, will not prescribe it. Now I still prescribe it, although most of my patients can't seem to afford it anymore because of the high cost. But like any other drug that's not FDA approved for that condition, we can prescribe it if we think it's medically warranted. We've always been able to do that, and until 2005 every single drug that I prescribed for restless legs was not FDA approved, but I still did it. Again, this is just a new warning, so the average doctor usually gets pretty scared by stuff like that and will not do that. But doctors like myself who are very familiar with quinine – in fact, I wrote an article about it in one of the Nightwalker several years ago, because it kind of overlaps – I've prescribed a lot and am familiar with it, so it doesn't really bother me to prescribe it.

Q: What is the prevalence of debilitating 24/7 RLS?

Dr. B: I can answer you that we do not know the answer to that question definitively. But here's what we can tell from the stats that we have in general. Typically, if you look at the population studies, and the best study was the R.E.S.T. study done by Wayne Henning, and actually the R.E.S.T. study was done in primary care practices and then Richard Allen did a companion one in the general population. So there's two R.E.S.T. studies... where it occurs 24/7. They then found that roughly a third of the patients (a third of the 10%, so roughly 3%) had restless legs enough to be called RLS sufferers. The way they defined that was the restless legs had to occur twice a week or more, and they had to have negative impacts on their quality of life questionnaires, significant. So these were the people we called sufferers.

Q: I've been on Lexapro for years, and developed RLS a few months ago. Should I try to get off of Lexapro, or what would you recommend?

Dr. B: We get this situation quite often, and my recommendation for anyone with depression and restless legs goes as follows. If the depression occurred before the restless legs ever occurred, and it's quite significant depression, and the medication you're getting is helping it, I would not consider stopping the medication. I would just treat around the medication, despite the fact that the medication may be worsening the restless legs. Now, if you haven't tried Wellbutrin (the generic on that is bupropion, but it's easier to say Wellbutrin), it may be worth a trial of going on Wellbutrin which is a RLS-friendly antidepressant. It's actually a pretty good one, but antidepressants are very peculiar from person to person. What works for one doesn't work for the other, even ones that are chemically very close. So Wellbutrin won't work for everyone. It's worth a try. Now on the other hand, if someone comes to me, and the RLS was pretty bad – was there for a while and pretty bad – and then the depression occurs and the patient was treated, I know there's a reasonable chance that the medication given to the patient may have been given for untreated RLS symptoms. They've caused depression and anxiety. Then I try to get the patient off and see what happens. So in the case here, if the Lexapro really does a good job and you've tried other stuff and it doesn't work well, and that really takes care of the problem, I would probably stick on it because it sounds like you were on it well before the restless leg problem.

Q: My maternal grandmother and paternal grandfather both had Parkinsons. Could you explain how RLS and Parkinsons are related, or are they not?

Dr. B: That's a very common question, because obviously the two only approved drugs and best drugs for restless legs are the two Parkinsons drugs. So that question comes up often, and in fact in the book I wrote, Coping with Your Sleepless Nights, I wrote the section on the medication, and in a big box I put "RLS does not lead to Parkinsons disease." The fact that you have restless legs does not make Parkinsons more likely to ever occur, although people can have both. Now, in the group of Parkinsons patients, we do see more restless legs symptoms, so that part is true. However, they get these dopamine agonists right away and dopamine-type drugs, so often the RLS symptoms get

treated pretty quickly. So someone with a family history of Parkinsons, I would not worry about restless legs occurring any more readily, but once you have restless legs yourself, of course it's genetic, so your family is six times more likely to have restless legs – any member of your family.

Q: This is a follow-up question to what was talked about before with the augmentation. On the RLS forums there is some discussion about permanent augmentation, e.g. If you don't stop the Mirapex in time and you're being augmented, then over a period of time somehow that is going to become permanent. I don't think there's any proof of that, but if you have any educated opinion.

Dr. B: I can tell you that that's probably not the case. One of the things with augmentation is a receptor phenomenon. The receptor gets fatigued or irritated or who knows what. Once you stop the Mirapex or Requip, things will go back to baseline sooner or later. The problem many people have is they find they can't get to that point because they try to stop the medication and they're not being given something else, so they go into RLS hyper-drive and they feel they really can't get down or off the medication to really feel better. Now there may be some cases of people who are on Mirapex or Requip who get worse and then even stop the medication and aren't better, but I would bet that those are not true augmentation cases. Those may be cases where the RLS just got worse either due to time naturally, or maybe some other circumstances – increased stress, an offending medication, more iron deficiency, God knows what.

Q: That was myself who asked the Parkinsons question, because this is my concern because no one in my family has (?) to RLS except myself. Who has been your youngest patient, or how young have you been coming across patients, and how long have they had RLS?

Dr. B: I can answer that question very easily. First of all let me just say that of the group that has a family history of RLS, roughly a third will have the onset before age 21.

Q: I've had mine all my life.

Dr. B: You hear a lot of that. I'll give you a couple of statistics in a minute. Just to answer the question "what was my youngest patient", my youngest patient was four years old. In fact, this was a patient I had to treat, and his mother, who is also my patient, has restless legs. His grandmother, who is not my patient, had restless legs also, fairly severe. They noticed, the grandmother noticed that the grandson was kicking at about 6 or 7 months, and she looked and said, "I think this kid has restless legs." And they watched and watched, and by the time he was four years old, he had fairly bad restless legs, and in fact they brought him to a pediatric neurologist who runs a sleep lab down in Orange County, which is about 30-40 miles away from where I am, and the pediatric neurologist said, "Nope, restless legs doesn't occur in kids" and wanted to do some other tests and didn't have a clue. So they eventually got to me and we took care of this kid. What's interesting is that even though he was four years old he gave me a better history of RLS, the four criteria, than most adults do. Now, there's been some recent studies – this is

actually the R.E.S.T. study I just told you about, the R.E.S.T. study in adults. This is the R.E.S.T. study by Dan Picchietti. He's a pediatric neurologist who is very interested in restless legs, and he did the pediatric restless legs study. And what they found actually is in children age 8-18 – they just chose that age group to study. They could have done it earlier but they didn't. 2% of kids age 8-18 have restless legs, and about 40% of that 2% have it significantly enough to bother their daily lives.

Q: Dr. B, I asked a question on the discussion board some time ago, and I'd really like to have your input on this. I found that – and I'm very lucky, I get to see Dr. Becker, and I have somebody who's really well qualified in this area and just awesome. But my problem is now, on the list of medications that I take, and I'm not the only one either in this room or in our community, that our medications look so wild to anybody who is not educated in RLS, that I have a hard time going to other doctors for non-RLS reasons. Because I have to explain RLS, the list of medications, and if I ever have a problem that involves pain, then they think I'm looking for drugs. How do I go about seeing non-RLS doctors?

Dr. B: That actually is a very, very big problem. I've had patients who have refused to take some of the more potent opioids, especially, or change from one to a less potent, because of the looks they get from doctors, and even the looks they get from the pharmacist who's dispensing it to them. One of the things I tell patients to do – again, this may be slightly self-serving, but I'll explain the whole thing – is take my book along. You can highlight the area in my book, and I've had patients actually do this, they just take the book along and say, "Look." Some of them have spoken to me, or they say, "I'm doing this based on this information", and just have that area highlighted. And just let me add for any of you who don't have my book, the profits go to the RLS foundation, so it's not that self-serving for me to tell you to go out and get more copies of my book. But I have patients either do that or photocopy the page. And actually it does help the doctors when they can see a real book written by MD's who are experts in this, and that's what it says. And in fact – since I wrote the section I know what it says there. Even the third book, which is a doctor-oriented book on restless legs, I wrote the section on treatment and all that stuff, and I've written the same things in there that can be easily photocopied and shown to any doctor. I think in the doctor book I even have the references. There's a few references. One is by John Winkelman, who's a psychiatrist at Harvard who is very into restless legs, and he wrote a paper on methadone. And so did Bill Ondo. So there's a bunch of literature which you can either find it in a book, or Lynn, you can email me sometime and I can probably give you some of the references if you can't find it in the books.

Q: I am a long-term chronic pain patient. I have had to take opioids for 10 years, and after 10 years of Remeron it caused my RLS to worsen to a horrible point, but after stopping Remeron it's back to...

Dr. B: If you're talking about how to treat the depression, then we're kind of stuck, because there's only so many, and most of them worsen restless legs. It's hard to say what to do because you have a limited range of medications to take. In fact the only

patients I have trouble with are the patients who really give me a very tiny pool of medications I can use because they seem to be bugged by everything. When I have my hands tied like that, that's when I may have difficulty making patients better. Just let me add for everyone listening, in the right hands with all the available medications we have, we can make 98% of restless leg patients 95% better. There are exceptions. You heard me say earlier, to every rule that you'll hear me say or generalized statement there are exceptions. And there's always a few percent that no matter what you do, every medication they look at they have a reaction to, so it's hard to give specific advice. But what I would consider for patients who are having trouble with all the antidepressants, you may try things like the anticonvulsants like Lyrica and gabapentin or Neurontin. Sometimes you can get some added benefit there. But those are cases really that have to be gone over one by one with someone who's very familiar with restless legs to kind of come up with a plan. And often it's just a lot of trial and error. I often tell my patients what makes me better than most doctors who treat RLS is just that I've been there and done that so often. And I have tried everything and I'm willing to try just about everything. My high success rate often comes just from experience and persistence.

Q: I have no family history of RLS. The doctor said that it could be due to a back injury from a car accident when this person was younger. And also, the second question is have you heard of alcoholism causing RLS?

Dr. B: The first part of the question was would an old back injury cause RLS. To the best of our knowledge, that really shouldn't happen. However, what we do see a lot, and this is undocumented but I've written about it in some of my books, is that often an accident, especially trauma to the spine, may trigger restless legs or worsen it. Now some doctors have said something serious like that is something you remember, and you may coincidentally associate it with it. But I've seen this many times, and we do believe that there may be some link to trauma, especially trauma to the spine, whether it's surgery or a car accident, that may trigger or worsen restless legs. How and why that works – no clue at all. Now the second part of the question (alcoholism – can alcoholism cause RLS). Alcohol itself tends to worsen restless legs. So clearly if someone has a problem with alcoholism where they can't control the amount they drink, their restless legs may be ratcheted up to quite a degree. Again, alcohol and caffeine are probably the two biggest offending drugs we get in our diet or otherwise that may worsen restless legs.

Dr.B: ...Emory and the Iceland group with him that found a gene that was more with PLM's, but still correlated with restless legs, and that gene and two more were found by a totally independent group which is made up of the German group and French Canadian group. So, now that we know there's a gene or there's some genes involved, what makes this very interesting is, if we can figure out the proteins that these genes make, we may then through the back door try to figure out exactly what the real genetic problems are with restless legs and get a true cure. We're probably looking at a 10+ year time frame on this, but frankly these are some of the most exciting bits of data that have come out for RLS in the last 10 or more years.

Q: On the augmentation, I've been on my Sinemet and then Mirapex probably since '94. Is there any long term studies on the disadvantages of being on a dopamine agonist for that long? And with the augmentation, could I just take a drug holiday, go off of it I know with the two weeks of hell, probably, and then to go back on?

Dr. B: The answer to your question is there are no long term problems with being on Mirapex or Requip for restless legs, even if you're on it for years. I've had people on those drugs since '91 when I started doing this. Of course, Mirapex and Requip only became available in '96, so for those two drugs we only have about 12 years. But the only long-term effect we worry about is the augmentation itself. Now the drug holiday is a reasonable idea. But here's the thing about a drug holiday. First of all, you don't have to be worried about the hyper-drive of restless legs that occurs when you stop the drug if you can get your physician to prescribe some opioids, and that usually takes care of it. However, if you just go back on the same dose of the Mirapex, Requip, or whatever, Sinemet, you're almost guaranteed to get the problem back. Here's what I do. If the person got augmentation with Mirapex, I'll put him back after a drug holiday of a few weeks on Requip. If he was on Requip I'll put him on Mirapex. But the trick is, use a lower dose. If you use a lower dose, you may have a good shot at not getting the augmentation back. However, since a lower dose may not work as well, you typically have to add another medication. And what I'll do is I'll add a low dose of maybe gabapentin or an opioid or Ultram or something. And that way I can get by with smaller doses of a couple of drugs, which may be less bothersome.

Moderator: Dr. B, I often quote you saying something that I heard you say at the very first, maybe not, it might have been in San Antonio or Atlanta – who knows. But I often quote you saying that when you were talking about medications, that it's a very good idea to take the lowest class at the lowest dose in the cleanest form for the longest time. Do you still believe that that's the way to go about this? I mean long term care.

Dr. B: Sure, what I always do with restless legs, or with any problem, I'm always trying to look at the lowest dose I can get the person on that does the job. And if you're using an opioid, you start with the weakest you can and work up only when you have to. In fact, I didn't like the Requip titration kit that doctors were given because they kind of went up too quickly and not with the slower increments that I did. Like they would go from 0.25 for 2 days, then right to 0.5, and then from 0.5 to 1. What I would do is I'd give the patient 0.25 for 5 days, and every 5 days you go up by 0.25. So I had a lot of patients who would end up on 0.75. And sometimes with Mirapex, I even go more slowly. I'll have patients sometimes start with ½ a tablet of Mirapex and go up by ½ tablets. So I'll have patients on really weird doses like 0.375 of Mirapex, sometimes 1 ½ tablets of the 0.25 or 3 tablets of the 0.125. And I get these weird doses which are just a little lower, and I think in the long run, by just being a little more careful getting slightly lower doses than you can with titration kits, I end up with patients who have less problems.

Moderator: I would agree, but you're the very first expert I've ever heard that said that about the Requip kit.

Dr. B: You know, I'll tell you something. Actually, I was involved in designing the Requip kit, as was Mirapex, along with some of the other doctors who you probably know. And here's what's very interesting. When we were at the meetings advising the companies on what to do, when they came out with the kit which we presently have now, especially the Requip one, here's what happened. A third of the doctors like me, in my camp, said "too fast". A third of the doctors said "just right", and a third said "way too slow" and wanted to go much faster. It just shows you the difference of opinion among experts. Now one of the things I can say is that in the group, most of the doctors except a few of us were also movement disorder specialists, neurologists who do a lot of Parkinsons, and they use massively higher doses and are very comfortable with it. But in different diseases, I've said, what works for one doesn't work for the other. And I think what the difference is that people like myself who are not neurologists, so I've come from a different camp, a different viewpoint on this, and I have a zillion restless leg patients, probably more than almost anyone as far as assisting people on a day to day in the trenches as an outpatient. You know you just learn kind of to be a little more conservative, and you see it works better. When you're not looking as closely you may miss these little finer things. I've had some patients who end up on like 2 mg, and I say, "Why did you go to 2 mg?" "Well, my doc who gave it to me said just keep increasing the dose." So they don't always realize that lower is better and that once you're nailed, don't go any higher. So you do tend to see a little more problems in those who... In general, what I've seen is people who go a little higher will have a higher degree or higher incidence of side effects. So lower is always better. And one of my things with restless legs is, hey, before you guys get to a doctor, it has been years or decades. So, you know, if you've gone that long, does it really make a difference to me whether I get someone well in a few days or in a couple of weeks? Not really, especially if I tell them before they leave, "Hey, it's going to take a while. Kind of like an antidepressant, it's going to take two or three weeks. But just keep... but sooner or later it will probably help you." But in my book, slower has always been better. If you want to learn the brand names and generics, you're all free to look at my website, which is www.rls-help.org, and if you turn to the treatment page, I have all the medications pretty well listed with their generic and trade names, and you can look at them. I even have for the opioids a little chart with their potency.

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