

Dr. Bateman delivered a presentation to an audience of scientists and clinicians at the ME/CFS International Conference 2021: RID-Research Innovation and Discovery. The following is a transcript of her online presentation. The video can be viewed at:
<https://youtu.be/7M7AjSdgJpE>

Addressing Orthostatic Intolerance In ME/CFS

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Hi, it's a pleasure to be here with you today even if it's remotely. It's a great honor to be part of your conference. I'm going to talk to you today about addressing orthostatic intolerance in ME/CFS. So first of all what do I mean when I say orthostatic intolerance? I mean a symptom.

Orthostatic intolerance is the development of symptoms in upright posture that are relieved or partially relieved by reclining. Orthostatic intolerance symptoms basically come from cerebral under perfusion symptoms and signs and peripheral cardiovascular symptoms and signs. There are many. It can be as subtle or as obvious as fainting, or as subtle as impaired cognition, disorientation, visual changes, unusual neurologic symptoms, palpitations, nausea, pallor, cold hands and feet, shortness of breath, etc. We know that orthostatic intolerance symptoms are worsened by heat, dehydration, prolonged sitting or standing, deconditioning and weakness, medications, and it can also worsen immediately after exercise.

So why is it important to assess and treat orthostatic intolerance? Well first of all it's reportable and observable. It's measurable and it's treatable and treatment can improve symptoms and function in ME/CFS and may lead to insight about the underlying disease processes. Remember that OI can occur in someone who has low, normal, or high blood pressure seated position at rest as we traditionally check blood pressure. You need to do a differential diagnosis to make sure that the patient doesn't have underlying heart disease or lung disease or other severe contributing factor to orthostatic intolerance. Most of all don't miss noticing certain drug side effects can worsen orthostatic intolerance: diuretics, tricyclic antidepressants, some blood pressure drugs, drugs used for prostate disease, and particularly missed often is the oral contraceptives that contain drospirenone.

But what we're talking about is really orthostatic intolerance that comes from either the central or peripheral nervous system kind of illness that we see in ME/CFS and related conditions. There are some defined syndromes of orthostatic intolerance that we learned about in medicine: orthostatic hypotension, postural orthostatic tachycardia syndrome, neurally mediated hypotension. They're actually several kinds of definitions and several different terminologies to refer to these but um these are generally the categories that I follow. However, I want to make clear that orthostatic intolerance and reduced cerebral blood flow are

manifestations of ME/CFS that don't necessarily have to be manifest in the traditional primary orthostatic intolerance syndromes and this is just a little series of articles by this group Linda Van Campe, Peter Rowe, and Frans Visser showing that cerebral blood flow is reduced even in the absence of hypotension or tachycardia during mild orthostatic testing and severe ME/CFS and that deconditioning alone does not explain orthostatic intolerance and that the cerebral blood flow remains reduced for a time after tilt table testing in their studies.

So how does one go about assessing orthostatic intolerance? In addition to those symptoms, we talked about, I use a few tools. One is a simple question about hours of upright activity (HUA). This is defined as the number of hours spent with feet on the floor in 24 hours so that includes sitting standing and walking. Typical hours of upright activity in 24 hours for normal people are usually 14 to 17. In many chronic illnesses including fibromyalgia 10 to 12 but ME/CFS patients have very low hours of upright activity some of that may come from orthostatic intolerance. We utilize a questionnaire called the Orthostatic Hypotension Questionnaire that has two components. Six items that ask about symptoms and four items that ask about activity. Each of those domains is scored on a 1 to 10 scale. When we give this test to patients we substitute the word hypotension with orthostatic intolerance. We did a small study and published it showing that hours of upright activity correlate with the orthostatic hypertension questionnaire. I can show you here these are the six scores on symptoms. The panel in blue are the scores the average scores in each domain on a scale of one to ten in healthy controls and then the CFS groups are separated based on their hours of upright activity tolerance into mild, mild-moderate, moderate-severe, and severe. With the moderate-severe and severe in the red. You can see again these are each domain scores of zero to ten and you can see how high the scores are for ME/CFS particularly as they become more severe. This shows in our 25 healthy controls in ME/CFS patients the correlation of hours of upright activity with their activity as reported on the OHQ. Again, you can see that the scores for the healthy controls are approximately one on a scale of one to ten in the healthy group and get higher and higher in the ME/CFS group but are particularly high and abnormal from standing a long time or walking a long time.

So, head-up tilt table testing is the gold standard of course but we like to use the 10-minute NASA Lean Test because of its convenience and use in the clinic. This is just the form we use you can see that patients lie down in a quiet room for 10 or 15 minutes before starting the test then we measure two values supine in the rested state and then they stand quietly against the wall with the pulse ox on one hand and measuring blood pressure in the other with obtaining measurements every minute for 10 minutes. You can also do it every two minutes for 10 minutes.

So, this is an example of and one of my ME/CFS patients who had been sick for a number of years eight or ten years you can see her lying. First of all, she has two to four hours of upright

activity per day normal seated blood pressure 112 over 75 and a heart rate of 77. You can see her values lying down and as she stands during the lean test you can see that initially her heart rate goes up as it would in a case of POTS from 68 to 100 to 111 but then at six minutes, she drops her blood pressure and her heart races and she begins to have a syncopal episode. So, she starts with low blood pressure, looks like she's going to meet POTS but then she has an episode of syncope that we call neurally mediated hypotension. She's now doing very well by the way this was some years ago.

So, what do we do to manage orthostatic intolerance? We improve perfusion, expand volume, constrict blood vessels, control rapid heart rate and do what we can to modulate the autonomic nervous system. There are triggers to avoid, getting overheated, dehydrated, standing or sitting too long with your feet on the floor, prolonged bed rest can make orthostatic intolerance worse, weakness of the muscles, and then the medications we talked about. So just basics about interventions increase volume in the blood vessels. So, this can be done with fluids and sodium intake. There is a drug called fludrocortisone that can help with sodium retention rapid water ingestion is helpful and IV normal saline is especially helpful during times when people are doing worse, dehydrated, or more ill. Then you can do internal or external compressions so compression socks, pants, sleeves, abdominal binder. Midodrine is an example of a drug that works on the peripheral alpha-1 receptors as an agonist and is like wearing compression on the arms and legs. Other interventions if the heart rate response is extremely rapid which may reduce cardiac output due to slow filling of the heart chambers we use very low dose beta-blockers like propranolol and sometimes metoprolol that to just put a little bit of a cap on the heart rate to keep the heart rate from going excessively fast. We've also been very successful in ME/CFS patients with POTS using pyridostigmine and if they can adapt to the short-acting formulation sometimes they can be changed over to the extended-release formulation. We work on strengthening the lower leg muscles for better venous return as well.

So just a quick case I'm going to present for you, this is a 21-year-old male with ME/CFS and POTS. He was a competitive high school athlete before he became ill. He became ill during his senior year of high school four years ago but is slowly getting worse. He's being managed by a POTS specialist but someone who doesn't understand ME/CFS and before I saw him, he wrote me an email and said I'm struggling to perform any daily activity: showering, eating, walking up the stairs. I'm struggling to walk, stand, or sit without nearly falling. I feel as though my muscles are too weak to hold me and my brain fog is too great to provide any sense of what is going on around me. So, this was his initial 10-Minute NASA Lean Test. He actually did it at home with some help or with his primary care but it was before he came to my office. You can see his supine blood pressures are around 112 over the 60s heart rate in the mid-50s. When he stood up his systolic pressures gradually marched down and his heart rate went up immediately from the mid-50s to over a hundred and he was very symptomatic: short of breath, dizzy, nauseated. So, we were able to reproduce many of his symptoms and toward the end, it felt like he was

going to pass out. So he met criteria for orthostatic hypotension because his blood pressure dropped more than 20 systolic he also met the criteria for POTS with a heart rate that went 62 beats a minute faster. This is the same patient a month later pushing fluids, consuming a thousand milligrams of sodium chloride daily, wearing compression pants and socks, taking propranolol extended release 60 milligrams at bedtime, and small doses of pyridostigmine through the day. So, I asked him to do this after his second dose of pyridostigmine and you can see by looking his blood pressure and heart rate are very similar. Actually, his heart rate is a little bit higher which is a little ironic there are reasons for that but you can see when he stands up there's a little bit of adjustment but his heart rate never goes above 90 and his blood pressure for the most part, doesn't go below 100 systolic. This correlates with improved function in his case as well. He has been able to continue finishing his last semester of college partly online but he's going into his classrooms two days a week and it looks like he's going to be able to finish. He has to continue to pace and be careful and avoid inducing post-exertional malaise.

So why assess and treat orthostatic intolerance? I'm going to just remind you it's reportable in other words, patients can give a history that's consistent with orthostatic intolerance. It's observable. You can see it in terms of signs of patient on physical exam especially during the orthostatic testing it's also measurable based on heart rate and blood pressure and other parameters during the lean test and it's treatable. Treatment can improve symptoms and function and may lead to insight about the underlying disease processes.

So, I'm not going to spend too much more time going into detail because what I believe clinicians need to do is to do this orthostatic testing in their patients. I do orthostatic testing using the 10-Minute NASA Lean Test in every ME/CFS patient. Then we adapt treatment to their manifestations. We also do the test multiple times to assess the benefit of treatment.

Thank you for an opportunity to talk about this. I'm enjoying the conference and look forward to hearing additional talks and also presenting later on. Thank you.

We advise viewers to carefully review and understand the ideas presented and seek the advice of medical providers with any questions you may have as it relates to your patient-specific situation.

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