

# DYSAUTONOMIA INTERNATIONAL



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## **Research Highlights from the 24<sup>th</sup> International Symposium on the Autonomic Nervous System**

October 28, 2013

Dear Friends,

As we at Dysautonomia International believe it is important for dysautonomia patients and family members to be informed about the latest research pertaining to their health conditions, we are providing this summary of research abstracts presented at the 24<sup>th</sup> International Symposium on the Autonomic Nervous System, which was held earlier this month. Research symposiums are a way for physicians and researchers to present new ideas to each other. We do not recommend changing your treatment plan based on any of this research without speaking with your doctor first.

Much of the research presented at this year's conference was conducted by the members of our Medical Advisory Board, including Dr. Julian Stewart from New York Medical College, Dr. Satish Raj from Vanderbilt University, Dr. Kamal Chémali from Eastern Virginia Medical School, Dr. Paola Sandroni from Mayo Clinic, and Amanda Ross from our Patient Advisory Board -- our POTS patient turned POTS researcher and Neuroscience Ph.D. candidate. We are honored to have them on our boards and we would like to thank *all* of the physicians and researchers who participated in this year's conference for their efforts to help individuals living with autonomic disorders.

After a competitive application process with input from patients and researchers, our first round of POTS research grants will be issued in December 2013. We are very excited about the prospect of funding research that could lead to a better understanding of autonomic disorders, better treatments, and hopefully someday a cure. This is made possible by the individuals and businesses who have generously donated their time, talents and financial resources to Dysautonomia International since our launch last October. We encourage everyone to donate what you can and get involved, so that we can continue to fund research and raise awareness about dysautonomia.

Sincerely,

The Board of Directors  
of Dysautonomia International

## POTS Related Research Highlights:

1. Researchers from Oklahoma University and Vanderbilt University found that POTS patients have elevated alpha1-andrenergic receptor antibodies in their blood, which diminishes a blood vessel's ability to constrict, and which causes the body to need higher amounts of vasoconstrictive substances, like norepinephrine, to constrict. They also found beta1-andrenergic and beta2-andrenergic antibodies in the blood of POTS patients, which may contribute to tachycardia. They concluded that “[t]hese findings provide strong support for an autoimmune basis for the increased upright plasma norepinephrine and excessive tachycardia observed in POTS patients.” In plain language – POTS might actually be an autoimmune condition. This is a preliminary study and more research is needed to know if this finding applies to a broad range of POTS patients.
2. Researchers from Vanderbilt University studied the effect of IV saline on the exercise capacity of POTS patients. They noted that **saline infusions improved hemodynamics at rest, but saline did not increase exercise capacity in POTS.**
3. Researchers at New York Medical College have documented that postural hyperapnea causes hyperadrenergic POTS. In plain language, when some POTS patients stand up, they have a reduction in blood flow to their brain and they begin to breathe rapidly. Why this occurs is not fully understood yet, but the researchers believe it may have to do with the parasympathetic nervous system. When these patients hyperventilate, it causes them to breathe out too much carbon dioxide. This causes even more reduction in blood flow to the brain. This stimulates the sympathetic nervous system, which produces panic like sensations. **By having patients breathe in a controlled amount of carbon dioxide during tilt testing, the researchers were able to prevent the reduction of cerebral blood flow, upright tachycardia and hyperventilation.** Please note, no one is advising POTS patients to intentionally breathe in carbon dioxide, but this may explain why some POTS patients feel some symptom improvement when they learn how to slow gently down their respiration rate.
4. Researchers at Mayo Clinic took a closer look at the gastrointestinal symptoms often seen in POTS patients. They looked at 228 adult POTS patients who had gastric emptying studies while seen at Mayo between 1998 and 2012. **20% of the patients had delayed gastric emptying, 33% had normal gastric emptying and 46% had rapid gastric emptying.** The rapid gastric emptying group had more deconditioning, anxiety, sleep problems, migraines, abdominal pain and bloating. The delayed gastric emptying group had more weight loss, vomiting, early satiety (feeling full) and was associated with greater cardiovascular andrenergic impairment, lower blood pressure upon standing, and greater increase in heart rate upon standing.
5. Researchers at Mayo Clinic sought to determine whether the deconditioning that is seen in a large percentage of patients with orthostatic intolerance was the cause of their orthostatic intolerance, or a consequence of it. The conclusion they reached was that “[m]arkers of deconditioning are not or are only marginally associated with the orthostatic HR [heart rate] response in patients with OI. This finding suggests that **a high prevalence of deconditioning in these patients is a phenomenon associated with OI but unlikely to be the primary causative factor of OI.** Although OI patients clearly benefit from physical reconditioning programs, our findings may in part explain the variable and often incomplete response to this approach.”
6. Researchers from Johns Hopkins and New York Medical College conducted a survey of 346 pediatric POTS patients and found that the **most commonly reported triggers for the onset of POTS** were viral illness (31%), surgery or trauma (26%), puberty (22%) and bacterial infection (14%). **Patients had been**

**diagnosed with a number of other conditions:** migraine (45%), chronic fatigue syndrome (33%), gastrointestinal reflux (32%), Ehlers Danlos or joint hypermobility syndrome (29%), irritable bowel syndrome (28%), sleep disorders (27%) and gastroparesis (21%). **Food intolerances were common:** dairy (44%), wheat/gluten (29%), artificial sweeteners (17%), refined sugar (13%) and peanuts (12%). **The top five most troubling symptoms reported** were fatigue (70%), lightheadedness (60%), cognitive complaints/"brain fog" (52%), nausea/gastrointestinal complaints (43%), and palpitations (36%).

7. Researchers at Eastern Virginia Medical School compared the co-morbidities (other diagnoses) found in neuropathic POTS patients with those found in autonomic neuropathy patients who didn't have POTS. **10 of the 11 most common co-morbidities found in POTS and autonomic neuropathy patients were the same**, including migraines, CFS, fibromyalgia, IBS. 30% of the non-POTS autonomic neuropathy patients had diabetes and 46% had high cholesterol.

8. Researchers at Eastern Virginia Medical School found that repeating tilt tests on patients who had increased orthostatic tachycardia, but not enough to meet the 30 bpm adult diagnostic criteria for POTS, resulted in **48% of them being diagnosed with POTS on the second tilt, when the tilt test was extended to 30 minutes**. During the prolonged tilt, "patients who reached POTS criteria did so between the onset and 30 min of tilt, suggesting that tilting to a maximum of 30 min will diagnose the large majority of "late POTS" patients.

9. Mayo Clinic researchers reviewed the records of 92 adolescent POTS patients who had undergone a colonoscopy or endoscopy with anesthesia while at Mayo Clinic. **Post-procedure complications occurred in 19% of patients**, including increased pain, need for medication changes, ER visits, worsened POTS symptoms and headaches. They recommended a follow up visit be planned within 7 days after the procedure to minimize complications and avoid ER visits. They noted that significant post-procedure complications were not found in adult POTS patients in a prior study.

10. Mayo Clinic researchers sent follow up surveys to pediatric POTS patients who were seen at the Mayo Clinic between 2003 and 2010. **18.2% of those who responded reported a complete resolution of their POTS symptoms, while 52.8% reported persistent but improved symptoms. The remaining 29% had no improvement or worsened over time. Male patients were twice as likely to report recovery.** An evaluation of the **mental health of all of these patients was similar to the national norm.**

11. Researchers from the Medical College of Wisconsin evaluated co-morbidities in pediatric POTS and in patients who presented with POTS like symptoms who didn't meet the diagnostic criteria for POTS. **The co-morbidities were the same in both groups.** 90.5% had migraines, 21% had fibromyalgia and 29% had hypermobility. **The complaint of lightheadedness/dizziness did not predict which patients had POTS, which the authors suggest indicates the contribution of an afferent processing disturbance.**

12. Researchers at New York Medical College found that **cerebral blood flow decreased by 26% in patients who had been diagnosed with Chronic Fatigue Syndrome and POTS** upon being tilted upright, and that **cognitive functioning was reduced with increasing time being upright (orthostatic stress).**

## Non-POTS Research Highlights:

13. Researchers from the University of Texas-Houston studies nine families in which non-specific dysautonomia was present in multiple generations, and concluded that **dysautonomia in these families was inherited in an autosomal dominant pattern**. (Note: Autosomal Dominant means that it is a non-sex linked inheritance pattern, and you only have to get the bad gene from one parent to have the disease. A carrier of the bad gene will have the disease, and that person's children will have a 50% chance of inheriting the bad gene, and thus the disease. Children who do not have the bad gene will not get the disease, and will not pass it on to their offspring.).

14. Researchers at Harvard performed a 10 year follow up with patients who had Orthostatic Hypotension (blood pressure drop within 3 minutes of tilt) and Delayed Orthostatic Hypotension (blood pressure drop after 3 minutes). Over a 10 year period of time, 60 % of the OH patients had died. The underlying causes of the OH in the patients who died were diabetes and synucleinopathies (such as MSA, Parkinson's, and other degenerative brain diseases). Of the OH patients who were still alive at the 10 year mark, 6 were diagnosed with Pure Autonomic Failure, 4 with Parkinson's, 5 with diabetes and 2 with cardiac disease. **More than half of the patients who had initially been diagnosed with Delayed OH were later diagnosed with OH within the 3 minute window.** Those who did not progress from Delayed OH to OH were generally younger. 27% of the patients originally diagnosed with Delayed OH died over the 10 years window (from diabetes, synucleinopathies and cardiac disease). **“These findings suggest that Delayed OH is part of the continuum of patients with autonomic dysfunction, and carries significant long term risks. These findings highlight the importance of autonomic testing in long term outcome data.”**

15. Researchers at the University of Massachusetts **identified 18 cytokines (inflammatory markers) that are elevated in MSA patients**, indicating the potential for drugs that alter the immune system as a potential treatment too. The researchers conducted a small trial of Intravenous Immunoglobulin (IVIG) on seven MSA patients to evaluate the safety and preliminary efficacy of IVIG in MSA patients, to assist with the development of future research studies. There were no serious adverse events. **Both the activities of daily living and motor functions improved significantly after treatment with 8 months of IVIG.** Future studies need to be conducted to further evaluate IVIG as a potential therapeutic tool for MSA.

All abstracts summarized were published in Clinical Autonomic Research (2013) 23:225-288. Abstract authors are as follows:

1. Autoimmune basis for postural tachycardia syndrome (POTS)  
D.C. Kem, H. Li, X. Yu, L.E. Okamoto, S.R. Raj Oklahoma University Health Sciences Center and VAMC, Oklahoma City, OK, USA and Vanderbilt University and VAMC, Nashville, TN, USA
2. The effect of acute volume loading with saline on exercise capacity in postural tachycardia syndrome  
R.A. Figueroa, A.C. Arnold, L.E. Okamoto, A. Diedrich, S.Y. Paranjape, B.K. Black, V.C. Nwazue, I. Biaggioni, S.R. Raj, A. Gamboa Department of Medicine, Division of Clinical Pharmacology, Vanderbilt University, Nashville, TN, USA
3. Postural hyperpnea causes hyperadrenergic POTS  
J.M. Stewart, C.E. Schwartz, A. Del Pozzi, M.S. Medow Department of Pediatrics, New York Medical College, Valhalla, NY, USA
4. Gastrointestinal dysmotility in postural tachycardia syndrome  
A. Loavenbruck, W. Singer, J. Itturino, D.M. Sletten, P.A. Low, A.E. Bharucha Department of Neurology, Mayo Clinic, Rochester, MN, USA; Department of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA

5. Deconditioning in orthostatic intolerance: chicken or egg?

W. Singer, T.G. Allison, P. Sandroni<sup>1</sup>, P.A. Low Department of Neurology and Cardiology, Mayo Clinic, Rochester, MN, USA

6. Risk factors for postural tachycardia syndrome in adolescents and young adults

A.J. Ross, J.M. Stewart, M.S. Medow, P.C. Rowe Department of Behavioral Biology, Johns Hopkins University, Baltimore, MD, USA; Departments of Pediatrics and Physiology, New York Medical College, Valhalla, NY, USA; Department of Pediatrics, Johns Hopkins School of Medicine, Baltimore, MD, USA

7. A comparison of the co-morbidities of neuropathic postural orthostatic tachycardia syndrome and autonomic neuropathies

K. McNeeley, K.R. Chémali Department of Neurology, Eastern Virginia Medical School, Sentara Healthcare, Norfolk, VA, USA

8. Repeating and prolonging the tilt table test help confirm the diagnosis of postural orthostatic tachycardia syndrome (POTS)

K.R. Chémali, K. McNeeley Department of Neurology, Eastern Virginia Medical School, Sentara Healthcare, Norfolk, VA, USA

9. Post-procedural complications after anesthesia in adolescents with postural orthostatic tachycardia syndrome

J. Bartlotti Telesz, R.M. Antiel, D.D. Joyce, P.R. Fischer, K.J. Grim Departments of Anesthesiology, General Surgery, and Pediatric and Adolescent Medicine, Mayo Clinic, Rochester MN, USA

10. Long-term outcomes of adolescent-onset postural orthostatic tachycardia syndrome

S.J. Kizilbash, S.P. Ahrens, R. Bhatia, J.M. Killian, S.A. Kimmes, E.E. Knoebel, P. Muppa, A.L. Weaver, P.R. Fischer Mayo Clinic Children's Center, Rochester, MN, USA

11. The co-morbidities of pediatric POTS: will the real "POTS" please stand up?

K. Kovacic<sup>1</sup>, T.C. Chelimsky, A. Rozmarynowski, M. Sood, P. Simpson, M. Nugent, G. Chelimsky Department of Pediatric Neurogastroenterology, Motility and Autonomic Disorders, Division of Pediatric Gastroenterology, Medical College of Wisconsin, Milwaukee, WI, USA; Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, USA; Department of Pediatrics, Division of Quantitative Health Sciences, Medical College of Wisconsin, Milwaukee, WI, USA

12. Cerebral blood flow regulation and orthostasis in chronic fatigue syndrome

M.S. Medow, S. Sood, Z. Messer, S. Dzogbeta, J.M. Stewart Department of Pediatrics, New York Medical College, Valhalla, NY, USA

13. Dysautonomia in young adolescents and their families has a dominant inheritance pattern

R.E. Martinez, I.J. Butler<sup>1</sup>, J.E. Lankford, M.T. Numan Department of Pediatric Neurology, University of Texas-Houston, TX, USA; Department of Pediatric Cardiology, University of Texas- Houston, TX, USA

14. Delayed orthostatic hypotension: long term consequences and follow up

C.H. Gibbons, R. Freeman Department of Neurology, Harvard Medical School Beth Israel Deaconess Medical Center, Boston, MA, USA

15. Inflammatory mechanisms and preliminary study of IVIG in MSA

P. Novak, University of Massachusetts Medical School, Worcester, MA, USA

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