DYSAUTONOMIA INTERNATIONAL

AWARENESS ADVOCACY ADVANCEMENT

New York Regional Office (Main)
Post Office Box 596
East Moriches, NY 11940

Washington, D.C. Regional Office
6151 Executive Boulevard
Rockville, MD 20852-3901

July 15, 2017

Walter Koroshetz, MD
Director, National Institutes of
Neurological Disorders and Stroke
P.O. Box 5801
Bethesda, MD 20824

Re: Postural Tachycardia Syndrome Research

Dear Dr. Koroshetz,

Thank you very much for agreeing to speak at Dysautonomia International's 5th Annual Conference. We are truly honored to have you join us to help kick-off our conference weekend.

We have prepared this letter to provide you with a summary of our patient community's perspectives regarding NIH funding for postural orthostatic tachycardia syndrome (POTS) research. We hope that this weekend will be the first step in an ongoing dialogue about what we can do to advance the pace of POTS research and bring new and more effective therapies to our patient community.

Our Organization's Focus

Dysautonomia International advocates for individuals with autonomic nervous system disorders, including POTS, neurocardiogenic syncope, pure autonomic failure, multiple system atrophy, neurogenic orthostatic hypotension, autoimmune autonomic ganglionopathy, dopamine beta-hydroxylase deficiency, post-TBI autonomic dysfunction, and autonomic neuropathies of any origin. We provide physician education programs, public awareness, and patient support for all of these conditions, but our research efforts have been focused on POTS to date.

Key Facts About POTS

According to Mayo Clinic and Vanderbilt estimates, POTS impacts an estimated 1-3 million Americans, and 90% of patients are female. Approximately half of POTS patients experience an onset of symptoms during adolescence (peak age of onset at 14), and half experience an onset in adulthood (most before age 50). Half of patients develop POTS shortly after an infection, 10% after a concussion, and lesser percentages report onset after pregnancy, surgery, anesthesia, bodily injuries, vaccination and significant blood loss. There are some POTS patients who have a more insidious onset, often in association with Ehlers-Danlos syndrome.

The disability seen in POTS is similar to what is seen in congestive heart failure and COPD, and the quality of life POTS patients experience is similar to what patients with end stage kidney disease experience. Half of adult POTS patients are unable to work. Of those who are employed, 67% would work more hours if not for their POTS symptoms. 21% have lost a job due to POTS. One-third of POTS patients have applied for social security disability, and 62% of those who apply are approved.

While doctors are fond of telling adolescent onset patients that “everyone grows out of it in five years,” we now have the first longitudinal data from Mayo Clinic showing that this is false. Five years after their visit to Mayo Clinic, only 19% of adolescent POTS patients report “recovery” from POTS, and within that 19%, some patients were still using POTS treatments like beta-blockers and a high salt/fluid diet. Some adolescent onset patients experience a period of sustained improvement as they reach adulthood, only to develop POTS again later in life after a pregnancy, surgery, infection, etc. Adult onset patients appear to be less likely to experience improvement than adolescent onset patients, but we do not have data on this yet.

There are no FDA approved treatments for POTS, and the off-label treatments that are used are not very effective for the majority of patients. One prominent autonomic neurologist tells us that he considers it a success if his patients get back to 60% of their pre-POTS functioning, but even with optimized pharma and non-pharma treatment, the majority of patients do not reach that goal.

Misdiagnosis is common, with 77% of patients being told their symptoms are “all in their head” prior to POTS diagnosis, despite data from Mayo Clinic and Vanderbilt showing that POTS patients have psychological profiles similar to national norms. Misdiagnosis and lack of physician awareness contributes to an average diagnostic delay of 4 years.

Far from being “all in their head,” 50% of POTS patients have an objectively verifiable sudomotor neuropathy and 20% have reduced cardiac MIBG uptake, which correlates to the severity of the small fiber neuropathy. Recent research at Harvard’s autonomic lab has identified a vasomotor neuropathy even in POTS patients who don’t have a sudomotor deficit, and over 80% of patients report burning, numbness and tingling in the limbs, suggesting that the small fiber deficit also includes somatic fibers.

While POTS is considered heterogeneous, recent research suggests that a sizeable portion of POTS patients may have an autoimmune condition causing or contributing to their symptoms. An assortment of neural receptor antibodies of have been identified in POTS by the University of Oklahoma (alpha and beta adrenergic and muscarinic receptor antibodies), University of Texas Southwestern (muscarinic 1-3 receptor antibodies), Mayo Clinic (thyroid and assorted neural receptor antibodies). 20% of POTS patients have an established autoimmune disease, most commonly Hashimoto’s, Sjogren’s and Celiac (Sjogren’s and celiac are the #2 and #3 causes of autonomic neuropathy). Pilot investigations are underway using immunotherapy, and early results look very promising. Mayo Clinic recently published a case series on patients with POTS and Sjogren’s, and those who had follow-up after IVIG showed dramatic improvement or complete resolution of POTS symptoms. A retrospective case series is being presented during our conference this weekend by University of Colorado – 56 of 60 POTS patients with co-morbid Sjogren’s or antiphospholipid syndrome who received IVIG responded with dramatic improvement autonomic symptoms and overall functioning.

NIH Investment in POTS Research

We reviewed the online NIH rePORTER database to identify POTS research funding between FY2012 and FY2017. **NIH funded only four POTS studies in the past five years**, with an average annual investment of $679,196. Only one of the grants came from NINDS, a Mayo Clinic grant averaging $174,030 per year. Other funding came from NHLBI.

NIH funded eight other studies that mention POTS in the grant summary between FY2012 and FY2017, but these are not really POTS-focused grants. For example, one was a study on mastocytosis. Mastocytosis is an extremely uncommon co-morbidity in POTS, so this study is unlikely to provide meaningful information on the POTS population.

We realize that every patient organization approaches NIH claiming their disease is not receiving enough funding, but we doubt there is any other disease that impacts 1-3 million Americans, results in a quality-of-life similar to COPD and congestive heart failure, leaves half of its patients unable to work, and only receives $679,196 a year from NIH. I have attached a spreadsheet with the NIH reporter data, as well as two charts providing funding comparisons between POTS and comparable diseases for FY 2016.

We also realize that NIH can only fund what researchers apply for. We asked the autonomic researchers whether they had applied for other NIH POTS grants that were not funded. They said yes. They also said that the fact that POTS does not have a "home" institute at NIH means no one is really focused on it, and that NINDS has rejected most of their POTS applications, which is why they apply to NHLBI, despite the fact that POTS is very clearly a neurological disorder. They also raised concerns that the program managers and grant reviewers, like the majority of physicians in the US, don't have enough expertise in autonomic disorders or familiarity with what's going on in the field to provide an informed review of their applications. One of the autonomic researchers said he intentionally doesn't mention POTS in his NIH applications because that increases the chances of rejection, since many reviewers incorrectly believe that POTS is a mild teenaged psychosomatic problem that self-resolves.

Our Next Steps

Our purpose in writing this letter is not to complain, but to let you know of the dire situation our patients are facing, and to ask what resources NIH can leverage to accelerate the pace of meaningful POTS research, to help us find effective treatments and improved diagnostics.

Can we set up an working group or coordinating committee at NIH to identify POTS research needs, establish priorities, and eventually secure dedicated funding for an RFA, similar to what has been done recently with chronic fatigue syndrome?

We would also like to know what we can do to improve the understanding of POTS amongst program staff and grant reviewers. Does NIH offer in-house Grand Rounds or CME programs for staff? Can we work with you to plan a POTS symposium at NIH to increase the profile and understanding of POTS amongst NIH staff? Are there standing review committees likely to review POTS related grants that we can send POTS education materials to, or invite to educational programs?

Last, but not least, we would like to see some intramural NIH research dedicated to POTS. Dr. David Goldstein runs an autonomic lab at NINDS. He used to do POTS research, but has focused on autonomic failure/Parkinson's related catecholamine research for the past few years. Can NIH support a fellow or a research assistant dedicated to POTS research working under Dr. Goldstein's supervision? Are there others at NINDS or elsewhere who may have an interest in POTS that can be expanded upon?

We welcome any other ideas you may have on how to increase the pace of research to deliver improved treatment options and diagnostics to the millions of Americans living with POTS.

Thank you very much for your time this weekend and your consideration of these issues.

Sincerely,

Lauren Stiles, JD
President & Co-Founder
Dysautonomia International

Encs.