

## Care of the Patient with Electrophysiological Abnormalities

### Postural orthostatic tachycardia syndrome: Diagnosis and treatment

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#### ABSTRACT

**BACKGROUND:** Postural orthostatic tachycardia syndrome (POTS) is an autonomic disorder characterized by an exaggerated increase in heart rate that occurs during standing, without orthostatic hypotension. Women are most frequently affected, and may present with palpitations, chest discomfort, shortness of breath, weakness, exercise intolerance, lightheadedness, presyncope, and syncope.

**METHODS:** We present three cases of POTS in otherwise healthy women, and discuss the clinical management of different types of this orthostatic intolerance.

**RESULTS AND CONCLUSION:** The diagnosis was established with a tilt-table test in 1 patient who became symptom-free with  $\beta$ -blockade and nonpharmacologic treatment, including fluid therapy, liberal sodium intake, support hose, and a reconditioning exercise program. The other 2 were diagnosed through a standing test, serum norepinephrine levels, and red-cell volumes. One patient had neuropathic POTS and partially responded to  $\beta$ -blockade and non-pharmacotherapy. The other patient had hyperadrenergic POTS and responded well to nonpharmacotherapy, a dualacting  $\beta$ -blocker, and a vasoconstrictor agent. Postural orthostatic tachycardia syndrome is not an uncommon clinical entity and making a correct diagnosis is crucial in providing appropriate treatment to restore patients' functional capability and quality of life.

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Postural orthostatic tachycardia syndrome (POTS) is a form of orthostatic intolerance characterized by orthostatic tachycardia in the absence of hypotension.<sup>1-4</sup> Patients with POTS manifest either an increased heart rate (HR) of  $\geq 30$  beats per minute (bpm) above their supine HR, or a persistent standing HR of  $> 120$  bpm. Postural orthostatic tachycardia syndrome represents

a heterogeneous group of autonomic disorders with similar clinical characteristics.<sup>1,3,4</sup> Patients may experience palpitations, chest discomfort, shortness of breath, weakness, exercise intolerance, lightheadedness, presyncope, syncope, and other symptoms related to selective peripheral autonomic dysfunction.<sup>1-4</sup> This clinical disorder is not new and was previously referred

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to as mitral valve prolapse syndrome, neurocirculatory asthenia, orthostatic tachycardia, or orthostatic intolerance.<sup>3,5</sup> More recently, this clinical entity was referred to as POTS because of its underlying characteristic autonomic dysfunction.<sup>3</sup>

## EPIDEMIOLOGY

Approximately 500,000 patients in the United States suffer from POTS, and 25% of them are disabled and unable to work.<sup>1,3,6</sup> Most patients are women between the ages of 20 and 50 years, with a female predominance of 5:1.<sup>1,4,7</sup> The reason for this female predominance is unknown, but may be related to the greater susceptibility of women to orthostatic intolerance.<sup>8,9</sup> Postural orthostatic tachycardia syndrome is not an uncommon clinical entity, although it is frequently under-recognized, and patients with POTS are often misdiagnosed with severe anxiety or panic disorders.<sup>1,3</sup> Effective treatment options are available, and establishing a correct diagnosis is crucial in providing appropriate treatment to restore patients' functional capability and quality of life.<sup>1,3</sup>

## ETIOLOGY

Postural orthostatic tachycardia syndrome is attributed to autonomic failure in response to standing, without orthostatic hypotension. The underlying pathophysiology of POTS involves patchy, sympathetic denervation in the lower extremities and kidneys, which causes orthostatic venous pooling and relative hypovolemia.<sup>1,3,10</sup> Cerebral and cardiac sympathetic innervations remain intact.<sup>1,3</sup> The compensatory increase in cerebral sympathetic outflow leads to elevated norepinephrine (NE) levels, which result in an increase in HR, myocardial contractility, and the characteristic POTS symptoms of palpitations and lightheadedness.<sup>1,3</sup> Evidence for partial dysautonomia includes abnormal thermoregulatory sweat and sudomotor reflex test results in the presence of intact autonomic adrenergic reflexes, which were demonstrated in more than 50% of patients diagnosed with POTS.<sup>4</sup> Postural orthostatic tachycardia syndrome can be primary or secondary.<sup>1,3</sup> The primary form is often idiopathic, and is categorized as neuropathic or hyperadrenergic. Neuropathic POTS is the most common primary form, and is usually precipitated by a febrile illness, sepsis, pregnancy, surgery, or trauma.<sup>1,3,4</sup> The sympathetic response is not excessive, and serum NE levels may be high normal or slightly elevated.<sup>4</sup> Some patients with neuropathic POTS may demonstrate a mild decrease in standing BP (<20/10 mm Hg) in addition to orthostatic tachycardia.<sup>1</sup> The ganglionic acetylcholine receptor antibody is present in a substantial percentage of patients with neuropathic POTS, indicating a possible autoimmune etiology in some cases.<sup>4</sup>

In hyperadrenergic POTS, the underlying pathophysiology involves excessive cerebral sympathetic outflow, mostly with patchy, peripheral sympathetic denervation, leading to a markedly elevated standing NE level (>600 pg/mL, and frequently >1000 pg/mL).<sup>1,3,4</sup> Isolated, excessive sympathetic discharge was documented in some patients.<sup>3,4</sup> Patients with hyperadrenergic POTS sometimes exhibit elevated standing BP, and more than 50% may also suffer from migraine headaches.<sup>1</sup> Hyperadrenergic POTS is less common and has a more insidious course than the neuropathic type.<sup>3,4</sup> This type of POTS is usually idiopathic, but it may be genetically linked and may be present in more than 1 family member.<sup>3,7</sup> A point mutation in NE transport was documented in these patients, leading to excessively high serum NE levels because of a diminished clearance of NE.<sup>7</sup>

The secondary form of POTS occurs in association with a variety of other medical illnesses, such as diabetes mellitus, amyloidosis, sarcoidosis, alcoholism, lupus, Sjögren syndrome, chemotherapy, paraneoplastic syndrome, multisystem atrophy, or heavy metal poisoning.<sup>1,4</sup> Prolonged bed rest and medications that impair autonomic regulation or NE levels (vasodilators, diuretics, antidepressants, anxiolytic agents, or central  $\alpha$ -2 agonists) may also cause a secondary form of POTS.<sup>1,3</sup>

## PRESENTATION

Patients with POTS may experience a combination of symptoms related to autonomic hyperactivity, cerebral hypoperfusion, and dysautonomia.<sup>1–4</sup> More than 50% of patients present with palpitations, lightheadedness, presyncope, exercise intolerance, and weakness.<sup>4</sup> These symptoms can lead to a high degree of functional disability, and some patients can only achieve symptom relief with recumbence.<sup>4,11</sup> Other less common symptoms include acrocyanosis, fatigue, chest discomfort, shortness of breath, abdominal bloating, nausea, sleep disturbances, tremulousness, and syncope.<sup>3,4</sup> Some patients may also experience various symptoms of autonomic dysfunction, such as disturbances in sweating or thermoregulation, and bowel or bladder dysfunction.<sup>1,3,4</sup> The onset of the symptoms of POTS may be acute or insidious, and can be precipitated by an acute medical illness.<sup>3,4</sup> Postural orthostatic tachycardia syndrome is also associated with a seemingly unrelated group of disorders including migraine headache, joint hypermobility, irritable bowel syndrome, autoimmune disease, and abnormalities of sudomotor regulation.<sup>3,4,12</sup>

## DIAGNOSIS

The initial evaluation involves a detailed history and physical examination, with a particular focus on the onset and duration of symptoms, precipitating events,

any family history of similar problems, and medical illnesses known to be associated with primary or secondary POTS.<sup>1</sup> Postural orthostatic tachycardia syndrome is considered a chronic disease, and many authors specify that the symptoms be present for more than 3 months, whereas others propose even a longer duration of illness.<sup>1,3,4</sup> Both HR and BP should be measured in supine and standing positions.

The diagnosis of POTS may be established with a standing test in the office or at bedside, or with a tilt-table test in a hospital facility.<sup>1–3</sup> In the standing test, HR and BP are obtained at 2, 5, and 10 minutes after the patient assumes a supine position, and at 2, 5, and 10 minutes after standing.<sup>1</sup> Tilt-table testing is normally performed in patients with suspected neurally mediated or orthostatic syncope, but it may also be used to diagnose POTS.<sup>1–3,13</sup> Patients are secured to a tilt table, and HR and BP are monitored every 2 minutes for 10 minutes. Patients are then tilted upward at angles between 60° and 80° for 30 to 60 minutes, with regular monitoring of clinical response, HR, and BP.<sup>13</sup> The test is considered positive for POTS if the patient develops orthostatic tachycardia associated with symptoms similar to those of spontaneous POTS in the absence of orthostatic hypotension.<sup>1,2,4</sup> Both tilt-table and standing tests are sensitive for the diagnosis of POTS. Tilt-table testing provides a more controlled setting, with fewer variables in HR and BP.<sup>1,3,4</sup> The standing test has a higher specificity because patients use their skeletal muscles for standing and balancing, which is more physiologic than passive standing during tilt-table testing.<sup>1,3,4,14</sup>

Supine and standing serum NE levels should be obtained because they may have both diagnostic and therapeutic implications.<sup>1,3,4</sup> Samples are obtained 15 minutes after the patient assumes a supine position, and 15 minutes after the patient assumes an upright position.<sup>3</sup> Most patients with POTS have increased standing NE levels. A NE level of >600 pg/mL was proposed as 1 of the diagnostic criteria.<sup>3,4,9,15</sup> However, standing NE levels are not always consistent, and may vary widely. Some studies reported markedly increased levels of NE (>1000 pg/mL), whereas others found only mildly elevated levels (>400 pg/mL).<sup>4,15</sup> In fact, some patients may have normal or low standing levels of NE (<400 pg/mL).<sup>4</sup> No relationship is evident between levels of NE and symptoms of POTS, and a low or normal level of NE does not rule out the diagnosis.<sup>4</sup> A high standing level of NE (>600 pg/mL) simply identifies patients with hyperadrenergic POTS, and predicts their responses to  $\beta$ -blockade.<sup>1,4</sup> Certain medications commonly used to treat patients with POTS, such as  $\beta$ -blockers, may increase levels of serum NE, and their effect on catecholamine levels in these patients has not been addressed in the literature.<sup>1,3,4,16</sup>

The assessment of intravascular volume may be performed in these patients by measuring plasma or red cell volume (RCV). Patients who have a low RCV indicative of low intravascular volume may benefit from volume expansion therapy.<sup>3,17,18</sup> A determination

of levels for NE and RCV may have to be specifically requested, because they are not routinely measured during tilt-table testing in most facilities.

## TREATMENT

Educating the patient about the chronic nature of the disease and about avoidance of aggravating factors, such as dehydration or extreme heat, is important.<sup>3,4</sup> The patient may be instructed to rise slowly, in stages, from supine to seated and to standing positions. Any medication that could worsen the symptoms should be discontinued, such as vasodilators, diuretics, antidepressants, anxiolytic agents, central  $\alpha$ -2 agonists, and over-the-counter products that contain ephedrine or pseudoephedrine.<sup>1,3</sup> The consumption of alcohol should be discouraged, because it may worsen symptoms.<sup>1</sup> The treatment of POTS may consist of nonpharmacologic and pharmacologic corrections of autonomic imbalance and hypovolemia (Table 1).<sup>1,3,4</sup> Treatment strategies should be individualized according to the appropriate subtype of POTS and the patient's responses.<sup>1,3</sup>

## NONPHARMACOTHERAPY

Nonpharmacologic treatment focuses on increasing intravascular volume with either oral or intravenous fluid or dietary sodium. An oral fluid intake of 2 L and a sodium intake of 3–5 g per day should be encouraged.<sup>1,3</sup> Acute blood volume expansion with an infusion of 1 L of physiologic saline over 1–3 hours is effective in decreasing orthostatic tachycardia and rapidly improving other symptoms of POTS.<sup>19</sup> However, this is not practical on a day to day basis, because this treatment requires the insertion of an intravenous catheter and a medical facility for saline infusion.<sup>3</sup> Support hose may be used to increase venous return. The most effective kinds of support hose are waist-high, and provide at least 30 to 40 mm Hg of ankle counterpressure.<sup>1,3</sup> Routine exercise with aerobic activity and gentle resistance training of the abdomen and lower extremities may be beneficial in expanding blood volume and improving lower extremity and abdominal vascular tone.<sup>3,20</sup> The majority of patients (92.5%) in 1 study reported using volume expanders, whereas over two thirds (71.0%) included resistance training in their treatment regimen, and only 10.7% wore support hose.<sup>4</sup>

## Pharmacotherapy

Some patients require pharmacotherapy because of severe symptoms. The initial goal of treatment is to stabilize patients so that they can begin a reconditioning exercise program.<sup>1</sup> No drug has been approved by

**Table 1 – Nonpharmacotherapy and pharmacotherapy for postural orthostatic tachycardia syndrome**

Agent	Dose	Effective in	Side effects
<b>Nonpharmacotherapy</b>			
Reconditioning training	Aerobic exercise 20 minutes, 3 times/week Resistance training of abdomen/lower extremities	N, H N, H	If too vigorous, may worsen symptoms
Fluid therapy	2 L/day	N, H	Edema, hyponatremia
Increase in dietary salt/Na salt tablets	2-4 g/day, 1 tablet (1 g) orally three times daily	N	Difficult to augment/poor taste, dyspepsia, nausea, edema
Elastic support hose (waist high)	30-40 mm Hg counterpressure	N, H	Uncomfortable, hot, itchy
Parenteral fluid therapy	1 L over 1-3 hours, every 1-2 days	N, H	Edema, inconvenience, medical setting needed
<b>Pharmacotherapy</b>			
<i>Volume expander</i>			
Fludrocortisone acetate	.1-.2 mg orally every day	N	Hypokalemia, hypomagnesemia, edema, hypertension, headache
Desmopressin acetate	.1-.2 mg orally at every bedtime	N	Hyponatremia, edema, headache
Erythropoietin (Epogen, Procrit)	10,000-20,000 U SC/week	N	Pain at injection site, expensive
<i>Beta-adrenergic receptor antagonist or <math>\beta</math>-blocker</i>			
Atenolol (Tenormin)	25-50 mg orally twice daily	N	Hypotension, fatigue, drowsiness, wheezing, insomnia
Propranolol (Inderal)	10-20 mg orally twice daily or four times daily	N	Hypotension, fatigue, drowsiness, wheezing, insomnia
<i>Beta/alpha adrenergic receptor antagonist or dual-acting <math>\beta</math>-blocker</i>			
Carvedilol (Coreg)	3.125-6.25 mg orally twice daily	H	Fatigue, dizziness, headache
Labetalol HCl (Trandate, Normodyne)	100-200 mg twice daily	H	Fatigue, dizziness
<i>Sympatholytic agent</i>			
Clonidine HCl (Catapres) or $\alpha$ -2 adrenergic receptor agonist	.1-.3 mg orally twice daily; .1-.3 mg patch/week	H	Dry mouth, blurred vision, drowsiness, constipation, fatigue
Methyldopa (false neurotransmitter)	125-250 mg orally three times daily	H	Hypotension, drowsiness, headache, constipation
<i>Alpha-1 adrenergic receptor agonist</i>			
Midodrine (Proamatine)	5-10 mg orally three times daily	N	Nausea, itching scalp, supine hypertension
<i>Acetylcholinesterase inhibitor</i>			
Pyridostigmine bromide (Mestinon)	30-60 mg orally every day	N	Nausea, diarrhea
<i>SSRI</i>			
Escitalopram oxalate (Lexapro)	10 mg orally every day	N, H	Tremor, agitation, sexual problems
<i>SSNRI</i>			
Duloxetine HCl (Cymbalta)	20-30 mg orally every day	N, H	Nausea, sleep disturbance
Venlafaxine HCl (Effexor)	75 mg orally every day or twice daily	N, H	Nausea, anorexia, tremor
<i>NDRI</i>			
Bupropion (Wellbutrin XL)	150-300 mg orally every day	N, H	Tremor, agitation, insomnia

H, hyperadrenergic POTS; HCL, hydrochloride; N, neuropathic POTS; NDRI, norepinephrine-dopamine reuptake inhibitor; SC, subcutaneous; SSRI, selective serotonin reuptake inhibitor; SSNRI, selective serotonin norepinephrine reuptake inhibitor.

the United States Food and Drug Administration for the treatment of POTS, and all currently used medications are “off-label.”<sup>1,3,4</sup> Treatment strategies have resulted in varying degrees of success, and often require combination therapy.<sup>21</sup> Patients with neuropathic POTS may respond favorably to volume expanders (fludrocortisone or oral vasopressin), vasoconstrictors ( $\alpha$ -1 adrenergic receptor agonist), or agents that prevent an elevated HR in response to standing (a  $\beta$ -blocker or acetylcholinesterase inhibitor).<sup>1,3,4</sup> Erythropoietin was used successfully in a few patients.<sup>1</sup> A combined  $\beta$ -blocker and  $\alpha$ -blocker (dual-acting  $\beta$ -blocker) may be more effective than a pure  $\beta$ -blocker in patients with hyperadrenergic POTS.<sup>1,4</sup> Some of these patients may respond better to central sympatholytic agents such as clonidine or methyl dopa.<sup>1,3,4</sup> Selective serotonin (SSRI), serotonin-norepinephrine, and norepinephrine-dopamine reuptake inhibitors have provided symptom relief in selected patients with both neuropathic and hyperadrenergic POTS.<sup>1-4</sup>

A  $\beta$ -blocker is the most commonly prescribed medication for the treatment of POTS (76.7%), and approximately 30% to 50% of patients have used either an SSRI, pharmacologic volume expander, or  $\alpha$ -1 adrenergic receptor agonist in their treatment regimen.<sup>4</sup> Other pharmacologic agents are used sparingly ( $\leq 10\%$ ) in combination therapy, mostly in patients who do not respond well to more commonly used medications.<sup>4</sup>

## PROGNOSIS

Information on the prognosis of POTS is limited, and the course of this illness is variable.<sup>1</sup> Approximately 40% to 90% of patients may respond to a combination of nonpharmacotherapy and pharmacotherapy.<sup>1,3,4</sup> Younger patients respond better to treatment, and recovery from postviral POTS usually occurs in 2 to 5 years.<sup>1</sup> Some patients manifest progressive symptoms, and those with hyperadrenergic POTS may require therapy indefinitely.<sup>1</sup>

## CASE REPORT

### Case 1

K.H. is an 18-year-old woman with a 6-month history of a fast heart rate associated with anxiety, sweating, and shortness of breath. Her symptoms usually lasted about 10 minutes, but reoccurred several times on a given day. The patient did not recall any precipitating medical illness.

K.H. had a normal BP of 120/60 mm Hg, a HR of 88 bpm, a systolic murmur, and frequent sinus tachycardia, with a HR as high as 190 bpm on a 24-hour Holter monitor. Tilt-table testing was positive for POTS, with a supine HR of 87 bpm, increasing to a tilt HR of

141 bpm, associated with near syncope, nausea, and vomiting, and without evidence of orthostatic hypotension. Levels of NE and RCV were not obtained. The patient responded to a treatment regimen that included Metoprolol extended-release tablets (25 mg daily) and nonpharmacotherapy (fluid therapy and liberal sodium intake) to increase intravascular volume, support hose, and a routine exercise program with aerobic exercise and resistance training of the lower extremities and abdomen. The patient has remained symptom-free for 18 months.

### Case 2

S.K. is a 19-year-old woman who presented with a 4-year history of dizziness and persistent rapid heartbeats  $>120$  bpm during exercise (while cheerleading in high school). She had been self-medicating with her father's  $\beta$ -blocker. Since graduation, she no longer engaged in cheerleading, but continued to experience intermittent palpitations associated with chest discomfort, dizziness, weakness, anxiety, diaphoresis, insomnia, diarrhea, and a feeling of “losing control.” These symptoms had become much worse after an induced abortion 7 months earlier, and she was having difficulty keeping up with her daily routine, despite the continued use of her father's  $\beta$ -blocker.

S.K. had a BP of 102/60 mm Hg, a pulse of 98 bpm, normal results of a cardiac examination, and frequent sinus tachycardia on a 24-hour Holter monitor. A standing test for POTS was positive, with supine and standing HRs of 82 and 114 bpm (HR increase of 32 bpm), respectively, and associated palpitations, dizziness, weakness, and cold in her extremities. No orthostatic hypotension was evident. The patient demonstrated a normal supine NE level (129 pg/mL) and a mildly elevated standing NE level (400 pg/mL), with a subnormal RCV (21 mL/kg). The patient partially responded to medical treatment that included atenolol (12.5 mg daily), nonpharmacologic therapy to increase intravascular volume, support hose, and routine aerobic exercise and resistance training of her lower extremities and abdomen. The patient manifested fewer symptoms, with occasional palpitations, and has been able to function adequately for 12 months.

### Case 3

L.K. is a 41-year-old woman with a 7-month history of palpitations followed by brief chest discomfort, fatigue, diaphoresis, and nausea, which became worse upon standing. L.K. had a BP of 144/92 mm Hg, sinus tachycardia (120 bpm), a systolic murmur, and frequent sinus tachycardia on 24-hour Holter monitoring. A standing test for POTS was positive, with an increase in standing HR of 38 bpm above her supine HR (141 versus 103 bpm, respectively), which was persistently  $>120$  bpm and associated with palpitations, lightheadedness, and weakness. No orthostatic

hypotension was evident, and supine and standing levels of NE were markedly elevated (513 and 862 pg/mL, respectively). The patient also manifested decreased RCV (18 mL/kg), indicating a low intravascular volume. L.K. was initially treated with a dual-acting  $\beta$ -blocker (carvedilol, 3.125 mg daily) and non-pharmacotherapy to increase her intravascular volume, support hose, and a routine aerobic and resistance exercise program. She demonstrated residual fatigability without any other symptoms, and subsequently received a vasoconstrictor agent (midodrine, 10 mg three times daily) 6 months ago, with good response.

## DISCUSSION

Three cases of POTS are presented to demonstrate clinical presentations, diagnostic approaches, classification, and treatment strategies. All 3 patients had orthostatic tachycardia and other symptoms of POTS for longer than 3 months, without any apparent precipitating events, except for Case 2 (S.K.). This patient (S.K.) may have been suffering from a mild form of POTS with only palpitations for the past 4 years, and began experiencing other symptoms when she stopped her cheerleading activity. A recent aborted pregnancy probably worsened her symptoms. Tilt-table testing without measuring NE levels or RCV was used for the diagnosis of Case 1 (K.H.). This patient most likely had neuropathic POTS, because she became asymptomatic with nonpharmacologic treatment and a pure  $\beta$ -blocker. The other 2 women were diagnosed with a standing test, NE levels, and RCVs. Both suffered from similar symptoms despite varying levels of NE. One patient (S.K.) had a normal supine and mildly elevated upright level of NE, consistent with neuropathic POTS. All of her symptoms, except for occasional palpitations, subsided with nonpharmacologic treatment and a low-dose  $\beta$ -blocker. The other patient (L.K.) had hyperadrenergic POTS, with markedly elevated standing levels of NE, and was free of symptoms with nonpharmacologic treatment, a dual-acting  $\beta$ -blocker, and a vasoconstrictor agent.

## CONCLUSIONS

Healthcare providers should be cognizant of POTS when treating young women who present with symptoms of orthostatic imbalance, particularly in the absence of orthostatic hypotension. Postural orthostatic tachycardia syndrome can be a chronic disease, and patients may present at either a physician's office or an emergency department because of worsening symptoms. The diagnosis may be confirmed with a standing or tilt-table test. Because of

the debilitating nature of the disease and its recurrent symptoms despite ongoing therapy, patients may feel discouraged and will benefit from both physical care and psychological support. Awareness of this syndrome is important in rendering the proper diagnosis and providing appropriate treatment for this autonomic disorder.

## REFERENCES

1. Grubb B. Postural tachycardia syndrome. *Circulation* 2008;117:2814-7.
2. Karas B, Grubb B, Boehm K, Kip K. The postural tachycardia syndrome: a potentially treatable cause of chronic fatigue, exercise intolerance and cognitive impairment. *Pacing Clin Electrophysiol* 2000;22:344-51.
3. Raj S. The postural tachycardia syndrome (POTS): pathophysiology, diagnosis and management. *Indian Pacing Electrophysiol J* 2006;6:84-99.
4. Thieben M, Sandroni P, Sletten D, et al. Postural tachycardia syndrome: the Mayo Clinic experience. *Mayo Clinic Proc* 2007;82:308-13.
5. Wieling W, Shepherd J. Initial and delayed circulatory responses to orthostatic stress in normal humans and in subjects with orthostatic intolerance. *Int Angiol* 1992;11:69-82.
6. Goldstein D, Robertson D, Esler M, Straus S, Eisenhofer G. Dysautonomias: clinical disorders of the autonomic nervous system. *Ann Intern Med* 2002;137: 753-63.
7. Shannon J, Flattum N, Jordan J, et al. Orthostatic intolerance and tachycardia associated with norepinephrine-transporter deficiency. *N Engl J Med* 2000;342:541-9.
8. Fu Q, Arbab-Zadeh A, Perhonen M, et al. Hemodynamics of orthostatic intolerance: implications for gender differences. *Am J Physiol Heart Circ Physiol* 2004;286:H449-57.
9. Shoemaker J, Hughson R, Sinoway L. Gender affects sympathetic neurovascular control during postural stress. In: Warmbein B, editor. Proceedings of "Life in Space for Life on Earth." 8th European Symposium on Life Sciences Research in Space. 23rd Annual International Gravitational Physiology Meeting, 2-7 June 2002, Karolinska Institutet, Stockholm, Sweden. Noordwijk, Netherlands: ESA Publications Division; 2002. p. 187-8.
10. Jacob G, Costa F, Shannon J, et al. The neuropathic postural tachycardia syndrome. *N Engl J Med* 2000; 343:1008-14.
11. Grubb B, Kosinski D, Boehm K, Kip K. The postural orthostatic tachycardia syndrome: a neurocardiogenic variant identified during head-up tilt table testing. *Pacing Clin Electrophysiol* 1997;20: 2205-12.
12. Gazit Y, Nahir A, Grahame R, Jacob G. Dysautonomia in the joint hypermobility syndrome. *Am J Med* 2003; 115:33-40.
13. Miller T, Kruse J. Evaluation of syncope. *Am Fam Phys* 2005;72:1492-500.
14. Raj S, Dzurik M, Biaggioni I, Black B, Paranjape S, Robertson D. Diagnosing postural tachycardia syndrome: comparison of tilt versus standing. *Circulation* 2005;112:U765.

15. Raj S, Black B, Biaggioni I, Harris P, Robertson D. Acetylcholinesterase inhibition improves tachycardia in postural tachycardia syndrome. *Circulation* 2005; 111:2734-40.
16. Fossum E, Olsen M, Høieggen A, et al. Long-term plasma catecholamines in patients with hypertension and left ventricular hypertrophy treated with losartan or atenolol: ICARUS, a LIFE substudy. *J Hum Hypertens* 2004;18:375-80.
17. Raj S, Biaggioni I, Yamhure P, et al. Renin-aldosterone paradox and perturbed blood volume regulation underlying postural tachycardia syndrome. *Circulation* 2005;111:1574-82.
18. Streeten D, Thomas D, Bell D. The roles of orthostatic hypotension, orthostatic tachycardia, and subnormal erythrocyte volume in the pathogenesis of the chronic fatigue syndrome. *Am J Med Sci* 2000;320:1-8.
19. Jacob G, Biaggioni I. Idiopathic orthostatic intolerance and postural tachycardia syndromes. *Am J Med Sci* 1999;317:88-101.
20. Winker R, Barth A, Bidmon D, et al. Endurance exercise training in orthostatic intolerance: a randomized, controlled trial. *Hypertension* 2005;45:391-8.
21. Medow M, Stewart J. The postural tachycardia syndrome. *Cardiol Rev* 2007;15:67-75.