Postural orthostatic tachycardia syndrome (POTS) is a clinically defined syndrome with many possible symptoms that relate to dysfunction of the autonomic nervous system. Although the syndrome has been known by the acronym POTS for the last few decades, it has probably also been described under other monikers, such as DaCosta syndrome, mitral valve prolapse syndrome, neurocirculatory asthenia, and chronic orthostatic intolerance.1 Neurologists are among the many medical specialists to whom people with POTS may present, making knowledge of this disorder important. The main symptoms of POTS are related to intolerance of upright posture (eg, standing, prolonged sitting). Light-headedness, palpitations, tremor, generalized weakness, blurred vision, exercise intolerance, and fatigue are the most common symptoms. Other common symptoms include headache, cognitive dysfunction (brain fog), gastrointestinal symptoms (eg, nausea, early satiety, and constipation), and sleep disturbances.2

**Epidemiology**

The prevalence of POTS is likely unknown, but current epidemiologic studies suggest that up to 1% of the US population may be affected. Onset is often between age 15 to 25 years, and more than 75% are in girls and women.3 Symptom onset can be insidious, occurring over months to years or may occur directly after illness (viral), surgery, injury, or concussion.

**Pathophysiology**

The pathophysiology of POTS is poorly understood. Although POTS is considered an autonomic disorder, it is likely related to multiple convergent physiologies resulting in the disparate symptoms. Theoretical POTS subtypes are discussed in the literature, but no definitive testing or evidence exists to confirm these entities. Individuals with the putative neuropathic subtype of POTS are considered to have some degree of small fiber and autonomic nerve dysfunction. In these individuals, venous pooling and limb temperature and color change are a common finding on exam. People with the putative hyperadrenergic subtype have an exaggerated cardiovascular response to standing that is thought to be caused by sympathetic overdrive. It is theorized that these individuals may have an enhanced beneficial reaction to beta blockers. The hypovolemic subtype includes an overall lower blood volume from postulated abnormalities in the renin-aldosterone system required for salt and water balance.

People with POTS have a higher incidence of autoimmune disease than the general population, including Sjogren syndrome, lupus, Hashimoto thyroiditis, celiac disease, and rheumatoid arthritis.4 An up to 10% occurrence of antibodies to the acetylcholine receptor ganglionic (G-AchR) antibody and other autoantibodies has been reported, although the titers are often very low, and the clinical significance of these antibodies remains unclear.4 In approximately 12.5% of cases, there is a family history of POTS symptoms, suggesting a genetic contribution to the disorder.3

**Diagnosis**

Consensus diagnostic criteria for POTS were developed by the American Rhythm Society in 2015 (Box).2 Diagnosis should be considered based on symptoms present, including an increase in heart rate of ≥30 beats per minute (bpm) when moving from lying to standing (or ≥40 bpm in individuals age 12-19 years); and the absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure). The standing heart rate of individuals with POTS is often >120 bpm at baseline. Transient symptoms of POTS can be seen in viral and other infections such that POTS, a chronic medical disorder, should not be diagnosed unless the symptoms have been present for more than 6 months. Symptoms of POTS can also be caused by other systemic conditions, including dehydration, deconditioning, medication effects (eg, anticholinergics, withdrawal from beta blockers, sympathomimetics), anemia, hyperthyroidism, and inappropriate sinus tachycardia syndrome. Although lightheadedness is among the most common symptoms, fainting is relatively rare in persons with POTS.

A detailed medical history should be taken, including personal and family history of cardiac disease, joint hypermobility, autoimmunity, neurologic disorders, symptom triggers and circumstances as well as the effect on daily functioning.
Box: Diagnostic Criteria for Postural Orthostatic Tachycardia Syndrome

1. Symptoms
   - light-headedness
   - palpitations
   - tremor
   - generalized weakness
   - blurred vision
   - exercise intolerance
   - fatigue
2. Heart rate increased by ≥30 bpm when moving from a recumbent to a standing position (or ≥40 bpm in individuals 12-19 years of age)
3. The absence of orthostatic hypotension (>20 mm Hg drop in systolic blood pressure

A complete physical examination is warranted and should include orthostatic heart rate and blood pressure obtained after 5 minutes of recumbency, immediately upon standing, and at 1, 3, 5 and 10 minutes of standing. Because individuals with POTS symptoms frequently complain of numbness of extremities, a detailed sensory exam is often warranted to evaluate for possible small fiber neuropathy. A resting 12-lead ECG should be obtained. Laboratory testing for anemia and thyroid function should be considered. A clinical diagnosis of POTS is appropriate if the symptoms and cardiovascular criteria are fulfilled. Evaluations including tilt-table testing, autoimmune panels, serum catecholamine levels, urinary histamine metabolites, estimates of blood volumes, and evaluations for small fiber neuropathy are not standardly pursued at our pediatric institution, but can be considered on a case-by-case basis.

Treatment
The current evidence for optimal management and treatment of POTS is extremely limited. Treatment options are symptom based, with no disease-modifying therapy available or even in development. Treatments can be divided into nonpharmacologic and pharmacologic strategies. The nonpharmacologic strategies target cardiovascular reconditioning and optimization and should be started and optimized before initiating pharmacologic treatments. Improvement in POTS symptoms can be expected with multimodal treatments. It is not well known, especially in pediatric and adolescent patients, how often the disorder may remit. In most series there is consistent improvement over time in the majority of patients.

Nonpharmacologic Strategies
Increasing blood volume through increases in salt and fluid intake is the cornerstone of nonpharmacologic therapy. The optimal amount of fluid intake for individuals with POTS is unknown and very likely needs to be individualized for each person. In general, the recommendation is 1 to 3 L / day. Fluid alone, however, is likely insufficient to expand blood volume and needs to be paired with an increase in salt intake. Dietary salt intake is encouraged, but if insufficient, salt supplements can be considered. Salt tablets can cause gastrointestinal upset, so 0.5 to 1 g tablets of sodium are paired with meals, up to 3 times daily, to reduce intolerance. The maximum recommended amount of sodium is 10 g/day. Use of sports drinks containing electrolytes can help some individuals reach their sodium and fluid goals through the day.

Exercise is necessary to improve cardiovascular endurance and reverse the deconditioning that is so often seen in POTS. People with POTS often report that “overdoing it” with exercise increases their symptoms. For that reason, a structured exercise program with gradually increasing intensity and duration of exercise is often prescribed. Exercise programs often begin with recumbent exercise to reduce orthostatic symptoms when upright. Targeted strength training in the lower body is thought to gradually improve venous return. Physical therapists and personal trainers can be allies in supervising exercise programs and helping individuals with POTS meet their exercise goals.

Sleeping in a reverse Trendelenburg position has been recommended for people with POTS. The head of the bed should be elevated 4 to 6 inches higher than the foot of the bed. This is postulated to cause mild orthostatic stress, activating the renin-aldosterone system to increase total blood volume. Compression stockings are recommended as an additional measure to reduce venous pooling in the legs.

Pharmacologic Treatments
Pharmacologic treatments can be added to address POTS symptoms when nonpharmacologic treatments are insufficient. Medication can be used to expand blood volume, reduce heart rate, induce peripheral vasoconstriction, and for sympatholysis. Medications can also be used to target the comorbidities of POTS; these are symptom driven.

Evidence for pharmacologic treatments for POTS is limited and varies in the types of individuals and disease subtypes studied, treatments and doses used, and outcomes measured. This is especially true for children and adolescents with POTS. Before starting medications for POTS, it is important to have a discussion about the potential benefits and risks of each medication. In general, the lowest effective dose should be used, and medications should be titrated, starting low and slowly increasing doses as the patient can tolerate (Table). If medications are ineffective after 4 to 6 weeks, they should be discontinued.

Fludrocortisone is a mineralocorticoid that increases blood volume through activation of the renin-aldosterone system. Doses up to 0.2 mg/day do not suppress the hypo-
Dizziness and Tachycardia in Postural Orthostatic Tachycardia Syndrome

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose range</th>
<th>Common side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fludrocortisone</td>
<td>0.1-0.2 mg every morning</td>
<td>Headache, irritability, rash, ankle swelling</td>
</tr>
<tr>
<td>Midodrine</td>
<td>5-15 mg 2-3 times/day</td>
<td>Scalp tingling, goose bumps, supine hypertension  Give only while awake</td>
</tr>
<tr>
<td>Desmopressin</td>
<td>0.1-0.4 mg twice daily</td>
<td>Bloating, headache, hyponatremia</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>12.5-100 mg at bedtime</td>
<td>Headache, nausea, fatigue, dizziness</td>
</tr>
</tbody>
</table>

Anxiety and depression symptoms are common in POTS, although not necessarily more common than in the general population. Both anxiety and depression contribute to reduced quality of life that is already reduced in POTS and may be treated effectively with cognitive behavioral therapy (CBT). Screening for anxiety and depression and referral to a mental health professional as needed is recommended.

Cognitive dysfunction, often described as brain fog or mental clouding, and fatigue are often present in POTS. The pathophysiology of cognitive changes is poorly understood, but the symptoms affect daily function and quality of life in most individuals with POTS. Intellectual ability is not reduced, but standardized testing may reveal impairments in attention, processing speed, memory function, and executive function. The clinical approach to brain fog is to optimize fluid and salt intake and exercise, improve the quality and quantity of nighttime sleep, evaluate and treat anxiety and depression (which can both contribute to brain fog), consider neuropsychologic testing, and consider a trial of a stimulant medication.

Joint hypermobility syndromes are a type of connective tissue disorder that present with joint hypermobility, skin hyperextensibility, and tissue fragility. There is a recognized spectrum of symptom severity resulting in a new clinical diagnostic paradigm. These disorders, previously known in general as Ehlers-Danlos syndrome, have long been recognized to co-occur with chronic fatigue symptoms, and orthostatic intolerance. The Brighton scale is a 9-item examination that can be administered in the medical outpatient setting and reliably predicts significant joint hypermobility. The importance of recognizing and diagnosing joint hypermobility lies in the propensity to physical injury and the development of appropriate exercise regimens.

Mast cell-activation syndrome (MCAS) presents with episodes suggestive of excessive histamine release—recurrent flushing, anaphylaxis, crampy abdominal pain, diarrhea, and itching. Elevated urinary methylhistamine levels during flushing episodes and symptom improvement with histamine antagonist treatment confirm diagnosis. An association of MCAS with POTS has been reported but is poorly understood. Allergists may be helpful in the evaluation of these symptoms.

Fatigue and sleep problems are both common in POTS and correlate directly with reduced quality of life. Differentiating fatigue from sleepiness is key to diagnosis and treatment. For the person who describes an overwhelming desire to sleep or nap during the day or finds themselves dozing off during activities, a sleep disorder such as narcolepsy or obstructive sleep apnea should be suspected and a polysomnogram should be considered. For those who describe a sensation of muscle tiredness or body exhaustion but do not have the need or desire for naps during the day, fatigue is more likely. Fatigue should be addressed with optimization.
of fluid and salt intake and exercise as well as strategies to improve the quality and quantity of sleep. Insomnia is common, and should be addressed with cognitive behavioral therapy, melatonin and the judicious use of medications.

Gastrointestinal symptoms are common in POTS, including early satiety, diarrhea and constipation, reflux, and abdominal pain, all of which can be symptoms of disordered gastric motility. Referral to gastroenterology is recommended for full evaluation of these symptoms.

Summary

Increasingly recognized as a cause of dizziness, fatigue, cognitive dysfunction, and headaches, POTS can significantly contribute to poor quality of life. The diagnosis of POTS, which is clinical and does not require ancillary testing, should be considered in individuals presenting with these symptoms. Nonpharmacologic treatment with fluids, salt, and exercise are recommended as first-line therapy for POTS. The use of medications can be considered with the knowledge that evidence for their use is suboptimal. There are many medical conditions comorbid with POTS for which screening and evaluation may be necessary. Although POTS should be considered a chronic disorder, appropriate multimodal treatment can improve and potentially resolve symptoms.