POTS
Postural Orthostatic Tachycardia Syndrome

As a pediatrician:

Fascinating Condition
Fun Opportunity to Learn
Great Privilege to Help Adolescents and Families
POTS
Postural Orthostatic Tachycardia Syndrome

For a Patient:

Misery
Upright Dizziness, Debilitating Fatigue
Often Nausea, Pain
Loss of “Best Years of Life”
Hopeless
# Pediatric Disorders of Orthostatic Intolerance

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Adolescent POTS
North American Pediatric Guidelines
or
A Personal Perspective from North America

Phil Fischer, MD
General Pediatric and Adolescent Medicine, Mayo Clinic
8 September 2017
Definitions

Orthostatic Intolerance: difficulty tolerating the upright posture because of symptoms which abate when returned to supine (chronic if > 3 mo)

• Symptoms: sense of impending loss of consciousness, cognitive deficits (memory loss, decreased reasoning and concentration), visual difficulties, lightheadedness, headache, fatigue, weakness, nausea and abdominal discomfort, tremulousness, exercise intolerance

• Signs: pallor, diaphoresis, tachycardia, bradycardia or hypotension
Definitions

POTS:

chronic orthostatic intolerance
daily symptoms
excessive upright tachycardia,
  > 40 bpm change
without preceding orthostatic hypotension,
  > 20 mm Hg drop in systolic blood pressure
How Common is Fatigue in Adolescents?
Fatigue is Common During Adolescence

31% with morning fatigue more than weekly

21% with significant fatigue for > 3 months

Dutch Boys  Pediatrics 117:e1078, 2006
7% with significant fatigue for > 3 months

British Teens  Pediatrics 119:e603, 2007
2% with chronic disabling fatigue
How Common is Dizziness in Adolescents?
Dizziness is Common During Adolescence

25% report postural dizziness.

Skinner. *J Child Neurol*, 2010

0.1% see a physician for syncope.

How Common is POTS in Adolescents?
Prevalence of POTS

Studies of chronic fatigue find half to two-thirds of patients have concurrent evidence of abnormal autonomic function, if tested.

If 2% of teens have debilitating chronic fatigue, maybe half to two-thirds of them have POTS.

So, is the prevalence of POTS about 1% during adolescence? Maybe…
Typical Presentations of Adolescent POTS

67-80% female

Previously “high achievers”

Caucasians >> Blacks

~15% with similar symptoms in family

Hypermobility common

Often within 1-2 years of menses or growth spurt

Sudden (after illness or injury) or gradual onset

Worse with bedrest and central hypovolemia
# POTS - Presentations

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
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</thead>
<tbody>
<tr>
<td>Postural Dizziness</td>
<td>Almost Always</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Almost Always</td>
</tr>
<tr>
<td>Pain (head, abdomen)</td>
<td>~ 65%</td>
</tr>
<tr>
<td>Nausea</td>
<td>50-60%</td>
</tr>
<tr>
<td>Anxiety/Depression</td>
<td>20-30% (↑ over time?)</td>
</tr>
<tr>
<td>Disordered Sleep</td>
<td>50+%</td>
</tr>
<tr>
<td>Brain Fog</td>
<td>≠ Cognitive Dysfunction?</td>
</tr>
</tbody>
</table>
Co-Morbidities

Not Uncommon:

- Hypermobility Syndromes
- Iron Deficiency (~45%)  
- Hypovitaminosis D (~33%)  
- Mast Cell Activation Disorder (<5%?)

*Uncommonly Seen*

- Attention Deficit Hyperactivity Disorder

*Also Seen:*

- Almost Anything Else!
Pathophysiology of POTS

Multifactorial?

Multiple Phenotypes?
Putative Causes/Mechanisms of POTS

Autoimmune

Ganglionic Acetylcholine Receptor Antibodies
- not very common
- not clearly linked to other findings
Isolated Sympathetic Failure With Autoimmune Autonomic Ganglionopathy


Introduction

In adults, antibodies against the nicotinic ganglionic acetylcholine receptor have been associated with subacute auto-
Putative Causes/Mechanisms of POTS

Autoimmune

Ganglionic Acetylcholine Receptor Antibodies
- not very common
- not clearly linked to other findings

Voltage-Gated Potassium Channel Antibodies
- not linked to having POTS
- linked to higher HR change if had POTS

Others – you heard it during the last session!
Vaccine-Related? NO!

Human Papillomavirus Vaccine and Postural Orthostatic Tachycardia Syndrome: A Review of Current Literature

Breann N. Butts, MD¹, Philip R. Fischer, MD², and Kenneth J. Mack, MD, PhD³

Abstract

The human papillomavirus (HPV) vaccine is efficacious in preventing complications of human papillomavirus infection including cervical cancer. However, there have been case reports of adverse events occurring after vaccination, one being postural orthostatic tachycardia syndrome (POTS). This article reviews published data and other available information regarding the relationship between the human papillomavirus vaccine and POTS. Background information is provided regarding the human papillomavirus vaccine and the proposed post-vaccination adverse event POTS. Peer-reviewed literature, statements by government and medical advisory committees, and publicly available information published on this topic are examined. At this time, there is no conclusive evidence supporting a causal relationship between the human papillomavirus vaccine and POTS. Though a causal relationship has been postulated, it is of utmost importance to recognize that while temporal associations may be observed, conclusions of causality cannot be drawn from case reports and case series due to the small sample size and lack of control population.
Putative Causes/Mechanisms of POTS

Deconditioning

identified in 68% of adolescent POTS patients
Exercise Performance in Adolescents with Autonomic Dysfunction

Barbara E. U. Burkhardt, MD, Phil R. Fischer, MD, Chad K. Brands, MD, Co-bum J. Porter, MD, Amy L. Weaver, MS, Paul J. Yim, BA, and Paolo T. Pianosi, MD

Objective To test the hypothesis that excessive postural tachycardia is associated with deconditioning rather than merely being an independent sign of autonomic dysfunction in patients with postural orthostatic tachycardia syndrome (POTS).

Study design We retrospectively analyzed records from 202 adolescents who underwent both head up-tilt and maximal exercise testing. Patients were classified as POTS if they had ≥30 min⁻¹ rise in heart rate (HR) after tilt-table test; and deconditioned if peak O₂ uptake was <80% predicted. Changes in HR during exercise and recovery were compared between groups.

Results Two-thirds of patients were deconditioned, irrespective of whether they fulfilled diagnostic criteria for POTS, but peak O₂ uptake among patients with POTS was similar to patients without POTS. HR was higher at rest and during exercise; whereas stroke volume was lower during exercise, and HR recovery was slower in patients with POTS compared with patients without POTS.

Conclusions Most patients who presented with chronic symptoms of dizziness, fatigue, or pre-syncpe, were deconditioned, but, because the proportion of deconditioned patients was similar in POTS vs non-POTS groups, we conclude that HR changes in POTS are not solely because of inactivity resulting in deconditioning. (J Pediatr 2011;158:15-9).
Putative Causes/Mechanisms of POTS

Deconditioning
identified in 68% of adolescent POTS patients
might be more consequence than cause

Low – Normal - High Flow
possibly related to peripheral pooling
partly related to cardiac conditioning

Pianosi PT et al. *Physiol Reports* 2:e12122, 2014
Putative Causes/Mechanisms of POTS

Hyperadrenergic
	norepinephrine

elevated at rest

> 4-fold increase with standing

not clearly related to symptoms

rarely associated with mild increase in upright BP

no clear impact on therapy, outcomes
Parents Relevant to Symptom Severity

Catastrophizing parents >> Less patient function

Guidelines, Consensus, or Review?
Pediatric Disorders of Orthostatic Intolerance

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Guidelines, Consensus, or Review?

Diagnostic Evaluation

Treatment
Diagnosis of POTS

Remember the Definition
- chronic intolerance of upright position
- excessive postural tachycardia
- no preceding orthostatic hypotension

Monitor Closely During Evaluation

Proper HR Criteria (>40 bpm change)

Diagnosis of POTS

- Based on symptoms PLUS postural tachycardia
- Can check supine (calm for several minutes) and standing (still like a statue for at least three minutes) heart rates

OR

- Can do formal tilt table testing
Diagnosis of POTS

Standing vs Tilting

Small, unpublished study – p=0.04

Large, formal study – being planned
Treatment of POTS

Non-Pharmacologic Therapy >> Medications

Personalized Management Plan

Team-Based Care

Supportive Follow-Up
Adolescent Fatigue, POTS, and Recovery: A Guide for Clinicians

Sarah J. Kizilbash, MD, Shelley P. Ahrens, RN, CNP, DNP, Barbara K. Bruce, PhD, Gisela Chelimsky, MD, Sherilyn W. Driscoll, MD, Cynthia Harbeck-Weber, PhD, Robin M. Lloyd, MD, Kenneth J. Mack, MD, PhD, Dawn E. Nelson, RN, MSN, Nelly Ninis, MD, MSc, MBBS, Paolo T. Pianosi, MD, Julian M. Stewart, MD, PhD, Karen E. Weiss, PhD, and Philip R. Fischer, MD

Many teenagers who struggle with chronic fatigue have symptoms suggestive of autonomic dysfunction that may include lightheadedness, headaches, palpitations, nausea, and abdominal pain. Inadequate sleep habits and psychological conditions can contribute to fatigue, as can concurrent medical conditions. One type of autonomic dysfunction, postural orthostatic tachycardia syndrome, is increasingly being identified in adolescents with its constellation of fatigue, orthostatic intolerance, and excessive postural tachycardia (more than 40 beats/min). A family-based approach to care with support from a multidisciplinary team can diagnose, treat, educate, and encourage patients. Full recovery is possible with multi-faceted treatment. The daily treatment plan should consist of increased fluid and salt intake, aerobic exercise, and regular sleep and meal schedules; some medications can be helpful. Psychological support is critical and often includes biobehavioral strategies and cognitive-behavioral therapy to help with symptom management. More intensive recovery plans can be implemented when necessary.

Approach to Treatment of Adolescent Autonomic Dysfunction

• According to doctors:
  • Non-pharmacologic therapies
  • Pharmacologic therapies

• According to recovered patients:
  • Go to school!
  • Exercise daily!
STEPS Treatment Plan

- Salt
- Take in fluids
- Exercise
- Prescriptions
- Sleep, school, support system, safety
Salt

- Take in as much as your taste buds can tolerate.
- Salt, salt, and more salt.
- Good nutrition
  - 3 well balanced meals
  - 2 salty snacks

*Salt helps the body keep the fluid in the blood vessels.
*Target urinary sodium of >170 mmol per day
Take in Fluids

- Take in 2-4 liters of fluid per day
  - Water (should be majority of fluid)
  - Sports drinks
  - Milk/juice
- Avoid caffeinated beverages

- Goal:
  * Produce colorless urine at least four times a day.
How many glasses should I drink?
Exercise

• Overall movement goal - 60 minutes 7 days a week
  • Break it down into cardio (aerobic) and “other physical activity”
    • 30 minutes cardio
    • 30 minutes other physical activity
• Exercise should make teen breathy & sweaty
• Incrementally increase to goal (over months)
Exercise

- Upright
- Sustained
- Vigorous

“If you don’t push it, you’ll never get past it.”

• Exercise every day before dinner, even on bad days
Exercise
Prescriptions

Must be in conjunction with other strategies

My “Top Three”

1. Beta Blocker - metoprolol, 25 mg po BID
2. Alpha Agonist - midodrine, 2.5 – 10 mg po TID
3. SSRI – citalopram, 10-20 mg po daily

Other Options – many!
Remember to Treat Identified Co-morbidities

- Life out of Balance
- Sleep Disorders
- Depression
- Other Diagnoses
- Iron Deficiency
  - 4-6 mg elemental iron/kg/d for 3+ mo
- Hypovitaminosis D
  - 400 – 2000 IU daily for months
Review Article

Postural Orthostatic Tachycardia Syndrome: A Clinical Review

Jonathan N. Johnson, MD*, Kenneth J. Mack, MD, PhD†, Nancy L. Kuntz, MD†,
Chad K. Brands, MD‡, Coburn J. Porter, MD*, and Philip R. Fischer, MD‡

Postural Orthostatic Tachycardia Syndrome
An Approach to Treatment

↑ hydration: >2 L/day
↑ salt intake: >200 mEq/day
Support stockings: 30 mm Hg
Poor adherence in teenagers

Non-pharmacologic (all patients)

Family education
Psychophysiologic therapy
Exercise – aerobic and lower extremity strengthening:
≥5x/week

Pharmacologic (case by case)

1st line
Beta blocker
↓ heart rate, block peripheral vasodilation
Metoprolol 12.5-50 mg 2-3x daily

1st or 2nd line
Alpha agonist
Peripheral vasoconstriction
Midodrine 2.5-12.5 mg 1-3x daily

2nd line/adjunct
Mineralocorticoid
↑ salt retention and plasma volume
Fludrocortisone 0.05-0.2 mg 1-2x daily

3rd line
SSRIs/SSNRIs
Improves serotonin regulation
eg, citalopram, fluoxetine, venlafaxine

Rarely used
Alternate medications (pyridostigmine, EPO, ddAVP, clonidine, methylphenidate)

Tritrate all meds to effect and tolerance

Sleep

• Recommend 8.5-9.5 hours of sleep
• Many POTS patients struggle with sleep

Tips
• No cell phones in bedroom
• Avoid caffeine
• Bedtime routine
• No naps
• No screen for 30-60 minutes before bed
• Go to bed and get up at same time each day
School

• Go!
• Discontinue homebound schooling
• Create a return to school schedule
• Prefer no online schooling – teens need social experience of school.
• When to stay home from school
  • Never for POTS
  • Only if another new problem develops
Support

• A good support system
  • Includes family, friends and school
• Cognitive behavioral therapy works!

“Hanging out with my friends makes me feel like things are getting back to normal…its definitely worth it!”
POTS and Pain – Persistent

Cognitive behavioral therapy works
Increasing exercise is better than “pacing”

McCrone et al. *PLOS One* 7:40808, 2012

A 3-week “rehab” program leads to lasting:
decreases in depression, anxiety, disability
decreases in dizziness, nausea

Outcomes?
What should I tell my patient?

Most teens outgrow POTS and return to normal health

“...I was scared. My first day felt like boot camp. But my mom and dad helped me to stick to it. Today my life is better than it used to be.”

Start with STEPS

You can beat autonomic dysfunction
What are the Data?

Adolescents and Adults – 34% recovered at 1 yr
Kimpinski K et al. *Mayo Clin Proc* 2012;87:746

Adolescents – 100% improved with beta blocker, 62% improved with midodrine
Lai CC et al. *PACE* 2009; 32:234
Outcomes: POTS in Adolescents

Outcomes of Adolescent-Onset Postural Orthostatic Tachycardia Syndrome

Roma Bhatia, BS¹, Sarah J. Kizilbash, MD¹,²,*, Shelley P. Ahrens, DNP¹,², Jill M. Killian, BS¹,³, Stephanie A. Kimmes, CNP¹,², Erin E. Knoebel, MD¹,², Prasuna Muppa, MBBS¹,², Amy L. Weaver, MS¹,³, and Philip R. Fischer, MD¹,²

Objectives To determine the clinical course of adolescent-onset postural orthostatic tachycardia syndrome (POTS) and to assess health-related quality of life, 2-10 years after diagnosis.

Study design Pediatric patients, 13-18 years of age, diagnosed with POTS at Mayo Clinic, Rochester, from 2003 to 2010 were mailed a questionnaire if they were at least 18 years of age at the time of the mailing. The primary outcome measures were norm-based, age- and sex-adjusted, 36-Item Short Form Health Survey physical composite score and mental composite score.

Results The survey was mailed to 502 patients with a response rate of 34% (n = 172). The mean duration from diagnosis to survey completion was 5.4 (SD, 1.9) years; the mean age of the respondents at the time of the survey was 21.8 (2.2) years. The responders were predominantly females (84% vs 68% of nonresponders; P < .001). Only 33 (19%) respondents reported complete resolution of symptoms, and an additional 51% reported persistent but improved symptoms, and 28 (16%) had only intermittent symptoms. The majority (71%) consider their health at least “good.” The mean physical composite score was significantly lower than the population norm (mean [SD], 36.6 [15.8] vs 50; P < .001), however, the corresponding mean mental composite score was normal (56.1 [11.2]).

Conclusions Overall, 86% of adolescents with POTS report resolved, improved, or just intermittent symptoms when assessed via questionnaire at an average of 5 years after initial treatment. Patients with persistent symptoms have more physical than mental health concerns. (J Pediatr 2016;173:149-53).
POTS and Pain – Outcomes

I am just stunned at the difference in E since we have returned from Mayo's. She is exercising daily without prompting, following her regimen exactly, and is back to work and out and going places every day.

I could go on and on. It is just amazing and such a joy! If there is one thing I could pin it on, I believe that our trip to Mayo's gave E back HOPE!

Mother of “E” – a 14 year old with POTS and Pain
Closing Comment

A Helpful Framework?

Structural versus Functional

Hardware versus Software

Phone versus App
## An Approach to Patients with Functional Disorders

<table>
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<th>Validate</th>
<th>Your symptoms are miserable.</th>
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<tr>
<td>Affirm</td>
<td>This is a real problem. It’s not in your head.</td>
</tr>
<tr>
<td>Share</td>
<td>What are YOUR goals?</td>
</tr>
<tr>
<td>Focus</td>
<td>Let’s go beyond discovery to recovery.</td>
</tr>
<tr>
<td>Explain</td>
<td>Use science of neural networking.</td>
</tr>
<tr>
<td>Plan</td>
<td>Let’s review our specific next steps.</td>
</tr>
<tr>
<td>Be There</td>
<td>You are not alone; we’re in this together!</td>
</tr>
<tr>
<td>Believe</td>
<td>Be optimistic. (Maximize placebo’s power.)</td>
</tr>
<tr>
<td>Laugh</td>
<td>Humor goes a long way.</td>
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http://heartsinhealthcare.com/ten-practical-steps-towards-healing-consultations/
Heal the sick. Advance the science.