Postural Tachycardia Syndrome and Hypermobility Syndrome

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Supine  Standing

- ↓ CBV
- ↓ Arterial pulse pressure
- Mechanoreceptor unloading
- ↑ Sympathetic outflow
- ↓ Vagal tone
- Veno-arteriolar reflexes
- Activation of renin angiotensin system

Central venous pressure
5 mmHg  100
0 mmHg  50
Periods of autonomic decompensation resulting in hypotension (with or without Bradycardia) may have a wide variety of clinical manifestations, such as:

Vertigo/dizziness
Lightheadedness
Convulsive Activity
TIAS
Syncope/near syncope
Fatigue
Cognitive Impairment
Head Upright Tilt Table Testing

Abnormal Response Patterns

- NCS
- POTS
- Dysautonomic
- Cerebral Syncope
- Psychogenic Syncope

Vasod. Cardio-inhib.
Classic Neurocardiogenic (Vasovagal) Response

HR/BP

Tilt

Head Down

Blood Pressure
Heart Rate
POTS

H.R. 160

B.P. 90/60

70 b/m

100/70 mm/hg
Supine  Standing

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- ↓ Vagal tone
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- Activation of renin angiotensin system

Central venous pressure
5 mmHg  0 mmHg
Venous Pooling in POTS

Supine

Normal

Upright

Pooling
Postural Tachycardia Syndrome (POTS)

Symptoms of orthostatic intolerance accompanied by a heart rate increase of at least 30 beats/min (or a rate that exceeds 120 beats/min) that occurs in the first 10 minutes of upright posture or head up tilt occurring in the absence of other chronic debilitating disorders.

Joint Consensus Statement of the AAS and AAN
Orthostatic Intolerance:

Provocation of symptoms upon standing that are relieved when becoming supine

Symptoms include exercise intolerance, fatigue, lightheadedness, diminished concentration, tremulousness, nausea, headache, near syncope, and syncope

Joint Consensus Statement of the American Autonomic Society and the American Academy of Neurology

“Dizziness, headache, chest pain, faintness and Extreme fatigue associated with a rapid heart rate upon Standing that fell to normal levels with recumbency”

Case # 12 : 122 beats/min standing- 90 bpm supine

“in all, the immediate effect of the Exchange in position was most striking”
Lewis T. The soldier’s heart and the effort syndrome. London, Shaw and Sons: 1919

“among them fatigue is an almost universal complaint, Which is aggravated by exertion, associated with chest Pain, excessive sweating, fainting spells, palpations and Giddiness”

“when completely rested the heart rate averaged 85 bpm And when up and about would rise to rates of 120 bpm” He documented BP drop of between 20 - 40 mmHg upon Standing

“the potential reservoir in the veins takes up the blood, The supply to the heart falls away , and arterial pressure Falls rapidly”
POTS - History

*MacLean et al – 1944*

Reported on patients with orthostatic tachycardia with only a mild drop in BP.
POTS – History: MacLean 1944

Pts complained of weakness, fatigue, palpitations.

Felt that it might be due to reduced venous return.
Criteria for POTS

1. Longstanding (>6 months) and disabling orthostatic symptoms
2. Orthostatic Tachycardia:
   >30 bpm increase of HR on tilt or standing
   >120 bpm HR on tilt on standing
3. Absence of an underlying cause (debilitating disease, dehydration, medications, etc…)
4. Upright plasma norepinephrine ≥600 pg/ml
5. Excessive isoproterenol response
## Symptoms in POTS Pts. (%)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Lightheadedness</td>
<td>85-95</td>
</tr>
<tr>
<td>Dizziness</td>
<td>60-80</td>
</tr>
<tr>
<td>Palpitations</td>
<td>40-55</td>
</tr>
<tr>
<td>Exercise Intolerance</td>
<td>50-85</td>
</tr>
<tr>
<td>Blurred Vision</td>
<td>70</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>60</td>
</tr>
<tr>
<td>Clammineness</td>
<td>60</td>
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</tbody>
</table>
Symptoms in POTS Pts. (%) cont.

- Near Syncope: 50%
- Anxiety: 50%
- Flushing: 50%
- Syncope: 40-45%
- Fatigue: 45-75%
- Headache: 50%
- Dyspnea: 40%
Figure I: Subtypes of Postural Tachycardia Syndrome

POTS = Postural Tachycardia Syndrome
JHS = Joint Hypermobility Syndrome
All subjects underwent head up tilt table testing
Over the years it became evident that many of the patients referred to the MCO Syncope/Autonomic clinic looked remarkably similar in appearance:

Pale, fair skinned, caucasian women. Usually blond haired, blue eyed, often tall and thin. Many complained of joint pain and easy bruising. Stretch marks were common.
In the late 1990s investigators at the Johns Hopkins Hospital realized that many of these patients met the criteria for Type III Ehlers-Danlos Syndrome (now called the joint hypermobility syndrome).

*J Pediatrics 1999;135:494-9*
So just what is Joint Hypermobility/Ehlers-Danlos Syndrome?
Ehlers-Danlos Syndrome (Type III or joint hypermobility syndrome))

- Heterogeneous disorder of connective tissue
- Prevalence unknown, perhaps 1 per 5000
- Characterized by varying degrees of:
  - Skin hyperextensibility (not present in many)
  - Joint hypermobility
  - Cutaneous scarring
- Early varicose veins, easy bruising
- Easy fatigability and widespread pain common, of unclear etiology
Many EDS/JHS Pts also complain of

1. nausea and bloating (due to gastroparasis and GB disease)
2. orthostatic acrocyanosis
3. joint pain and dislocations
4. hernias
5. constipation
6. hemorrhoids
7. early arthritis
8. stretch marks
ORTHOSTATIC INTOLERANCE AND CFS ASSOCIATED WITH EDS

Among approximately 100 adolescents seen in the CFS/OI clinic at JHH over a 1 year period, they identified 12 subjects with EDS

11 females, 1 male

All had either POTS or NMH

6 classical-type, 6 hypermobile-type EDS

# FEATURES ASSOCIATED WITH CFS IN 12 WITH EDS

<table>
<thead>
<tr>
<th>Feature</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Fatigue &gt; 6 mo</td>
<td>100</td>
</tr>
<tr>
<td>Post-exertional malaise</td>
<td>100</td>
</tr>
<tr>
<td>Unrefreshing sleep</td>
<td>100</td>
</tr>
<tr>
<td>Impaired memory/concentration</td>
<td>92</td>
</tr>
<tr>
<td>Multi-joint pain</td>
<td>83</td>
</tr>
<tr>
<td>New headaches</td>
<td>83</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>58</td>
</tr>
<tr>
<td>Sore throat</td>
<td>25</td>
</tr>
<tr>
<td>Tender glands</td>
<td>25</td>
</tr>
</tbody>
</table>
Revised Criteria for JHS (EDS III)

MAJOR CRITERIA:
1. A Beighton score 4/9 or more (current or historically).
2. Arthralgia for longer than 3 months in 4 or more joints

MINOR CRITERIA:
1. Beighton score of 1, 2 or 3/9 (0, 1, 2 or 3 if aged 50+)
2. Arthralgia (>3 months) in 1-3 joints or back pain (>3 M) spondylosis, spondylosis/spondyloisthesis
3. Dislocation/subluxation in more than one joint
4. Soft tissue rheumatism >3 lesions (epicondylitis etc.)
5. Marfanoid habitus
6. Abnormal skin: striae, hyperextensibility, thin, scarring
7. Eye signs: drooping eyelids or myopia
8. Varicose veins, hernia or utero/rectal prolapse
Diagnosis is made by the presence of:

1. two major criteria
2. one major and two minor criteria
3. four minor criteria
4. two minor criteria with an unequivocally affected first degree relative

Diagnosis excluded by presence of Marfans or the other EDS subtypes

J Rheumatology 2000;27:1777-1779
A picture from childhood from one of our patients
Another picture from a patients childhood

Many of these patients excelled at gymnastics and dance
JOINT HYPERMOBILITY IS MORE COMMON IN CHILDREN WITH CFS

Study question: do children with CFS have a higher prevalence of joint hypermobility?

Beighton scores obtained in 58 new & 58 established CFS patients, and in 58 controls

Median Beighton scores higher in CFS (4 vs. 1)

Beighton score ≥ 4 higher in CFS (60% vs. 24%)


48 pts with Joint Hypermobility Syndrome (JHS) were compared to 30 healthy controls with a battery of Autonomic Tests: HUTT, Valsalva Ratio, HRV, catecholamine levels and baroreflex testing.

78% of JHS pts demonstrated Orthostatic intolerance and abnormal autonomic testing (on every one of the tests mentioned above), as compared to 10% of control subjects.

They concluded that JHS/EDS III predisposed people to develop OI.
**Methods:**

- This retrospective study was approved by our local Institutional Review Board (IRB).
- Over a period of 10 years, 26 patients of POTS were identified for inclusion in this study.
- All these patients had features of Joint Hypermobility Syndrome (by Brighton criterion).
- A comparison group of 39 patients with other forms of POTS were also followed in the autonomic clinic during the same time.
- We present a descriptive report on the comparative clinical profile of the clinical features of Postural Orthostatic Tachycardia patients with and without Joint Hypermobility syndrome.
- The data is presented as a mean±SD and percentages wherever applicable.
Results:

- Out of 65 patients, 26 patients (all females, 20 Caucasians) had POTS and JHS.
- The mean age at presentation of POTS in JHS patients was $24 \pm 13$ (range 10-53 years) vs $41 \pm 12$ (range 19-65 years), $P=0.0001$,
- Migraine was a common co morbidity 73 vs 29% $p=0.001$.
- In two patients POTS was precipitated by pregnancy, and in three by surgery, urinary tract infection and a viral syndrome respectively.
- The common clinical features were fatigue (58%), orthostatic palpitations (54%), presyncope (58%), and syncope (62%).
Conclusion:

- Patients with POTS and JHS appear to become symptomatic at an earlier age compared to POTS patients without JHS.
- In addition patients with JHS had a greater incidence of migraine and syncope than their non JHS counterparts.
Figure 1. Disorders of the Autonomic Nervous System Associated with Orthostatic Intolerance

- **ANS Disorders**
  - POTS
  - Secondary
    - Diabetic
    - JHS
    - Other
  - Primary
    - Partial Dysautonomic
    - Beta Hypersensitivity
  - Reflex Syncope
    - Situational
      - Micturition
      - Defecation
      - Other
    - CSH
  - Acute Autonomic Neuropathy
  - Chronic
    - Paraneoplastic
    - Diabetic
    - Other
  - Pure Autonomic Failure
    - Parkinsonian
    - Mixed
    - Cerebellar
  - Multiple System Atrophy
    - Parkinson's Disease

NCS: Neurocardiogenic Syncope
CSH: Carotid Sinus Hypersensitivity
POTS: Postural Orthostatic Tachycardia Syncope
JHS: Joint Hypermobility Syndrome
Before embarking on Medical Therapy one must:

1. Avoid predisposing conditions or medications
2. Have adequate fluid & salt intake
3. Reconditioning and lower extremity strength building
   a. aerobic training 30 min. 3/week
   b. resistance training
Pharmacotherapy is employed to make the patient feel well enough so that they can begin a reconditioning program.
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Pharmacotherapy

1. Fludrocortisone / DDAVP
2. Methylphenidate
3. Midodrine
4. Beta blockers
5. SSRIs
6. Clonidine
7. Erythropoietin
8. Yohimbine
9. Pyridostigmine
10. Norepinephrine reuptake inhibitors
11. Octreotide
12. droxidopa
13. ivbradine
Illness effects and can disrupt the entire family dynamic. Counseling is often critical in getting the patient and the family through this difficult period.
For Barbara Straus MD
1950 - 2015
Physician, Mother, Dancer, Wife, Soul Mate, Community leader, Educator, Adventurer

“May her memory be for a blessing...”
“If I have accomplished anything in life it is all because of you”
"She was unstoppable. Not because she did not have failures or doubts, but because she continued on despite them."

Beau Taplin || Unstoppable.
“I would like to be known as an intelligent woman, a courageous woman, a loving woman, a woman who teaches by being...”

Maya Angelou

Barbara Lynn Straus
“A Life well Lived”