**Postural tachycardia syndrome (POTS)**
- POTS is the most common form of orthostatic tachycardia syndrome.
- All patients were treated at time of symptom assessment.
- Pathophysiology of POTS remains unclear. Several causes have been proposed, including autonomic dysfunction, autonomic neuropathies, and autoimmune autonomic failure.
- Radioimmunoprecipitation of ganglionic acetylcholine receptor (gAChR) antibodies has been used to study POTS.
- Patients with AAG typically have autoantibodies against ganglionic acetylcholine receptors.
- In 2000, in the initial report of POTS patients, 6 patients were seropositive for gAChR antibodies.
- In a 2009 review of POTS patients, 20% of patients were seropositive for gAChR antibodies.
- The seroprevalence of gAChR antibodies in POTS patients is 5% (using a cutoff of 0.05 nmol/L).
- However, only one patient (seronegative) on IVIG had a lower antibody level.
- The seroprevalence of gAChR antibodies was higher in female POTS patients, but the significance is questionable.
- The clinical characteristics of POTS with gAChR antibodies were otherwise not different.
- The ganglionic acetylcholine receptor (gAChR) is responsible for synaptic transmission in autonomic ganglia.
- Antibodies against gAChR cause autoimmune autonomic ganglionopathy (AAG). Patients with AAG typically have severe autonomic failure with orthostatic hypotension, postural dizziness, and menstrual irregularities.
- Patients with AAG typically have gAChR antibodies higher than 0.2 nmol/L.
- The ganglionic acetylcholine receptor (gAChR) antibody in patients with POTS is 0.11 nmol/L.
- In a 2007 retrospective series of 152 POTS patients, 6/42 patients (14%) were positive (0.07–0.28 nmol/L).
- In a 2009 review of gAChR antibodies, the Mayo autonomic group reported positive antibodies in 25% of POTS in their clinical practice.
- The seropositive rate in these studies may be artificially higher due to possible retrospective & referral bias at a tertiary referral center, Mayo Clinic.
- Previous unpublished retrospective experience, 3 of 25 (12%) consecutive POTS patients seen at UT Southwestern were seropositive.
- However, 2 of the 3 patients were referred because of positive Ab result elsewhere.

**Results**
- 11 POTS patients had gAChR antibody (0.02–0.10 nmol/L).
- 5 POTS patients had Ab level > 0.05 (0.06–0.13 nmol/L).
- Ab-positive POTS more likely to be male (but the number of male subjects in this study was small).
- The clinical characteristics of POTS with gAChR antibodies were otherwise not different.

**Design/Methods**
- Prospective study of POTS volunteers
- Participants at 2014 meeting of Dysautonomia International (a patient support and advocacy group) were invited to participate in a serological study.
- Demographics and supine/standing vital signs
- All subjects completed VOSS (Vanderbilt Orthostatic Symptoms Score); a rating of 9 common POTS symptoms on a scale of 0-10 (max score is 90).
- Blinded serum sample sending for antibody testing.
- 102 POTS patients (self-reported diagnosis).
- Mean VOSS = 25.3
- 64 control subjects (healthy family members).
- 18% male, mean age 50 years
- Mean VOSS = 3.5

**Clinical characteristics of POTS with & without gAChR antibody (0.02 nmol/L)**

<table>
<thead>
<tr>
<th>POTS</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>29±13</td>
</tr>
<tr>
<td>Males (%)</td>
<td>22%</td>
</tr>
<tr>
<td>Height (in)</td>
<td>65±5</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>168±45</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>89±18</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>118±18</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>75±14</td>
</tr>
<tr>
<td>VOGS Standing Symptoms Score</td>
<td>32±14</td>
</tr>
</tbody>
</table>

**NS**
- No significant differences using antibody > 0.05 nmol/L

**Anecdotal case**
- 17 year male - onset of orthostatic intolerance after recovery from a foot injury
- gAChR antibody positive – 0.13 nmol/L
- Autonomic testing normal aside from postural tachycardia (HR increase from 77 to 117 bpm on tilt)
- Plasma NE normal: 284 (supine), 641 (upright)
- Trials of iv and oral steroids and 5 days of IVIG produced no subjective or objective benefit

**Specificity of low level gAChR antibodies**
- High levels of gAChR Ab (>0.5 nmol/L) are frequently associated with autoimmune autonomic failure.
- Low Ab levels (<0.1 nmol/L) are much less specific.
- Patients with low Ab have various disorders, including degenerative and non-neurological disorders.
- False positives (in healthy controls) do occur, ranging from 0.6% to 3%.
- Low gAChR antibody may be a useful non-specific marker of autoimmune but needs to be interpreted critically, according to the clinical context.
- Very low gAChR Ab levels ≤ 0.05 nmol/L appear to have questionable significance.

**Summary**
- A small minority of unselected patients with POTS and healthy controls were seropositive for gAChR antibodies.
- Prevalence of gAChR antibody in POTS patients (5%, using a cutoff of 0.05 nmol/L) was lower than previous reports.
- All had low antibody levels (≤0.13 nmol/L).
- Neither the seroprevalence nor antibody level was significantly different from the healthy control group.
- Seropositive POTS patients were not different in clinical characteristics compared to seronegative POTS, except for a greater number of males.
- Limitations of the study:
- POTS diagnosis and healthy controls were self-reported.
- All patients were treated at time of symptom assessment.
- However, only one patient (seronegative) on IVIG was seropositive for gAChR antibodies.
- No low gAChR antibody appears to have little clinical significance in otherwise typical POTS.

**References**