“People who know what they’re talking about don’t need PowerPoint.”

— Steve Jobs

From Walter Isaacson’s book *Steve Jobs*
The problem:
# nothing is certain
# this is what I’ve learnt from patients
# others in the audience may do different things and neither of us is wrong!

We don't know a millionth of one percent about anything.

~ Thomas A. Edison
PoTS; my approach

HRC 2018
FAILURE OF THE SYSTEM TO COPE WITH UPRIGHT POSTURE

Disorders of the Autonomic Nervous System Associated with Orthostatic Intolerance

Reflex Syncope
- NCS
- CSH
- Situational
  - Micturition
  - Defecation
  - Other
  - Partial Dysautonomic
  - Beta Hypersensitive

POTS
- Primary
  - Pure Autonomic Failure
  - Multiple System Atrophy
  - Parkinson’s Disease

Secondary
- Diabetic
- JHS
- Other

Autonomic Failure
- Acute Autonomic Neuropathy
- Chronic
- Secondary
  - Paraspastic
  - Diabetic
  - Other

NCS: Neurocardiogenic Syncope
CSH: Carotid Sinus Hypersensitivity
POTS: Postural Orthostatic Tachycardia Syncope
JHS: Joint Hypermobility Syndrome
What is PoTS?

A subtle failure of the system to move blood upwards

- Insufficient blood volume
- Failure of vasoconstriction
- Blood is directed to the wrong place at the wrong time in the wrong quantity
- Inappropriate heart rate response
HYPERMOBILITY
PoTS IS A SYNDROME NOT A DISEASE – CONSIDER HEART FAILURE!
A definition:

**Definition: Postural Tachycardia Syndrome**

Postural tachycardia syndrome (POTS) is defined as a clinical syndrome that is usually characterized by (1) frequent symptoms that occur with standing such as lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue; (2) an increase in heart rate of ≥ 30 bpm when moving from a recumbent to a standing position held for more than 30 seconds (or ≥ 40 bpm in individuals 12 to 19 years of age); and (3) the absence of orthostatic hypotension (> 20 mm Hg drop in systolic blood pressure).

The heart rate increase needs to be sustained over 10 minutes.
Finally some guidelines!
MANAGEMENT

STEP 1: RECOGNISING YOUR PATIENT
Who is the right patient?

Relatively common: 170/100,000

5-6:1 female to male ratio

Usually young, 15 – 35y/o

Often beginning after a clinical event e.g. viral illness
Clinical features

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthostatic symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Light headed or dizziness</td>
<td>118</td>
<td>78</td>
</tr>
<tr>
<td>Palpitations</td>
<td>114</td>
<td>75</td>
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<tr>
<td>Presyncope</td>
<td>92</td>
<td>61</td>
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<tr>
<td>Exacerbation by heat</td>
<td>81</td>
<td>53</td>
</tr>
<tr>
<td>Exacerbation by exercise</td>
<td>81</td>
<td>53</td>
</tr>
<tr>
<td>Sense of weakness</td>
<td>76</td>
<td>50</td>
</tr>
<tr>
<td>Tremulousness</td>
<td>57</td>
<td>38</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>42</td>
<td>28</td>
</tr>
<tr>
<td>Chest pain</td>
<td>37</td>
<td>24</td>
</tr>
<tr>
<td>Exacerbation by meals</td>
<td>36</td>
<td>24</td>
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<tr>
<td>Exacerbation associated with menses</td>
<td>22</td>
<td>15</td>
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<tr>
<td>Hyperhidrosis</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Loss of sweating</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Nonorthostatic symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>59</td>
<td>39</td>
</tr>
<tr>
<td>Bloating</td>
<td>36</td>
<td>24</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td>Constipation</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>23</td>
<td>15</td>
</tr>
<tr>
<td>Bladder symptoms</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Pupillary symptoms (glare)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Diffuse associated symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>73</td>
<td>48</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>48</td>
<td>32</td>
</tr>
<tr>
<td>Migraine headache</td>
<td>42</td>
<td>28</td>
</tr>
<tr>
<td>Myofascial pain</td>
<td>24</td>
<td>16</td>
</tr>
<tr>
<td>Neuropathic type pain</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>
What do you hear in the cardiology clinic (1)?

- NB HYPERBOLE IS COMMON – DO NOT CONFUSE FOR ANXIETY

- Chest pain
  - Common and unexplained
  - MSK, upper GI, central tightness like angina

- SOBOE
  - More breathless than they should be
  - Gasping respiration, sighing, hyperventilating
  - Sometimes even lying flat

- SOA
  - When sedentary, in the heat; acrocyanosis
What do you hear in the cardiology clinic (2)?

- Palpitations:
  - Persistent sinus tachy’, inappropriate for the circumstance
  - Ectopics, sudden tachys ?SVT
- Dizziness / LOC
  - Faintness on standing, head rush and with prolonged standing
  - Improved lying down etc
  - Worse in extremes of temperature, with temperature changes, when unwell, after a meal, time of the month, after alcohol etc.
You might have the right patient...
It's not always that simple!

The HR changes are unfortunately variable and are perhaps not the whole story.

**Definition: Postural Tachycardia Syndrome**

Postural tachycardia syndrome (POTS) is defined as a clinical syndrome that is usually characterized by (1) frequent symptoms that occur with standing such as lightheadedness, palpitations, tremulousness, generalized weakness, blurred vision, exercise intolerance, and fatigue; (2) an increase in heart rate of \( \geq 30 \) bpm when moving from a recumbent to a standing position held for more than 30 seconds (or \( \geq 40 \) bpm in individuals 12 to 19 years of age); and (3) the absence of orthostatic hypotension (\( > 20 \) mm Hg drop in systolic blood pressure).
Did you know?

- Symptoms change from day to day, hour to hour.....

Diagnosing Postural Tachycardia Syndrome: Comparison of Tilt Test versus Standing Hemodynamics

Walker B Plash, BS¹, André Diedrich, MD, PhD¹,²,³,⁴, Italo Biaggioni, MD¹,²,³,⁵, Emily M Garland, PhD, MSCI¹,²,³, Sachin Y Paranjape, BS¹,²,³, Bonnie K Black, RN, CNP¹,²,³, William D Dupont, PhD¹,⁶, and Satish R Raj, MD, MSCI¹,²,³,⁵

- Tested 8-9am, fasted, medication stopped >5 half-lives before
The world is not divided into normal, mad and PoTS!
The haemodynamic changes vary!

THE CLASSICAL PATTERN
Orthostatic intolerance
Reflex syncope is not required for the diagnosis.
Is this really our patient?

STEP 2:
LET’S MAKE SURE WE’RE NOT MISSING SOMETHING!
The guidelines will help us?! Tiny evidence base!

### Recommendations—Investigation of POTS

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>E</td>
</tr>
<tr>
<td>IIa</td>
<td>E</td>
</tr>
<tr>
<td>IIb</td>
<td>E</td>
</tr>
<tr>
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<td>E</td>
</tr>
</tbody>
</table>

- A complete history and physical exam with orthostatic vital signs and 12-lead ECG should be performed on patients being assessed for POTS.
- Complete blood count and thyroid function studies can be useful for selected patients being assessed for POTS.
- A 24-hour Holter monitor may be considered for selected patients being assessed for POTS, although its clinical efficacy is uncertain.
- Detailed autonomic testing, transthoracic echocardiogram, tilt-table testing, and exercise stress testing may be considered for selected patients being assessed for POTS.
Our approach to testing is empiric and cardiological - because they keep pitching up with cardiac symptoms!

- Tilt / active stand
- Echo
- 7 day Holter
- CPET
- Respiratory function tests
Holter – the HR trend is helpful

Prolonged Holter to:

- Exclude arrhythmia
- Assess the persistence of the daytime tachy’
- Consider whether rate slowing may be of assistance
**CPET**

Very complex investigation

Good assessment of physiology overall, exclude other conditions

Assessment of deconditioning

Dysfunctional breathing

Respiratory function tests can help with CPET, asthma etc
Other things....

- **BLOOD TESTS**
  - FBC, ESR, CRP
  - U&Es, LFTs, TFTs, Glc
  - (CK)
  - Ferritin, B12, folate, Vitamin D
  - (Coeliac, autoantibodies, anti-PL etc)
  - (EBV serology)
  - (Lyme serology)
Results

Cardiovascular reflexes: Resting cardiac vagal tone (CVT): was 6.2 units in the linear vagal scale (LVS) which is a normal vagal tone, (Normal range, 3.5-15 units in the LVS). Resting heart rate: was 78.0 beats/min, which is a normal heart rate for this level of CVT. Breathing: there was normal breathing at the rate of 14.0 breaths/min. Deep breathing: CVT was 11.5 units and the maximum CVT was 14.4 units in the LVS indicating normal respiratory effect on CVT in the brainstem during deep breathing. Carotid massage: CVT increased by 5.8 units in the LVS showing a normal cardiodepressor effect (normal increase 3.5-20 units), blood pressure (BP) changed by -19.0 mmHg indicating a normal vasodepressor effect (normal drop 10-25 mmHg). Baroreflex responsiveness in isometric exercise: was 1.85 ms/mmHg but 1.42 ms/mmHg was predicted from the patient’s height, indicating a normal central gain of the baroreflex system. Phenylephrine injection test: there was no measurement. Valsalva’s ratio: was 2.39 indicating a high Valsalva’s ratio (normal range, 1.2-1.8).

Orthostasis: Cardiac response: showed an abnormally low response in a 30:15 ratio test. BP stability: was good, systolic BP varied by -15.0 mmHg, normal variation is <25 mmHg. Mean supine arterial BP was 77.5 mmHg indicating normal supine BP (the normal range of supine mean arterial BP, 70-110 mmHg). Orthostatic hypotension: Postural change in diastolic BP was +20.7 mmHg. Therefore, no postural hypotension was detected.

Sympathetic function in general: There was no test done for postganglionic damage. Control of resistance blood vessels in skeletal muscles during isometric exercise: showed normal muscle sympathetic tone. Cardioaccelerator function in isometric exercise: showed normal cardioaccelerator function. Blood pressure response to Valsalva’s manoeuvre: BP change in phase Ile was 4.9 mmHg and in phase III was 9.9 mmHg showing evidence of normal venous return. BP change in phase III was 48.9 mmHg indicating raised splanchnic sympathetic tone.

Cutaneous sympathetic function:

<table>
<thead>
<tr>
<th>Sudomotor function</th>
<th>Vasomotor function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotional sudomotor function</td>
<td>Thermoregulatory vasomotor function was not assessed</td>
</tr>
</tbody>
</table>

Interpretation: The results show evidence of normal muscle sympathetic tone, normal cardioaccelerator function and raised splanchnic sympathetic tone in the deep targets of the sympathetic division of the autonomic nervous system. There was evidence of normal venous return to the heart. In the cutaneous targets, there was no sudomotor measurement and there was no vasomotor measurement. Postganglionic sympathetic fibres were not assessed for damage.

In the parasympathetic division, there was normal vagal tone. Baroreflex system had a normal central gain and there was normal respiratory effect on the CVT in the brainstem during deep breathing. There were normal cardiodepressor and normal vasodepressor effects of the carotid reflex.

Of the non-specific tests, there was no postural hypotension, a high Valsalva’s ratio and an abnormally low response of the heart to standing upright. HR increased from 91 to 100 bpm and there were runs of Mayer type waves which were associated with her symptoms of icy legs and headache.

Clinical Interpretation: Despite the relatively modest HR change with standing the Mayer type waves were convincing and were symptomatic. This is more the picture of dysregulation rather than a major autonomic neuropathy.
The tilt can help though.....
Let’s get the treatment started....

STEP 3:
MAKING A DIFFERENCE TO THE ORTHOSTATIC INTOLERANCE
<table>
<thead>
<tr>
<th>Recommendation</th>
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</tbody>
</table>
Non-pharmacological therapy

IT’S NOT SEXY BUT NOTHING WORKS IF THEY’RE NOT DOING THIS!!

REMEMBER THE DIET (INDIVIDUAL)

---

**Box 4 | Key nonpharmacological measures in PoTS**

The primary nonpharmacological measures used in the management of PoTS.

**To be avoided**
- Sudden head-up postural change (especially on waking)
- Prolonged recumbency
- High environmental temperatures (including hot baths)
- Large meals (especially of refined carbohydrate)
- Alcohol
- Undue exertion
- Drugs with vasodepressor and/or vasodilator properties (such as diuretics, nitrates and nifedipine)

**To be introduced**
- High salt intake (in patients who do not have hypertension)
- Water repletion (especially in the morning on wakening)
- Small, frequent meals
- Judicious regular exercise (including swimming)
- Head-up tilt at night
- Physical countermaneuvers to include activation exercises

**To be considered**
- Elastic stockings
- Abdominal binders

Abbreviation: PoTS, postural tachycardia syndrome.
IV Saline (1L) Acutely Decreases Orthostatic Tachycardia

Forensic aspects of water intoxication; Forensic Science International 2012:

- ‘the kidneys of a healthy adult can process a maximum of 15L a day’

- Although...symptoms of intoxication are headache, behaviour changes, muscle weakness, twitching, cramping, nausea, vomiting, sensory disorders, confusion, irritability and drowsiness.....!!

G Jacob et al. Circulation 1997;96:575-580
Dietary Salt in POTS: Raj et al...Study Design

**Design**
- Low Na⁺ Diet (LS) (10mEq/day)
- High Na⁺ Diet (HS) (300mEq/day)

**Endpoints:**
- Plasma volume
- Norepinephrine levels
- Orthostatic vital signs

**Screening**
- POTS/Controls (HC)

**6 day diet**
Dietary Salt in POTS: Summary

- In POTS patients, a HIGH SALT DIET
  - Increases plasma volume
  - Decreases standing plasma norepinephrine
  - Decreases orthostatic tachycardia

- HOWEVER, this did not normalize POTS patients

- POTS patients on a HIGH SALT DIET physiologically resemble Healthy subjects on a LOW SALT DIET
Is salt bad for you?

- Lancet, July 2016:
  - "little robust evidence exists to support a reduction in salt for the general population....the level at which salt intake is regarded as high is not, however, agreed’

  - Pooled analysis of 133118 patients
  - 63559 hypertensive

- Aim for urine excretion >170mmol Na+ in 24 hours
Compression clothing:

- Too complicated....?
- Unacceptable to patients?
- Doesn’t always work!

- But..... Dangerous.....?!?!
  - It’s a problem in fragile skinned, elderly varicose vein sufferers
  - It’s a problem in peripheral vascular disease with an ABI <0.5. Not Raynaud’s.

Table 1. Differences in compression standards

<table>
<thead>
<tr>
<th>Class</th>
<th>British standard</th>
<th>French standard</th>
<th>German (RAL) standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>14–17 mmHg</td>
<td>10–15 mmHg</td>
<td>18–21 mmHg</td>
</tr>
<tr>
<td>II</td>
<td>18–24 mmHg</td>
<td>15–20 mmHg</td>
<td>23–32 mmHg</td>
</tr>
<tr>
<td>III</td>
<td>25–35 mmHg</td>
<td>20–36 mmHg</td>
<td>34–46 mmHg</td>
</tr>
<tr>
<td>IV</td>
<td>N/A</td>
<td>&gt;36 mmHg</td>
<td>&gt;49 mmHg</td>
</tr>
<tr>
<td>Recommendations — Treatment for POTS</td>
<td>Class</td>
<td>Level</td>
<td></td>
</tr>
<tr>
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</table>
PoTS Patients almost invariably describe exercise intolerance

- Deconditioned patients appear rather like POTS patients
- A POTS-like condition can be caused by deconditioning alone / space flight
- Exercise appears to improve clinical findings in POTS

POTS patients have lower stroke volume and higher heart rates compared to controls (although in proportion to their abilities)

- Not clearly a HR control problem but due to the smaller stroke volume

Training increases blood volume, cardiac size, improves orthostatic tolerance, although still not the same as normal.
Fu 2011 Hypertension:
- Exercise when compared to beta-blockers produced favourable cardiac changes and improved quality of life.

Figueroa 2014 J Appl Physiol:
- IV fluids do not improve VO2 max.

Oldham 2016 Pulm Circ:
- Invasive CPET study investigated POTS patients:
  - Had lower stroke volume compared to normal but it couldn’t be normalised with IV fluid.
  - Their problem seemed to relate to venous capacitance and directing blood to the wrong vascular bed.
  - Dilutional effect on haemoglobin meant that vasoconstriction may be better than fluid.
Not all POTS patients are the same with exercise!

- **Pianosi Physiol Reports 2016**
  - Assessed POTS patients on CPET including cardiac output
  - Three different groups:
    - Cardiac output increases with oxygen consumption
    - Cardiac output increases more than expected
    - Cardiac output increases less than expected
  - Couldn’t tell the difference at rest or on the tilt!

- One group ‘hyperkinetic’ – can’t tighten blood vessels to get the blood to the right area

  Vs

- Another group ‘hypokinetic’ – under-filled and blood vessels tightened excessively to maintain some perfusion
Introduction:

- In the research setting exercise leads to better oxygen uptake, larger hearts, larger blood volumes, fewer symptoms – *in fact they suggest in most cases ‘symptom free’* – four refs:
  - Shibata 2012 *J Physiol* – NO assessment of symptoms
  - Fu 2011 *Hypertension* - assessed quality of life
  - Winker *Hypertension 2005* – in Austrian military recruits
  - Fu *JACC 2010* – assessed quality of life

- An attempt at a ‘real-world study’
The International POTS registry

- Screened 304 and enrolled 251 from 36 states and 7 countries. All had POTS by standard criteria.

- Stopped medication, stand test, assessed quality of life

- Then three month exercise program
  - Cardio’ and weights
  - For those who were too unfit, a 2 month lead in program first

- Then re-assessment with stand test and quality of life
Screened (n=304)

Excluded (n=48);
- DNQ per stand test (n=35)
- DNQ tilt test (n=5)
- Age (n=3)
- Incomplete data (n=5)

Enrolled (n=251)

Completed (n=103)
- Full data (n=78)
- Partial data (n=11)
- Completed training, no follow-up data (n=14)

Enrolled

Did not finish program (n=117)
- Other medical problem (n=35)
- Personal reasons (n=23)
- Training difficulty (n=59)
  - Continued training at lower intensity (n=7)

Withdraw prior to enrollment (n=5)

Unable to contact (lost to follow up) (n=31)
The International POTS registry

- Completion rate 41% - similar to cardiac rehab’
  - 24% did not finish because of other things: Lyme, epilepsy, coeliac disease, migraines, SVT and hospitalization
  - 16% for personal reasons: couldn’t afford the gym or lack of access to exercise equipment
  - 21% no contact made
  - 40% as it was ‘too difficult’

- BUT
  - 71% no longer qualified for HR criteria: ‘in remission’ / ‘cured’
  - Continuing exercise maintained the response
Is it all deconditioning?

Joyner 2008 Clin Auton Res: Some postulate that it is all deconditioning developing after an illness associated with somatic hypervigilance and worsened by over-medicalization.

Not all patients with orthostatic intolerance are deconditioned.

- Parsaik 2012 Neurology: 90% deconditioned in one study.

- Burkhardt 2011 J Paeds: Exercise studies in teens: 2/3 of their cohort with OI and CF were deconditioned. When dividing OI from POTS and deconditioning from normal there was no correlation.
Advice for cardio’ exercise based on the papers

### Table 2: Short-term exercise training program

<table>
<thead>
<tr>
<th>Training type</th>
<th>Month 1</th>
<th>Month 2</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base pace (RPE 13–15)</strong></td>
<td>10 × 30 min</td>
<td>6 × 30 min</td>
<td>5 × 35 min</td>
</tr>
<tr>
<td><strong>Maximal steady state (RPE 16–18)</strong></td>
<td>1 × 20 min</td>
<td>3 × 35–40 min</td>
<td>4 × 45–60 min</td>
</tr>
<tr>
<td><strong>Recovery (RPE 6–12)</strong></td>
<td>1 × 25 min</td>
<td>1 × 25 min</td>
<td>1 × 30 min</td>
</tr>
<tr>
<td><strong>Strength training</strong></td>
<td>2 × 40 min</td>
<td>1 × 35 min</td>
<td>1 × 40 min</td>
</tr>
<tr>
<td><strong>Cardiovascular modes</strong></td>
<td>8 × 15–20 min</td>
<td>8 × 20–25 min</td>
<td>8 × 30 min</td>
</tr>
<tr>
<td>Recumbent bike</td>
<td>Swimming</td>
<td>Month 1 modes plus</td>
<td>Month 1 and 2 modes plus elliptical and treadmill walking</td>
</tr>
<tr>
<td>Rowing</td>
<td></td>
<td>upright bike plus</td>
<td></td>
</tr>
</tbody>
</table>

RPE = rating of perceived exertion (subjective rating of the entire cardio workout on a scale of 6–20: 6 is very, very easy; 11 is fairly easy; 13 is somewhat hard; 15 is hard; 17 is very hard; 19 is very, very hard).

### Rating of Perceived Exertion Borg RPE Scale

<table>
<thead>
<tr>
<th>RPE</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Very, very light</td>
<td>How you feel when lying in bed or sitting in a chair relaxed. Little or no effort.</td>
</tr>
<tr>
<td>7</td>
<td>Very light</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Fairly light</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Somewhat hard</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Hard</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Maximum exertion</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Very hard</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Very, very hard</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Maximum exertion</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>How you felt with the hardest work you have ever done.</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Don’t work this hard!</td>
<td></td>
</tr>
</tbody>
</table>

Target range: How you should feel with exercise or activity.
Advice for cardio’ exercise based on the papers

Table 5. Frequency, intensity, time, and type (FITT) prescription.

| FREQUENCY:     | Physical Therapy: 1 time per week sessions (4 total visits over 4 weeks) |
|               | Home program: 4 times per week ENDURANCE training sessions (see below). |
|               | 1–2 times per week STRENGTHENING sessions (see below). |
| INTENSITY:     | Endurance training: Ideal target HR range: 159–170 bpm (75–85% HRmax); and/or; |
|               | BORG RPE scale (6–20): 11–12 for warm up & cool down; 13–16 during endurance training. |
|               | Strength training: 2–3 interval circuits with each exercise done for 30–40 seconds followed by rest for 20–30 seconds |
| TIME:          | Endurance training: Target duration of 30–45 min (10 min warm up & cool down) |
|               | Strength training: Target duration of 20–40 min |
| TYPE:          | Endurance training: The patient only had access to an elliptical trainer at home. Since the patient safely performed the 1-MWT, the physical therapist felt that this was a safe option that would improve patient adherence. |
|               | Strength training: The physical therapist collaborated with the patient to design an interval resistance program of 9–11 general exercises that progressed from semi-recumbent to upright positions and addressed the hip and trunk weakness. |

HR = heart rate, bpm = beats per minute, RPE = rate of perceived exertion, 1 MWT = 1 mile track walk test, min = minutes.
### Strength training program

<table>
<thead>
<tr>
<th>Exercise Duration (sec)</th>
<th>Rest Interval (sec)</th>
<th>Repetitions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>On Back</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bridge</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Lower Trunk Rotation</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Abdominal Curl</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Dumbbell Flies (3-5 lbs)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>In Sidelying</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hip ABD</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Side Plank</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>On Stomach</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plank on elbows</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>With Chair</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse Dip</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Arm Curls (3-5 lbs)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td><strong>Upright Progression Strength Training Program (Weeks 3-4)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physio Ball (lying on back)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Abdominal Curl</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Dumbbell Bench Press (3-5 lbs)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Dumbbell Flies (3-5 lbs)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>In Sidelying</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side Plank (on elbow or hand) with arm opening</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>On Stomach</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plank on elbows or hands</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>With Chair</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reverse Dip (feet propped if tolerated)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Seated AFR overhead press with twist (3-5 lbs)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Sit to Stand (pushing with arms only as needed)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td><strong>Rest Interval</strong></td>
<td>1–2 minutes</td>
<td></td>
</tr>
<tr>
<td><strong>In Standing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm Curls (3-5 lbs)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
<tr>
<td>Hip ABD (with Elastic Band as tolerated)</td>
<td>30–40</td>
<td>20–30</td>
</tr>
</tbody>
</table>

2 weekly sessions initially 15–25 minutes & gradually progressing to 30–40 minutes as tolerated. 5–10 minute warm up and cool down with walking or on an Elliptical machine. The 30–40 second exercise interval should allow you to complete 20–30 reps. All Rest Intervals are as needed. Slow down or stop immediately and take a break if any of your POTS symptoms occur.
Spread the workouts during the week, don’t miss more than 2 days, if you can’t complete all of the sessions for one week, do that week again next week

If you stop for me than two weeks, start again

Once you’ve got there, keep doing month 3 INDEFINITELY

Can do strength and cardio’ on the same day

Have at least a day off between strength days
To summarise:

*(Raj S Heart Rhythm 2016)*

**Exercise** is a treatment not a cure

Recumbent exercise first

Comorbidities may cause problems

Need to exercise every other day

MAY NOT FEEL BETTER FOR FIRST 4-6 WEEKS

You may need a physio’ or PT to reproduce the studies BUT anything is better than nothing; focus on low-impact, horizontal exercise
<table>
<thead>
<tr>
<th>Therapeutic strategy</th>
<th>Drug class or mechanism of action</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reducing salt loss and/or plasma volume expansion</td>
<td>Mineralocorticoid</td>
<td>Fludrocortisone</td>
</tr>
<tr>
<td>Vasoconstriction</td>
<td>Sympathetic action on resistance vessels</td>
<td>Midodrine</td>
</tr>
<tr>
<td>Ganglionic nicotinic receptor stimulation</td>
<td>Anticholinesterase inhibitors</td>
<td>Pyridostigmine</td>
</tr>
<tr>
<td>Preventing vasodilatation and tachycardia</td>
<td>$\beta_2$-adrenoreceptor blockers, ideally cardioselective</td>
<td>Bisoprolol</td>
</tr>
<tr>
<td>Preventing postprandial tachycardia</td>
<td>Peptide release inhibitors, Somatostatin analogs</td>
<td>Octreotide</td>
</tr>
<tr>
<td>Directly reducing tachycardia</td>
<td>Selective sinus node blockade</td>
<td>Ivabradine</td>
</tr>
<tr>
<td>Lowering blood pressure if elevated and reducing tachycardia</td>
<td>Central sympatholytic</td>
<td>Clonidine</td>
</tr>
</tbody>
</table>
Small studies confirm haemodynamic benefit and symptom improvement

SR Raj et al. Circulation 2009;120:725-734
ST Coffin et al., Heart Rhythm. 2012;9:1484-90

SR Raj et al., Circulation 2005;111:2734-2740
SNRIs make it worse!

Orthostatic Change

Pre 1H 2H 3H 4H
15 20 25 30 35 40
Atomoxetine Placebo
P_{int} = 0.001

Time Post Dose

\Delta Heart Rate (bpm)

Symptoms: 0 to 2h

-8 -6 -4 -2 0 2 4 6
Atomoxetine Placebo
P = 0.028

\Delta Symptoms Score (a.u.)

SR Raj et al., AAS Presentation (2010)
So what do I do?

- Midodrine first (2.5 – 10mg TDS)
- Ivabradine second (2.5 – 5mg BD – TDS)

- Then think about something else
  - Beta blockers if high functioning (low dose)
  - Fludrocortisone (up to 200 mcg daily)
  - Slow sodium (600 – 1200mg TDS)
  - (Pyridostigmine etc - I don’t prescribe drugs I can’t spell........)
Other things that other people use

- Octreotide
- DDAVP
- SSRI
- EPO
- Pyridostigmine
- Droxidopa
- Modafinil / methylphenidate
- Clonidine / methyldopa
Consider the physiology...

- If it’s empty – fill it
  - Water, salt, fludrocortisone

- If it’s too baggy – tighten it
  - Compression, midodrine

- If it’s too fast – slow it
  - Beta blockers, ivabradine, pyridostigmine

- What works might tell you what’s wrong with their physiology!
But what about all of the other stuff?

STEP 4:
ALL OF THE OTHER SYMPTOMS
### Dysfunctional breathing – respiratory physio’

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Never – 0</th>
<th>Rarely - 1</th>
<th>Sometimes - 2</th>
<th>Often - 3</th>
<th>Very often - 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling tense</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Blurred vision</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Dizzy spells</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeling confused</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Faster/deeper breathing</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short of breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tight feelings in the chest</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bloated feeling in the stomach</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tingling fingers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unable to breathe deeply</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiff fingers or arms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tight feelings around the mouth</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold hands or feet</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feelings of anxiety</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL SCORE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A score of over 23 out of 64 suggests a positive diagnosis of hyperventilation syndrome.
Gastroenterology

- Often complain of:
  - Nausea / vomiting
  - Bloating
  - Pain
  - Constipation / Diarrhoea

- Find a helpful gastroenterologist and look for gastroparesis, SIBO, colonic dysmotility
  - Treat whatever you can!
  - Medications, diet (various)
Urology

- Often complain of:
  - Weak bladders
  - Frequency, urgency, incontinence
  - Recurrent UTI, pain

- Find a helpful urologist and look for a large, insensate bladder
  - Timed and double voiding
  - Antibiotics
  - Catheters etc
Neurology / Sleep / Audiovestibular medicine

- Lots of headaches esp. migraines
- Migraine variant balance disorder
- Psychophysiological insomnia
- Reassurance needed:
  - Neuropathic symptoms....
  - MS....
  - Chiari....
Other stuff that comes up....

STEP 4:
DAY TO DAY MANAGEMENT
Pregnancy implications

- No clear suggestion of adverse consequences
- Symptoms may well get worse – reassure
- Fludrocortisone and beta-blockade are safe
- Don’t do anything differently on our account
  - Standard analgesia and delivery in labour
Anaesthetic implications

- No adverse consequences
- Inform the anaesthetist that it is not a heart problem but is about managing the underfilled
  - Lots of IV fluid
  - TEDs
  - Slow mobilisation
  - Don’t panic with the tachycardia
Hypermobility is very common
- Pain, clicky joints, stretch marks, easy bruising
- PoTS vs hypermobility

Do we need to exclude an inflammatory arthritis?

Find a helpful rheumatologist
- Try to refer to the hypermobility experts for pain management, specialist physio etc
Complex 2017 classification

- Common forms have unknown genetic cause
- hEDS – very specific criteria
- HMSD – bendy but not fulfilling above criteria
Red flags for referral to genetics:

Joint hypermobility and FH if:
- Extensive, widened atrophic scars
- Significant sagging skin
- Premature aged appearance
- Significant kyphoscoliosis
- History of organ rupture
- Young onset unexplained arterial dissection
- Hand and foot deformities
- Young age unexplained significant / extensive varicosities
- Recurrent large hernias
- Recurrent pneumothoraces
Association with POTS etc

- Apparent association with PoTS, OI and NCS
- Many patients (94% in one series) with hEDS had autonomic symptoms
  - more than with other forms of EDS
  - more hypermobility correlated with greater haemodynamic change on tilting
- Cause uncertain
  - ?pooling
  - ?small fibre neuropathy
  - ?deconditioning
Why might it be relevant?

- Consideration of other family members (clear genetic association)
  - Including rare, dangerous conditions
- EDS effects e.g. wound healing, local anaesthetic, difficult intubation
- Exercise advice may need to be modified
  - Low impact
  - Use of splints for joint protection
- Aetiology in POTS may define clinical characteristics
  - JHS patients younger, no preceding viral illness, more headaches, poorer quality of life
  - Some of PoTS features may in fact be JHS features....
Mast cell activation syndrome

Cookson Clin Med 2016
Doherty Auton Neurosci 2018
Mast cell activation syndrome

Cardiovascular
Presyncope (lightheadedness, weakness, dizziness, vertigo) and/or syncope (71%), hypertension and/or hypotension, palpitations and dysrhythmias (47%), chest discomfort or pain (usually non-anginal in character (40%)), coronary and peripheral arterial atherosclerosis/spasm/infarction, aneurysms, hemorrhoids, varicosities, aberrant angiogenesis (hemangiomas, arteriovenous malformations, telangiectasias), migratory edema (often non-dependent and in spite of normal cardiac and renal function) (56%)

- Theoretical reasons why they might be involved
  - mast cell : nerve interaction, involvement in autoimmunity
  - Hypertryptasaemia patients commonly have PoTS
  - Mast cell activation increased in association with EDS

- Consider if allergies, rashes, bladder pain, abdo pain / diarrhoea, hypertensive PoTS

- Testing.....?!
  - Urinary methylhistamine / 11 beta PGF2 alpha / LTE4; serum tryptase
  - Likely imperfect investigations however

- Try to find an expert (and let me know when you do...)

- **Empirical treatment (high dose cetirizine, ranitidine, Na+ cromoglicate etc) for a limited time**
What effects does POTS have on the patient’s life?

5% bedbound
23% wheelchair users
11% lost driver’s license
To conclude:

- Recognise the patient by the symptoms more than the HR change
- Exclude other conditions
- Do the simple stuff extremely well
- Consider medications
- Treat the associated features
- Be honest and caring because we don’t have all of the answers!
...AND ON THAT DREADFUL DISAPPOINTMENT...

THANK YOU FOR YOUR ATTENTION