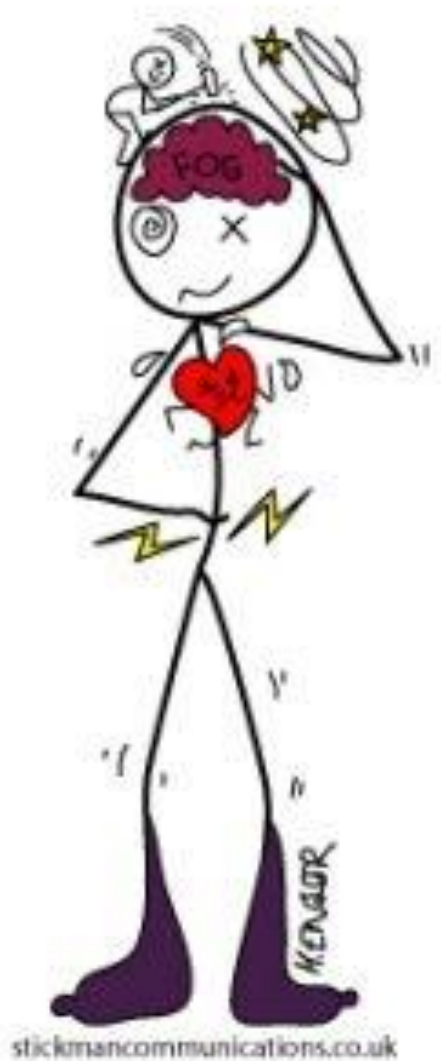




Hypermobility 102:

Postural Orthostatic Tachycardia Syndrome (POTS) and Mast Cell Activation Disorder (MCAD) Associated with Hypermobility Spectrum Disorder

Leslie N Russek, PT, DPT, PhD, OCS

Clarkson University, Canton-Potsdam Hospital, Potsdam, NY

Slides are available on my web site:

<https://webpace.clarkson.edu/~lrussek/hsd.html>



Who Am I?

- Professor Emeritus, Physical Therapy Department, Clarkson University
- Staff PT, St. Lawrence Health System, Potsdam NY
 - Clinical specialties: hypermobility, fibromyalgia, headaches, temporomandibular disorders
- Frequent presenter to professional and patient groups at national conferences
- Author of multiple review and research articles on hypermobility
- Author of "Chronic Pain" chapter in *Physical Rehabilitation* textbook for PT students
- Lrussek@Clarkson.edu
- <https://webpace.clarkson.edu/~lrussek/>

**I do not have any
conflicts of interest to report**

DISCLAIMER

- I cannot provide individual medical advice in this presentation: I cannot diagnose or provide personal treatment recommendations.
- The information provided here is generally applicable to HSD/hEDS, but your personal situation may be different.
- You should discuss options with your healthcare provider before starting a new management approach.



“HSD 101” Lecture Series

I will refer to
these if you
want more info

- HSD 101: Basics of HSD/hEDS and self-care
- HSD 102: POTS and POTS self-care, basics of MCAD
- HSD 103: Pain management in HSD/hEDS
- HSD 104: Safe exercise selection and progression with HSD/hEDS
- HSD 104 part 2: Nuts and bolts of modifying exercise with HSD and POTS
- HSD 105: Posture and joint protection
- HSD 106: Gut issues in HSD/hEDS, POTS, MCAD
- HSD 107: Fatigue in HSD/hEDS and POTS
- HSD 108: Headaches, migraines, and TMJ pain in HSD, POTS and MCAD
- HSD 109: Breathing dysfunctions in HSD
- HSD 110: Lumbar instability
- HSD 111: Cervical instability
- HSD 112: The vagus nerve
- HSD 113: The importance of fascia
- HSD 114: Surgery and hospitalization precautions
- HSD 115: Functional Neurological Disorder



Relevant Handouts Available



Scan for website link.
Will show again at end.

- <https://webpace.clarkson.edu/~lrussek/research.html>
- **POTS**
 - [Overview of POTS symptoms and causes.](#)
 - [Checklist for POTS self-care management.](#)
 - [Flow charts for POTS management, including fatigue and sleep.](#)
- **MCAD self-care**
 - [Suggestions for managing MCAD.](#)
 - [How to check your medications for \(MCAD\) sensitivities.](#)
- **General Self-Care Strategies**
 - [Breathing.](#) Breathing incorrectly can increase pain sensitivity, headaches, jaw pain, and more.
- **Links to other resources**
 - www.potsuk.org POTS-UK
 - <http://www.dysautonomiainternational.org> Dysautonomia International.
 - <https://www.dysautonomiasupport.org/handbooks/> Disautonomia Support has excellent suggestions about school and work accommodations for POTS
 - <https://tmsforacure.org> The Mast Cell Disease Society.
 - <https://www.mastzellaktivierung.info/en/introduction.html>. (has English language pages)



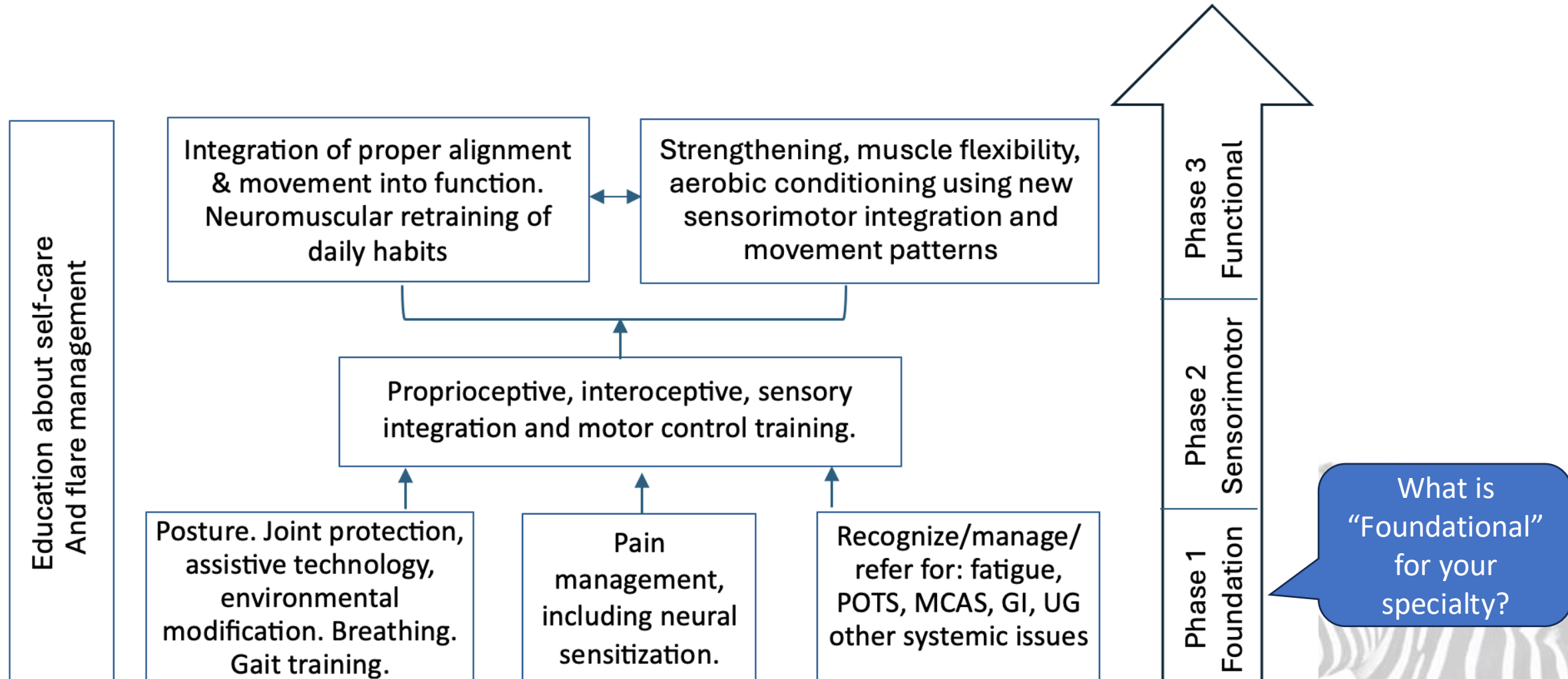
Learning Objectives

At the end of this session, participants will be able to:

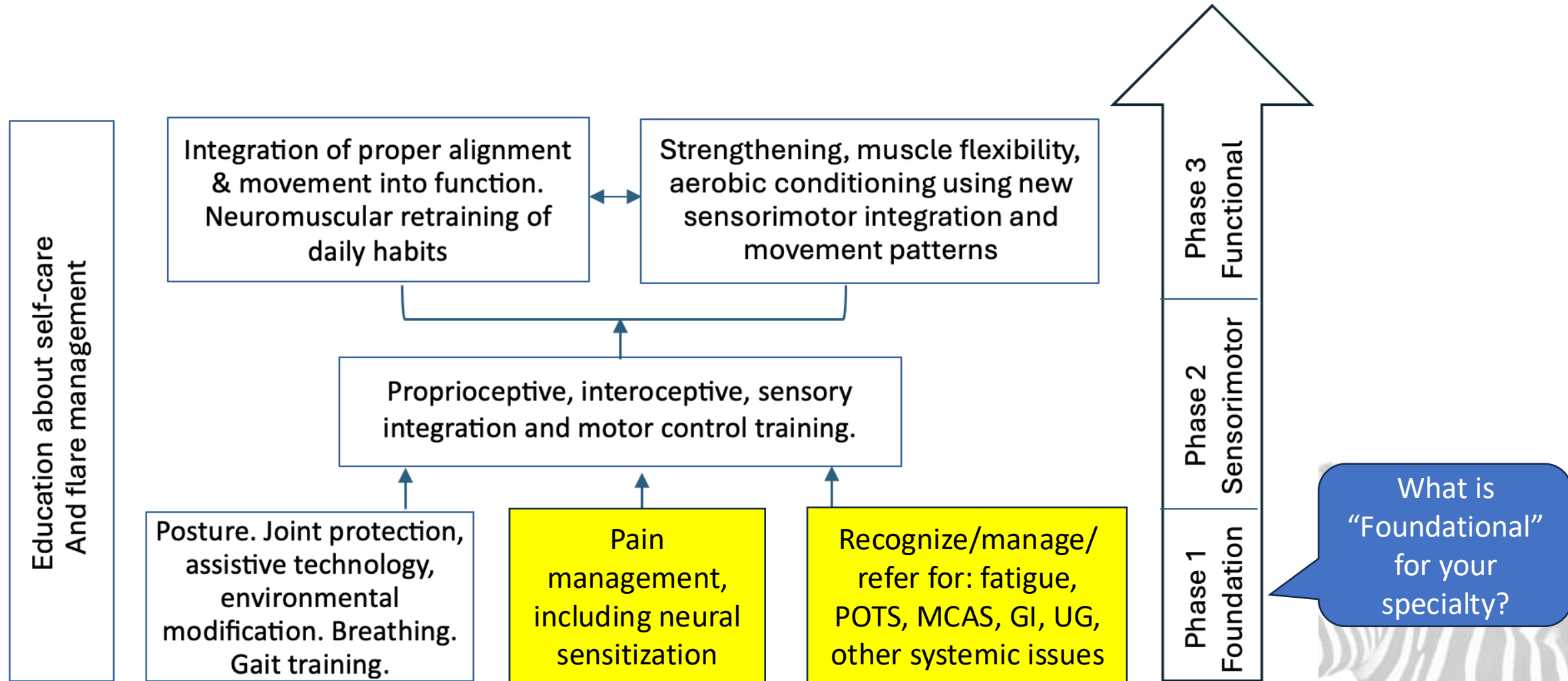
1. Describe the possible relationships among HSD, POTS and MCAD
2. Recognize signs and symptoms of Postural Orthostatic Tachycardia Syndrome (POTS) as the most common form of dysautonomia; contrast with Orthostatic Intolerance (OI)
3. Describe self-management strategies for POTS
4. Identify medical approaches to POTS management
5. Recognize signs and symptoms of Mast Cell Activation Disorder/Syndrome (MCAD/S)
6. Describe self-management approaches for MCAD/S.



PT Approach to Managing HSD



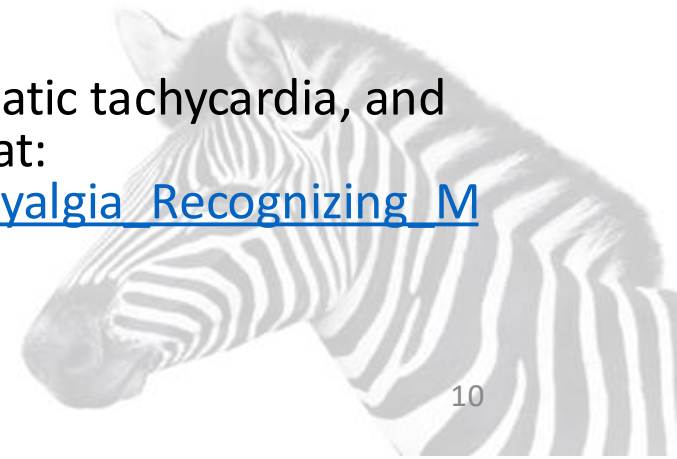
PT Approach to Managing HSD



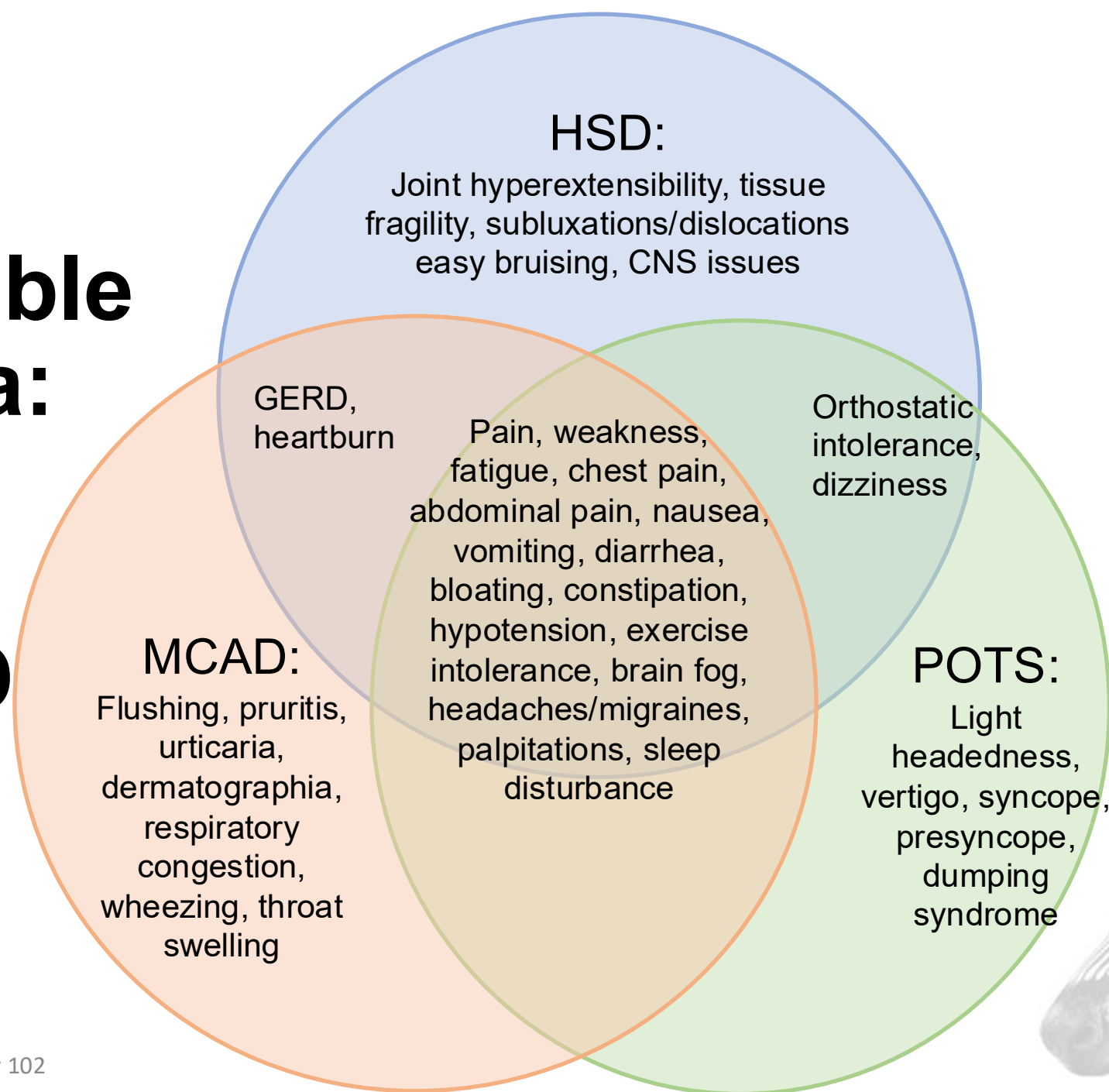
Why Discuss POTS, MCAD Here?

Why are we talking about POTS and MCAD in “HSD102”?

- POTS, MCAD and Hypermobility frequently co-exist as **“The Terrible Trifecta”**
- Together, HSD, POTS, and MCAD look like fibromyalgia
- Interestingly... POTS, MCAD & Chronic Fatigue Syndrome/Myalgic Encephalitis look like Long-COVID
- Russek LN. Is it really fibromyalgia? Recognizing mast cell activation, orthostatic tachycardia, and hypermobility. *Orthopaedic Practice*. 2018;30(3):187-193. Available on-line at: https://www.researchgate.net/publication/326426655_Is_It_Really_Fibromyalgia_Recognizing_Mast_Cell_Activation_Orthostatic_Tachycardia_and_Hypermobility ..



The Terrible Trifecta: HSD POTS MCAD

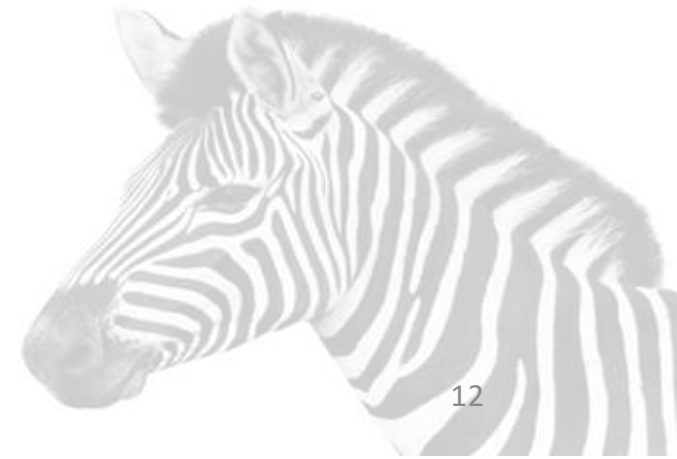


Dysautonomia & POTS

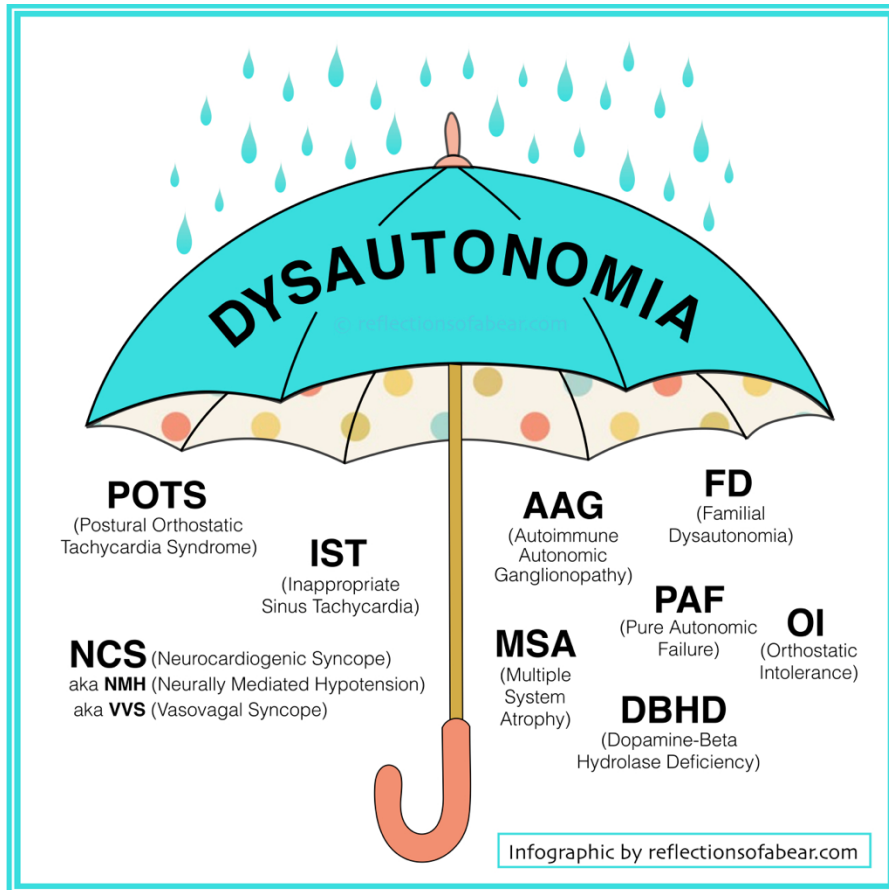


Why is it so common in HSD?

- Mechanical reasons
- Neurological reasons



Types of Dysautonomia



If your body is able to compensate with increased heart rate:

- Postural Orthostatic Tachycardia Syndrome (POTS) – most common

If your body is NOT able to compensate with increased heart rate (e.g. 'just because' or due to meds such as anxiety meds):

- Orthostatic hypotension/ intolerance (OI) is also common.
 - Tinkle et al, 2017
 - Blitsheyn, 2022

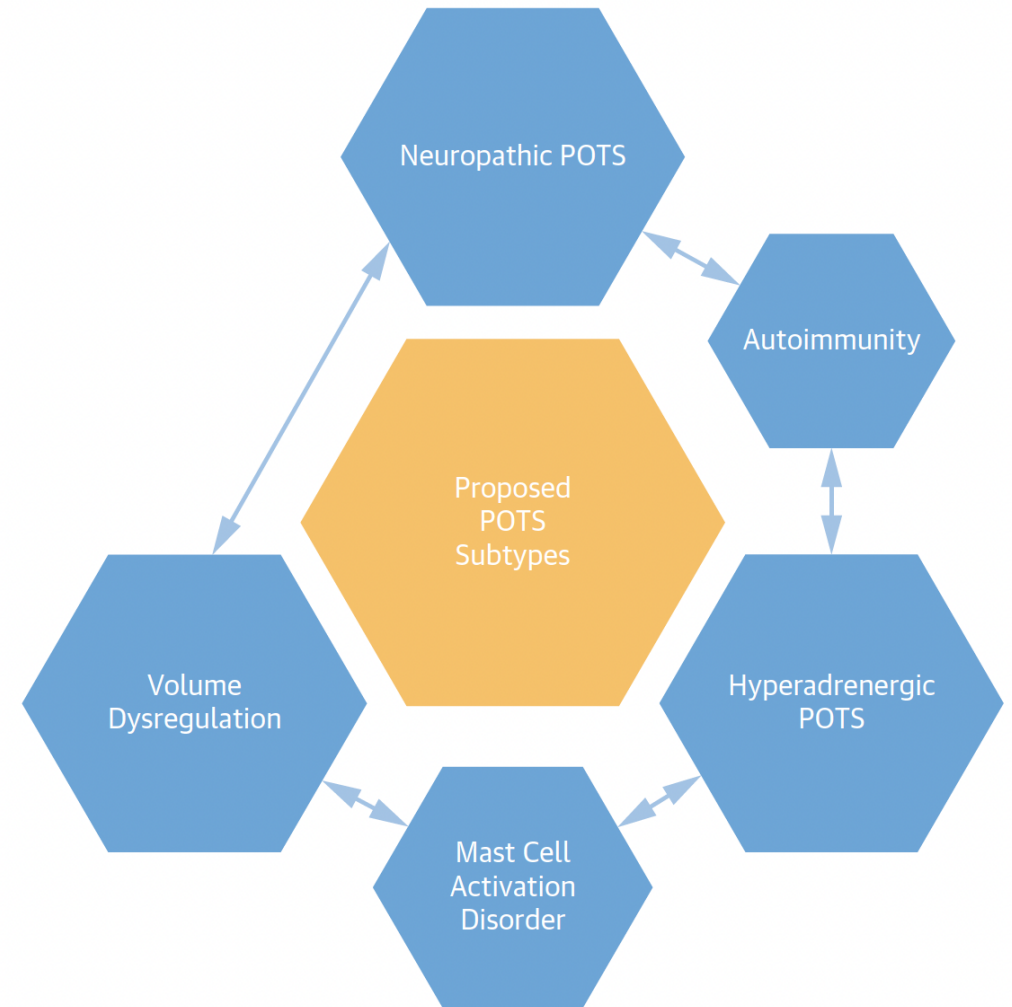
Types of POTS

- Volume dysregulation (30%)
 - Due to stretchy veins, pooling
 - Maybe common in HSD?
- Neuropathic POTS (>50%)
 - Decreased autonomic nerve function
 - Less anxiety & depression, ↓ sweating
 - Maybe associated with neck problems?
- Mast Cell Activation (controversial)
 - Flushing, short of breath, headache, lightheaded, ↑ sweating, GI symptoms
 - Maybe contributes to POTS & HSD?
- Hyperadrenergic (30-60%)
 - Palpitations, tremulous, sweating, nausea
 - Increased by exercise & stress
- People may have multiple types or switch among different types
- Non-pharmacological management probably the same

(Bryarly, 2019)

L. Russek, Hypermobility

FIGURE 3 POTS and Proposed Subtypes



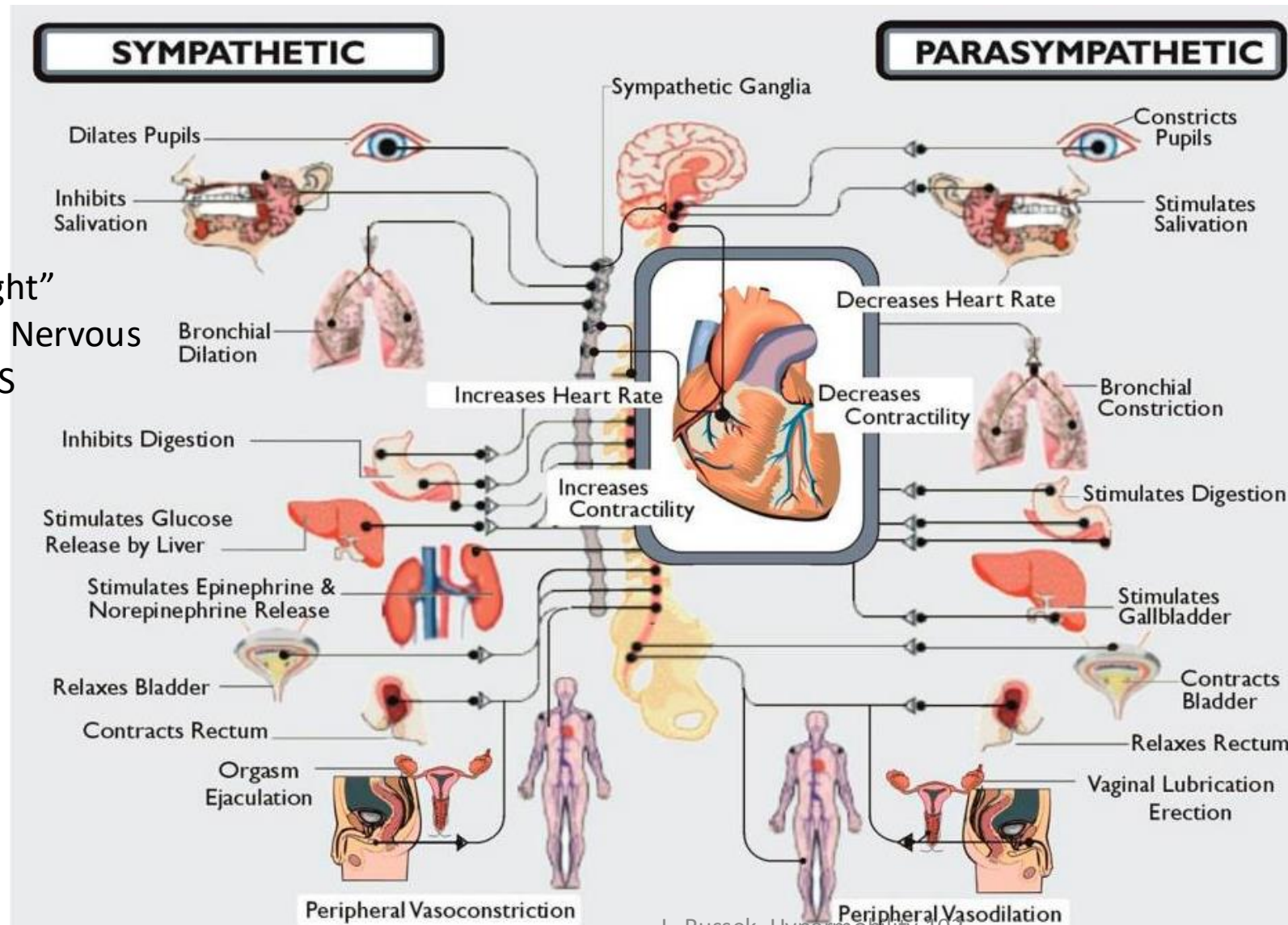
Several subtypes of POTS have been proposed and include neuropathic POTS, autoimmunity, hyperadrenergic POTS, mast cell activation disorder, and volume dysregulation. These subtypes are not mutually exclusive or clearly independent. POTS = postural orthostatic tachycardia syndrome.

Prevalence of POTS

- Prevalence not known, as it is often undiagnosed
- Diagnosis often requires ≥ 4 years, 7 MDs
- Maybe 0.5-3M in US
 - This is more than all MS and Parkinson's together
- Maybe 1% of all teenagers
 - 52% have onset ≤ 18 years old..
- (Stiles, 2017)



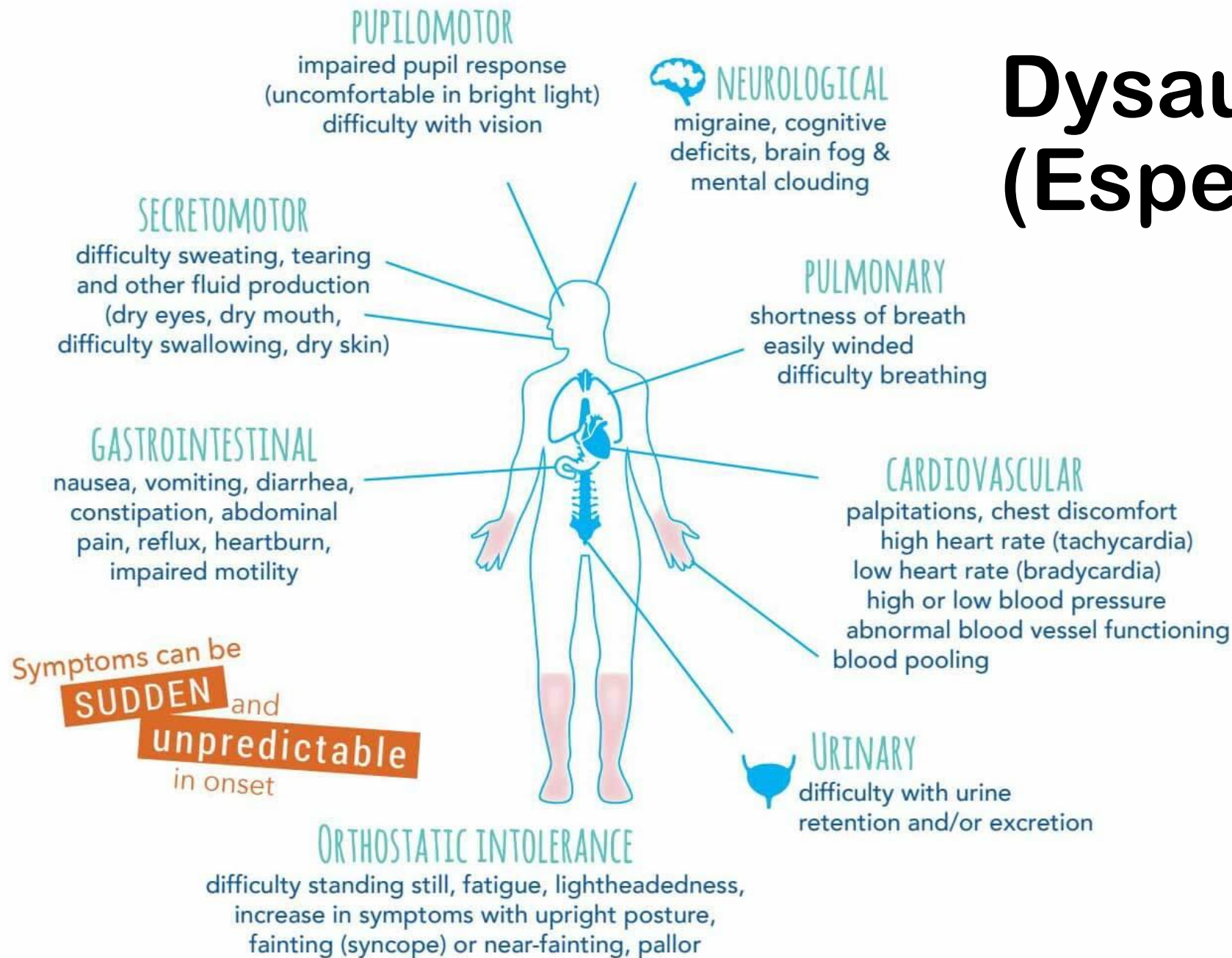
The Autonomic Nervous System



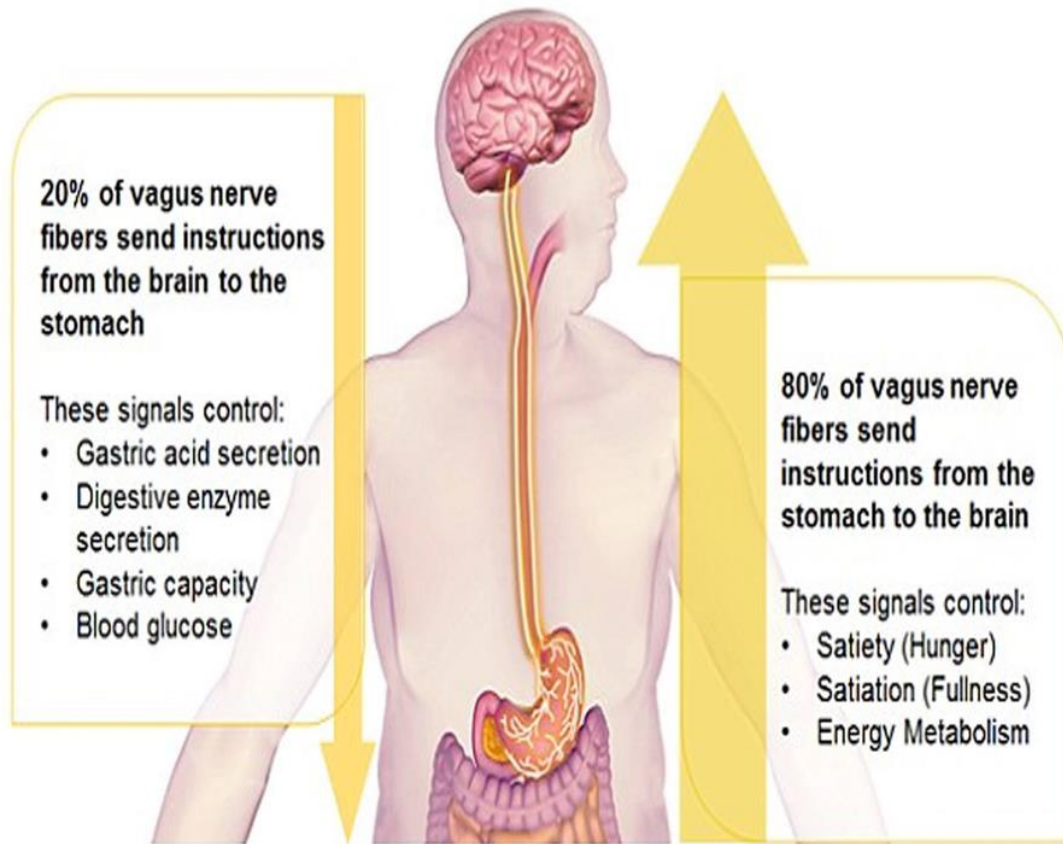
"Rest and Digest" or
"Breed and Feed"
Parasympathetic
Nervous System = PNS



Dysautonomia (Especially POTS)



Vagus Nerve and Dysautonomia



- Vagus nerve:
 - Controls autonomic function (sympathetic/ parasympathetic activity)
 - Communicates from the body to the brain
- Vagus nerve function is disrupted in POTS

- Anjum, 2018

<https://www.facebook.com/IBSHelpisHere/photos/pcb.326199840910720/326199620910742/>



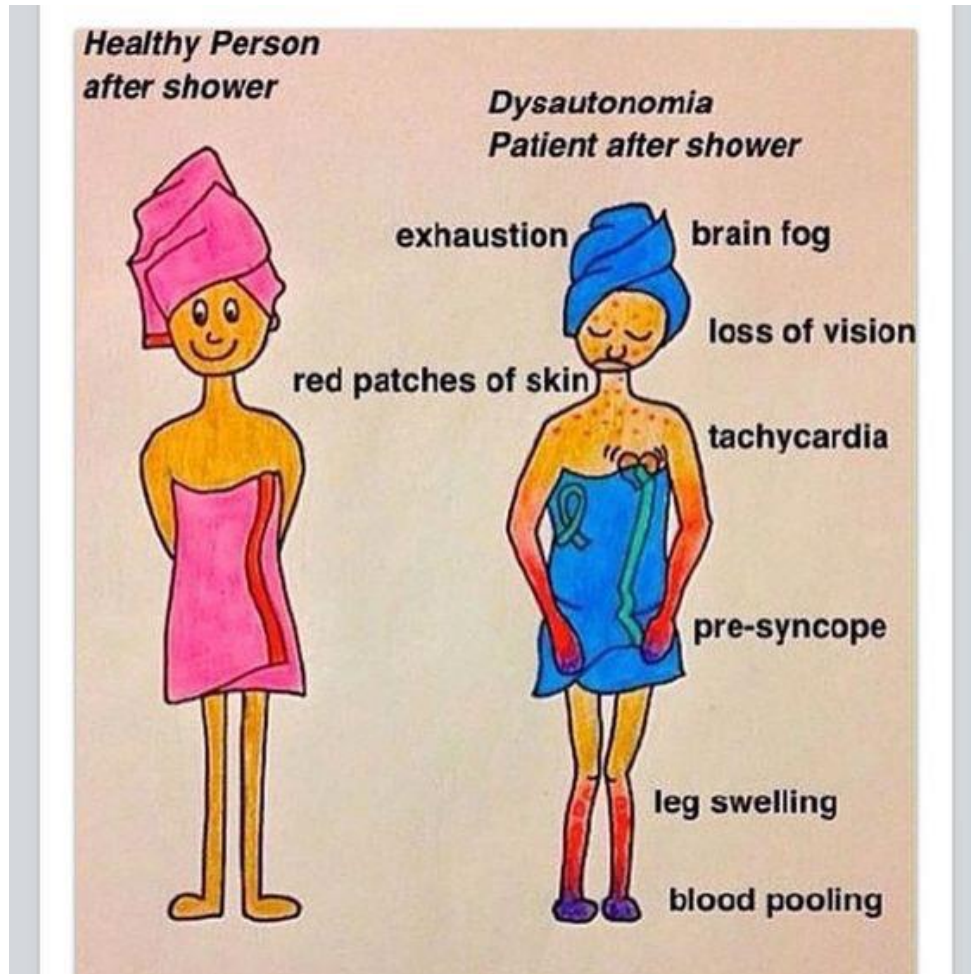
Pain, Inflammation and Autonomic System

- The autonomic and immune systems interact
- Increased SNS balanced with decreased PNS
- Increased SNS:
 - Triggers local inflammatory response, muscle spasm and contraction of fascia
 - SNS forms abnormal connections to neurons transmitting pain info
- Decreased PNS:
 - Decreased vagus nerve function of suppressing inflammation leads to increased local or systemic inflammation
 - Disrupts gut function, and gut sends signals to the brain that amplify pain processing and neural inflammation

Elenkov, 2000 (5); Guo, 2019 (5); Johnson, 2018 (5)

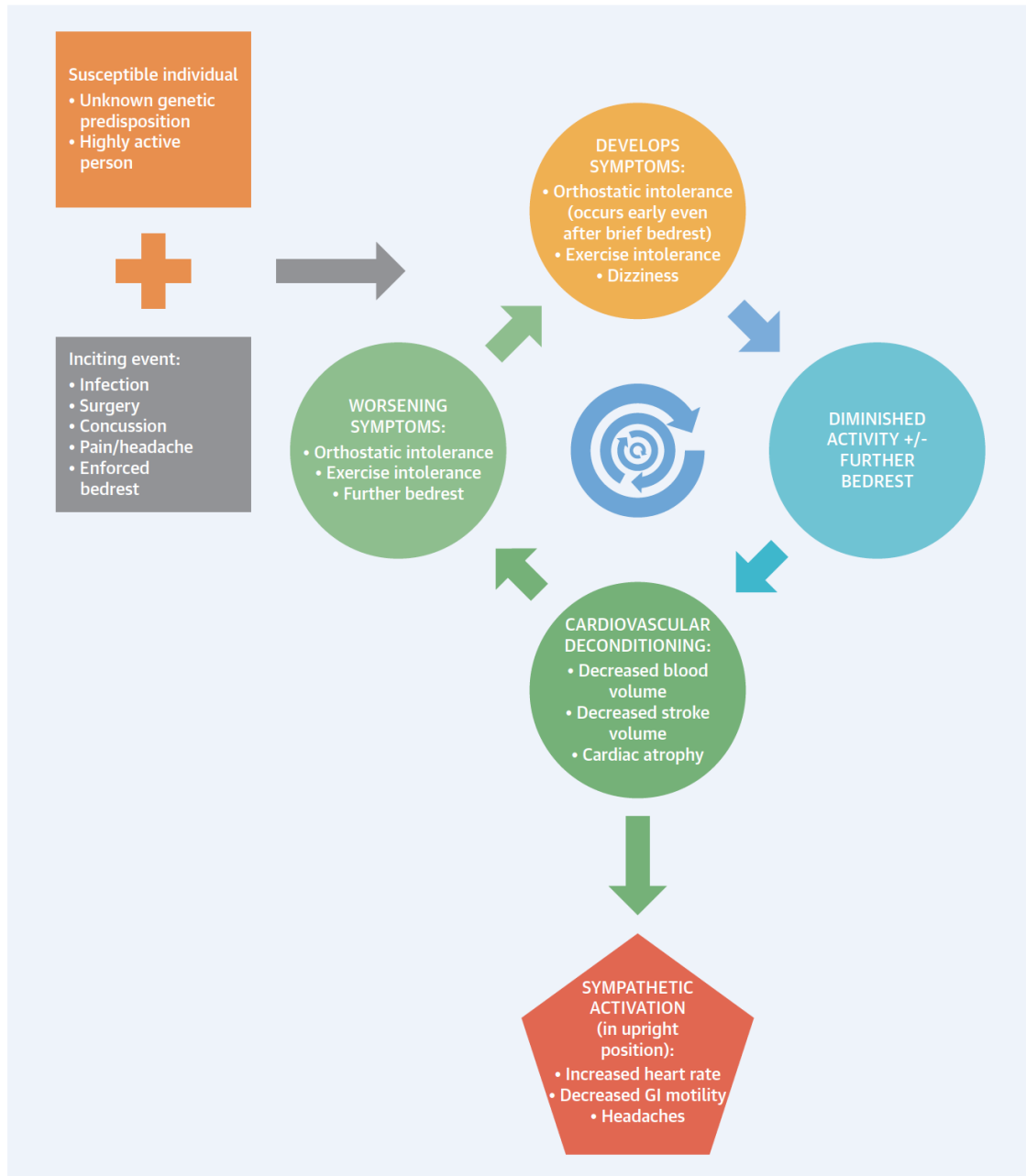


POTS Looks Like...



Acrocyanosis
Stiles, 2017





POTS Downward Spiral

- HSD is a risk factor
- Common triggers:
 - Puberty
 - Concussion or trauma
 - COVID or other viral illness
 - MCAD flares
 - Upper cervical instability
- Prevalence 6.8% in children/teens

Chen, 2020; Zhang, 2020
Wells, 2018; Fedorowski, 2019



Characteristics of POTS

- In a sample of 779 people with POTS in the UK
 - 92% were female
 - 81% were 18-49 years old
 - Most common symptoms:
 - Fatigue: 91%
 - Dizziness & near-fainting: 90%
 - Palpitations: 86% (may present as anxiety)
 - Fainting or blackouts 58%
 - Brain fog, trouble concentrating 40%
 - 37% stopped working due to POTS
 - Of school age respondents, 50% missed 3 months or more of school..

• Kavi, 2016

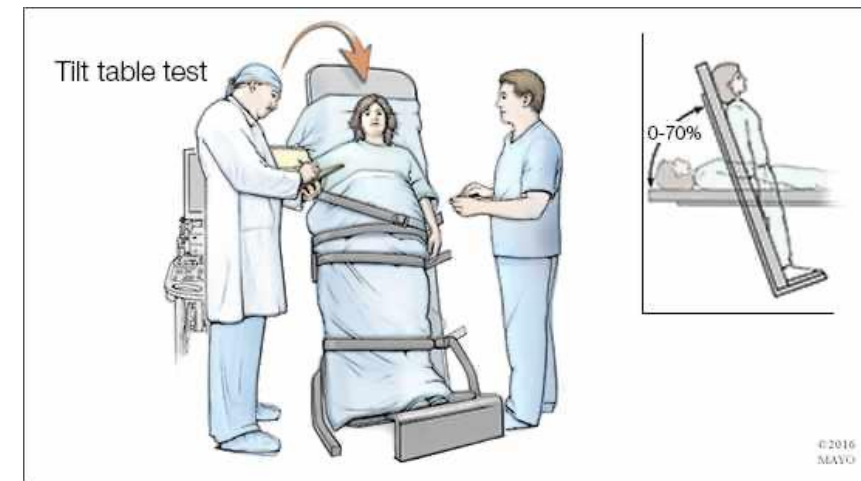


POTS-Related Headaches

- Headaches and migraines are common in POTS: 41-96%
- Migraines most common in POTS
- Sleep-disturbance HA
- Coat-hanger HA
- POTS is commonly overlooked in patients with migraine
- (Cook, 2018; Wig, 2019; Fedorowski, 2019)



POTS Diagnostic Criteria



- Stand Test, Lean Test, Tilt Table Test:
- Adults: Heart rate increases (and remains high for several minutes) ≥ 30 bpm from lying down to upright (10 min). BP drop $< 20/10$
- Children: HR increases ≥ 40 bpm
 - OR maximum HR > 130 BPM, (6-12 y/o), 125 BPM (13-18 y/o)
- Symptoms worsen with standing and improve lying down
- Symptoms last ≥ 6 months
- Absence of other obvious cause of orthostatic symptoms or tachycardia (e.g., active bleeding, acute dehydration, medications)..

Instructions for POTS Stand Test available at:

<https://batemanhornecenter.org/assess-orthostatic-intolerance/>

Raj et al, 2013

Common Triggers of POTS Episodes

POTS Checklist

- Excess heat (hot weather, showers, etc.)
- Eating – especially refined carbohydrates & sugar
- Rapid position changes, sitting/standing up quickly
- Dehydration
- Time of day (especially mornings)
- Menstrual period (for women)
- Alcohol (which dilates blood vessels)
- Inappropriate or unaccustomed exercise

<https://www.potsuk.org/symptoms> ..



Pectus Excavatum

- The ribcage dips in at the breastbone
- **Symptoms overlap with POTS!**
- More common in EDS
- Sometimes, there are no physical symptoms
- Symptoms can include:
 - Decreased exercise tolerance
 - Fatigue
 - Respiratory problems
 - Palpitations or tachycardia
 - Chest pain
 - Dizziness
- Difference: PE is worse when lying down, better when upright





Questions?



Orthostatic Intolerance and Postural Orthostatic Tachycardia Self-Care Checklist

POTS/OI Self-Care

1. Identify and avoid your triggers

a. Physical triggers:

- .. Extreme heat, hot showers/baths.
- .. Standing up quickly or for long periods.
- .. Holding arms up for an extended time.
- .. Lifting objects over 10–15 pounds.
- .. Climbing long flights of stairs.
- .. Donating blood.

b. Food/beverage triggers:

- .. Getting dehydrated.
- .. Caffeine (especially energy drinks).
- .. Extra-large meals, especially high carbohydrate or sugar meals.
- .. Alcohol.
- .. Foods high in gluten or other allergens.

c. Psychological triggers:

- .. Stress at home or work; (note that POTS is not just anxiety and is not caused by anxiety).

2. Learn short-term 'countermeasures' to control acute onset of symptoms

a. Standing:

- .. Cross and squeeze legs and buttocks; Squat; Do calf raises, Stand with one leg on a chair.
- .. Shift weight side-to-side, bounce on your toes, fidget, walk in place.
- .. Bend slightly forward from the waist (such as leaning over a shopping cart).

b. Sitting:

- .. With knees tucked to your chest.
- .. With feet propped/elevated.
- .. Leaning forward with hands on the knees.

c. Lying down:

- .. With feet propped up on a chair or against a wall; pumping your feet helps even more. Try not to lie still for a long time, as this can make POTS symptoms worse.

d. Other:

- .. Before sitting or standing up, pump the ankles, then tense and release your thighs, then your buttocks; Squeeze a ball to pump your arms.
- .. Take deep belly breaths to help return fluids to your heart. Inhale against resistance (like sucking in air through a straw). Cough.
- .. Cool your skin with a water mister or cold wet cloth on your face. Finish showers with cool water.

3. Implement long term prevention/self-care

a. Food/beverage strategies

- .. Drink lots of fluid and electrolytes (100 ounces, or 3L, per day). Avoid sugary drinks.
- .. Eat lots of salt (8-10 grams per day) and/or use an electrolyte supplement.
- .. Eat small, frequent meals (with salt); avoid high sugar/carbohydrate foods.

b. Physical strategies

- .. Get up and move around frequently throughout your day. This decreases blood pooling.
- .. Practice deep, diaphragmatic breathing at least once a day, preferably more often.
- .. Use compression socks/stockings (20-40 mmHg, waist high works best) or an abdominal binder.
- .. Participate in an appropriate exercise program. Some people need to start in a reclined position and focus on leg and core strength. (i.e.: recumbent bike, swimming, row machine, leg machines). Progress gradually.

c. Psychological strategies

- .. Relaxation practice through diaphragmatic breathing, meditation, biofeedback, etc.

Leslie Russek, PT, DPT, PhD, Clarkson University

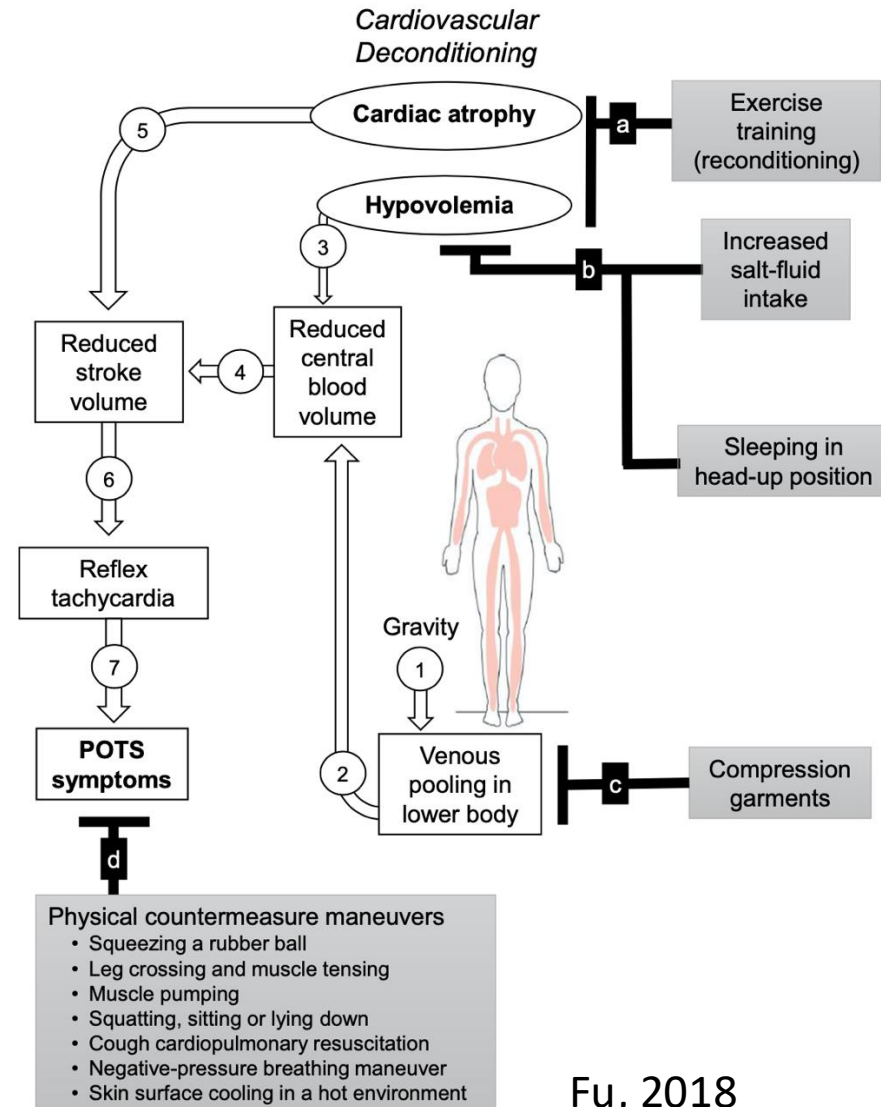


1. Avoid POTS/OI Triggers

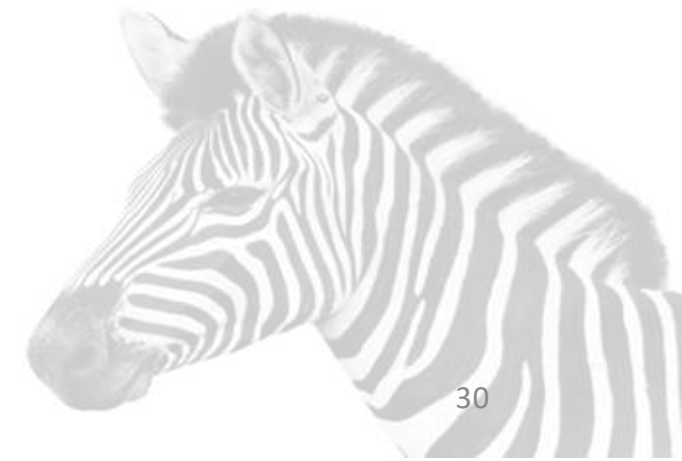
- **Physical triggers:**
 - Extreme heat, hot showers/baths.
 - Standing up quickly or for long periods.
 - Holding arms up for an extended time or Lifting objects over 10–15 pounds.
 - Climbing long flights of stairs.
 - MCAD flares
- **Food/beverage triggers:**
 - Getting dehydrated.
 - Caffeine (especially energy drinks).
 - Extra-large meals, especially high carbohydrate or sugar meals.
 - Alcohol.
 - Foods high in gluten or other allergens.
- **Psychological triggers:**
 - Stress at home or work; (note that POTS is not just anxiety and is not caused by anxiety).



Overview of POTS Management

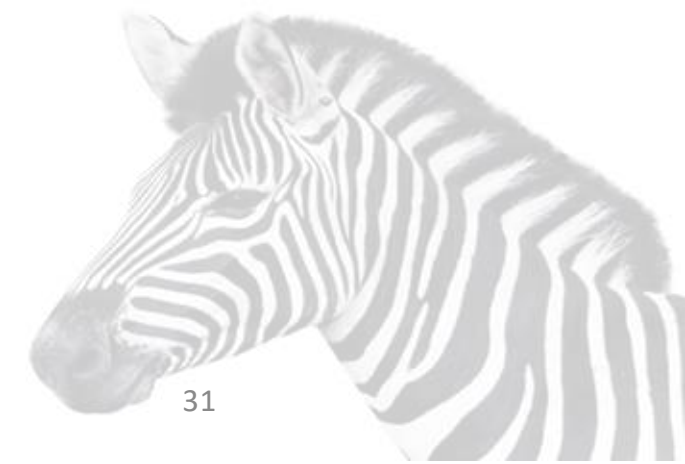
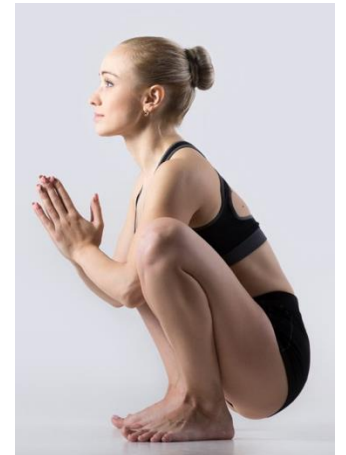


- Countermeasures for acute symptoms
- Long term management to prevent/control symptoms



Maneuvers	Brief description	Action mechanisms
Squeezing a rubber ball	Static or rhythmic muscle contraction to increase mean arterial pressure and prevent orthostatic intolerance or syncope	Sympathetic activation, vagal withdraw, or both via the exercise pressor reflex
Leg crossing and muscle tensing	Crossing one foot in front of the other and squeezing the thighs and gluteal muscles together	Restoration of venous return and prevention of further blood pooling in the lower body
Muscle pumping	Swaying, shifting, tiptoeing, or walking	Activation of the muscle pump in the legs to increase venous return
Squatting, sitting, lying down	Squatting is a combination of sitting, bending and muscle tensing; sitting and lying down to reduce/eliminate gravitational stress	Facilitating venous return from the legs to the heart and increasing central blood volume
Cough cardiopulmonary resuscitation	Forceful coughing	Increasing intrathoracic pressure to force blood out of the chest into the aorta and its branches
Negative-pressure breathing maneuver	Breathe through an inspiratory impedance threshold device	Using endogenous respiratory pump to increase venous return and central blood volume
Skin surface cooling	Spray cold water, use fan and cooling towel to cool the skin in a hot environment	Decreasing blood supply to the skin and reducing clinical symptoms

2. Physical Countermeasures For Immediate Relief



3. Long-Term Control of POTS/OI

- **Food/beverage strategies**

- Drink lots of fluid and electrolytes (100 ounces, or 3L, per day). Avoid sugary drinks.
- Eat lots of salt (8-10 grams per day) and/or use an electrolyte supplement.
- Eat small, frequent meals (with salt); avoid high sugar/carbohydrate foods.
- Gluten-free diet may be helpful for some people (Zha, 2023)

- **Physical strategies**

- Get up and move around frequently throughout your day. This decreases blood pooling.
- Practice deep, diaphragmatic breathing at least once a day, preferably more often.
- Use compression socks/stockings (20-40 mmHg, waist high works best) or an abdominal binder.
- Appropriate exercise. May need to start in a reclined position and focus on leg and core strength. (i.e.: recumbent bike, swimming, row machine, leg machines). Progress gradually.
- Place 6" blocks under the head of your bed; this helps you retain fluid overnight.
- Manage MCAD, if present/flared.

- **Psychological strategies**

- Relaxation practice through diaphragmatic breathing, meditation, biofeedback, etc.



Managing Poor Quality Sleep

Sleep Hygiene & Positioning

- Address pain interfering with sleep

- Positioning for decreased pain
- General pain management
- Mindfulness meditation/relaxation

- Sleep hygiene

- Cool, dark room; winding down routine; avoid screens 1-2 hrs before bed

- Physiological quieting, relaxation training

- Regular exercise

- Good information at <https://sleep.org> .



HSD 107:
Fatigue in
HSD & POTS



Post-Exertional Malaise (PEM)

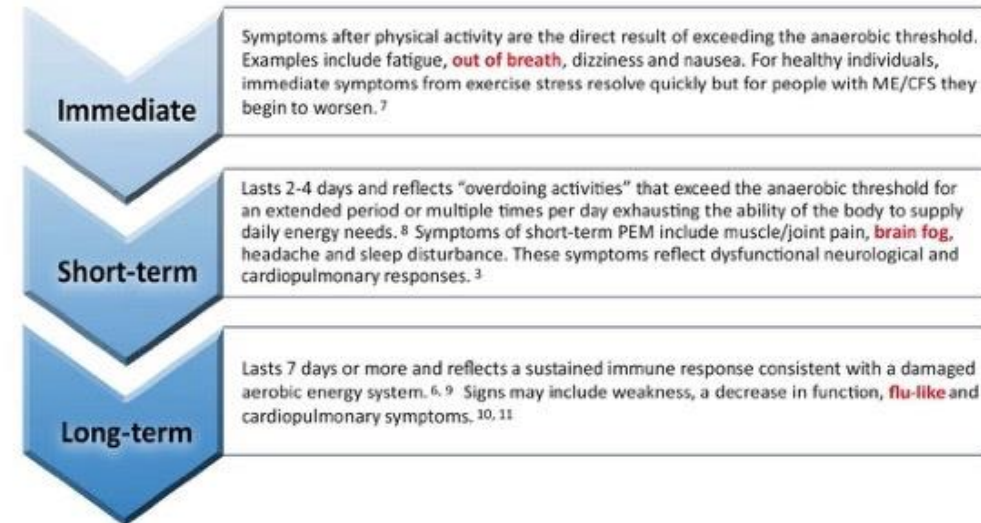
- Commonly seen in Chronic Fatigue Syndrome/Myalgic Encephalitis (ME/CFS)
- Good resources about ME/CFS info from Workwell Foundation:
 - <https://workwellfoundation.org/resources/>
- Important to not push through the fatigue

Post-exertional Malaise (PEM) Timecourse for ME/CFS

What is Post-exertional Malaise Following Physical Activity?

Post-exertional malaise (PEM) is considered the hallmark clinical feature of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). PEM is the worsening of symptoms and decreased function following physical, cognitive, or emotional effort. The onset may occur immediately after activity or be delayed.^{1, 2} Immediate, short-term and long-term PEM symptoms following physical activity can be explained in terms of the damaged energy systems found in ME/CFS.^{3, 4, 5} Overload in other areas (cognitive, emotional, sensory, upright posture, etc) can also cause immediate and longer-term symptoms, but responses to these stressors are less well documented in the literature.⁶

PEM Timecourse



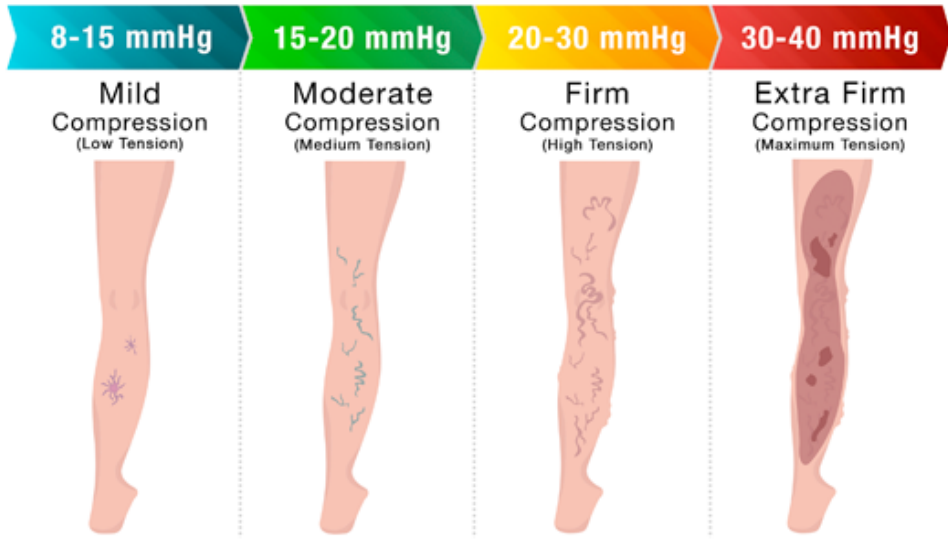
Identifying PEM After Activity

1. Do you experience severe fatigue with at least 3 symptoms in the categories below?
a. feel unwell b. feel weak c. don't sleep well d. have pain
2. Does it take a day or more to recover from exertion?^{10, 12}

Preventing PEM

1. What is your first symptom of PEM?^{2, 13}
2. How long does your PEM last?
3. Do your symptoms progress or change over the immediate/short-term/long-term?

Compression Garments for POTS



MILD COMPRESSION (8-15 mmHg)

Best for healthy legs with few or no visible symptoms. For proactive and preventative wear.

MODERATE COMPRESSION (15-20 mmHg)

Best for legs with minor to moderate symptoms. The common starting point for first time wear.

FIRM COMPRESSION (20-30 mmHg)

Best for legs with major symptoms and/or severe conditions. Wear when specifically directed by a doctor or health care provider.

EXTRA-FIRM COMPRESSION (30-40 mmHg)

Best for legs with severe conditions. Wear when specifically directed by a doctor or health care provider.



Knee high socks are no longer recommended!

- Compression stockings 20-40 mmHg
 - Consider compressive sports clothing or slimwear
 - Abdominal binder/compression or compression shorts
 - Compression tights for PoTS should be waist high for maximum benefit. Knee high socks seldom ideal.
 - CWX brand, Old Navy, FourYourLegs, BrightLifeDirect, etc.
 - If you have trouble putting compression stockings on because of finger instability, try using a 'stocking assist' or use 2 layers of 20 mmHg stockings.

- https://www.potsuk.org/compression_clothing



POTS Exercises: Starting Out

If you are very deconditioned, start easy:

- Lying down exercises encourage blood return to heart
 - Squeeze pillow between legs; Pillow between palms
 - Ankle alphabets; Leg lifts
 - Core exercises (lying down)
 - Muscle stretching (careful to protect hypermobile joints)
- Progress exercises gradually
 - Start horizontal, progress to vertical
 - Start with lower extremity exercise, add upper
 - May need to start with compression garments
- Recumbent (horizontal) cardio exercises:
 - Pool exercise (preferably cool pool), recumbent bike, rowing



POTS Exercise Protocols

- Old exercise protocols – you should not be doing these
 - CHOP (Children's Hospital of Philadelphia)
 - Lavine protocol
- NEW'ish exercise protocols
 - CHOP AADP (Children's Hospital of Philadelphia Acquired Autonomic Dysfunction Protocol)
 - ADaPT (Autonomic Disorder *adaptive* Physical Therapy)
 - Exercise only enough to increase HR 15-20 BPM
 - Exercise ≥ 5 days/week, don't miss more than 2 days in a row
- Research shows that ≥ 3 months of exercise is safe and effective for POTS (Peebles, 2024)
- But essential to start with self-care strategies – exercise alone isn't enough

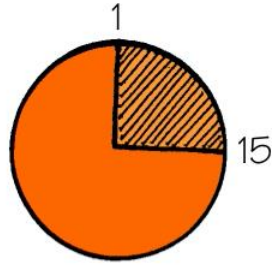
Gastrointestinal Issues in POTS

HSD 106: Gut
Issues in HSD,
MCAD & POTS

- Nausea and/or vomiting
- GERD/indigestion
- Abdominal pain & bloating
- Early satiety (feeling full)
- Rapid or delayed gastric emptying
- Constipation or diarrhea
- Increased POTS symptoms after eating..
- POTS and GI: Primer for Gastroenterologist (DiBaise, 2018)
 - <https://www.proquest.com/docview/2124758833/fulltextPDF/9AE27033078D48C5PQ/1?accountid=37646>

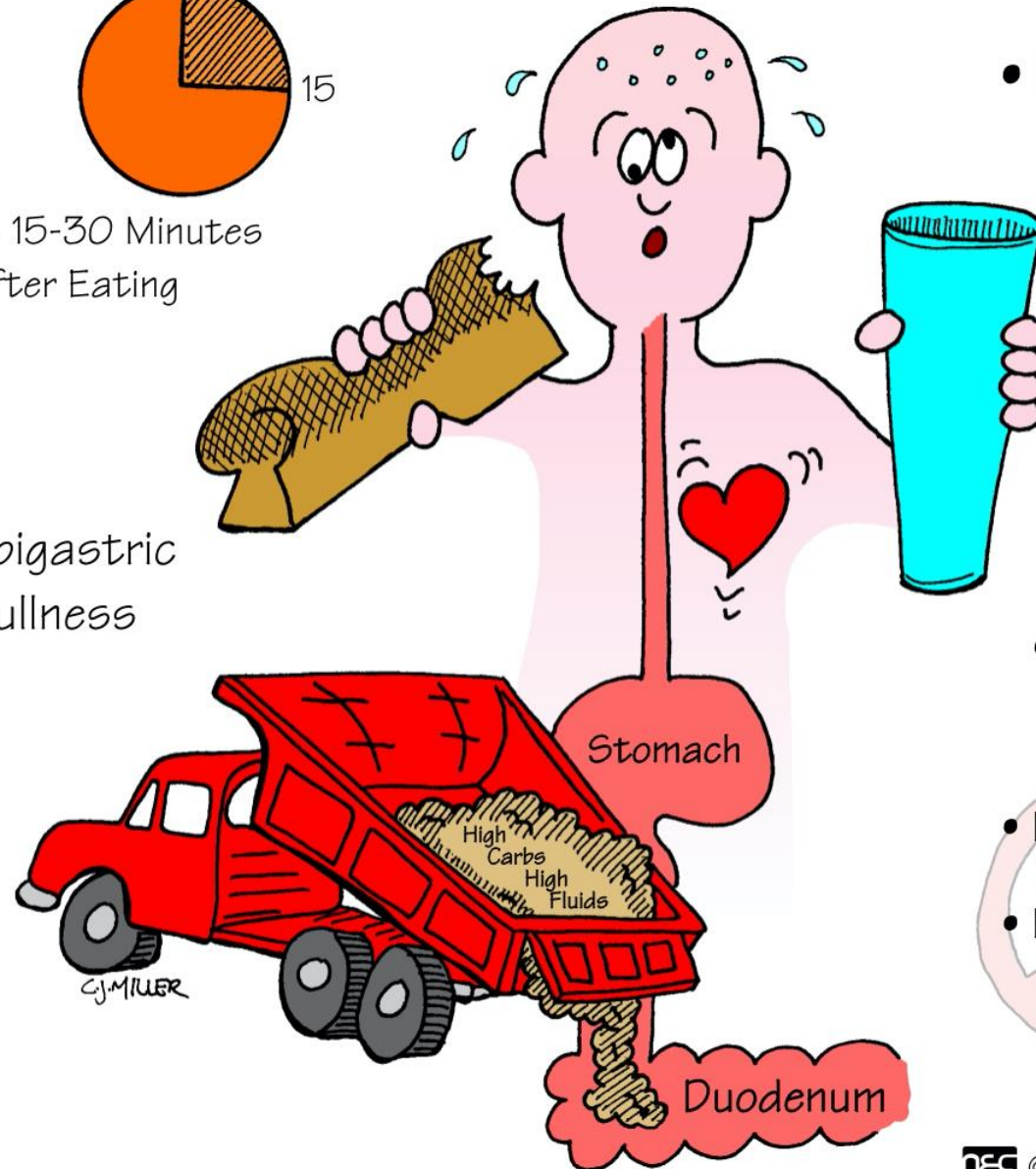


DUMPING SYNDROME



Occurs 15-30 Minutes
After Eating

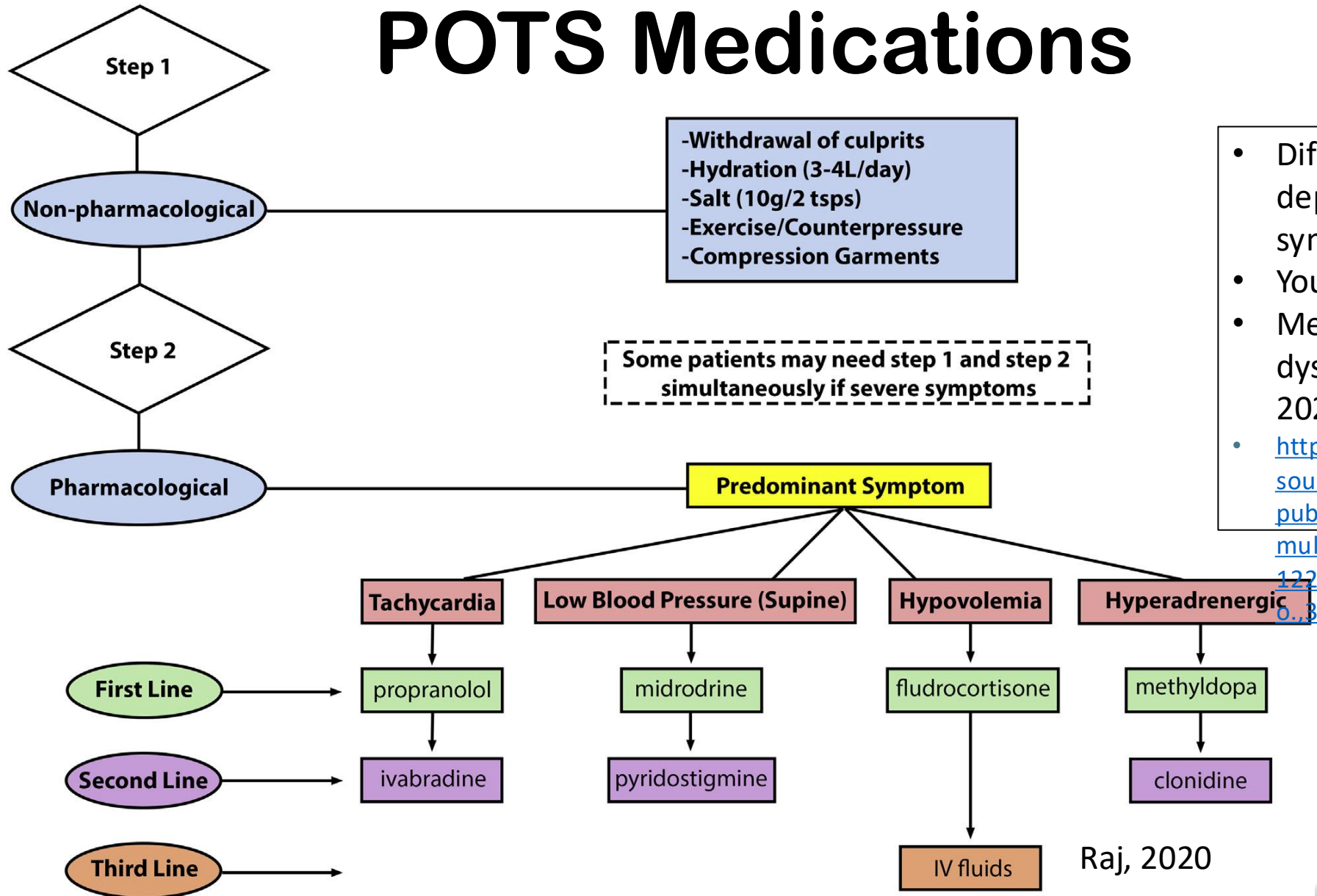
- Epigastric Fullness



- Weakness
 - Dizziness, vertigo
 - Diaphoresis
- Tachycardia
- Abdominal Cramping
- Self-Limiting

- No Fluids With Meals
- No High Carbs i.e., Bread, Potatoes

POTS Medications



- Different medications depending on primary symptom.
- You might need to treat MCAD
- Medications for all types of dysautonomia (Blitshteyn, 2022):
- https://www.aapmr.org/docs/default-source/news-and-publications/covid/covid-blitshteyn-multi-disciplinary-tables-1222.pdf?sfvrsn=92702a7c_0#:~:text=N

Raj, 2020



POTS Emergency Pack

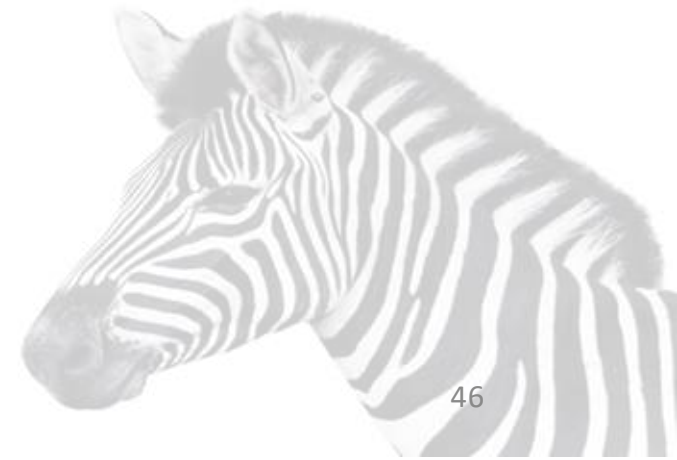
- It can be helpful to have a fanny pack or small bag with emergency supplies for your POTS
 - Water bottle
 - Electrolytes
 - Salty foods or salt tablets
 - Compression socks/leggings
 - Cooling towel (cools when wet), hand-held fan or misting sprayer
 - Peppermint oil for nausea, or passing out
 - POTS rescue medications, if you have any
 - More at <https://www.awarenessforpotsies.org/car-togo-packs>



Accommodations for POTS

Once you have done as much as possible to manage POTS...

- Primary school accommodations:
 - <http://www.dysautonomiainternational.org/page.php?ID=107>
 - <https://www.dysautonomiasupport.org/handbooks/>
- College students:
 - https://www.standinguptopots.org/sites/default/files/images/College_Accommodations_for_Students_with_POTS_-_2018.pdf
 - <https://www.dysautonomiasupport.org/handbooks/>
- Workplace accommodations
 - <https://www.dysautonomiasupport.org/handbooks/>



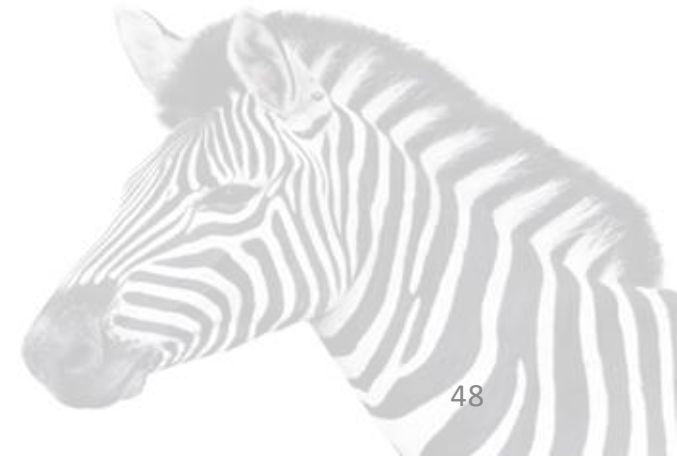


Questions?



Mast Cell Activation Disorder/Disorder MCAD/MCAD

Why is it so common in HSD?



What is a MAST CELL?

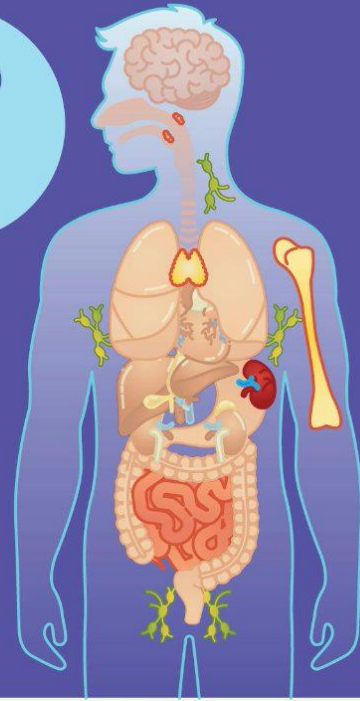
Mast cells are a part of the immune system.

1

Mast cells are well-known for releasing histamine during allergic reactions, such as in pollen or insect sting allergies.

2

They're found in most tissues throughout the body, especially those that interact with the outside environment including the lungs gastrointestinal tract and skin.



They play an important role in anaphylaxis!

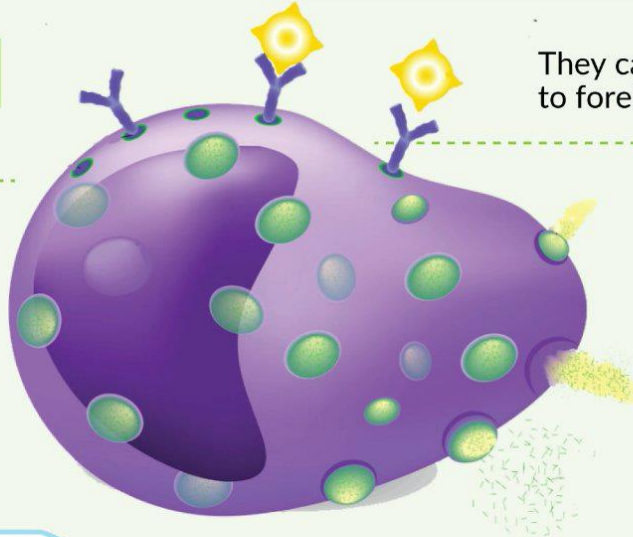
3

Mast cells play a role in inflammation, help defend against pathogens and are involved in wound healing and tissue repair

4

They can detect and respond to foreign substances.

5



When a mast cell is activated by a trigger, these granules release many mediators (chemicals that mediate reactions leading to symptoms) Histamine is one of the most common example of the many mediators that can be released during degranulation.

6

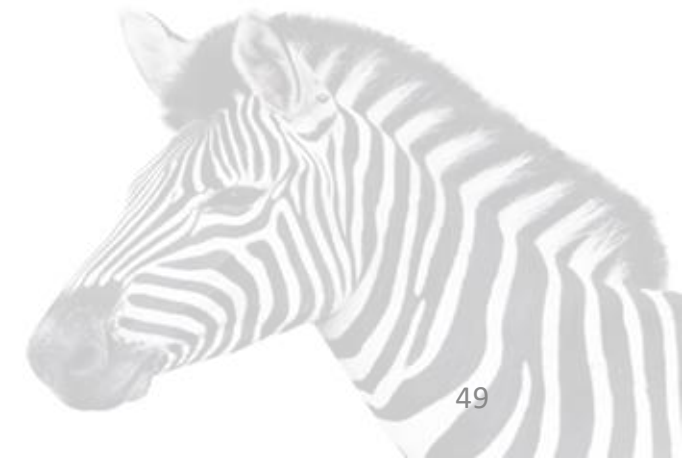


MAST CELL DISEASE

Happens when these cells aren't behaving normally.

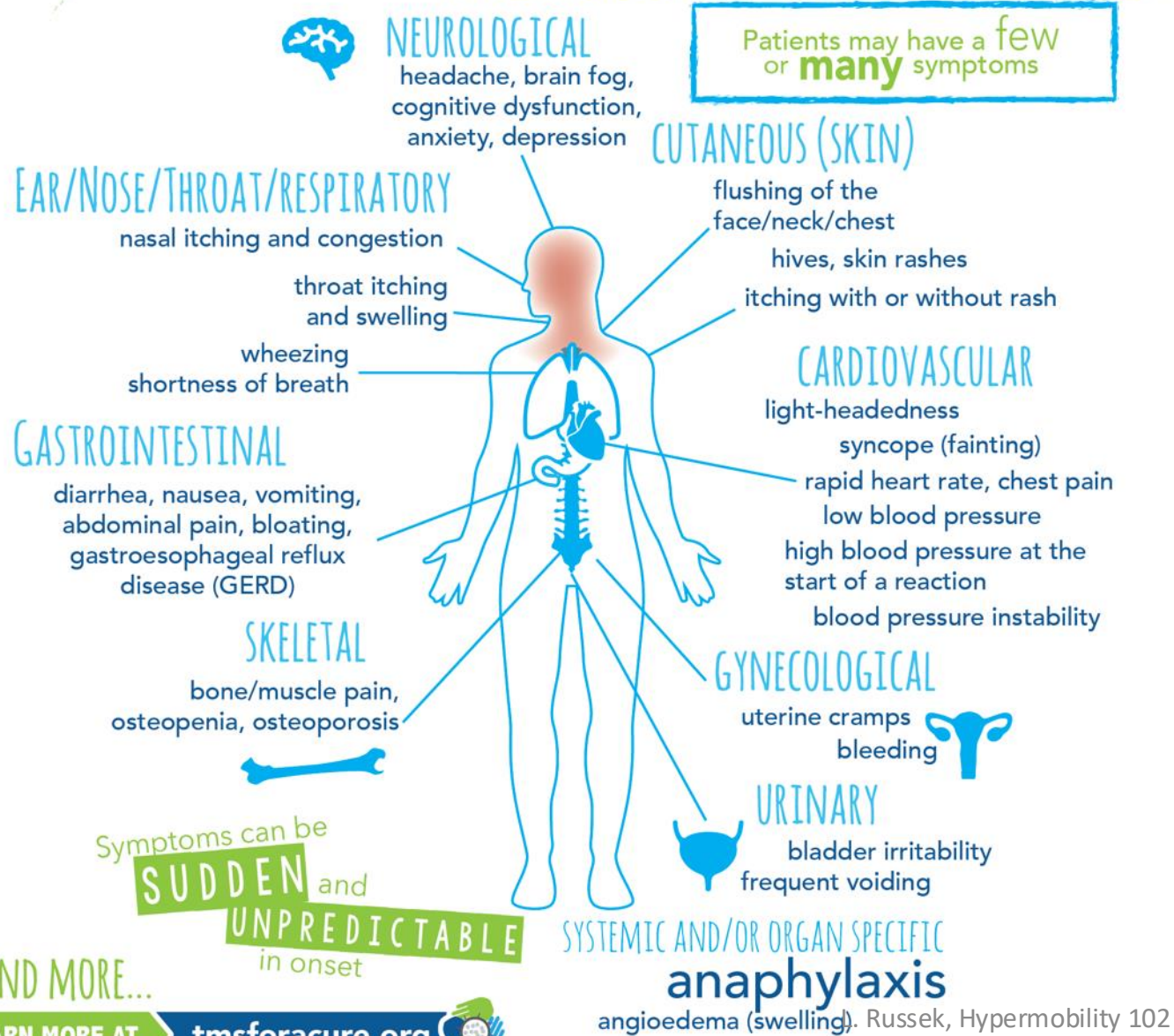
TickedOffMastCells.Org

- Mast cells mediate an allergic response
- Mast cells do not cause autoimmune disorders, but can aggravate them



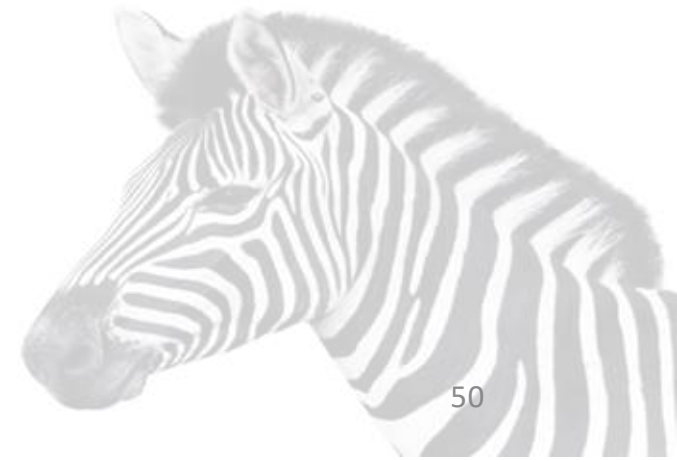
Some common SYMPTOMS of MAST CELL DISEASE

that are caused by mast cell mediator release



Prevalence estimated at 17%

- Molderings, 2013



MCAD: Skin Problems



MCAD: Diagnostic Criteria

- It is really difficult to formally diagnose
 - Blood tests are technically difficult and often have false negative results
- Official diagnostic criteria are still argued. One version:
 - A. Typical symptoms of severe, recurrent (episodic) systemic MCA, involving ≥ 2 organ systems
 - B. Involvement of MC documented by biochemical studies (increased serum tryptase is preferred marker) – must be DURING MCAD event, and using careful sample management (on ice)
 - C. Response of symptoms to therapy with MC-stabilizing agents or drugs blocking mediator release (Valent, 2019; Gulen, 2024)
- **Use the Mast Cell Activation Disease Questionnaire**
 - <https://www.humangenetics-bonn.de/wp-content/uploads/2024/01/Fragebogen-englisch-1-15-20-LW-GJM.pdf>
 - Don't worry about the questions you can't answer
 - Score ≥ 14 indicates systemic mast cell mediator release Disorder.
 - Score 8 - 14 indicates a pathological activation of mast cells.



MCAS/D Diagnosis is Still Controversial

- There are many publications stating that MCAS (the Syndrome) is over diagnosed.
- MCA “Disorder” is more vague (Theoharides, 2023; Gulen, 2024)
- So: use MCAD strategies if they help manage symptoms

MCAS - what isn't?

Symptoms/conditions that are not diagnostic for MCAS

Fatigue, fibromyalgia-like pain, chronic low back pain, recurrent edema, dermatographism, warts, alopecia, tinnitus, adenopathy, weight change, endocrinologic conditions (metabolic syndrome, type 2 diabetes mellitus, hypothyroidism, hyperthyroidism, abnormal electrolytes), gastroenterological conditions (constipation, irritable bowel syndrome, inflammatory bowel disease, gastroesophageal reflux disease, celiac disease and non-celiac gluten intolerance), neuropsychiatric disorders (headache, mood disturbances, anxiety, attention deficit/hyperactivity disorder, depression, posttraumatic stress disorder, restless leg syndrome, schizophrenia), essential hypertension, atherosclerosis, idiopathic non-ischemic cardiomyopathy, pulmonary hypertension, chronic kidney disease, endometriosis, polycystic ovarian syndrome, prostatitis, multiple chemical/food sensitivity syndrome, autoimmune disorders, solid organ malignancies, blood disorders (polycythemia, anemia, an increased or decreased level of immunoglobulin isotypes), nonspecific peripheral blood mutations, dysautonomia (postural orthostatic tachycardia syndrome, neurocardiogenic syncope), hypermobile Ehlers-Danlos syndrome, chronic fatigue syndrome

Gulen, 2024

≥2 of the below with or without known trigger

Cutaneous

Flushing
Pruritus
Urticaria
Angioedema

Gastrointestinal

Vomiting
Abdominal cramps
Diarrhea

Respiratory

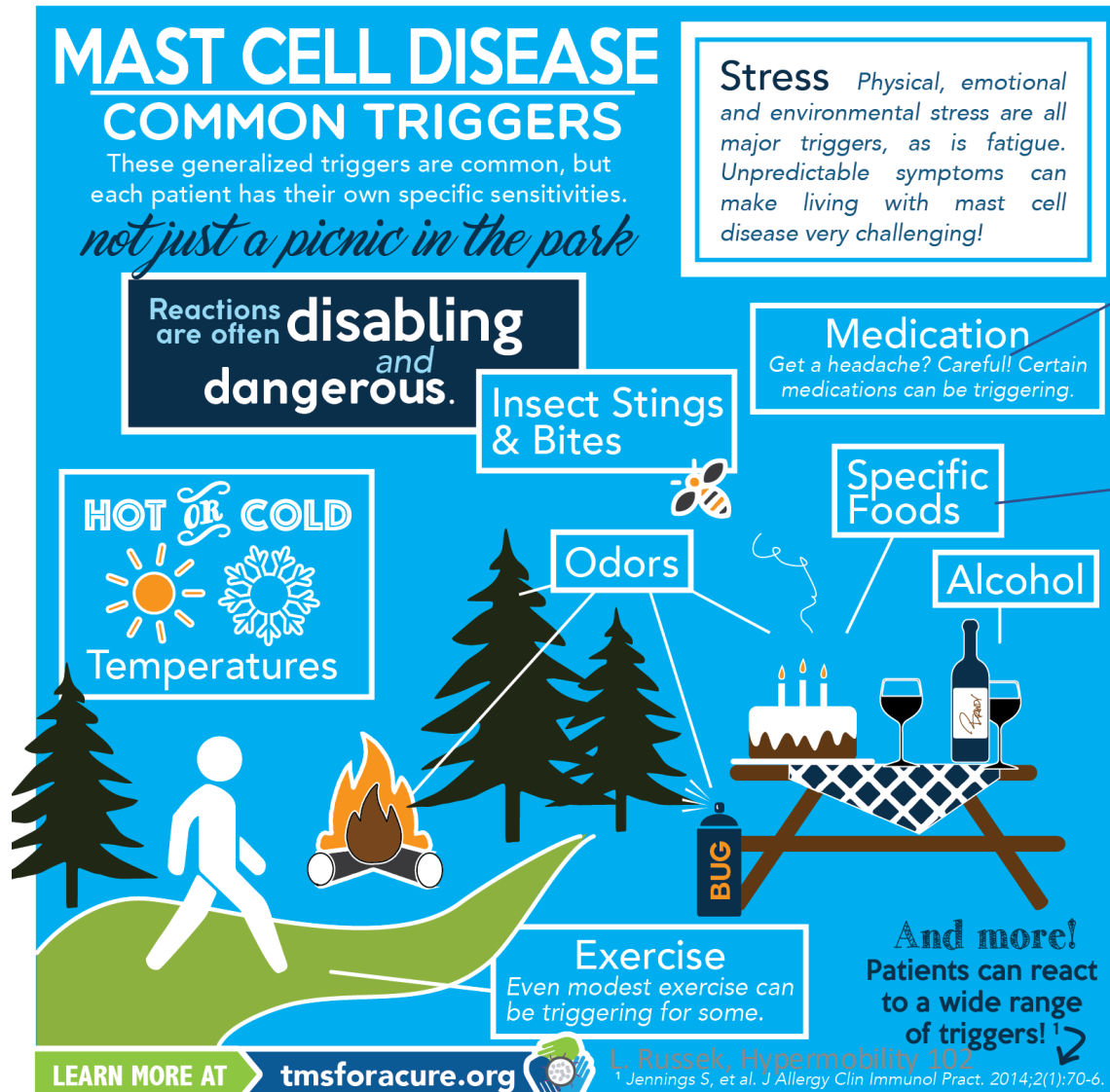
Laryngeal edema,
Shortness of breath,
Cough/Stridor
Wheeze/bronchospasm

Cardiovascular

Low blood pressure
Abnormal heart rhythm
Syncope
Loss of consciousness

MCAS diagnosis can be obtained, if laboratory and response criterion are also fulfilled

MCAD Common Triggers



Check your meds for MCAD sensitivity

Opiates & NSAIDs, medication 'excipients' (inactive ingredients)

Especially histamine containing or releasing foods



Migraine & MCAD Triggers

- Migraines & headaches reported in 63% of people with MCAD (Afrin, 2017)
- Mast cells contribute to migraines through a neuroinflammatory process
- Histamine in the CNS causes migraines

Migraines:

- Stress
- Changes in sleep schedule
- Alcohol (especially red wine)
- Diet: histamine, MSG, chocolate, cheese, dairy, artificial sweeteners, cured meats
- Strong smells
- Sunlight
- Dehydration
- Hormones
- Caffeine
- Weather changes
- (<https://americanmigrainefoundation.org/resource-library/top-10-migraine-triggers/>)

Mast Cell Activation:

- Stress
- Fatigue, changes in sleep schedule
- Alcohol (especially red wine)
- Diet: ripe cheese, dried meat or sausage, tomato, nuts, pickled foods, cured meats fish, food additives
- Strong smells
- Sunlight
- Exercise
- Medications (NSAIDs, antibiotics, opioids)
- Insect and other venoms
- Infections (viral, bacterial, fungal)
- Mechanical irritation, friction

Are migraines
really a mast
cell reaction?

MCAD Management

Managing MCAD

See “Suggestions for
Managing MCAD”
Handout

- Avoid triggers, especially foods
 - Probably histamine containing or releasing foods
- Substitute ‘safe’ meds for mast cell activators
- Physiological quieting
 - Relaxation, meditation, yoga, Tai chi, etc.

- Medication

(Molderings, 2016)

- <https://tmsforacure.org/treatments-2/medications-treat-mast-cell-disorders/> ..
- What every gastroenterologist should know about MCAD
 - Weinstock, 2021 (<https://link.springer.com/article/10.1007/s10620-020-06264-9>)

Molderings, 2016; Theoharides, 2023

Dietary Histamine Intolerance

- Histamine that crosses from the gut to blood stream causes systemic effects
- Some foods contain a lot of histamine, or cause mast cells to release histamine
- Histamine is normally metabolized in the gut by DAO (diamine oxidase)
 - Some people lack DAO
 - Some foods and medications inhibit DAO
 - There is a blood test for DAO, but it is tricky, expensive, and not often available
 - You can take DAO supplements

Comas-Basté, 2020



Low Histamine Diet

Low Histamine Foods to Eat

- Fresh meat and freshly caught fish.
- Non-citrus fruits.
- Eggs, mozzarella, ricotta.
- Gluten-free grains, such as quinoa corn and rice.
- Dairy substitutes, such as coconut milk and almond milk.
- Fresh vegetables except as noted
- Cooking oils, such as olive oil.

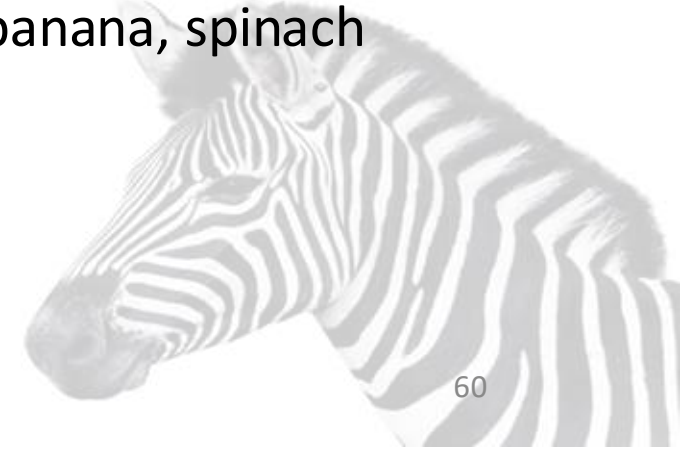
High Histamine Foods to Avoid

- Fermented dairy products, such as cheese (especially aged), yogurt, sour cream, buttermilk, and kefir.
- Fermented or pickled vegetables
- Vinegar, kombucha, miso, soy sauce
- Cured or fermented meats, such as sausages, salami, and fermented ham.
- Wine, beer, alcohol, and champagne
- Fermented grains: sourdough bread
- Tomatoes, eggplant, banana, spinach
- Soy milk
- Most nuts..

<https://www.healthline.com/health/low-histamine-diet>

Good resource at:

https://www.histaminintoleranz.ch/downloads/SIGHI-Leaflet_HistamineEliminationDiet.pdf



MCAD Medications

Talk to your
doctor

- **H1 antihistamines**: help with itching, abdominal pain, flushing, headaches, brain fog
 - **H2 antihistamines**: help with gastrointestinal symptoms and overall mast cell stability
 - **Mast cell stabilizers**: help with stomach and intestinal symptoms and brain fog
 - **Leukotriene inhibitors**: help with respiratory symptoms and overall mast cell stability (all mast cell activation symptoms)
 - **Aspirin therapy** (*only under direct supervision of a physician*): if tolerated and if prostaglandins are elevated, helps with flushing, brain fog and bone pain
- <https://tmsforacure.org/treatments-2/medications-treat-mast-cell-diseases/> ..
(more on medications in the 'appendix' slides)



ALL PATIENTS:

Self-Injectable Epinephrine (two doses; e.g., EpiPen®/EpiPen Jr®) should be carried by all patients with a mast cell disease at all times, even if previous anaphylaxis has not occurred. Both the patient and family members/caregivers should be trained on administering the epinephrine!

Please visit the American Academy of Allergy, Asthma and Immunology (AAAAI) website for more information on anaphylaxis.

<http://www.aaaai.org/conditions-and-treatments/allergies/anaphylaxis>

Basic Medications for Symptomatic Patients with Mast Cell Diseases¹⁻⁴

- **H1 antihistamines:** help with itching, abdominal pain, flushing, headaches, brain fog
- **H2 antihistamines:** help with gastrointestinal symptoms and overall mast cell stability (all mast cell activation symptoms)
- **Mast cell stabilizers:** help with stomach and intestinal symptoms and brain fog
- **Leukotriene inhibitors:** help with respiratory symptoms and overall mast cell stability (all mast cell activation symptoms)
- **Aspirin therapy** (under direct supervision of a physician): if tolerated and if prostaglandins are elevated, helps with flushing, brain fog and bone pain
- **Other medications may include:** omalizumab (Xolair®, anti-IgE therapy), steroids, and proton pump therapy (for additional control of gastroesophageal reflux (GERD), but proton pump therapy may not replace the H2 antihistamine necessary to stabilize mast cells)

Please see **Table 1- Table 6** for lists of some specific drugs in these different categories.

Please see **Table 7** for a list of some specific drugs for advanced systemic mastocytosis.

Table 1. Some First Generation H1 Antihistamines

Brand Name	Generic Name
Atarax®	Hydroxyzine hydrochloride
Benadryl®	Diphenhydramine
Chlor-trimeton®	Chlorpheniramine
Doxepin®, Sinequan®	Doxepin hydrochloride
Tavist®	Clemastine

Table 2. Some Second Generation H1 Antihistamines (may tend to cause less drowsiness)

Brand Name	Generic Name
Allegra®	Fexofenadine
Claritin®	Loratidine
Clarinex®	Desloratidine
Zaditor®/Zaditen® (in Europe)*	Ketotifen
Xyzal®	Levocetirizine
Zyrtec®	Cetirizine

*Zaditor® is only available in the US as eye drops; Zaditen® is available by prescription, but it must be obtained from a compounding pharmacy or from abroad.

Table 3. Some H2 Antihistamines

Brand Name	Generic Name
Axid®	Nizatidine
Pepcid®	Famotidine
Tagamet®	Cimetidine
Zantac®	Ranitidine

Continued on page 28

Medication Options

- Over the counter:
 - H1 inhibitor
 - H2 inhibitor
- Prescription
 - Cromolyn
- Guide to MCAD medications:
<https://tmsforacure.org/treatments/medications-treat-mast-cell-diseases/>



Medications to Treat Mast Cell Diseases

Supportive Care for Symptoms



Self-Injectable Epinephrine (two doses; e.g., EpiPen®/EpiPen Jr®)

Should be carried by all patients with a mast cell disorder at all times, even if previous anaphylaxis has not occurred. Both the patient and family members/caregivers should be trained on administering the epinephrine!

Second Generation H1 Antihistamine¹

Help with itching, abdominal pain, flushing, headaches, and brain fog

First generation anti-histamines (e.g. Diphenhydramine or Benadryl®) are also available but have a risk of drowsiness.



Brand Name	Generic Name
Allegra®	Fexofenadine
Claritin®	Loratidine
Clarinex®	Desloratidine
Zaditor®/Zaditen®* (in Europe)*	Ketotifen
Xyzal®	Levocetirizine
Zyrtec®	Cetirizine

* Zaditor® is only available in the US as eye drops; Zaditen® is available by prescription, but it must be obtained from a compounding pharmacy or from abroad.

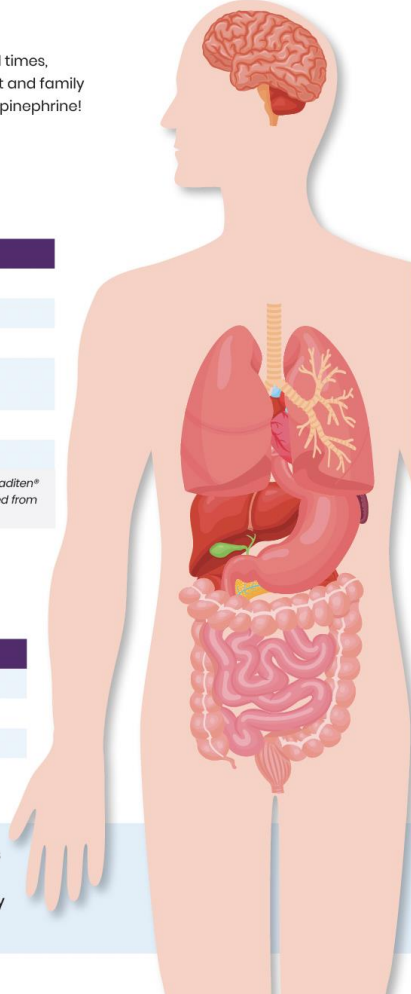
H2 Antihistamines¹

Help with gastrointestinal symptoms, pruritus and flushing



Brand Name	Generic Name
Axid®	Nizatidine
Pepcid®	Famotidine
Tagament®	Cimetidine

¹Note: The H1 and H2 antihistamines are necessary to stabilize receptors on the mast cell. Therefore, if additional medication is required for control of gastroesophageal reflux (GERD), a proton pump inhibitor may be added to this protocol, but it cannot replace the H2 antihistamine.



Medications to Treat Mast Cell Diseases

Supportive Care for Symptoms

Leukotriene Inhibitors



Helps with respiratory symptoms and cutaneous symptoms

Brand Name	Generic Name
Singulair®	Montelukast
Accolate®	Zafirlukast
Zyflo®/Zyflo CR®	Zileuton

Mast Cell Stabilizers



Helps with stomach and intestinal symptoms and brain fog

Brand Name	Generic Name
Gastrocrom®	Oral cromolyn sodium
Zaditor®/Zaditen®* (in Europe)*	Ketotifen
Algonot, Neuroprotect, etc.	Food supplements containing bioflavonoids such as quercetin and luteolin

* Zaditor® is only available in the US as eye drops; Zaditen® is available by prescription, but it must be obtained from a compounding pharmacy or from abroad.

Aspirin Therapy

^{*} Under direct supervision of a physician

If tolerated and if prostaglandins are elevated, helps with flushing, brain fog and bone pain



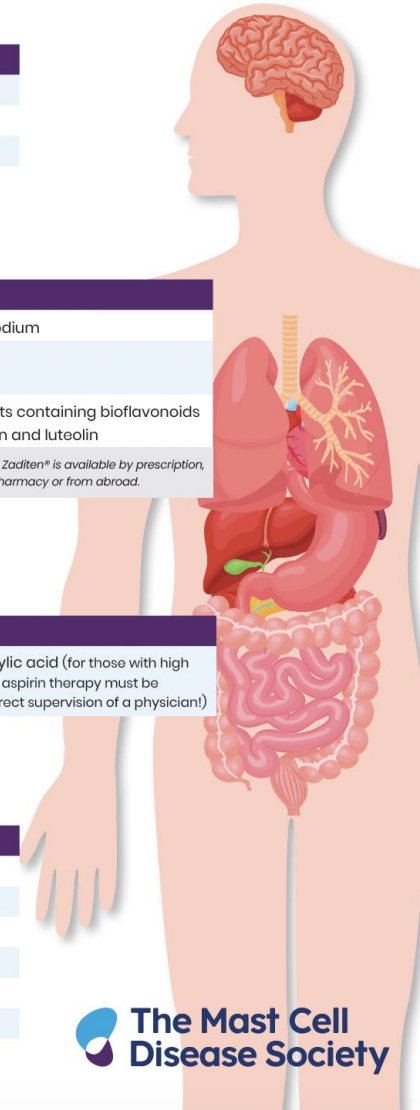
Brand Name	Generic Name
Bayer® Aspirin; Aspirin; ASA	Aspirin, acetylsalicylic acid (for those with high prostaglandin levels; aspirin therapy must be initiated under the direct supervision of a physician!)

Proton Pump Inhibitors

Help with GERD
(Gastroesophageal Reflux)



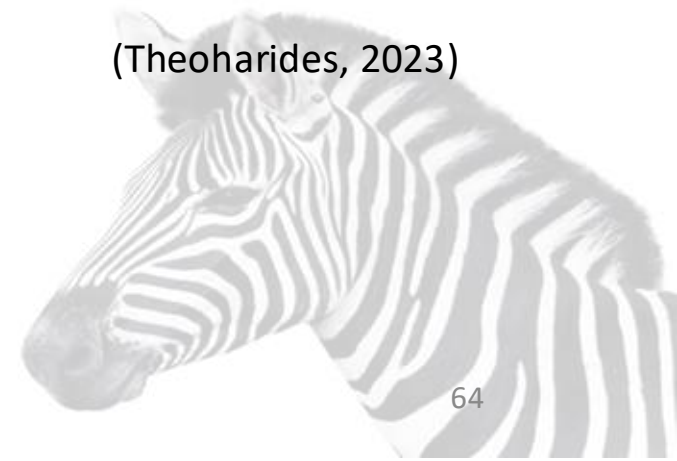
Brand Name	Generic Name
Aciphex®	Rabeprazole
Dexilant®	Dexlansoprazole
Nexium®	Esomeprazole
Prevacid®	Lansoprazole
Prilosec®	Omeprazole
Protonix®	Pantoprazole



New
Infographic!

MCAD Supplements

- Research is moderate for the following:
 - Diamine oxidase (DAO) enzyme: breaks down histamine in the gut
 - Good research that migraine is associated with DAO deficiency and DAO supplements can help treat migraines (Comas-Baste, 2020)
 - Vitamin C
 - If you don't tolerate ascorbic acid, e.g., citrus, try vitamin C made from broccoli
 - Vitamin D (Theoharides, 2023)
 - Quercetin: an antioxidant found in some berries



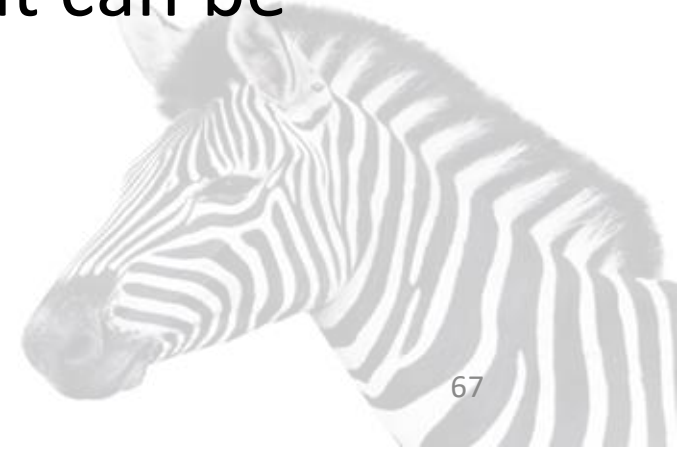
So, What Do I Do Now?

- HSD, POTS and MCAD are all quite variable, day to day. This makes it difficult to identify triggers or know whether a change has helped.
- Change one thing at a time
- Keep a wellness journal, tracking what you are changing and how you feel.
- Give it 2 weeks to see if it helps.
 - If it does help, keep it and change something else
 - If it doesn't help, eliminate it and wait 1 week to make sure it wasn't actually helping.
- Be patient. Each change might only help 5-15%.



Summary

- POTS/Dysautonomia and MCAD are common in people with hypermobility/hEDS
- POTS and MCAD are often overlooked by MDs
- Understanding these conditions can help you avoid aggravating factors and do more to care for yourself
- Improvements are often slow (~6-12 months) but can be dramatic!



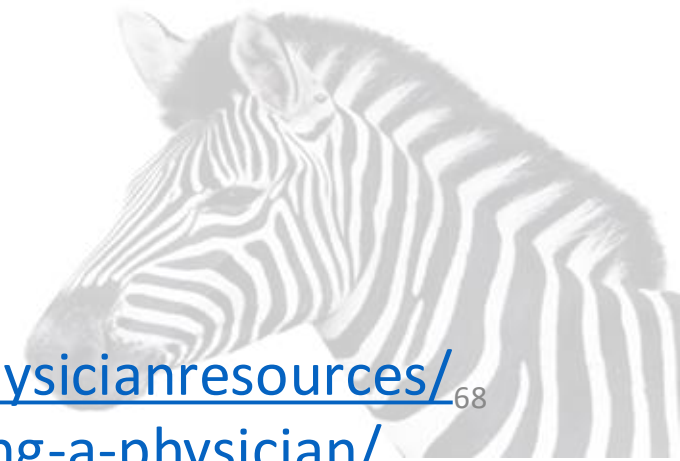
Web Resources

- POTS:

- www.potsuk.org
- <http://www.dysautonomiainternational.org>
 - POTS video: <http://www.dysautonomiainternational.org/page.php?ID=50>
 - School accommodations: <http://www.dysautonomiainternational.org/page.php?ID=107>
 - Extensive patient guide POTS: <http://www.dysautonomiainternational.org/pdf/RoweOlsummary.pdf>
- Guidelines for providers: [https://www.onlinecjc.ca/article/S0828-282X\(19\)31550-8/fulltext](https://www.onlinecjc.ca/article/S0828-282X(19)31550-8/fulltext)
- List of POTS providers: <http://www.dysautonomiainternational.org/page.php?ID=14>

- MCAD:

- <https://www.tmsforacure.org>
- <https://www.mastzellaktivierung.info/en/introduction.html>
- Booklet for health care providers: <https://tmsforacure.org/physicianresources/>
- List of MCAD clinics: <https://tmsforacure.org/resources/finding-a-physician/>



Other Resources

- Books
 - The Trifecta Passport: Amber Walker
 - A free patient workbook available at <https://originwellnesscolorado.com/passport>
 - Mast Cells United: Amber Walker
- Excellent fatigue self-management resources at: <https://www.newcastle-hospitals.nhs.uk/services/chronic-fatigue/>
- Symptom tracking app: <https://www.flourish.care/>



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Questions?



Relevant Handouts Available



Scan for
website link.

- <https://webpace.clarkson.edu/~lrussek/research.html>
- **POTS**
 - [Overview of POTS symptoms and causes.](#)
 - [Checklist for POTS self-care management.](#)
 - [Flow charts for POTS management, including fatigue and sleep.](#)
- **MCAD self-care**
 - [Suggestions for managing MCAD.](#)
 - [How to check your medications for \(MCAD\) sensitivities.](#)
- **General Self-Care Strategies**
 - [Breathing.](#) Breathing incorrectly can increase pain sensitivity, headaches, jaw pain, and more.
- **Links to other resources**
 - www.potsuk.org POTS-UK
 - <http://www.dysautonomiainternational.org> Dysautonomia International.
 - <https://www.dysautonomiasupport.org/handbooks/> Dysautonomia Support has excellent suggestions about school and work accommodations for POTS
 - <https://tmsforacure.org> The Mast Cell Disease Society.
 - <https://www.mastzellaktivierung.info/en/introduction.html> (has English language pages)

