EDS, Autonomic Dysfunction and MCAS – Putting It Together

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Ehlers-Danlos Syndromes

**Are a Clinical Subtype of Connective Tissue Disorders**

They can be *inherited* and are *varied* in:

- How they affect the body
- In their genetic causes

**Characterized by:**

- **Joint Hypermobility** (*joints that stretch further than normal*)
- **Skin Hyper Extensibility** (*skin that can be stretched further than normal*)
- **Tissue Fragility, Easy Bruising**
The 2017 International Diagnostic Criteria for hEDS have:

**Generalized Joint Hypermobility**

Three Criteria (A,B,C)

\[ \downarrow \]

**ALL** of which **MUST** be present:

**A**
- Five or more of the following:
  - Soft velvety skin
  - Skin hyper extensibility
  - Striae (stretch marks)
  - Piezogenic heel papules
  - Hernias
  - Atrophic scarring
  - Prolapse of pelvic floor
  - Rectum or uterus
  - Dental crowding and high palate
  - Arachnodactyly (long, slender fingers)
  - Arm-span-to-height ratio $>1.05$
  - Mitral valve prolapse or aortic root dilatation

**B**
- Positive family history
  - In first-degree relatives diagnosed with these criteria

**C**
- Pain in two or more extremities
  - For three + month
  - Recurrent joint dislocations
  - Atraumatic joint instability
Evaluation of HSD

The Beighton Score is a Screening Technique for hypermobility

Used to Evaluate/Assess the Range Of Movement in some joints

There are **NO Diagnostic Laboratory Tests** for HSD
Joint Hypermobility or Laxity is the hallmark of most types of EDS. The Beighton Hypermobility Scale is widely used.

The following maneuvers are performed:

- Flexion of waist with palms on the floor (and with the knees fully extended)
- Hyper extensibility of the knee >10 degrees
- Hyperextension of the elbow >10 degrees
- Passive dorsiflexion of the fifth finger >90 degrees with forearm flat
- Passive apposition of the thumb to the flexor aspect of the forearm
• Assessed in the context of **Age and Sex Matched Norms**

Scores which identify - Generalized Joint Hypermobility:

- ≥6 in children
- ≥5 in adolescents and younger adults
- ≥4 in adults aged 50+ years

According to an **Analysis Of Population Data** the use of these definitions may:

- Fail to identify Males with unusually high levels of joint hypermobility
- Over-diagnose young females as having joint hypermobility

Not a perfect tool!
Clinical Subtypes:

- Classical EDS (cEDS)
- Classical-like EDS (clEDS)
- Cardiac-valvular EDS (cvEDS)
- Vascular EDS (vEDS)
- Hypermobile EDS (hEDS)
- Arthrochalasia EDS (aEDS)
- Dermatosparaxis EDS (dEDS)
- Kyphoscoliotic EDS (kEDS)
- Brittle cornea syndrome (BCS)
- Spondylodysplastic EDS (spEDS)
- Musculocontractural EDS (mcEDS)
- Myopathic EDS (mEDS)
- Periodontal EDS (pEDS)
Most common disorder among Hereditary Disorders of connective tissue

Affects a subset of 10-20% of the general population with joint hypermobility

Genetic testing unavailable

Note: Patients with Vascular EDS may not be hypermobile
Additional

HSD/EDS / hEDS Testing

- Imaging (MRI Brain/spine)  
  **Chiari 1**

- Labs

- Echocardiogram  
  *(Rule out - MVP)*

- Dexa-Scan  
  *(Rule out - osteopenia/osteoporosis)*

- Dysautonomia Evaluation

- Gastrointestinal  
  *(Caution – Complications during colonoscopy/endoscopy such as perforations & bleeding can occur)*

- Bladder Dysfunction

- Pain Evaluation  
  *(Neuropathic/Musculo skeletal)*

- Spinal Instability

- Median Arcuate Ligament  
  *(Celiac Artery Ultrasound)*

- Sleep Apnea

- Genetic testing  
  *(Family history of Aneurysm Deaths or spontaneous bowel perforation)*
The presence of any of the following features suggests a need for further evaluation by a Medical Geneticist or EDS Specialist:

- Extensive widened atrophic scars
- Significant sagging skin
- Premature aged appearance
- Severe periodontal disease
- Severe corneal thinning, retinal detachment
- Significant kyphoscoliosis
- History of organ rupture
- Young-onset unexplained aortic root dilation, arterial dissection, or aneurysm
- Hand and foot deformities
- Unexplained significant or extensive varicosities at a young age
- Recurrent large hernias
- Recurrent pneumothorax
- Hypertelorism (wide-set eyes), bifid uvula, or cleft palate
- Intellectual disability
Dysautonomia: IS NOT a specific medical diagnosis, instead, an umbrella term used to describe any malfunction of the autonomic nervous system

Dysfunction of the Autonomic Nervous System (ANS)

Failure of the Sympathetic or Parasympathetic components of ANS (Affecting multiple organs)

Excessive or Overactive ANS actions

Autonomic Dysfunction can affect you from Head to Toe.
### Symptoms of Dysautonomia

<table>
<thead>
<tr>
<th>Blurred vision</th>
<th>Dry eyes/Dry Mouth</th>
<th>Lightheadedness</th>
<th>Fainting</th>
<th>Headaches/Migraines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity to light and noise</td>
<td>Difficulty Swallowing</td>
<td>Insomnia</td>
<td>SOB/Palpitations</td>
<td>Chest Pain</td>
</tr>
<tr>
<td>Nausea/Bloating</td>
<td>Abdominal Pain</td>
<td>Intolerance to large meals</td>
<td>Constipation/ Diarrhea</td>
<td>Bladder Dysfunction</td>
</tr>
<tr>
<td>Heat/Cold Intolerance</td>
<td>Orthostatic Intolerance</td>
<td>Profound Fatigue</td>
<td>Brain Fog</td>
<td>Abnormal Sweating</td>
</tr>
</tbody>
</table>

**NOTE:** Many of these symptoms can be caused by things other than autonomic nervous system dysfunction *Ex. Medication*
Primary Causes of Disability

in patients w/ Autonomic Dysfunction

- Orthostatic Intolerance
- Fatigue
- Brain Fog

Patient Evaluation

in patients w/ Autonomic Dysfunction

- Are there other Medical and Neurological conditions?
- Determining the need for a referral to a Specialist
- Psychiatric/Psychological evaluations
- Determination the extent of disability
- Medication evaluation
**Diagnosis of Autonomic Disorders**

<table>
<thead>
<tr>
<th>Tilt-Table Test</th>
<th>Evaluates the patient's blood pressure regulation in response to orthostatic stresses</th>
</tr>
</thead>
<tbody>
<tr>
<td>QSART</td>
<td>Measures the function of the post-ganglionic autonomic nerves that control sweat glands</td>
</tr>
<tr>
<td>Cardiac Workup</td>
<td>Electrocardiography, Echocardiogram</td>
</tr>
</tbody>
</table>

**Lab Tests**

- CBC
- B12
- Folate
- Vitamin D
- Celiac panel
- Ana DS DNA
- SSA SSB
- Complement Total
- C3, C4
- Iga, Igm, Igg

- Tryptase
- Thyroid Function
- Cortisol
- Metanephrines
- Urine
- Beta Prostaglandin f2 (mast cell)
- N-methylhistamine
- Leukotriene E4
- Lupus Anticoagulant

- Beta2glycoprotein
- Antiphospholipid
- Paraneoplastic Panel (Autoimmune Dysautonomia) also w/u for amyloid immunoglobulin free light chain assay
- Small Fiber Neuropathy Skin Biopsy
Postural Orthostatic Tachycardia Syndrome (POTS) - cause of POTS is unknown

- A condition characterized by too little blood returning to the heart when moving from a lying down to a standing up position

Orthostatic Intolerance

- Causes lightheadedness or fainting that can be eased by lying back down

- In people with POTS - these symptoms are also accompanied by a rapid increase in heart rate
Common and can be disabling ……

Estimated to impact between 1,000,000 - 3,000,000 in United States and millions more around the world

- Affect men and women of all ages
- Most cases are diagnosed in women between the ages of 15 and 50
- Associated with the presence of excessive tachycardia and other symptoms upon standing

POTS

Orthostatic Intolerance
How to do a *Poor Man’s Tilt Table Test* at home:

- Lay flat for 2-3 minutes. Take your bp & pulse and write it down.
- Stand up for 10 minutes without moving from side to side and take BP & Pulse every 2 minutes and write down the results.
- Record any Symptoms while standing every minute during the test.
- Lay back down for another 2 minutes, check BP & Pulse and record if your symptoms go away.
- If it’s too difficult to stay standing, then sit or lay back down and stop the test.

**Take Note:**

- What time of day you took the test
- When your last meal was
- What medications or supplements you were taking, *if any*
Examples of...  
Drugs that can **cause or exacerbate** symptoms of **Orthostatic Hypotension**:

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha Blockers:</td>
<td>Terazosin</td>
</tr>
<tr>
<td>Antidepressants:</td>
<td>Selective Serotonin Reuptake inhibitors, Trazodone, Monoamine, Oxidase Inhibitors, Tricyclic antidepressant</td>
</tr>
<tr>
<td>Anti-hypertensives:</td>
<td>Sympathetic Blockers</td>
</tr>
<tr>
<td>Anti-Parkinsonism Drugs:</td>
<td>Levodopa, Pramipexole, Ropirol</td>
</tr>
<tr>
<td>Antipsychotics:</td>
<td>Olanzapine, Risperidone</td>
</tr>
<tr>
<td>Beta Blockers:</td>
<td>Propranolol</td>
</tr>
<tr>
<td>Diuretic Drugs:</td>
<td>Hydrochlorothiazide, Furosemide</td>
</tr>
<tr>
<td>Muscle Relaxant Drugs:</td>
<td>Tizanidine</td>
</tr>
<tr>
<td>Narcotic Analgesic Drugs:</td>
<td>Morphine</td>
</tr>
<tr>
<td>Phosphodiesterase Inhibitors:</td>
<td>Sildenafil, Tadalafil</td>
</tr>
<tr>
<td>Sedatives/Hypnotic Drugs:</td>
<td>Temazepam</td>
</tr>
<tr>
<td>Vasodilator Drugs:</td>
<td>Hydralazine, Nitroglycerin, Calcium Channel Blockers</td>
</tr>
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</table>
Mast Cell Activation Syndrome (MCAS)

Mast Cells are:
- Part of the immune system
- Mast Cells are white blood cells found throughout the body
- 1st responder for your Immune System

When Mast Cells come in contact with antigens, they decide whether to create an Immune Response to protect you

Symptoms of MCAS

- Flushing
- Urticaria (Hives)
- Angioedema
- Nasal Congestion
- Rhinorrhea Wheezing
- Bronchospastic Cough
- Multiple Allergies
- Intolerances ex. Foods, medicines, smells
- Unexplained rashes
- Allergic Hypotension
- Headache

- Diarrhea
- Gastric Hyperacidity
- Abdominal Cramping
- Nausea +/- Vomiting
- Hypotension
- Tachycardia
- Fatigue, Lethargy
- Memory/Concentration Issues
Diagnosis of MCAS

- **Tryptase Levels** Before And After A Reaction
- Consistent *Tryptase Levels >20 may indicate other Mast cell disorder*
- Multiple Allergies/Or Inflammation (*not IgE mediated*)
- Anaphylaxis with Hypotension (*in response to a bee/wasp sting*)
- Search for Allergic Diseases like Immunocap

Citation: Up to Date Clinical Software Application: Mast Cell
## Symptoms and some Co-Morbidities of HSD/EDS/hEDS Dysautonomia MCAS

### HSD/hEDS
- Joint and Muscle Pain/Stiffness
- Back/Neck
- Clicking Joints
- Joint Dislocation
- Early onset Arthritis
- Pain from Soft Tissue Injuries (Sprains)
- Connective Tissue Weakness
- Easy Fractures from Osteoporosis/Osteopenia
- Varicose Veins
- Mitral Valve Prolapse (Palpitations)
- Poor Coordination
- Bladder Symptoms from Prolapse
- Sleep Disturbances
- Widespread Pain
- Hiatal Hernia w/GERD
  - Bloating
  - Early Satiety
  - Abdominal Pain

### Dysautonomia
- Dizziness/Fainting
- Dry Eyes/Dry Mouth
- Difficulty Swallowing
- Shortness of Breath
- Heat/Cold Intolerance
- Bladder Symptoms
- Neuropathic Pain
- Sleep Disturbances
- Widespread Pain
- Adrenalin Rushes
- Headaches
- Flushing (Generalized)
- Nausea/Vomiting
- Hypotension/Hypertension
  - Fast Heart Rate
  - Palpitations
- Sweating
- Chest Pains

### MCAS
- Hives
- Swelling
- Nasal Congestion
- Nasal Discharge
- Wheezing
- Bronchospastic Cough
- Multiple Allergies
- Anaphylaxis (hypotensive)
- Intolerance of Foods, Meds, Smells
- Rashes (Unexplained)
- Irritability
- Painful Urination
- Gastric Hyperacidity/GERD
- Headaches
- Flushing (Generalized)
- Nausea/Vomiting
- Hypotension (Allergic)
  - Fast Heart Rate
  - Palpitations

### Cognitive Issues
- Memory/Brain Fog

### GERD
- Diarrhea
- Abdominal Pain
- Extreme Fatigue
- Urination Urgency/Frequency

### Fatigue

### References
Citation: Up to Date Clinical Software: EDS
Management of Pain
• Musculoskeletal and Neuropathic
  • (ex. Fibromyalgia)
• Muscle Relaxants may help with spasms but can make subluxations worse

Physical Therapy
• Muldowney or Divon Protocols
• 30 Minutes/Day or Every Other Day
• In A Laying Down Position

Avoid Exercises That Over Stretch Your Joints
• ex. Yoga, Competitive Dancing, Cheerleading, Some Martial Arts
• Physical Exercise is an important part of the Treatment of EDS
• Playing certain sports is ok, however, you must take extra caution to ensure your joints aren’t being over stretched during the exercise/sport

Extra care for Invasive Procedures
Informing Physician:
• That you may bleed more
• Lidocaine/Novocaine May Not Work
• That all tissues involved should be handled gently because of increased risk of perforation ex. Colonoscopy/Endoscopy
• It may take 3X longer to heal, possibly requiring additional pain medicine

Joint Subluxation > Ice
Muscle Spasm > Heat

Sleep Study (If needed)
Treatment for Dysautonomia/Autonomic Dysfunction

- Improve Orthostatic Intolerance
- Improve Fatigue and Brain Fog
- Heat/Cold Intolerance
  - Use an umbrella to block the sun
  - Limit the amount of time outside
  - Use a wheelchair instead of walking

Compression garments 30-40 mmh

- Compress from knees up to belly button
- Better than just lower legs Ex. Brands: Mediven, Jobst, Sigvaris, Sankom
- Put on first thing in the morning/Take off at bedtime
- Frequent small meals vs. 3 meals/day
- Helps with intestinal pooling and Gastroparesis

Extra salt and water

- Recommendation:
  - 4 Grams of Sodium =10 grams/2 teaspoons of Salt
  - 4 liters of fluid
  - Electrolyte drinks: Nuun, Liquid IV, Drip Drop, Scratch Labs

Diet

- Organic/Whole Foods
- Gluten and Dairy Free for at least 30 days
- See if your intestinal symptoms improve

Exercise in lateral (flat) position ex. Swimming, Rowing, Recumbent Bike

- Goal – Slowly increase exercise to 30 minutes/day or every other day
- If you’re deconditioned, start with 1 or 2 minutes
- Note: You may need to be on medications like Midodrine before you have enough energy to exercise!

Avoid Post-exercise Fatigue:
Exercise Laying Down
Stay Hydrated
Go Low And Slow

Keep from getting Deconditioned!

It takes a lot of time and effort to get conditioned and Very Little Time to get Deconditioned!
Pooling makes the BP Drop

Signaling Adrenal Glands to produce more Adrenaline

Commonly referred to as Adrenaline Rushes

Causing you to feel

Treatment for Dysautonomia

• Reduce Blood Pooling by wearing compression garments and you will Reduce Adrenaline Rushes

• Shaky
• Nervous
• Sob
• Jittery
• Palpitations
When taking Multiple Medications – ("Polypharmacy")

Use Caution

Orthostatic Intolerance
- Ex. Midodrine, Northera, Mestinon, Florinef, Beta Blockers, Clonidine, Corlanor

Migraines
- Ex. CGRP (Aimovig), Triptans

Adrenaline Rushes
- Ex. Beta blockers Propranolol, Central Alpha Agonists, Clonidine

Gastrointestinal
- Ex. Zofran, Prochlorperazine, Rabeprazole, Carafate, Reglan

Bladder Dysfunction
- Based on underlying causes

Insomnia
- Ex. Belsomra, Ambien, Trazodone, Hydroxyzine HCL

Fatigue/Brain Fog
- Mestinon, Possibly amphetamines Ex. Adderall, Provigil
Treatment for Mast Cell Activation

Therapeutic Trial with H1 Blockers, H2 Blockers, Leukotriene Inhibitors, and Cromolyn

If response is noted

MCAS can be diagnosed and may warrant other treatments like Ketotifen, Xolair

Important

- With Mast Cell always start with the lowest dose and increase slowly
- One drug at a time
- May need to compound medications
COVID 19 Vaccine

In general all patients should be vaccinated
• MCAS patients should pre-medicate with H1 Blockers, H2 Blockers, Leukotriene Inhibitors, and Cromolyn
• Ensure you wait 30 minutes after the vaccination before leaving the facility
• Have the vaccine at a medical facility in case there’s a reaction
• Expect to have Flu Like symptoms and a Sore Arm for a few days
• Patients who experience Anaphylaxis should consult a Mast Cell Specialist prior to getting vaccinated

COVID 19 is causing Autonomic Dysfunction (Long Haulers)
Helpful Hints....

Migraine Prevention
- FeverFew • 100mg daily
- COQ 10 • 150mg daily
- Magnesium

Sleep Habits
- Have a Set Schedule
- Avoid Alcohol, Caffeine, and Exercise Before Bed
- Avoid Naps When Possible
- Optimize Bedroom Comfort • ex. Lighting and temperature
- Use Natural Products • ex. Sleep Well, Valerian Root, Lemon Balm, Passion Flower, Melatonin, THC/CBD
- Keep Head Raised In Your Bed • About 6-10” higher than your body
- Optimize Bedroom Comfort • ex. Lighting and temperature

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Sodium Supplements for Dysautonomia

Liquid IV
- 500mg Sodium, 370mg Potassium

Salt Stick Vitassium
- 500mg Sodium, 100mg Potassium

Nuun
- “Sport” Formula = 300mg Sodium, 150mg Potassium
- “Endurance” Formula = 380mg Sodium, 200mg Potassium

Others:
- NormaLyte, Drip Drop, Skratch Labs

Use Code POTS30 for 30% off
Contains helpful links, handouts, videos for Patients, Employers, Educators, and Physicians

- Annual Conference Information

www.DysautonomiaInternational.org

Provides support and education to patients and their families while promoting information sharing and meetups

- Note: On Home page, fill in the Search field with what you’re interested in researching

https://www.facebook.com/groups/DysautonomiaInternationalFLSupport
Dedicated to patient support, scientific research, advocacy, and increasing awareness for the Ehlers-Danlos syndromes, hypermobility spectrum disorder, and related medical disorders
https://www.ehlers-danlos.com/

Dedicated to supporting patients affected by Mastocytosis and Mast Cell Activation Diseases as well as their families, caregivers and physicians through research, education and advocacy
https://tmsforacure.org/
Published in December 2018 by President and Co-founder of Dysautonomia International Lauren Stiles with 40+ Leading Dysautonomia Physicians throughout the world

Search: ScienceDirect.com
Journal: Autonomic Neuroscience
Volume: 215

Pharmacotherapy
Headaches & Chronic Pain
Cognitive & Psychological Issues
Managing Fatigue
Sleep Disorders
Gastrointestinal Symptoms
Autoimmunity
Mast Cell Activation
Ehlers-Danlos Syndrome
Adolescents
Pregnancy
Surgical & Dental Considerations

"Postural Orthostatic Tachycardia Syndrome"
(Please note there is a fee of $35.95 to view. Make sure you download or print within 24 hours)

Additional Articles in ScienceDirect.com
How to Prepare for a New Patient Doctors Appointment

- Ensure you submit all of you new patient paperwork
- Preform the Beighton Scale test at home prior to appointment
- If you’ve never had a Tilt Table Test: Preform a Poor Man’s Tilt Table test at home if you’re not on any medications. If you’re on medications, wait for your appointment
- If the visit is virtual: Ensure you have a blood pressure cuff available for the day of your appointment
- Select the top 3 most disabling issues to discuss at each appointment
**Things to Remember**

- It takes **time** to find the right diagnosis and treatment plan
- Include your family and community
- Try new things and be flexible enough to change your day to day activities so that you can move forward and lead your best life with your diagnosis/disability
- This is a chronic condition with ups and downs
- When you get your period, get a virus, or intestinal flu, it’s going to knock you back down and you will have to fight to get yourself back up
- With time and persistent effort, the crashes will be shorter and less severe and recovery will get easier

**Goal of Therapy:**
Getting patients from a **9 out of 10 Disability Level** to a **2 out of 10 Disability Level**

**Note:** Patients who achieve optimal results are the ones who follow all recommendations every day