Dysautonomia in Ehlers-Danlos Type III

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7 Mars 2015. Paris

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Finantial disclosure

None

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What is Dysautonomia

- Dysautonomia = alteration of the autonomic nervous system.
- It is a condition in which patients tire easily, after activity, after a big lunch or at the end of the day, they feel sleepy and usually feel “like their batteries have become discharged” and have no energy.
- Due to the chronic fatigue, and episodic sensation of weakness, is that in many cases the wrong diagnosis of Depression, Fibromyalgia, Chronic Fatigue, Hypothyroidism or Hypoglycemic crisis is made.
- Family and friends usually see them as being lazy and unsociable, since they lack the energy to participate in social meetings or to interact with other people.

Dysautonomia in EDS-III

- Dysautonomia is a frequent condition that can cause poor quality of life and usually goes undiagnosed. It is particularly frequent in people with the EDS-III. These people may not even know that they have hypermobile joints and physicians usually pay no attention to this condition and do not make the diagnosis.

- EDS-III can produce musculoskeletal complaints (joint pain, recurrent tendinitis, joint sub-luxations, etc) and problems derived from weak tissues (Dysautonomia, hernias, varicose veins, uterine and mitral valve prolapse, myopia, spinal disc disease, early osteoarthritis and early osteoporosis).

- Note: I prefer the term EDS-III rather than Hypermobility type EDS, since in my study of 1751 pts, 55% had a Beighton score of 3/9 or less.

Symptoms of Dysautonomia

- Chronic fatigue, with somnolence.
- Pre-syncope or syncope.
- Low blood pressure.
- Cold intolerance.
- Poor memory, concentration and disorientation.

Why is Dysautomia associated with SED-III

- The reason is the weak collagen of the venous walls in the lower extremities. In a patient with normal veins the blood progresses up to the brain, but if the vein dilates, due to poor collagen, then the blood pools in the lower extremities and has more difficulty to get back to the heart and brain, causing brain hypoxia , which causes the symptoms of Dysautonomia.

Symptoms of Dysautomia

Sudden changes, such as getting out of bed abruptly, or standing in line or while walking slowly in malls or supermarkets, or after eating a big meal, specially with alcohol, the blood return to the heart diminishes and as a result the blood pressure drops suddenly and the brain oxygenation decreases.

When someone stands up suddenly, 300 to 800 ml of blood stay in the veins of the abdomen or lower extremities and in patients with Dysautonomia the body is incapable to compensate rapidly and symptoms appear (dizziness, head aches, severe fatigue, syncope).

Causes of Dysautonomia

- **Primary:** Idiopathic

- **Secondary:** A.- Autonomous Nervous System:
  a) Chronic polyneuropathies (Diabetes, Amyloidosis, uremia). Thiamine deficiency. Chronic alcoholism. Other toxic, hereditary or inflammatory diseases.
  b) Acute polyneuropathies (Guillen-Barre, Porfiria).
  c) Other diseases of the Nervous System (Multiple sclerosis, encephalic or hypothalamic lesions, infections). **Dysautonomia of Ehlers-Danlos Syndrome,** Familial Dysautonomia.

  B.- Spinal cord injury.

  C.- Other diseases (see next slide).

  D.- Medications: especially cardiovascular and antidepressants.

Ref.: Modified from Alter JB. Textbook of Internal Medicine. William N. Kelly. 3th ed. 1997.

Causes of Dysautonomia (cont.)

Other diseases:

- Chronic diseases.
- Depression.
- Chronic Fatigue Syndrome.

  Rowe found that 60% of patients with CFS had Joint Hypermobility (JH) compared to 24% in controls [1].

- Fibromyalgia.

  Oflougu noted that 64% of adults with FM had JH [2].

- **Ehlers-Danlos type III**

  Is the most frequent cause of Dysautonomia seen by rheumatologists. (80% of young females with EDS-III, in my studies).

Ref.: 1.- J Pediatr 2002; 141:421-25.
2.- Clin Rheumatol 2005; 16;1-3.

Causes of Dysautonomia in EDS-III

A.- Autonomic Nervous System dysfunction, characterized by:

Orthostatic hypotension or
Postural orthostatic tachycardia (POTS).

Symptoms: Palpitations, lightheadedness, tiredness, dizziness, somnolence, poor thermostat regulation, chronic fatigue, pre-syncope or syncope.

B.- Increased venous pool in the lower extremities, derived from collagen weakness of the venous wall.

Since physicians believe that low blood pressure is normal, Dysautonomia frequently goes undiagnosed. These patients with low blood pressure, usually have a poor quality of life.

In EDS-III the veins in the legs and abdomen act as a blood pool

A good analogy is what happens to fluids inside half-filled bottles. When moved from a horizontal to a vertical position, the fluids remain close to the bottom of the bottle. Something similar occurs to people with Dysautonomia, reason for which, when they stand up abruptly, they can develop dizziness and even syncope, due to lack of oxygen to the brain.

Causes that agravate Dysautonomia

- Dehydration, due to: Excessive heat
  Fever
  Vomiting and diarrhea
  Diuretics
- High altitude, in cities like Mexico City.
  and in mountain climbing.
- Standing at church or in a line for too long or when getting up suddenly from bed or from a sitting position.
- Phobic reaction to close surroundings (Claustrophobia).
- The sight of blood, especially if from a relative or close friend.
- Frightening.
- Severe pain or pain associated with anxiety, such as when getting an injection.

Causes that agravate Dysautonomia (Cont.)

- Sexual relations.
- Menstrual periods.
- Pregnancy.
- A prolonged hot bath (bathtub, shower, sauna, jacuzzi) or Bikram yoga, which is done at 42° C.

Causes that agravate Dysautonomia (Cont.)

- With a strong emotion or with nervousness, such as when taking an exam.
- Acute anemia.
- Walking slowly, like when walking in malls or at the super markets.
- With certain BP medicines that can produce orthostatic hypotension, as a secondary effect.
- Standing for a long period, without moving.
- After a big meal or alcohol in excess.

Dysautonomia in the Joint Hypermobility Syndrome

Gazit Y, Nahir M, Grahame R, Jacob G

- 48 JHS patients; 20 controls responded to ANS-linked questions: Syncope, pre-syncope, palpitations, chest discomfort, fatigue and heat intolerance were significantly more common among JHS patients.
- 27 patients and 21 controls underwent autonomic evaluation: orthostatic test, cardiovascular vagal and sympathetic function. Orthostatic hypotension (OH), postural orthostatic tachycardia syndrome (POTS), and uncategorized orthostatic intolerance (UOI) was found in 78% of JHS patients and in 10% of controls.
- They conclude that Dysautonomia is part of the extra-articular manifestations of JHS (EDS-III).

Ref. Amer J Med 2003;114:33-40

Frequency of Different types of Dysautonomia in Gazit's study

	JHS n = 27	Control n = 21	ρ
Postural Orthostatic Tachycardia Syndrome (POTS)	4 (15%)	0 (0%)	0.12
Orthostatic Hypotension (OH)	4 (15%)	0 (0%)	0.12
Unclassified Orthostatic Intolerance (UOI)	13 (48%)	2 (9.5%)	0.004
Dysautonomia, Total	21 (78%)	2 (9.5%)	<0.001

Ref. Gazit Y, Nahir M, Grahame R, Jacob G 2003. Amer J Med 2003;114:33-40

Dysautonomia and Osteoporosis in EDS-III in Chilean Studies

In our study of 1734 patients :

- In the group younger than 30 y/o (235 pts):

Dysautonomia was present in: Males 56.1% .

- Females 79.5%

- Bone mineral density was performed in 830 of these EDS-III patients, In the group younger than 30 y/o (89 pts):

Osteoporosis was present in: Males 13.6%

Females 14.9%.

Ref. .-Bravo JF. Presented as a Poster. First International Symposium on Ehlers-Danlos. Ghent. Belgium. Sept. 2012

Treatment of Dysautonomia

A.- General measures:

- Avoid standing or sitting without moving arms or legs.
- Avoid walking slowly in a Mall or supermarket, for prolonged periods of time.
- When sitting in a bus or an airplane, it is necessary to move the knees and ankles frequently and to get up and walk.
- After a big meal or heavy drinking it is necessary to lie down for 15 minutes or more. Do this also, when noticing early signs of Dysautonomia.

Treatment of Dysautonomia (Cont.)

- We recommend drinking liquids until the urine is clear like water.
- Use of elastic stockings, with a pressure at the ankle of at least 20 mm of Hg, to increase blood return from the lower extremities.
- Tight body garments are very useful (Hamonet).
- In the absence of hypertension or kidney damage, we recommend adding to the diet 6 to 9 g of salt a day (measured).
- Moderate aerobic exercises are useful.

Treatment of Dysautonomia (Cont.)

B.- Medications.

- 1.- Fludrocortisone (Florinef). It is a mineralo-corticoid. 0.1 mg/day. Effect lasts 24 to 36 hours.
- 2.- Midodrine (Gutron). 2.5 to 5 mg 2 to 3 times a day. Effect lasts only 4 hours.
- 3.- Atenolol can be added to reduce tachycardia in POTs.

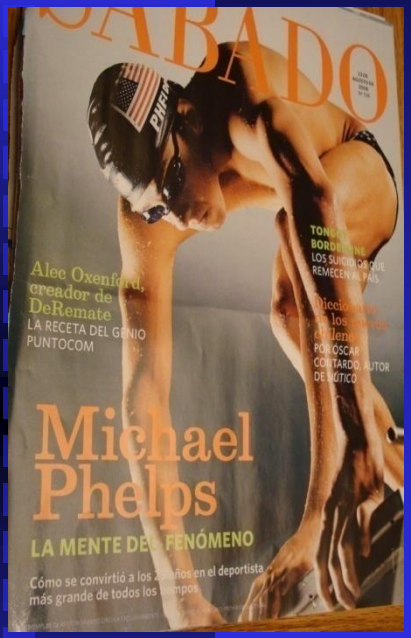
Treatment of Dysautonomia (Cont.)

- Anti-depressants: Fluoxetine
  Sertraline
  Cytalopram
  Escytalopram
  Paroxetine
- Ansyolitics. Alprazolam or others

In case of anemia it is necessary to correct it, because it aggravates Dysautonomia.

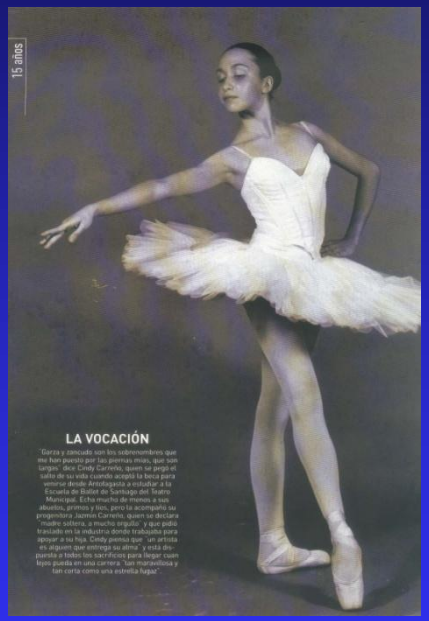
A pacemaker may be indicated in a few cases, to prevent recurrent syncopal episodes.

Hypermobility can be an Asset

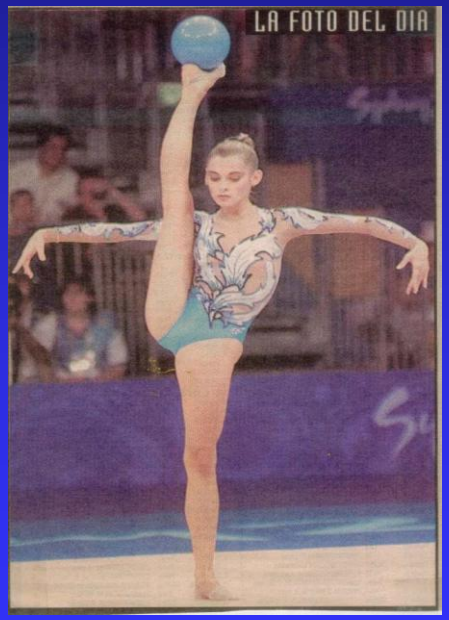


Olympic swimmer

(Marfanoid)



Ballet dancer



Contorsionist

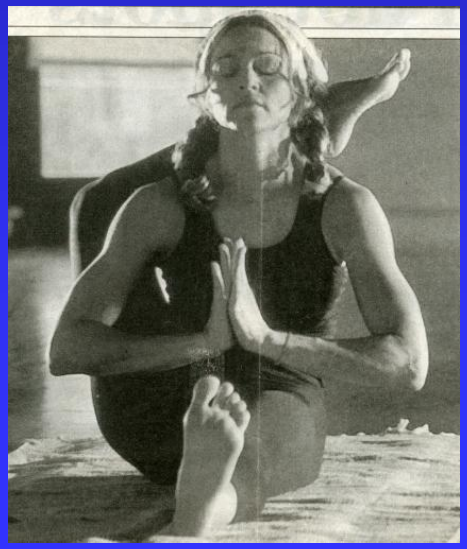
Michel Petrucciani

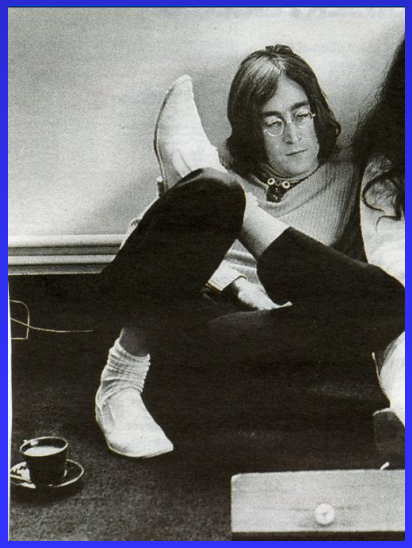
Osteogenesis Imperfecta

One of my JHS patients with marfanoid habitus

Virtuos pianists such as Rachmaninov and violinists such as Paganini had Marfán Syndrome.

Hypermobility can be an Asset





Lake Area. Southern Chile

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