

In This Issue:

Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance	1
Dysautonomia and Menopause: As if Hot Flashes Weren't Enough	5
Fast Facts: Did You Know...	6
NDRF Patient Conference 2002 Notes	6
Contributors	7
The Patient's Voice	7
Glossary	8

Dysautonomia research is continually evolving. Future research may change or disprove some currently held beliefs. Information in several of the articles in this newsletter contains the author's interpretation. As always, readers are encouraged to confirm all information with other sources and a physician.

Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance

For years, researchers have wondered why blood pools in the abdomen and limbs of some patients with **orthostatic intolerance**. Physicians hypothesized that these patients were experiencing abnormal **vasoconstriction** of the arteries, altered **capillary permeability, denervation**, impaired venous emptying and/or had abnormal veins that stretch excessively.

Research has suggested that some of these patients do indeed have blood vessels that stretch excessively¹. Some of these patients have a connective tissue disorder called Ehlers-Danlos syndrome (EDS).

Ehlers-Danlos syndrome is the name for a group of genetic

Continued on page 2

Ehlers-Danlos Syndrome Linked to Orthostatic

Intolerance *continued from page 1*

disorders that affect the structure and function of collagen. Collagen is a fibrous protein that is one of the main building blocks of connective tissues – such as skin, tendon, bone and cartilage. Each type of connective tissue requires a certain kind of collagen to function correctly. People with Ehlers-Danlos syndrome may experience symptoms such as fragile skin and/or unstable joints that result from faulty collagen.

There are different types of Ehlers-Danlos syndrome, each classified according to the manifestation of signs and symptoms². Each type includes a subset of the following symptoms³:

- skin problems
- soft, velvet-like skin
- fragile skin that bruises or tears easily
- stretchy rubber band-like skin
- easy or severe bruising
- poor and slow wound healing (usually taking weeks to months to heal)
- small harmless bumps under the skin
- joint problems
 - loose unstable joints causing frequent

dislocations usually occurring in the shoulders, knees, hips, collar bone or jaw

- double jointedness (hyperextension of the joints), may be extreme
- joint pain from frequent dislocation
- eye problems
 - nearsightedness, occasionally extreme
 - more serious eye conditions (EDS VI)
- gum disease (EDS VIII)
- curvature of the spine (EDS VI)
- problems with blood clotting (EDS X)
- pulmonary (lung) problems (EDS IV)
- weak blood vessels, intestines or uterus that may lead to more serious complications (EDS IV)

Orthostatic intolerance patients with Ehlers-Danlos syndrome usually have type III⁴. These patients tend to be female, **hypermobile, hyperflexible**, and often have blond hair, blue eyes and pale skin⁴.

A Johns Hopkins study of twelve orthostatic intolerance patients with Ehlers-Danlos syndrome reported the following findings¹:

-Six of the patients were classified as having EDS type II, the remaining six had EDS type

Continued on page 3

Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance *continued from page 2*

III. However, the authors of this study admit that the clinical distinction between mild classical EDS (formerly known as EDS type II), hypermobile EDS (formerly EDS type III), and the more common **benign familial hypermobility syndrome** is often difficult to make.

- All patients satisfied clinical criteria for chronic fatigue syndrome.
- Nine patients had neurally mediated hypotension; of those, seven had **postural tachycardia** within ten minutes of standing. Three others had postural tachycardia without **hypotension**.
- All subjects reported some degree of chronic joint or muscle pain in the absence of articular (joint) swelling or **erythema**.
- Five patients had **fibromyalgia**.
- Five patients had at least three episodes of fainting; the other seven had recurrent lightheadedness without fainting.

-All patients had experienced recurrent joint dislocations; six of which had temporomandibular (jaw) joint diseases (TMJ).

- All patients had soft skin with localized skin **hyperextensibility**; none showed evidence of extreme or generalized hyperextensibility.
- All patients had acrocyanosis (blueness of the extremities) when the limbs were in a dependent position.
- Six patients had wide, papyraceous (thin, paper-like) scars; the others had no scars.
- All of the patients had easy **eversion** of the upper eyelid.
- One patient had **mitral valve prolapse** and one patient had mild dilation of the **aortic** root.
- Eleven of the patients could place their leg behind their head and five could place their entire fist in their mouth.

Other features that presented in some of these patients included a high arched palate, scoliosis, easy bruising, delayed wound healing, piezogenic papules (small, soft skin-colored lumps that appear on the side of the heel when standing and disappear when the foot is

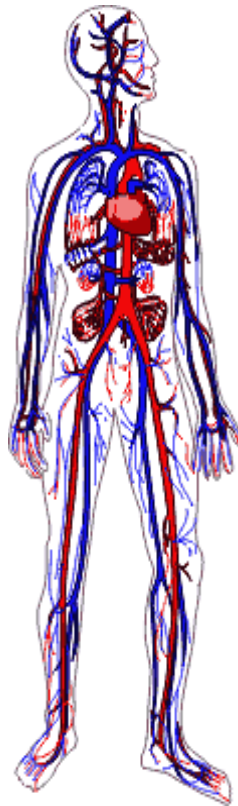
Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance *continued from page 3*

elevated), varicose veins, flat feet, ability to touch the tip of the nose with the tongue and **slipped rib syndrome**.

The authors of this twelve patient study propose that people with both Ehlers-Danlos syndrome and orthostatic intolerance have abnormal connective tissue in dependent blood vessels¹. This condition permits veins to distend excessively. Simply put, Ehlers-Danlos patients have flexible collagen in places where it should be firm, thus resulting in blood vessels stretching further than normal. This inappropriate stretchiness allows blood to pool in the vessels. The pooling of blood is exacerbated when these patients stand up, resulting in symptoms of orthostatic intolerance.

However, this phenomenon does not occur in all patients with Ehlers-Danlos syndrome. In fact, it has been reported that excess lower extremity pooling seems uncommon in common variants of EDS (eg, type III)⁵. Preliminary data also indicate no change or even a decrease in venous distensibility compared to reference ranges⁵.

So why do some patients with Ehlers-Danlos syndrome have orthostatic intolerance?



Research done by Dr. Giris Jacob may provide some answers. Jacob suggests that the blood vessels of EDS patients do not work well, even in those without symptoms⁴. The blood vessels do not respond normally to chemical provocation, and they may be more susceptible to damage. If

these blood vessels deteriorate further, a peripheral form of POTS may develop⁴.

Currently, there is little treatment for Ehlers-Danlos syndrome. However, this study raises the possibility that the fatigue reported by some EDS patients may be occurring as a result of orthostatic tachycardia and/or hypotension, and thus, may be treatable.

The connection between orthostatic intolerance and Ehlers-Danlos syndrome is still

Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance *continued from page 4*

in its infancy. Tomorrow's discoveries could render some of today's knowledge obsolete. Future research is needed to clarify the connection between orthostatic intolerance, chronic fatigue and Ehlers-Danlos syndromes. This research could then result in better treatment options for these baffling syndromes.

References

1. Rowe, P. C., Barron, D. F., Calkins, H., Maumenee, I. H., Tong, P. Y., & Geraghty, M. T. (1999). Orthostatic intolerance and chronic fatigue syndrome associated with Ehlers-Danlos syndrome. *Journal of Pediatrics*, 135(4), 494-499.
2. Ehlers-Danlos National Foundation, (2001). *The Facts About Ehlers-Danlos Syndrome* [Brochure]. Clarke, D. A., Czerpak, K. S., & Neumann-Potash, L: Authors.
3. Ehlers-Danlos Syndrome: Symptoms and Diagnosis. (2001). *University of Washington Orthopaedics & Sports Medicine*. <http://www.orthop.washington.edu/arthritis/types/ehlersdanlos/03?faq>
4. Grubb, B. P. (2002, October). The heterogeneity of symptoms related to dysautonomia. *Symposium conducted at the meeting of the National Dysautonomia Research Foundation Northwest Ohio Support Group*. Toledo, Ohio.
5. Stewart, J. M., & Erickson, L.C., (2002). Orthostatic intolerance: an overview. In Alejos, J. C., Konop, R., Chin, A. J., Herzberg, G., Neish, S. (Eds.). *emedicine Journal*, 3, (1). <http://www.emedicine.com/ped/topic2860.htm>

Dysautonomia and Menopause: As if Hot Flashes Weren't Enough

Women sometimes report a worsening of **dysautonomia** symptoms around menopause. This occurs due to the release of two chemicals, follicle-stimulating hormone (FSH) and luteinizing hormone (LH)¹.

FSH and LH are pituitary hormones that stimulate ovulation. The ovaries begin to fail as a woman enters menopause, and the brain releases excessive amounts of FSH and LH to try and get the ovaries to start working again².

FSH and LH are both vasodilators. Vasodilators cause dilation of blood vessels, which can worsen orthostatic hypotension. Sympathetic activity may increase in an attempt to constrict blood vessels as blood pressure falls. This combination of factors can result in a worsening of dysautonomia symptoms around menopause.

References

1. Grubb, B. P. (2002, October). The heterogeneity of symptoms related to

Ehlers-Danlos Syndrome Linked to Orthostatic Intolerance *continued from page 5*

dysautonomia. *Symposium conducted at the meeting of the National Dysautonomia Research Foundation Northwest Ohio Support Group.* Toledo, Ohio.

2. Menopause/FSH/LH. *Doc Trish Explains It All: Medicine You Can Understand.* Retrieved December 5, 2002. Full text:
<http://www.askdoctrish.com/bloodtests.htm>

Fast Facts: Did You Know...

- The average POTS patient is a highly educated woman¹.
- Sympathetic overactivity can result in reduced wrinkling².
- Vitamin B12 deficiency can cause pooling blood and orthostatic hypotension³.

References

1. Benrud-Larson, L. M., Dewar, M. S., Sandroni, P., Rummans, T. A., Haythornthwaite, J. A., & Low, P. A. (2002, June). Quality of life in patients with postural tachycardia syndrome. *Mayo Clinic Proceedings*, 77, 531-537. Full text: <http://www.mayo.edu/proceedings/2002/jun/7706a4.pdf>
2. Coghlan, H. C. (2002, July). Orthostatic Intolerance. *National Dysautonomia Research Foundation Patient Conference.* Washington, DC.
3. Coghlan, H. C. (2002, July). Open Session

with Panel. *National Dysautonomia Research Foundation Patient Conference.* Washington, DC.

National Dysautonomia Research Foundation Patient Conference 2002 Notes

Michelle Sawicki attended the NDRF conference in July of 2002. The following are segments of answers to questions she asked during one of the sessions.

Question: Why does walking up stairs induce symptoms in some people?

Answer by Dr. Blair Grubb: Walking up stairs puts an unusual amount of stress on the cardiovascular system because of the fact you are not using the skeletal pump in the same fashion as when you walk. You are going upwards against an incline, and this is a tremendous sudden workload on the body that is hard to accommodate to. Stair walking provokes symptoms in a variety of different cardiovascular conditions, be it an autonomic patient, a heart failure patient, a patient with angina, a patient with chronic obstructive

Continued on page 7

NDRF Patient Conference 2002 Notes *continued from page 6*

pulmonary disease..all of these people have an extremely difficult time walking up stairs because it is a greater than normal physiological stress.

Question: What, if any, are the negative effects of high circulating **norepinephrine** levels on the body?

Answer: In general, the physicians on the panel did not feel POTS patients were at risk for **cardiomyopathy** resulting from elevated norepinephrine levels. Dr. David Robertson and Dr. Blair Grubb stated they had each had (only) one patient develop cardiomyopathy. Dr. Robertson explained that his patient had developed cardiomyopathy due to a genetic factor. Dr. Blair Grubb explained that there was no way of knowing whether his patient's cardiomyopathy was due to high **catecholamine** levels or not.

**We Value Newsletter
Contributions and
Suggestions!**

Contributors

We would like to thank the following people for contributing to this newsletter:

Judith Pettibone, Editor

Melanie Oliverio, Proofreader and Advisor

Dysautonomia News articles are written by Michelle Sawicki, unless stated otherwise.

The Patient's Voice

The Patient's Voice is an area for patients to express themselves and write about experiences relating to dysautonomia - both positive and negative. It is a place to share medical experiences, suggestions, short stories and poetry, etc. If you would like to contribute to The Patient's Voice, please email Michelle@potsplace.com or write to:

Michelle Sawicki
P.O. Box 55
Brooklyn, MI 49230

Views expressed in The Patient's Voice are not necessarily those of the Dysautonomia Information Network or its members.

The Relation Between POTS and Neurosurgery
By Sophie Hankes

Two women developed POTS after decompression of cranial nerves - a neurosurgical procedure. I am one of them and would like to know:

-are there more people who had this procedure and developed POTS?

-who was the neurosurgeon and how did he/she deal with you?

-were you referred to other physicians?

-can anyone recommend a physician who would be interested in researching POTS developing after surgery on cranial nerves?

Any information is welcome. Please email me at: srhankes@aol.com

Glossary

Aorta: the main trunk of a series of vessels, commencing at the upper part of the left ventricle, which convey the oxygenated blood to the tissues of the body for their nutrition.

Definition from: <http://www.bartleby.com> The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Aortic Root: The base of the aorta.

Benign Familial Hypermobility Syndrome –

The types of Ehlers-Danlos syndrome have been reclassified. See www.ednf.org for the latest classifications.

Capillary Permeability: property of blood capillary walls that allows for the selective exchange of substances.

Definition from: <http://cancerweb.ncl.ac.uk/>

Cardiomyopathy: heart muscle damage that is not related to hypertension, coronary artery disease, congenital (inherited) heart defects, or problems of the arteries, heart valves or pericardium (membrane around the heart).
Cardiomyopathy is a chronic condition, which often causes a

Dysautonomia News

Glossary *continued from page 8*

steady deterioration in heart function.

Definition from: <http://www.intelihealth.com/>

Catecholamine: Any of a group of amines derived from catechol that have important physiological effects as neurotransmitters and hormones and include epinephrine, norepinephrine, and dopamine.

Definition from: <http://www.bartleby.com> The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Denervation: To deprive (an organ or body part) of a nerve supply, as by surgically removing or cutting a nerve or by blocking a nerve connection with drugs.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Dysautonomia: dysfunction of the autonomic nervous system.

Erythema: a capillary congestion which results in reddened skin.

Eversion: The act of turning inside out.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Fibromyalgia: A syndrome characterized by chronic pain in the muscles and soft tissues surrounding joints, fatigue, and

tenderness at specific sites in the body.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Hyperextensibility: having the capacity to be hyperextended or stretched to a greater than normal degree.

Definition from: <http://www.fasthealth.com/> Published under license with Merriam-Webster, Incorporated. © 1997-2000.

Hyperflexible: Capable of being flexed or bent to a greater than normal degree.

Hypermobile: Capable of readily moving excessively from place to place.

Hypotension: Abnormally low blood pressure.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Mitral Valve Prolapse: a valvular heart disorder in which one or both mitral valve flaps close incompletely during systole usu. producing either a click or murmur and sometimes minor mitral regurgitation and which is often a benign symptomless condition but may be marked by varied symptoms (as chest pain, fatigue, dizziness, dyspnea, or palpitations) leading in some cases to endocarditis or ventricular tachycardia.

Definition from: <http://www.fasthealth.com/> Published under license with Merriam-Webster, Incorporated. © 1997-2000.

Dysautonomia News

Glossary *continued from page 9*

Norepinephrine: A substance, C₈H₁₁NO₃, both a hormone and neurotransmitter, secreted by the adrenal medulla and the nerve endings of the sympathetic nervous system to cause vasoconstriction and increases in heart rate, blood pressure, and the sugar level of the blood. Also called noradrenaline.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Orthostatic: Relating to or caused by standing upright.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Postural Tachycardia: a rapid heart rate, especially one above 100 beats per minute in an adult, related to positioning of the body or of body parts.

Combined definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Slipped Rib Syndrome: results from ligamentous injury trauma to the costal cartilage of (usually) the eighth, ninth, or tenth rib. When the ligaments are stretched or ruptured, they allow the cartilage tip of the rib to slip upwards and impinge on the intercostal nerve. Children are particularly vulnerable to slipped rib syndrome because their ligaments have not fully

matured and are naturally “loose”.

Definition from <http://www.healthyroads.com/>

Vasoconstriction: Constriction of a blood vessel, as by a nerve or drug.

Definition from: www.bartleby.com The American Heritage® Dictionary of the English Language: Fourth Edition. 2000.

Dysautonomia News will soon be part of the Dysautonomia Information Network. See future newsletters for more information on this nonprofit organization.

Subscribe to Dysautonomia News at:

<http://www.potsplace.com/newsletter.htm>