Ehlers-Danlos Syndrome

LEARN ABOUT YOUR PAIN

Definition and description of the disorder

The Ehlers-Danlos syndromes are inherited in the genes that are passed from parents to offspring. They are categorized according to the form of genetic transmission into different types with many features differing between patients in any given type. The fragile skin and loose joints and tissue fragility is often a result of abnormal genes that produce abnormal proteins that confer an inherited frailty of collagen (the normal protein "glue" of our tissues).

In 2001, researchers discovered a new form of Ehlers-Danlos syndrome that is caused by an inherited abnormality in a protein other than collagen that also normally plays a role in binding together the cells of our tissues (including the skin, tendons, muscle, and blood vessels). Abnormalities in this protein, called tenascin, also lead to a form of Ehlers-Danlos syndrome. Researchers suspect that tenascin could play a role in regulating the normal distribution of collagen in the connective tissues of the body.

SYMPTOM LIST

Migraines, allergies, hay fever, asthma, eczema, varicose veins, positive Gorlin's sign (ability to touch your nose with your tongue), IBS, gastric reflux, hernias, diverticulitis, bendy joints or hyper flexibility soft skin, easy bruising and bleeding, slow wound healing thin translucent skin that you can see the veins through or unusual scarring especially on the lower legs. Unusual stretch marks.

Joint pains, arthritis, TMJ, RSI, aneurysms and mitral valve problems. Also POTS/OI and ME of course - fainting dizziness etc. Overcrowding of teeth (orthodontic work needed), scoliosis. Unstable joints/proneness to sprains, dislocations, subluxations and hyperextension. Joints that click, early onset of osteoarthritis, chronic degenerative joint disease, muscle pain, frequent tearing of tendons or muscles, Reynaud's phenomenon, Dupuytren's contracture, scoliosis, costochondriatis, pectus scavatum, nearsightedness and other eye problems, blue sclera, carpal tunnel, neuropathy, keratosis pillarist (pimply red rash on upper arms that comes and goes), skin tags (small longish pedicles of skin overgrowth on various parts of the body) and pregnancy complications such as post-partum hemorrhage.

*TMJ = temper mandibular joint dysfunction - i.e. a saw jaw that hurts to chew or open your mouth.

YOU do NOT need to have ALL these symptoms of have EDS and few will have them all but your family members may have some and you will have some others.

The symptom list is so diverse as EDS is a connective tissue disease (CTD) and CT is nearly everywhere in the body; symptoms vary form person to person, even within the same family.

Other possible symptoms - dry lips, alcohol intolerance, clumsiness (? possibly due to poor proprioception) ganglions - eg on the wrists and a youthful appearance-few wrinkles, petechial (tiny red dots of blood just under the skin that appear for no apparent reason). Ear problems like "water in ear" or blocked ear feeling and tinnitus. Also avoidance of social situations can be a sign-they can be stressful and can involve a lot of standing, in

hot, crowded places and often alcohol (a vasodilator)- all factors that can exacerbate EDS symptoms.

There are many types of EDS and much crossover between the types - you do NOT need to be hypermobile or flexible to have EDS, as is commonly but wrongly stated. In fact it seems likely some people with it have very tight muscles by contrast (muscular hpertonicity).

There are six major types of EDS. The different types of EDS are classified according to their manifestations of signs and symptoms.

Classical Type

This type is characterized by highly elastic, soft, and doughy skin; unusual scarring; and loose joints. This type of Ehlers-Danlos Syndrome combines the types formerly called I and II. Ehlers-Danlos Syndrome, Classical Type is a subtype of Ehlers-Danlos Syndrome.

People with the Classical Type have smooth, velvety skin that is stretchy, fragile, and easily bruised. Wounds often split open with little bleeding, heal slowly, and leave characteristic thin, wide scars

("cigarette paper" scars). People with this condition also have loose joints with an unusually large range of movement (hypermobility). As a result, joints are prone to dislocation, sprains, and the early-onset arthritis. Non-cancerous fibrous growths on pressure points (such as elbows) and fatty growths on the forearms and shins are also common. Other manifestations include weak muscle tone in infants due to hypermobility, which can make them seem "floppy" and delay the development of motor skills such as sitting, standing, and walking. As many as half of the people with Classical Type Ehlers-Danlos Syndrome have a condition called mitral valve prolapse, which affects blood flow between the chambers of the heart.

The Classical Type is one of the most common forms of Ehlers-Danlos Syndrome. This condition is usually inherited in an autosomal dominant pattern, which means one copy of the altered gene is sufficient to cause the disorder. In the rare cases caused by TNXB mutations, the condition has shown an autosomal recessive pattern of inheritance, which means two copies of the gene must be altered for a person to be affected by the disorder.

Clinical Diagnosis

The clinical diagnosis of EDS, Classic Type is established by family history and clinical examination. Diagnostic criteria was developed by a medical advisory group in a conference (sponsored by the Ehlers-Danlos Foundation [USA] and the Ehlers-Danlos Support Group [UK]) at Villefranche in 1997**[Beighton et al 1998]** The combination of the first three major diagnostic criteria should have a high specificity for EDS, Classical Type. The presence of one or more minor criteria contributes to the diagnosis of the Classical Type of EDS but is not sufficient to establish the diagnosis.

Major Diagnostic Criteria for the Classical Type of EDS

- Skin hyper extensibility should be tested at a neutral site (one not subjected to mechanical forces or scarring), such as the volar surface of the forearm. It is measured by pulling up the skin until resistance is felt. In young children, hyper extensibility of the skin is difficult to assess because of abundant subcutaneous fat.

- Widened atrophic scars (a manifestation of tissue fragility)

- Joint hypermobility depends on age, gender, and family and ethnic backgrounds. Joint hypermobility in Classical Type EDS is general, affecting both large and small joints. It is usually noted when a child starts to walk. It should be assessed using the Beighton scale**[Beighton 1988]**, the most widely accepted grading system for the objective semi-quantification of joint hypermobility
- Positive Family History

Minor Diagnostic Criteria for the Classical Type of EDS

- Smooth, velvety skin
- Molluscoid pseudotumors: fleshy, heaped-up lesions associated with scars over pressure points such as the elbows and knees
- Subcutaneous spheroids: small, cyst-like, hard shot-like nodules, freely movable in the subcutis over the bony prominences of the legs and arms. They occur in about one-third of affected individuals, are numerous, and feel like hard grains of rice. X-ray reveals an outer calcified layer with a translucent core. The spheroids represent subcutaneous fat globules that have lost their blood supply, becoming fibrosed and calcified.
- Complications of joint hypermobility (sprains, dislocations,subluxations, pes planus)
- Muscle hypotonia, delayed gross motor development
- Easy bruising
- Manifestations of tissue extensibility and fragility (hiatal hernia, anal prolapse in childhood, cervical insufficiency)
- Surgical complications (postoperative hernias)

Hypermobility

This type is characterized by loose joints and chronic joint pain. This form of Ehlers-Danlos Syndrome was formerly called type III. Ehlers-Danlos Syndrome, Hypermobility Type is a subtype of Ehlers-Danlos Syndrome.

The most common sign of this condition is an unusually large range of joint movement, called hypermobility. Both large and small joints are unstable, and certain joints (such as the shoulder, knee, and jaw) tend to dislocate frequently. Chronic joint and limb pain often begins early in life. People with this condition may have skin that is soft, velvety, or stretchy; however, skin symptoms vary among people. Many affected people also have a condition called mitral valve prolapse, which affects blood flow between the chambers of the heart.

The Hypermobility Type is the most common form of Ehlers-Danlos Syndrome. The Hypermobility Type of Ehlers-Danlos Syndrome is most often inherited in an autosomal dominant pattern, which means one copy of the altered gene is sufficient to cause the disorder. In these cases, family members in each generation are usually affected, but the features of the condition may vary.

In some families, a recessive pattern of inheritance may be possible. This inheritance pattern means that two copies of the gene must be altered for a person to be affected by the disorder. Most often, the parents of a child with an autosomal recessive disorder are not affected but are carriers of one copy of the altered gene

Clinical Diagnosis

Clinical diagnostic criteria and a revised nomenclature for all forms of Ehlers-Danlos Syndrome (EDS) were proposed by **[Beighton et al 1998]**. EDS, Hypermobility Type is distinguished from EDS, Classical Type chiefly by milder and fewer skin and soft tissue manifestations. The diagnosis of EDS, Hypermobility Type is based entirely on clinical evaluation and family history. The criteria listed below reflect those proposed by **[Beighton et al 1998]** as modified by the author's experience.

Major Diagnostic Criteria for the Hypermobility Type or EDS

- Joint hypermobility, which usually is confirmed by a score of five or more on the nine-point Beighton scale **[Beighton et al 1973]**, including:

  -One point for passive dorsiflexion of each fifth finger >90°
  -One point for passive apposition of each thumb to the flexor surface of the forearm
  -One point for hyperextension of each elbow >10°
  -One point for hyperextension of each knee >10°
  -One point for ability to place the palms on the floor with the knees fully extended

- Soft or velvety skin with normal or slightly increased extensibility

  Skin hyper extensibility is assessed at a site lacking excess or loose skin and without evidence of prior trauma by gently pulling until resistance is met. Extensor surfaces of joints should not be used because of the presence of excess skin. An ideal location is the volar surface of the forearm, where the upper limit of normal is approximately 1-1.5 cm.

- Absence of skin or soft tissue fragility, which is suggestive of other types of EDS. Examples include:

  -Spontaneous or easily induced skin cuts or tears
  -Spontaneous or easily induced tears or ruptures of tendons, ligaments, vessels, or other internal organs
  -Atrophic ("cigarette paper") scars (although mildly atrophic scars are sometimes seen in the hypermobility type, especially in areas subject to physical stress, such as extensor surfaces and the abdominal wall)

- Molluscoid pseudotumors

- Surgical complications, such as incisional hernia, wound dehiscence, or sutures tearing through tissues and failing to hold

Minor Diagnostic Criteria for the Hypermobility Type of EDS

- Family history of similar features without significant skin or soft tissue fragility in a pattern consistent with autosomal dominant inheritance
- Recurrent joint dislocations or subluxations
- Chronic joint or limb pain
- Easy bruising
- Functional bowel disorders (functional gastritis, irritable bowel syndrome)
- Neurally mediated hypotension or postural orthostatic tachycardia
- High, narrow palate
- Dental crowding

The sensitivity and specificity of examination for joint hypermobility is dependent in part on the individual's age, gender, and medical history.

- Young children (approximately five years of age or younger) tend to be very flexible and are therefore difficult to assess.
- Women are, on average, more flexible than men
- Older individuals tend to lose flexibility, and post-surgical or arthritic joints often have reduced range of motion. A history of former joint laxity or clinical demonstration of substantial laxity in multiple joints is sometimes accepted in lieu of a positive Beighton score in such cases, if the family history and other minor criteria are strongly suggestive

There is disagreement as to whether the "benign familial articular hypermobility syndrome" is identical to EDS, hypermobility type or represents a unique condition **[Grahame 1999]**. The distinction is subtle and relates to degree of joint complications and presence or absence of skin manifestations. However, first-degree relatives of

probands with EDS, Hypermobility Type often have relatively asymptomatic joint laxity and mild or absent skin manifestations. Therefore, the benign hypermobility syndrome is included as EDS, Hypermobility Type for this review.

Vascular Type

This type is characterized by possible arterial or organ rupture as a result of spontaneous rupture of vessels or organs due to the result of even minor trauma. The Vascular Type of EDS is the most serious form of Ehlers-Danlos Syndrome.

If a patient presents with signs of chest, neck, abdominal pain (etc.) it should be considered a **TRAUMA SITUATION.** Patient complaints should be immediately investigated using an MRA, MRI or CT-Scan rather than x-rays since expedient diagnosis and treatment is so critical to the survival of a Vascular EDS patient.

Please keep in mind that the Vascular Type of EDS is extremely hard to diagnose. Since so many patients are misdiagnosed with another form of EDS extreme caution should be taken with all forms of this disorder. The Vascular Type is a subtype of Ehlers-Danlos Syndrome.

People with the disorder have thin, fragile skin that bruises easily. Veins are visible beneath the skin, particularly on the chest and abdomen, and hands and feet may have an aged appearance. Unlike people with other forms of Ehlers-Danlos Syndrome, people with the Vascular Type have skin that is soft but not overly stretchy. Facial features are often distinctive, including protruding eyes, a thin nose and lips, sunken cheeks, and a small chin.

Other signs of the disorder include an unusually large range of movement (hypermobility) of hand and foot joints, tearing of tendons and muscles, painfully swollen veins in the legs, lung collapse, and slow wound healing following injury or surgery. Infants with the condition may be born with hip dislocations and a foot disorder called clubfoot, which causes the foot to turn inward and downward.

Unpredictable ruptures of arteries and organs are the most serious complications of the Vascular Type of Ehlers-Danlos Syndrome. A torn artery can cause internal bleeding, stroke, or shock, and is the most common cause of death in patients with this disorder. Rupture of the intestine is seen in 25 to 30 percent of affected individuals and tearing of the uterus (womb) during pregnancy affects 2 to 3 percent of women. Although serious problems are rare in childhood, more than 80 percent of patients experience severe complications by the age of 40.

The vascular type is a rare form of Ehlers-Danlos Syndrome. Mutations in the COL3A1 gene cause the Vascular Type of Ehlers-Danlos Syndrome. The protein made by the COL3A1 gene is used to assemble larger molecules called type III collagens. Collagens provide structure and strength to connective tissue throughout the body. Type III collagen is mostly found in skin, blood vessels, and internal organs. If the structure or production of type III collagen is altered by a mutation in the COL3A1 gene, collagen fibrils cannot be assembled properly in these tissues, and the signs and symptoms of the Vascular Type of Ehlers-Danlos Syndrome result.

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene is sufficient to cause the disorder. About half of all cases are inherited from a parent who has the condition. The other half of cases occur in people whose families have no history of the disorder; these sporadic cases are caused by new mutations in one copy of the COL3A1 gene.

Clinical Diagnosis

Diagnostic criteria and standardized nomenclature for the Ehlers-Danlos Syndromes were suggested by a medical advisory group in a conference sponsored by the Ehlers-Danlos Foundation (USA) and the Ehlers-Danlos Support Group (UK) at Villefranche in 1997 **[Beighton et al 1998]**. Criteria are modified here to reflect the authors' experience.

The combination of any two of the major diagnostic criteria should have a high specificity for the Vascular Type of EDS. Biochemical testing is strongly recommended to confirm the diagnosis.
The presence of one or more minor criteria supports the diagnosis of the vascular type of EDS but is not sufficient to establish the diagnosis.

Major Diagnostic Criteria for the Vascular Type of EDS

- Arterial rupture
- Intestinal rupture
- Uterine rupture during pregnancy
- Family history of the vascular type of EDS

Minor Diagnostic Criteria for the Vascular Type of EDS

- Thin, translucent skin (especially noticeable on the chest/abdomen)
- Easy bruising (spontaneous or with minimal trauma)
- Characteristic facial appearance (thin lips and philtrum, small chin, thin nose, large eyes)
- Acrogeria (an aged appearance to the extremities, particularly the hands)
- Hypermobility of small joints
- Tendon/muscle rupture
- Early-onset varicose veins
- Arteriovenous carotid-cavernous sinus fistula
- Pneumothorax/pneumohemothorax
- Chronic joint subluxations/dislocations

- Congenital dislocation of the hips
- Talipes equinovarus (clubfoot)
- Gingival recession

Kyphoscoliosis Type

This type is characterized by generalized joint laxity and severe muscle hypotonia (weak muscle tone) at birth. The muscular hypotonia can be very pronounced and leads to delayed gross motor development. Individuals with the Kyphoscoliosis Type of EDS present with a progressive form of scoliosis at birth. The phenotype is most often severe, frequently resulting in the loss of ambulation in the second or third decade. Scleral fragility may lead to rupture of the ocular globe after minor trauma.

Tissue fragility including atrophic scars and easy bruising. Spontaneous arterial rupture can occur.

Other Findings May Include

- Marfanoid Habitus (Marfan like features)
- Micro Cornea (abnormally small cornea)
- Radiologically Considerable Osteopenia (diminished amount of bone tissue)

The Kyphoscoliosis Type of EDS is the result of a deficiency of lysylhydroxylase (PLOD), which is a collagen-modifying enzyme. This type of EDS is inherited in an autosomal recessive manner. The Kyphoscoliosis Type of EDS can be diagnosed through a urine test.

Arthrochalasia Type

This type is characterized by congenital hip dislocation which is present in all biochemically proven individuals with this type of EDS.

Severe generalized joint hypermobility with recurrent subluxations are seen in individuals with this type of EDS.

Other manifestations of this type may include

- Skin hyperextensibility with easy bruising
- Tissue fragility including atrophic scars
- Muscle Hypotonia
- Kyphoscoliosis
- Radiologically Mild Osteopenia.

The Arthrochalasia Type of EDS is caused by mutations leading to deficient processing of the amino-terminal end of proa1(I) [type A] or proa2(I)[type B] chains of collagen type I. It is inherited in an autosomal dominant manner. A skin biopsy can also diagnose this type of EDS.

Dermatosparaxis Type

This type is characterized by severe skin fragility and substantial bruising. Wound healing is not impaired and the scars are not atrophic. The skin texture is soft and doughy. Sagging, redundant skin is evident. The redundancy of facial skin results in an appearance resembling cutis laxa. Large hernias(umbilical, inguinal) may also be seen. The number of patients reported with this type of EDS is small.

The Dermatosparaxis Type of EDS is caused by a deficiency of procollagenI N-terminal peptidase. It is inherited in a autosomal recessive manner. A skin biopsy can diagnose this type of EDS.

Tenascin-X Deficient Type

This type is characterized by joint hypermobility, hyperplastic skin, and fragile tissue. Lacking multiple shrinking (atrophied) scars in the skin that is often seen in the Classic Type of Ehlers-Danlos Syndrome. Inherited as an autosomal recessive genetic trait (not seen in family members or only in one generation of members of the same family).

What people are saying

People look at those of us with this condition and frequently remark how good we look. These comments don't happen when we are in the wheelchairs or have our braces on, for then one is visually aware of problems existing. Many of us face judgment by others due to us looking "normal" and have to learn how to cope with this attitude that people have towards us.

Possible co-morbidities

Most people that are coping with EDS tend to have other conditions to deal with too. It is not unusual at all. For instance, many face pots with EDS and also are on celiac diets. Do not get alarmed if you get a diagnoses for more that just the EDS. Take it in stride and realize now that you know what else is going on, that you can begin to address the issues and try to improve the quality and safety of your life.

Treatment options

How are Ehlers-Danlos syndromes treated?

Ehlers-Danlos syndromes are treated according to the particular manifestations present in a given individual.

Skin protection (from injury of trauma and sun, etc.) is critical. Wounds must be tended with great care and infections treated and

prevented. Suturing can be difficult as the skin can be extremely fragile.

Joint injury must be avoided. Occasionally, bracing may be necessary to maintain joint stability. Exercises that strengthen the muscles that support the joints can help to minimize joint injury. Getting a good core program to follow will help to strengthen the muscles that are on overload taking over the job of the ligaments and tendons. Contact sports and activities involving joint impact should be avoided.

If surgery is necessary, be sure to deal with a doctor that is aware of this rare condition. Cadaver tendons used will help to strengthen joints that just no longer have the ability to hold the bones in position.

Low dose naltrexone – 4mg, can very effective since it triggers the endorphins giving you a feeling of peace in your body along with helping to support the immune system, allowing the body to heal itself.

Medical Marijuana is very effective for relieving the raw pain. It is safe, no invasive, does not make you feel high unless you over do it the amount, does no organ damage and allows you peace and the ability to sleep at night. There are two types of plants – sativa, that gives pain relief and stimulates you during the day and indica, that gives you pain relief and also allows your body to get the rest you desperately need.

Complementary therapies

Manual physical therapy is extremely helpful to reposition the body and also help it to relax. You may feel off for up to 24 hours after the treatment as the body fights to try to return to the wrong position, but in time, the body learns to remember where it is suppose to be positioned.

Prolotherpy is something to also consider to help strengthen the joints by injecting sugar water into the ligaments and tendons. The healing process causes fiber blasts, new tissue, thus providing strength.

Best nutrition

Many EDS'ers deal with issues with digestion. Due to this, I would encourage you to see a good nutritionist and learn what is it that you are not able to digest. Don't settle for someone telling you that the scratch tests are normal for many of us need to turn to the blood test that tells you the foods that you are allergic or reacting to. Many of us face issues with dairy, soy, and gluten. When you are able to identify what the problems are, you will feel so much better, eliminating the bloated stomach, gas, weight loss, and loose bowels. In time, you may be able to reintroduce many of these foods you had to stop enjoying.

It is always important to eat frequent, small well-rounded meals that include protein. It is best to stay away from a sugary, high carb diet. We tent to be prone to candida, and sugar and carbs feed that condition. If you experience a lot of gas and a bloated stomach frequently, consider approaching your doctor and requesting a blood test to be sure you are not infested with this form of yeast. If you are, simple medication will take care of the issue and you will feel so much better.

Best exercise regime

Moving your body is extremely important to your well being. You need to connect with a good physical therapist, preferably one that works in manual therapy. You need to develop a safe exercise routine that helps to strengthen your muscles, since they are doing not only their job but also that of the ligaments and tendons. Remember that one with this condition should not lift more that five pounds or you will stretch what you have and create damage in time along with unneeded pain. Swimming is a non invasive to this condition provided you have good movement with your neck and shoulders. When they become issues, you can resort to wearing a belt around the waist and jogging in the water. Walking is also a wonderful exercise that will keep those muscles strong.

Local support groups

RI has a new EDS support group – for more information, contact: Krista at kristalynn1977@hotmail.com or check the web site at http://eds.timix.org/

Links to other organizations and websites

www.invisibleproject.org

www.ednf.org

http://www.ehlersdanlosnetwork.org

* please not that much of this content was taken from the Ehler-Danlos Syndrome Network C.A.R.E.S. Inc site.