

TYPES OF EHLERS-DANLOS SYNDROME

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The Ehlers-Danlos National Foundation

(EDNF) is a 501(c)(3) non profit organization; founded in 1985 its purpose is to:

- Disseminate accurate information
- Provide a network of support and communication
- Foster and support research

The EDNF produces a range of educational media that is distributed free of charge to those who request it. Information leaflets, articles, multimedia programs, guides and newsletters are examples of the kind of programs that are available.

EDNF members are now able to communicate directly with each other through the interactive members area at www.ednf.org. With over 15,000 posts as of January 2004, EDNF members have built an extensive information repository on EDS and it is growing every day.

The EDNF currently has 36 local groups within the United States. By actively encouraging the development of such groups the Foundation is better able to meet the needs of communities at a local level.

Finally, with up to \$100,000 allocated for 2004, the EDNF is now directly funding research into the Ehlers-Danlos Syndrome.

To find out more about the Ehlers-Danlos National Foundation or to see if there is a local group in your area, please visit our easy to use web site at www.ednf.org or tear off the adjacent form and return it to us at the following address:

Ehlers-Danlos National Foundation
6399 Wilshire Boulevard #200
Los Angeles, CA 90048

Ehlers-Danlos syndrome (EDS) is a heterogeneous group of heritable connective tissue disorders characterized by articular hypermobility, skin extensibility and tissue fragility. Individuals with EDS have a defect in their connective tissue. It is this tissue that provides support to many body parts such as the skin, muscles, ligaments and organs. The fragile skin and unstable joints found in EDS are due to faulty collagen. Collagen is a protein that acts like glue in the body adding strength and elasticity to connective tissue.

There are six major types of EDS. The different types of EDS are classified according to the signs and symptoms that are manifested. Each type of EDS is a distinct disorder that "runs true" in a family. This means that an individual with Vascular Type EDS will not have a child with Classical Type EDS.

■ **Classical** (Formerly EDS Types I & II)

Marked skin hyperextensibility (stretchy) with widened atrophic scars and joint hypermobility are found in the Classical Type of EDS. The skin manifestations range in severity from mild to severe expression. The skin is smooth and velvety with the evidence of tissue fragility and easy bruisability. Examples of tissue extensibility and fragility include hiatal hernia, anal prolapse in childhood and cervical insufficiency. Hernias may be a post-operative complication. Scars are found mostly over pressure points such as the knees, elbows, forehead and chin. Molluscoid pseudo tumors (calcified hematomas) associated with scars are frequently found over pressure points such as the elbows, and spheroids (fat containing cysts) are usually found on the forearms and shins.

Complications of joint hypermobility include sprains, dislocations/subluxations and pes planus (flat foot) to name a few. Recurrent joint subluxations are common in the shoulder, patella and temporomandibular joints. Muscle hypotonia and delayed gross motor development may also be evident.

Clinical Testing - Abnormal electrophoretic mobility of

the proa1(V) or proa2(V) chains of collagen type V has been detected in several but not all families with the Classical Type. The Classical Type of EDS is inherited in an autosomal dominant manner.

■ **Hypermobility** (Formerly EDS Type III)

Joint hypermobility is the dominant clinical manifestation. Generalized joint hypermobility that affects large (elbows, knees) and small (fingers and toes) joints is evident in the Hypermobility Type. Recurring joint subluxations and dislocations are common occurrences. Certain joints, such as the shoulder, patella, and temporomandibular joint dislocate frequently. The skin involvement (hyperextensibility and/or smooth velvety skin) as well as bruising tendencies in the Hypermobility Type are present but variable in severity.

Chronic joint and limb pain is a common complaint amongst individuals with the Hypermobility Type. Skeletal X-rays are normal. Musculoskeletal pain is early onset, chronic and may be debilitating. The anatomical distribution is wide and tender points can sometimes be elicited.

To date, no distinctive biochemical collagen finding has been identified by researchers. The Hypermobility Type of EDS is inherited in an autosomal dominant manner.

■ **Vascular** (Formerly EDS Type IV)

This type is generally regarded as the most serious form of EDS due to the possibility of arterial or organ rupture. The skin is usually thin and translucent with veins being seen through the skin. This is most apparent over the chest and abdomen. There are certain facial characteristics present in some affected individuals. These manifestations include large eyes, thin nose, lobeless ears, short stature and thin scalp hair. Also evident is a decrease in subcutaneous tissue, particularly in the face and extremities. Minor trauma can lead to extensive bruising.

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Arterial/intestinal/uterine fragility or rupture commonly arise in this type of EDS. Spontaneous arterial rupture has a peak incidence in the third or fourth decade of life, but may occur earlier. Midsize arteries are commonly involved. Arterial rupture is the most common cause of sudden death. Acute diffuse or localized abdominal or flank pain is a common presentation of arterial or intestinal rupture. Life expectancy is shortened with a majority of individuals living only into their forties. Pregnancies may be complicated by intra-partum uterine rupture and pre- and postpartum arterial bleeding.

Joint hypermobility is usually limited to the digits. Tendon and muscle rupture can occur. Talipes equinovarus (clubfoot) is frequently seen at birth. Other manifestations that may be found in the Vascular Type include: acrogeria (premature aging of the skin of the hands and feet); early onset varicose veins; arteriovenous fistula (an opening between an artery and vein), carotid-cavernous fistula; pneumothorax (collapse of a lung)/pneumohemothorax (collapse of a lung with a collection of air or gas and blood); gingival recession and complications during and after surgery (i.e. wound dehiscence).

The Vascular Type of EDS is caused by structural defects in the proa1(III) chain of collagen type III encoded by COL3A1. This type of EDS is inherited in an autosomal dominant manner. A skin biopsy can diagnose this type of EDS.

■ **Kyphoscoliosis** (Formerly EDS Type VI)

Generalized joint laxity and severe muscle hypotonia (weak muscle tone) at birth are seen in this type of EDS. The muscular hypotonia can be very pronounced and leads to delayed gross motor development. Individuals with the Kyphoscoliosis Type present with Scoliosis at birth that is progressive. 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 may be seen in the Kyphoscoliosis Type. Spontaneous arterial rupture can occur. Other findings may include: marfanoid habitus (Marfan like features); micro cornea (abnormally small cornea); and radiologically considerable osteopenia (diminished amount of bone tissue).

Kyphoscoliosis Type 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. Kyphoscoliosis Type can be diagnosed through a urine test.

■ **Arthrochalasia** (Formerly EDS Type VII A&B)

Congenital hip dislocation has been 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 and radiologically mild osteopenia.

The Arthrochalasia Type 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** (Formerly EDS Type VIIC)

Individuals with Dermatosparaxis Type EDS have 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.

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

Other Types Of EDS

The current EDS type V (X-linked) has been described in a single family. It is a rare variant and the molecular basis of which remains unknown.

The current EDS type VIII is similar to the Classical Type except that in addition it presents with periodontal friability. This is a rare type of EDS. The existence of this syndrome as an autonomous entity is uncertain.

The EDS type IX was previously redefined as "Occipital Horn syndrome", an X-linked recessive condition allelic to Menkes syndrome. This was previously removed from the EDS classification.

The current EDS type X has been described in only one family.

The EDS type XI termed "Familial Joint Hypermobility syndrome" was previously removed from the EDS classification. Its relationship to the EDS is not yet defined.

Conclusion

This simplified classification system will facilitate an accurate diagnosis of the Ehlers-Danlos syndrome and allow a clearer distinction of disorders that overlap with EDS. It is important to note that each type of EDS is distinct. If you have one type of EDS, you cannot develop another type. However, individuals with the same type of EDS may have slightly different manifestations because each of us is a unique person.

Reference:

Beighton, P., De Paepe, A., Steinmann, B., Tsipouras, P., & Wenstrup, R (1998). Ehlers-Danlos Syndromes: Revised Nosology, Villefranche, 1997. *American Journal of Medical Genetics*, 77, 31-37.

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