

STARTING NO LATER THAN AGE 12 YEARLY EDS SCREENING RECOMMENDED

Traditionally it was problematic to consider Ehlers-Danlos syndrome in pre-adolescent children because normal growth variations can mimic some EDS symptoms, especially joint hypermobility. A more helpful approach would be:

Start EDS screening before age 12 if there is a family history of Ehlers-Danlos syndrome or an obvious developmental concern.

Connective Tissue Disorders and Ehlers-Danlos Syndrome

Collagen is the most abundant protein in the human body. It provides structural strength in human tissues, including heart and blood vessels, eyes and skin, cartilage and bone. When muscles, ligaments, tendons and even large organs are built with structurally defective collagen, there can be systemic weakness and instability evident throughout. Connective tissue disorders such as Ehlers-Danlos syndrome cause multiple manifestations that affect many functions of the human body.

Why Is Screening Important?

Children with a connective tissue disorder will usually display warning signs before any serious problems begin to arise. Recognizing these warning signs early provides the best opportunity to positively influence the course of patients' lives. Families with Ehlers-Danlos syndrome should be educated to be aware of the potential risks of contact sports, and how to preserve already unstable joints and general health.

What Can I Do?

The most common form of EDS is hypermobility, which is also the form for which genetic testing is unavailable (the genes involved have not been completely identified yet). So it is particularly important that primary care physicians screen for EDS. Refer the family to a geneticist, but:

You are in the best position to enable an EDS child's full and happy life.

The clues and complications listed here can help guide you and the families you serve in deciding whether a diagnosis of EDS may be worth pursuing further, and help those who have been diagnosed to stay as healthy as possible.

CARDIOVASCULAR

- Possibility of aortic root dilatation, mitral valve prolapse, other valvular abnormalities, enlarged right coronary artery.
- Postural orthostatic tachycardia, leading to chronic fatigue, is especially found in young persons with EDS.
- Some doctors have seen onset of lipid abnormalities in EDS youth; in any case, attention to heart health should begin early.

GASTROENTEROLOGY

- Irritable bowel syndrome with constipation and/or diarrhea, reflux, food allergies, gastroparesis.

RHEUMATOLOGY & ORTHOPEDIC

- Joint hypermobility can be assessed using the Beighton scale; however, joint hypermobility also depends on age, gender, family and ethnic background.

- Excessive flattening of feet when weight bearing, pronated or everted feet, plantar fasciitis, bunions.
- Joint dislocations & subluxations apparently unrelated to specific injury.
- Chronic unexplained joint pain, commonly out of proportion to physical and radiological findings.
- Scoliosis, kyphosis and leg length discrepancy, knee/hip alignment issues.
- Premature onset of degenerative disc disease and herniated discs in the spine.

SOCIAL & DEVELOPMENTAL

- Depression and withdrawal from social activities due to chronic pain.
- Physical awkwardness and clumsiness.

DERMATOLOGY & SPORTS MEDICINE

- Easy bruising, enlarged scars, stretch marks, poor wound healing.
- Frequent injuries.
- Joints may not be stabilized by adequate muscular control and appropriate physical therapy.
- Long-term damage resulting from hypermobile joint "party tricks", rotational stress, contact sports.

MAXILLOFACIAL/DENTAL

- High palate and teeth crowding (prior to orthodontic corrections).
- TMJ pain.
- Early onset gingival recession and gum problems.
- Cavities, dental discoloration and dental pits.

NEUROLOGY

- Cranio-cervical instability, cervical disc disease, Chiari I malformation.
- Syringomyelia.
- Tethered Cord Syndrome.
- Migraine headaches.

SCREENING AND MANAGEMENT FOR ADULTS WITH EDS

SKELETAL

Joint instability, pain, fatigue, osteoarthritis, bunions, osteopenia

- Low resistance muscle toning exercise to help stabilize joints.
- Minimize joint impact, hyperextension and resistance exercise.
- Avoid excess body weight.
- Myofascial release to reduce painful spasm (*heat, cold, massage, ultrasound, electric stimulation, acupuncture/acupressure, etc.*).
- Avoid or minimize use of high heels.
- Arch and/or heel support for foot complications.
- External bracing when necessary (*will not cause atrophy if toning exercise is continued*).
- Supportive mattress and pillow; keep head in neutral position while sleeping.
- Fat-grip writing utensils.
- Avoid joint stabilizing surgery (*high risk of failure*).
- Joint replacement surgery acceptable when necessary.
- Analgesic medication as needed.
- Calcium and vitamin D supplementation.
- Periodic bone density screening.

CARDIOVASCULAR

Aortic root dilation, neurally mediated hypotension (NMH), postural orthostatic tachycardia syndrome (POTS)

- Echocardiography annually if abnormal, every five years or longer if normal.
- Consider β -blockade for enlarging aortic root.
- Maintain adequate hydration and salt intake.

- Consider tilt-table test for dizziness, fatigue, tachycardia.
- Treat NMH and POTS as in patients without EDS.

GASTROINTESTINAL

GERD, gastritis, delayed gastric emptying, irritable bowel syndrome

- Smaller meals and avoid lying down for two hours after meals.
- Treat acid and functional bowel disorders as in patients without EDS.

SKIN

Soft, stretchy, easy bruising.

- Minimize trauma.
- Vitamin C 250–500 mg daily might be helpful.

ORAL/DENTAL

High narrow palate, dental crowding, periodontal disease, TMJ dysfunction

- Frequent brushing (soft bristles) and flossing.
- Dental exam and cleaning every six months.
- Appliances as needed for crowding, bruxism or TMJ pain.

PSYCHOSOCIAL

Isolation, depression, stigmatization

- Supportive, trusting, patient-centered care.
- Counseling for self-esteem, stress management and coping with chronic pain/disability.
- Counseling does not replace management of the underlying musculoskeletal and other systemic manifestations.

PREGNANCY

Anticipate increased pain and laxity in third trimester

- Possible rapid labor and delivery, including first pregnancy.
- No clear advantage between vaginal and Caesarean delivery.

- Premature rupture of membranes **only** in classical type, especially if fetus also has EDS.

SKIN/SOFT TISSUE FEATURES

Excluding hypermobility type: atrophic scars, skin fragility, wound dehiscence, prolonged bleeding

- Extra precautions against trauma.
- Adhesive bandages may tear skin.
- Avoid unnecessary surgery.
- Don't pull sutures tighter than necessary, but use more and leave them in longer.
- Treat prolonged bleeding similarly to von Willebrand disease.
- The skin involvement (hyperextensibility and/or smooth velvety skin) as well as bruising tendencies in the Hypermobility Type are present but variable in severity.

VASCULAR EDS

Rupture of intestines, medium-sized arteries, gravid uterus, and other internal organs

- Non-invasive arteriography head through pelvis (CT or MR) every 6-12 months.
- Cautious embolization, stenting or surgical management of enlarging aneurysms.
- Tissues are especially friable when there is concurrent inflammation.
- Repair of torn structures may be difficult, sometimes requiring sacrifice of downstream organ(s).

KYPHOSCOLIOSIS EDS

- Consider arterial screening as in the vascular type.
- Eye protection whenever there is risk of trauma.
- Regular ophthalmologic examination.
- Prompt evaluation and treatment of potential retinal detachment.
- Regular spine examination; surgery for kyphoscoliosis if necessary.

Ehlers-Danlos syndrome (EDS) is a group of inherited connective tissue disorders, caused by various defects in the synthesis of collagen. EDS is known to affect men and women of all racial and ethnic backgrounds.

There are six distinct types of EDS currently identified. All share joint laxity, soft skin, easy bruising, and some systemic manifestations. Each type is thought to involve a unique defect in connective tissue, although not all of the genes responsible for causing EDS have been found.

	Easy Bruising	Joint Laxity	Skin	Genetic Information
Hypermobility: Most common type	✓	✓	Soft	To date, no distinctive biochemical collagen finding has been identified by researchers. Inherited in an autosomal dominant manner.
Classical: Occasional internal organ fragility	✓	✓	Soft, fragile, elastic	In some families type V collagen is affected (abnormal electrophoretic mobility of proa1(V) or proa2(V) chains) as well as type I. Inherited in an autosomal dominant or recessive manner.
Vascular: Fragility of arteries, intestines & other internal organs	✓	✓	Soft, fragile, elastic, translucent	Caused by structural defects in the proa1(III) chain of collagen type III, encoded by the COL3A1 gene. Inherited in an autosomal dominant manner. VEDS incidence is estimated at one in 250,000; particularly serious because of possible arterial or organ rupture. See EDNF's <i>Vascular EDS Medical Resource Guide</i> and <i>Clinic Reference Manual: Vascular Type</i> .
Kyphoscoliosis: Very rare; kyphoscoliosis, hypotonia, fragility of eyes and arteries	✓	✓	Soft, fragile, elastic	Result of a deficiency of lysyl hydroxylase (procollagen-lysine 5-dioxygenase, or PLOD), which is a collagen-modifying enzyme. Inherited in an autosomal recessive manner. Can be diagnosed through urine test.
Arthrochalasia: Very rare	✓	Extreme	Soft, extremely fragile	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. Inherited in an autosomal dominant manner. Can also be diagnosed by skin biopsy.
Dermatosparaxis: Very rare	✓	✓	Sagging, redundant, doughy and extremely fragile	Caused by a deficiency of procollagen I N-terminal peptidase. Inherited in an autosomal recessive manner. Can be diagnosed by skin biopsy.

The types may appear clear and defined, but EDS rarely permits easy classification. Although the type almost always runs true within each family, the symptoms of individual family members can vary so widely from each other that EDS is either misdiagnosed or ignored, and therefore is probably more frequent than previously thought. Current research estimates incidence at one in 2,500 to 5,000.