

Classical Ehlers-Danlos syndrome (cEDS), previously called EDS-Classic type or Type I and II EDS, is a connective tissue disorder than can affect many different parts of the body, including the skin, arteries, muscles, and organs. Connective tissue is a type of tissue that helps to hold everything together, like a glue for your body.

People with cEDS can have some or many signs and symptoms, including:

- skin hyperextensibility
- smooth, velvety skin
- <u>atrophic scarring</u>
- splitting of the skin following relatively minor trauma
- delayed wound healing
- easy bruising
- hypermobility and complications of joint hypermobility (e.g., sprains, dislocations/subluxations)

Some individuals with cEDS may also experience low muscle tone (hypotonia), and some children show delayed gross motor development. Cardiac and vascular issues are less common, but there may be an increased risk for dilation of the aorta (stretching of the main blood vessel that carries blood from the heart to the body) and spontaneous rupture of the larger arteries.

Causes

More than 90% of cEDS is due to a pathogenic variants in the COL5A1 gene (75-80%) or the COL5A2 gene (10-15%). In more rare cases, classic EDS will be caused by a pathogenic variant in the COL1A1 gene (<1%), which is also associated with another form of EDS (EDS type VII, or the arthrochalasia type). Pathogenic variants in the genes that cause cEDS are inherited in an <u>autosomal dominant</u> pattern, meaning that anyone who carries the pathogenic variant has a 50% chance to pass it down to any children they have. About 50% of individuals with cEDS will have a positive family history and will have inherited it from an affected parent. The remaining 50% of people with cEDS that have no family history are the result of a new (de novo) variant and will be the first ones in their family to have it.

cEDS is thought to affect approximately 1 in 20,000 people, but it is likely that there are affected individuals who have more mild symptoms and have not been diagnosed so it could be more common that current estimates show.



Diagnosing Classical Ehlers-Danlos syndrome

While genetic testing for cEDS can be helpful, medical providers may use other pieces of information, such as a physical exam and family history, to help establish a diagnosis.

The diagnosis of cEDS is often made by a medical provider who is familiar with cEDS who can look for the signs on a physical examination. The criteria for a diagnosis of cEDS are broken down into two categories: major diagnostic criteria and minor diagnostic criteria. Major criteria include overly stretchy skin, <u>atrophic scarring</u>, and generalized joint hypermobility (this depends on age, gender, and family/ethnic background). Minor criteria include:

- Easy bruising
- Soft, doughy skin
- Fragile skin (breaks apart easily)
- Fleshy lesions called molluscoid pseudotumors that are associated with scars of pressure points such as your elbows and knees
- Small round hard masses called subcutaneous spheroids that are usually under the skin around the forearms and shins
- History of a hernia
- Epicanthal folds
- Complications associated with joint hypermobility (chronic pain, dislocations, sprains, etc)
- Family history of a first-degree relative (parent, sibling, child) who meets criteria for cEDS

Red flags that can increase the chance for someone to have cEDS would be if they have the major criteria of overly stretchy skin and <u>atrophic scarring</u>, or if they have the major criteria of generalized joint hypermobility combined with three or more of the minor criteria. Anyone who feels that they meet these criteria should seek consultation with a geneticist, genetic counselor, or other provider who is familiar with cEDS to get more information.

Medical Management for Classical Ehlers-Danlos syndrome

Treatment for cEDS can sometimes vary depending on the individual person and their specific health concerns, and should be discussed with a medical provider who is familiar with cEDS. Medical management can include blood tests, medications, physical therapy, and treatments to help with excessive bleeding or skin breakage. Imaging of the heart, called an <u>echocardiogram</u> may also be done to look for dilation of the aorta or <u>mitral valve prolapse</u>. It



is also recommended that individuals with cEDS avoid unnecessary trauma and make sure any wounds are being properly cared for. Young children with skin fragility may want to wear pads or bandages to avoid skin tears, and all individuals with cEDS should avoid sports with heavy strain on the joints (such as contact sports, running, etc).

For women, during pregnancy they should be followed by a high-risk OB/GYN due to potential complications both for mom and the baby.

Click <u>here</u> to learn more about scheduling a genetic counseling appointment for questions about pediatric or adult genetic conditions.

Resources

The Ehlers-Danlos Society

Ehlers-Danlos Support UK