

Loeys-Dietz Syndrome

General Facts

WHAT IS LOEYS-DIETZ SYNDROME?

Loeys-Dietz syndrome (LDS) is a genetic disorder of connective tissue that was identified and named in 2005. At that time doctors realized that even though LDS has some features of other connective tissue disorders, it is a distinct disorder. The other disorders that share features with LDS include Marfan syndrome, VEDS (Vascular Ehlers-Danlos) and Shprintzen- Goldberg syndrome.

WHAT CAUSES LOEYS-DIETZ SYNDROME?

LDS is caused by a pathogenic variant (disease-causing DNA variant or change) in one of the genes involved in the *tgf-beta* pathway. When a gene in this pathway has a pathogenic variant, the pathway does not function appropriately and the variable features of LDS result. The genes known to cause LDS are *TGFBR1*, *TGFBR2*, *SMAD3*, *TGFB3* and *TGFB2*.

WHO HAS LOEYS-DIETZ SYNDROME?

Many individuals diagnosed with Loeys-Dietz syndrome are first identified through cardiovascular features in themselves or family members such as aortic aneurysm or dissection. Many other individuals are suspected to have LDS because of skeletal features. The list below outlines some LDS features.

LDS affects both males and females. People can inherit LDS, meaning they get the pathogenic variant from a parent who has LDS. Others can have a spontaneous variant, meaning they are the first in the family to have LDS.

WHAT ARE THE FEATURES OF LOEYS-DIETZ SYNDROME?

Because connective tissue is found throughout the body, LDS features can occur in the heart, blood vessels, bones, joints, and skin. Some LDS features are easy to see, while others, such as heart and blood vessel problems, need special tests to find them.

Some LDS features are also found in Marfan syndrome. These include:

- Aortic dilation or aneurysm (enlarged or bulging aorta, the main blood vessel carrying blood from the heart)
- Aortic dissection (tear of the wall of the aorta)
- Mitral Valve Prolapse – MVP (“floppy” mitral valve)
- Pectus excavatum (chest wall deformity that pushes the sternum and breast bone inward) or Pectus carinatum (chest wall deformity that pulls the sternum and breast bone out)
- Scoliosis (s-like curvature of the spine) or Kyphosis (spine that curves from back to front)
- Flexible joints
- Flat feet
- Dural ectasia (swelling, bulging or widening of the spinal sac)

Some LDS features are different from Marfan syndrome features and are very important for making a correct diagnosis. When a person has these particular features, it is important that the doctor consider LDS.

Features that set LDS apart from Marfan syndrome and many other connective tissue disorders include:

- Arterial tortuosity (twisting or spiraled arteries)
- Aneurysms and dissections in arteries other than the aorta
- Hypertelorism (widely-spaced eyes)
- Bifid (split) or broad uvula (the little piece of flesh that hangs down in the back of the mouth)
- Cleft palate (a gap in the roof of the mouth)
- Club foot (when the foot is turned inward and upward at birth)
- Blue sclera (blue tinge to the whites of the eyes)
- Heart defects at birth such as atrial septal defect, patent ductus arteriosus, bicuspid aortic valve
- Features in the skin such as: easy bruising, wide scars, soft skin texture and translucent skin (almost see-through)
- Gastrointestinal problems such as difficulty absorbing food and chronic diarrhea, abdominal pain, and/or gastrointestinal bleeding and inflammation

- Allergies to food and things in the environment
- Cervical-spine instability (instability in the vertebrae directly below the skull)
- Osteoporosis (Poor mineralization of the bones) that can make the bones more likely to break

HOW IS LOEYS-DIETZ SYNDROME DIAGNOSED?

A medical geneticist is the kind of doctor most likely to know how to recognize and diagnose LDS. Some cardiology clinics are specialized and able to help facilitate evaluation for LDS.

To decide if you have LDS, your doctor will use:

- The health history of you and your family
- Your physical exam
- The results of an echocardiogram (ultrasound to study the heart, its valves and the aorta)
- Genetic testing to determine if there is a mutation in the TGFBR1, TGFBR2, SMAD3, TGFB3 or TGFB2 genes