

Loeys-Dietz Syndrome A Correct Diagnosis

HOW TO FIND OUT IF YOU HAVE LOEYS-DIETZ SYNDROME

In 2005, doctors identified and named a newly defined genetic connective tissue disorder called Loeys-Dietz syndrome (LDS). For some people, a diagnosis of LDS can now explain why they have certain features and medical problems. Here is what you need to do to find out if LDS is the correct diagnosis for you or a family member.

Talk over your concerns with your primary care physician or pediatrician. They can help guide and refer you to a doctor who knows about Loeys-Dietz syndrome and/or connective tissue disorders. The type of doctor most likely to know about LDS is a medical geneticist, a doctor who specializes in genetic disorders including Marfan syndrome (MFS), Ehlers-Danlos syndrome (EDS) and LDS. Some cardiologist offices also are capable of performing evaluations and other necessary testing.

You can find a medical geneticist by:

- Asking your primary doctor for a referral
- Calling the doctor referral service at your local hospital
- Using online resources including American College of Medical Genetics (www.acmg.net) or National Society of Genetic Counselors (www.nsgc.org)

LIST THE CONNECTIVE TISSUE FEATURES THAT ARE MORE COMMON IN LOEYS-DIETZ SYNDROME COMPARED TO OTHER CONNECTIVE TISSUE DISORDERS

Write down any of these features you or your family members have. They include:

- Arterial tortuosity (twisting or spiraled arteries)
- Aneurysms and dissections in arteries other than the aorta
- Heart defects at birth such as atrial septal defect, patent ductus arteriosus, bicuspid



aortic valve

- Hypertelorism (widely-spaced eyes)
- Blue sclerae (blue tinge to the whites of the 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)
- Gastrointestinal problems such as difficulty absorbing food and chronic (comes and goes but never really goes away) 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

MONITOR YOUR AORTA AND OTHER ARTERIES WITH IMAGING

Write down any of these features you or your family members have. They include:

- Aortic dilation or aneurysm (enlarged or bulging aorta, the main blood vessel that carries 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
- Features in the skin such as: easy bruising, wide scars, soft skin texture, and translucent skin (almost see-through)
- Rupture of the spleen or bowel
- Rupture of the uterus during pregnancy

TAKE YOUR LISTS TO YOUR DOCTOR

Explain the reasons why you think you might have LDS to your doctor. Also take lists of:

- your past illnesses, operations, and hospitalizations
- medications you are taking
- family members who have, or might have, LDS

Have your doctor do a thorough physical exam. This includes looking for LDS features in your bones, joints, skin, and face.

TALK TO YOUR DOCTOR ABOUT ORDERING MEDICAL TESTS

THESE TESTS INCLUDE:

- **Echocardiogram.** This ultrasound looks at the heart, its valves, and the aorta (vessel that carries blood from the heart) close to the heart.
- **Genetic testing that can find the TGFBR1, TGFBR2, SMAD3, TGFB3 or TGFB2 pathogenic variant (disease-causing genetic variant) that causes LDS.** This testing is most helpful when used in people who have LDS features not usually seen in other connective tissue disorders. Your doctor must order this testing and they may refer you to a medical geneticist. Testing typically includes ordering an aneurysm panel, a genetic tests that looks for DNA variants in many different genes that cause aneurysm syndromes or connective tissue disorders.

When genetic testing is positive for a pathogenic or likely pathogenic variant in one of these genes, the person most likely has LDS and needs special medical care and counseling. Ask your doctor how to take care of yourself. It is very important to follow these instructions. You also need to find out if there are other people in your family who also have LDS.

When genetic testing is negative for a pathogenic variant, the connective tissue features may still be due to a genetic syndrome, but possibly one in which the genetic cause is not yet identified. There are likely more genes in the LDS pathway that have not been discovered. In this case, talk to your doctor about developing a good medical plan if testing is negative. There are new genes discovered over time, so repeat aneurysm panel testing may be appropriate every few years. Ask your doctor if you have any other condition that needs medical care.