What is Loeys-Dietz Syndrome (LDS)?

Loeys-Dietz syndrome (LDS) is a rare genetic disorder of the connective tissue (the cells that support or connect different structures in the body). Women and men are equally affected. Patients diagnosed with LDS may present with varied pathological manifestations in the heart, lungs, skeleton, skin, eyes and intestines.

LDS patients are at risk for dissection and rupture of arteries at sizes that are not thought to be dangerousto the general population or to those with other connective tissue disorders.

How is it Transmitted?

There are six types of LDS, each caused by mutations in different genes: LDS1 (TGFBR1); LDS2 (TGFBR2); LDS3 (SMAD3); LDS4 (TGFB2); LDS5 (TGFB2); LDS6 (TGFB3). This syndrome may be inherited from a parent as patients have a 50% chance of passing their disease-causing mutation on to each child. Mutations in these 6 genes induce defective functioning of TGF-b protein, an important player in development of vessels and certain organs as well as in tissue strength and repair.

In most cases, LDS is caused by a spontaneous mutation and occurs with no family history.

How is it Diagnosed?

Confirmed diagnosis is made using a genetic test to detect mutations in one of the identified genes. However, as genetic tests are not 100% comprehensive, a negative genetic test does not necessarily mean that LDS can be excluded. Diagnosis is then based on clinical observations and imaging examinations.

As LDS can be inherited, some family members may have the genetic mutation without knowing it, hence it is important to ask your medical professional if family screening is necessary.

Is There a Treatment for LDS?

Currently, there is no treatment that can cure this disease. However, the pathological manifestations can be slowed down by various means. As soon as the diagnosis is established, regular medical follow-up is essential. Due to the generalized degradation of the connective tissue, follow-up requires various medical specialties and therapies. Management includes medical therapy, lifestyle modification, imagingsurveillance, and surgical intervention.

For children at school, an individual education plan can be put in place.

What can I do Every day?

1. Always carry an alert card and/or wear medical alert jewelry.
2. Follow prescribed medical follow-up, in collaboration with your attending physician.
3. Do not interrupt prescribed treatment without medical advice.
4. Inform the people around you about warning signs, so that they can help you, if necessary. Let them know you have an alert card or medical alert jewellery.
5. Inform your doctor if you are planning to become pregnant or are in early pregnancy.

What Physical Activity Can I Practice?

Do: Participate in light - moderate physical activity on a regular basis, such as walking, hiking, swimming or cycling; Ensure you are able to speak with ease during the exercise, without having to stop to catch your breath; Participate in rehabilitation programs for pain management.

Avoid: Exercises that require great muscular effort; Efforts that require rapid acceleration followed by deceleration or twists; Competitive sports, Contact sports or sports with a high risk of shock.

Depending on the involvement of the blood vessels, some people have to be more careful and do even lighter exercises.

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Loeys-Dietz Syndrome Manifestation & Recommendations

Body System & Manifestations	Treatment and Recommendations
Cardiovascular (Heart & Blood Vessels): Dilatation, dissection or rupture of the aorta and other arteries; Arterial tortuosity; Mitral valve prolapse; Bicuspid aortic valve (BAV), cardiomyopathy (weakness of the heart muscle)	**Imaging:** Echocardiograms, magnetic resonance imaging (MRI), and computed tomography (CT) imaging are used to image the heart, entire aorta, and smaller arteries for aneurysms, dissection, and tortuosity. The patient's age, specific genetic change, and other risk factors will guide frequency and type of imaging. **Medication:** Treatment with beta-blockers and/or angiotensin 2 receptor antagonists can reduce the progression of arterial damage by lessening the strain on the body's major arteries. **Vascular Surgery:** Preventative aortic root replacement is often performed to prevent type A aortic dissection and improve outcomes. Aortic surgery decisions should be informed by the aortic size, presence of specific genetic variant, patient age, aortic growth rate, family history, identification of high-risk features, and surgical risk. **In case of sudden pain,** call 911 or local emergency number to be transferred to hospital.
Skeletal (Bones): Clubfoot; Scoliosis or Kyphosois (curvature of the spine); Cervical spine instability (instability in the neck); Pectus excavatum/carinatum (chest wall deformities); Osteoarthritis; Joint hypermobility; Flat feet	**Imaging:** Spine X-rays, and sometimes MRI, are performed to evaluate for scoliosis/kyphosis & monitor the degree of any curve. X-Rays of the neck are performed to check for cervical instability. **Bracing/Orthotics/Harnesses:** For spine and other joints, foot deformities, and hip dislocations. **Surgery:** To repair pectus deformities (often cosmetic, sometimes needed to improve heart or lung function). Cervical spine fusion for instability. Spine surgery for scoliosis in severe cases. **Lifestyle:** Ensure adequate intake of calcium and vitamin D and calcium to help prevent osteoporosis. Minimize risk of falls and shocks. Avoid spinal manipulation by a chiropractor. An adapted lifestyle is necessary (regular and adapted physical exercise, relaxation). An occupational therapist can help adapt your environment and find technical solutions to facilitate the activities of daily life, at home, at work or outside.
Allergic/Inflammatory: Allergies; Gastrointestinal inflammatory disease; Eosinophilic esophagitis	**Medication/Surgery:** In case of known allergies, carry an adrenaline pen on you, if advised. **Feeding tubes:** help with caloric intake. Treatments may be prescribed by doctor. **Lifestyle:** Avoid certain foods or exposure to environmental allergens. Eat fiber-rich foods to avoid constipation. Ensure balanced and regular food intake.
Lungs: Pneumothorax (collapsed lung); Asthma; Sleep apnea	In case of sudden pain, call 911 or local emergency phone number to be transferred to hospital. In case of excessive fatigue during the day, talk to your doctor. Temporary tube insertion into the chest may be needed to treat a pneumothorax.
Eyes: Retinal Detachment; Blue tinge to the white of the eyes; Hypertelorism (widely spaced eyes)	Any visual disturbance, sudden onset should raise fears of a complication. Immediately call an ophthalmologist for an emergency consultation.

Other potential manifestations: Craniosynostosis (early fusion of the skull bones); Cleft palate (hole in the roof of the mouth); Bifid (split) or broad uvula (the little piece of flesh that hangs down in the back of the mouth); Translucent skin; Easy bruising; Wide scars; Chronic pain; Dural ectasia (swelling, bulging or widening of the spinal sac); Rupture of spleen or bowel; Rupture of uterus during pregnancy

*This is not an exhaustive list of manifestations. LDS patients will not present with all of these manifestations, and having these manifestations does not mean a person has LDS.

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