The Leeds Teaching Hospitals NHS Trust

Loeys-Dietz Syndrome

Information for patients

Leeds Pathology

This information leaflet describes what Loeys-Dietz syndrome is, how it is diagnosed and how it is inherited.

What is Loeys-Dietz syndrome?

Loeys-Dietz syndrome (LDS) is a genetic condition that affects the connective tissues. In this condition the connective tissues are weaker than usual. Connective tissue is important for supporting many parts of the body. Weak connective tissue can cause changes in the blood vessels, heart, skin, joints, intestines and the uterus.

What causes Loeys-Dietz syndrome?

LDS is caused by a change in a specific gene. Genes are the instruction manuals for how to build and operate all parts of the body. Currently the genes that are known to cause Loeys-Dietz syndrome are called TGFBR1, TGFBR2, SMAD3, TGFB2, TGFB3, and SMAD2. Changes in these genes can lead to the connective tissue not being assembled correctly.

In most cases (75% or 3 in 4 cases) the gene change happens for the first time in the affected person. This means that it has not been inherited from either of their parents. In 25% (1 in 4) cases the gene change has been inherited from a person's mother or father and may have been inherited from further back in the family.

How is LDS diagnosed?

Individuals with LDS can have the following features:

- Widening of the arteries (vessels) including the aorta (the main vessel leaving the heart).
- Bendy or twisty blood vessels (arterial tortuosity)
- Changes to the head or face; including widely spaced eyes (hypertelorism) and a split or wide uvula (the piece of tissue dangling down at the back of a person's throat).
- Skeleton changes including long fingers, changes to the shape of the chest or curvature of the spine.
- Skin or joint changes; such as having flexible joints, having joint pains, or very soft skin.

Not everyone with LDS will have all of these features. The condition is very variable from one person to another, even within the same family.

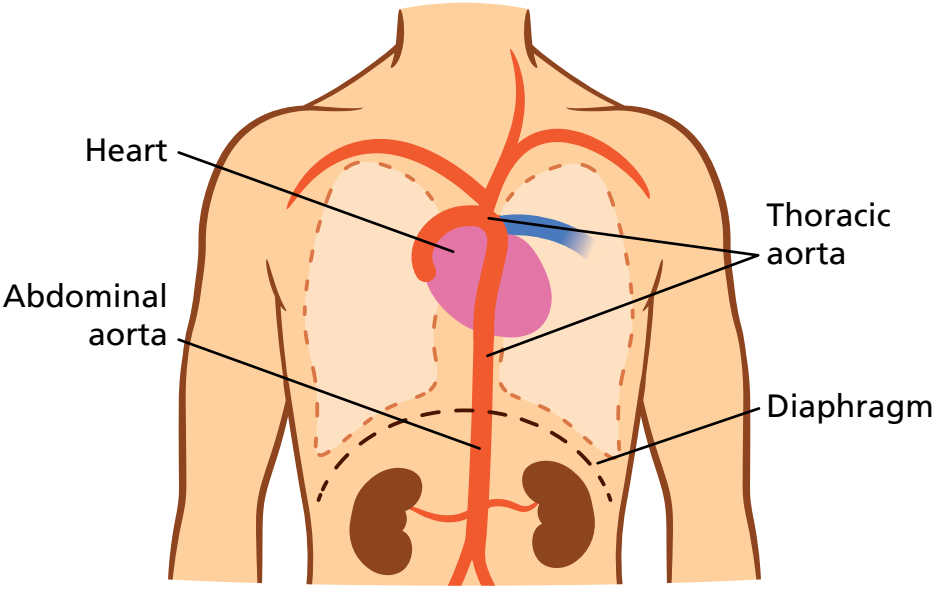
If a diagnosis of LDS is suspected then a genetic test may be carried out to look for a change in one of the associated genes. It is not always possible to find a gene change, even if a person has lots of features of LDS. This is because we do not yet know everything there is about all genes that could be linked to LDS.

What problems can LDS cause?

Aortic dilatation and dissection

The aorta is the main blood vessel which leaves the heart, to carry blood to the rest of the body (see diagram below). The walls of the aorta are made of connective tissue. In LDS, the weak connective tissue can mean that the aorta stretches outwards – similar to a bulge in a hosepipe. This is called dilatation.

In LDS this is most often in the thoracic aorta, which is the part of the aorta in the chest. As the walls stretch, they become weaker and it is possible that the aorta can burst, which can be life threatening. Therefore people with LDS should have regular scans of their aorta to check if it is becoming dilated. If it is, then this can be managed with medications, or sometimes surgery.



Arterial tortuosity and aneurysms in other blood vessels

Widening of other blood vessels can also occur in LDS. This can be anywhere in the body – such as the brain or tummy. In the same way as for the aorta, there is a chance that these aneurysms can burst.

When people are first diagnosed with LDS, they may be recommended to have a whole-body scan to look for any other aneurysms.

Cervical instability

Loeys-Dietz syndrome can weaken the ligaments which hold bones together. In some people this can make the bones at the top of the spine unstable. This means that there is a chance that they can move out of line. If this happens there is a risk of damage to the spinal cord. The spinal cord takes messages from the brain to the rest of the body to tell it how to move and to feel sensations.

When people are diagnosed with LDS, or before they have any operations, they may be recommended to have an X-ray of their neck to check that the bones are in-line. Some people need to have an operation to fix these bones in place so that they do not move.

Skeleton changes

The weakness of connections between the bones can cause physical changes for people with Loeys-Dietz syndrome. These include:

Changes to the shape of the chest bone which can stick in (pectus excavatum) or stick out (pectus carinatum)

- A curve in the spine (a scoliosis)
- 'Flat feet' (pes planus)
- Flexible joints

These features may not cause a person any problems.

However, they may contribute to joint and muscle pains and, in some cases, may be managed with an operation.

Allergies

People with Loeys-Dietz syndrome are more likely to have allergies to foods, as well as allergic conditions such as asthma and eczema.

These can be managed using the usual treatments.

Rupture of other organs

It is very unusual, but sometimes the spleen or intestine can burst in people with LDS. This needs rapid treatment in hospital and can be fatal.

Pregnancy in Loeys-Dietz syndrome

Pregnancy makes connective tissue more stretchy and puts the body under stress. In people with LDS, pregnancy can make aneurysms develop more quickly.

There is also a risk of the womb muscle tearing as the pregnancy gets bigger (this is called uterine rupture). This can be life threatening to mum and the pregnancy. Pregnant women with LDS should be monitored by a specialist and have extra heart and blood vessel scans during their pregnancies to monitor for aneurysms.

Problems affecting babies

Babies with LDS may have some difficulties.

Babies can be born with a gap in the roof of the mouth (a cleft palate). If this is large, then this can make feeding difficult and is usually repaired with an operation.

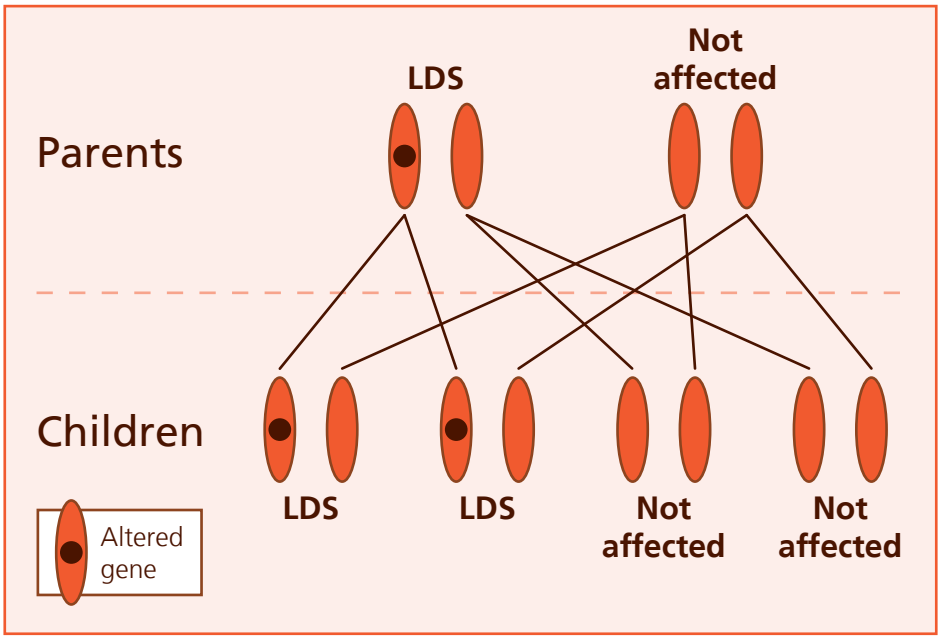
Some babies or people with LDS have a wide or bifid uvula (the floppy bit of tissue at the back of the throat). This doesn't cause any problems and doesn't need any treatment.

Babies can also have early fusion of the bones in the skull (craniosynostosis). The bones of the skull may stick together too early, giving a different head shape. This can be monitored to make sure there is enough space for the brain to grow. If there are concerns, then an operation may be offered.

How is Loeys-Dietz syndrome inherited?

Someone who has LDS can pass this on to their children. Everyone has two copies of the genes that can cause LDS. If someone has a genetic change on one copy of their gene pair, then they can develop features of LDS. When we have children we only pass on one copy of our gene pair. The other copy of the pair comes from the other parent. This means that for someone with LDS there is a 50% chance (1 in 2) chance of passing the condition on to each of their children.

This is called **dominant inheritance** (shown in the picture below).



If a person with genetically confirmed LDS is planning a family then there may be options for testing a pregnancy for the gene change, or a form of IVF where the embryos can be tested before implantation (Pre-implantation genetic testing; PGT).

Family screening

If someone is diagnosed with LDS then it is recommended that their first-degree relatives (parents, siblings and children) are offered testing for the gene. If they are found to have the LDS gene change, then they are at risk of developing features of the condition. We would recommend affected individuals have the following surveillance:

1. Regular ultrasound scans (echocardiograms) or other imaging of their aorta by a specialist cardiologist
2. Whole body MRI angiogram to look for tortuosity or aneurysms of their blood vessels
3. Flexion/extension X rays of their cervical bones.

Patient support organisations and more information

- The Marfan foundation (marfan.org) is an American group for patients with LDS and other connective tissue conditions. You do not have to be American to join or use their website.
- The Loeys-Dietz syndrome foundation (loeysdietz.org) had specific information about Loeys-Dietz syndrome. It is also an American website, but anyone can access it.
- Marfan Trust (marfantrust.org) supports patients and families with LDS and provides educational material.

If using these sites, please be aware that some recommendations might be different for patients living in the UK and under the care of the NHS.

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