Marfan Trust
Supporting Research into Inherited Aortic and Related Disorders
Loeys Dietz
CONNECTING THE UNCONNECTED AND STRENGTHENING LIVES

The ENT Aspects of Marfan and Loeys-Dietz Syndromes

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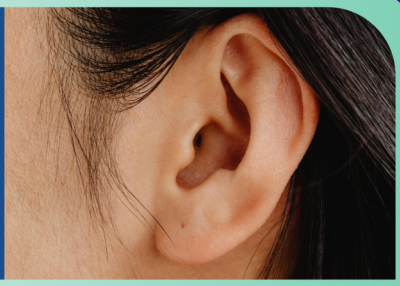

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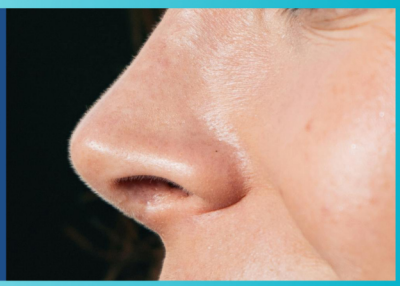

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What Are Marfan & Loeys-Dietz Syndromes?

Marfan and Loeys-Dietz syndromes are inherited genetic disorders of the body's connective tissue, affecting any gender, race or ethnic group. Connective tissue helps provide structure to the body, binding skin to muscle and muscle to bone. It is made of fine fibres and 'glue' called fibrillin. This tissue provides the stretchy strength of tendons and ligaments around joints and in blood vessel walls. It also supports the internal organs.

In Marfan syndrome (MFS), a change in the fibrillin-producing gene, fibrillin-1, means that this protein is deficient in connective tissue throughout the body, creating an unusual stretchiness and weakness of tissues. This has far-reaching implications and can affect the eyes, lungs, gut, nervous system, skeleton and, most dangerously, the cardiovascular system. Symptoms can vary widely from person to person with people experiencing mild to severe manifestations. MFS affects roughly 1 in 3,000 people which means that approximately 18,000 people in the UK have MFS. We estimate that half remain undiagnosed.

75% of patients inherit the condition whilst 25% develop it as a result of a spontaneous (new) gene change. Each child of an affected parent has a 50% chance of inheriting Marfan syndrome.

Every year, on average in the UK there are over 200 new cases of Marfan Syndrome diagnosed.

Marfan syndrome was first described by a French paediatrician, Dr Antoine Marfan, in 1896. It is caused by a change in the gene for fibrillin-1 on Chromosome 15.

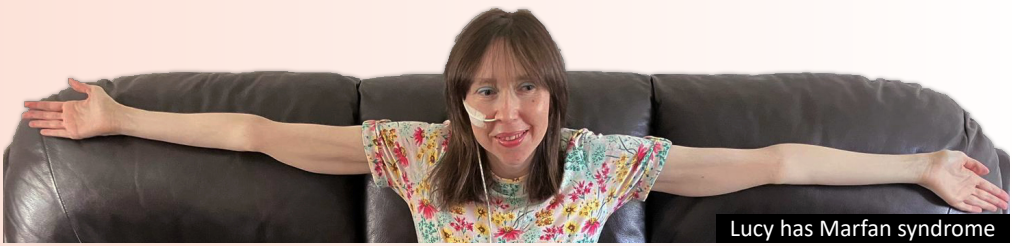
Patients with Loeys-Dietz syndrome (LDS), were once thought to have Marfan syndrome, such are the similarities between the two conditions.

Drs Dietz & Loeys

LDS was first described in 2005 by Drs Bart Loeys and Harry Dietz. It is caused by a variant in one of the genes in the transforming growth factor-beta signalling pathway, TGF-β. The genes that cause LDS are: TGFβR1, TGFβR2, SMAD3, TGFβ3 and TGFβ2. TGF-β is a crucial signalling pathway involved in various cellular processes, including cell growth and immune responses. It is a key player in development and tissue repair. When a gene change occurs, it has implications for many systems of the body. Whilst symptoms vary from patient to patient, the most characteristic are: arterial tortuosity, aortic enlargement, bifid uvula, curvature of the spine, high-arched palate and over-crowded teeth.

Loeys-Dietz syndrome is much rarer than MFS and the incidence is currently gauged to be 1 in 100,000 although this is probably an underestimation.

This pamphlet is intended for patients with both Marfan and Loeys-Dietz syndromes.

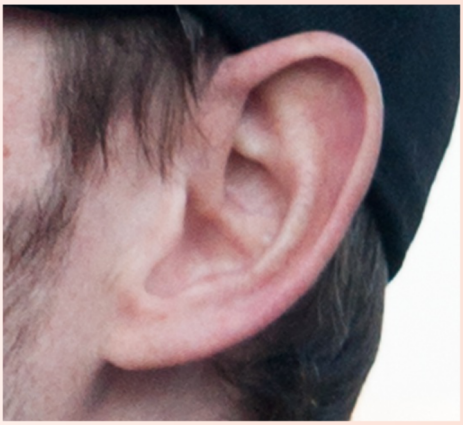


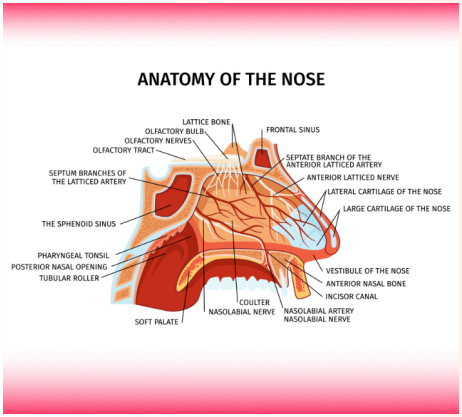
Lucy has Marfan syndrome

ENT Aspects

The clinical findings in the ear, sinuses, nose and throat display the same great variability in expression as found throughout the rest of the body in Marfan syndrome (Pyeritz et al, 1993). Important skeletal characteristics which contribute to ENT problems include a long, narrow face and skull (dolichocephaly), often associated with long lower jaw, high arched palate, crowded teeth, prominent eyebrow ridges, small upper jaw, and temporomandibular jaw joint hypermobility **(Cervino et al, 2020)**.

The ears are often large, simple, low-set and posteriorly rotated. Ear canals can be narrow and angulated upward and forward. Mild hearing loss is not uncommon, although the cause is obscure, possibly due to inner ear bone malformation during development, but most likely due to recurrent or chronic otitis media in childhood, which is common in any child.





The nose is long, often beaked and asymmetrical, with narrow cavities and frequently deviated septum, which may lead to nasal obstruction, and in some people mouth breathing may result. In addition, sinuses may be narrow and underdeveloped with narrow drainage channels, therefore recurrent sinusitis is a common problem **(Child, 2017)**.

Obstructive sleep apnoea (OSA) is a common associated feature, requiring referral for sleep studies. This happens when the upper airways are narrowed to start with, and can become blocked at night during sleep. One of the main risk factors is overweight and obesity but research has shown that people with Marfan syndrome (MFS) can also be at increased risk, probably due to some of the craniofacial features, for example, the abnormal position of the lower jaw and the increased collapsibility of the upper airways. The prevalence of sleep apnoea in MFS is estimated to be between 30-42% in the literature **(Gessler et al, 2022)**.

Frequent unexplained nosebleeds may be a feature in childhood and adolescence, probably due to blood vessel wall fragility.

Medical Management

Early recognition and prompt medical management of allergic rhinitis or sinusitis may prevent secondary infections. Antibiotics for infection may be required, but knowing that most infections in this area are viral, there needs to be clear discussion between the patients and the health care provider. Due to the risk of endocarditis, there should be a low threshold for antibiotics, and sometimes, there may be the need for a protracted course.

Surgical Management

Grommets for ‘glue ear’ may help resolve the problem of recurrent otitis media.Hearing aids can also be given to help hearing loss. For obstructive sleep apnoea early removal of tonsils and/or adenoids is recommended as surgical experience shows that these structures are surprisingly large and can actually contribute, through obstruction, to chronic otitis and sleep apnoea **(Rybczynski et al, 2010)**.

Surgical correction of deviated septum can be very helpful in the management of nasal obstruction, mouth breathing and aspects of sleep apnoea. Cautery (heat sealing) for recurrent nosebleeds may be necessary, if direct pressure is not effective.

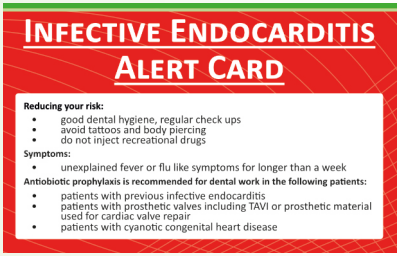
The possibility of a bleeding tendency, probably due to vascular fragility, has been noted in some affected individuals, and this should also be taken into consideration when planning surgery.

Bacterial Endocarditis Prophylaxis

The prevention of bacterial endocarditis is all-important because of the high incidence of heart valve involvement in MFS. High risk patients are those who have had cardiac valve replacement or repair or a previous episode of bacterial endocarditis. Guidelines for antibiotic prophylaxis are periodically updated and if surgery is planned, advice should be sought from the patient’s cardiologist to determine whether antibiotic prophylaxis is indicated.

The high-risk categories in both the European (2023) and American guidelines (updated 2021) include:

- People with previous IE
- People with replacement heart valves or those with artificial material used to carry out valve repair
- Those with certain types of congenital heart disease



General Anaesthesia

Patients with Marfan syndrome are recognised to have a slightly increased morbidity and mortality risk associated with general anaesthesia. Factors contributing to this are cardiovascular abnormalities and arrhythmia, impaired respiratory function, scoliosis, the potential to develop endocarditis and a tendency to spontaneous pneumothorax especially in adolescence. Rarely, difficulty with intubation has been reported, due to limited neck extension, high palate and narrow trachea. **(Verghese, 1984)**. An experienced anaesthetist should be involved and a smaller than usual tube for intubation may be indicated.

The pre-operative assessment should include a thorough medical examination, including a chest X-ray, electrocardiogram, and echocardiogram, to look for valvular insufficiency and aortic root dilatation in the sinuses of Valsalva. Any treatment must be carried out in conjunction with the patient's cardiologist.

Conclusion

In summary, the patient's doctor and ENT specialist must be aware of all the problems associated with treating a patient who has Marfan syndrome. Prompt management of ENT infections in childhood and surgical correction to improve the airway can be considered in conjunction with an ENT surgeon.

The classical marfanoid appearance of the face, mouth and ears can be recognised by a physician or surgeon and could be the first vital step towards a diagnosis of the underlying condition. If the diagnosis is suspected, the patient should be referred for echocardiography and genetic counselling through the general practitioner.

References

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The Marfan Trust

Co-founded in 1988, the Marfan Trust is the sole charity in the United Kingdom dedicated to improving and saving the lives of those with Marfan syndrome. It is estimated that approximately 18,000 people are living with Marfan syndrome in the United Kingdom and we estimate that half remain dangerously undiagnosed.

The Marfan Trust's three main objectives are to:

- provide personalised support and medical guidance through its helpline;
- conduct cutting-edge medical research through its self-funded Sonalee Laboratory, named after a young doctor who tragically died of complications from MFS during her ward round;
- continue to provide educational information and raise awareness of the condition.

How you can help

The Marfan Trust relies solely on the goodwill of its unstoppable supporters who tirelessly raise funds and awareness, allowing the charity to continue its good work and lift the shadow from this condition.

You can help to secure the Marfan Trust's future by becoming a member today for just £3 per month:

www.marfantrust.org/pages/10-membership

JustGiving

Just Giving – **http://bit.ly/3Scj51w**

PayPal

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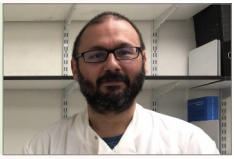
- BANK: Charities Aid Foundation (CAF) ACCOUNT NAME: Marfan Trust
- SORT CODE: 40-52-40
- ACCOUNT NUMBER: 00017677
- REFERENCE: Your Name (plus campaign name if relevant)

By donating to the Marfan Trust, you are contributing to an ever-growing body of knowledge on the condition, allowing more doctors and medical specialists to deliver the best possible treatment to patients affected by Marfan syndrome.

You can also help to fund a piece of equipment in Dr José Aragon-Martin's Sonalee Laboratory. Email **info@marfantrust.org** to find out more.



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