Translation from Romanian

MARFAN Syndrome

DEFINITION

Marfan syndrome is a systemic disease of the connective tissue characterized by a variable combination of cardiovascular, musculoskeletal, ophthalmic and pulmonary manifestations.

PREVALENCE

→ The prevalence is estimated at **1 / 5,000** and there are no differences between sexes, ethnic or geographical.

CLINICAL ASPECTS

→ **Clinical description:** Symptoms can occur at any age and vary greatly between individuals even within the same family. The usual age of diagnosis is in the second decade of life.

- **Cardiovascular manifestations are characterized by:**

1) progressive dilation of the ascending aorta accompanied by an increased risk of **aortic dissection**, which adversely affects the prognosis;

2) mitral valve prolapse, mitral regurgitation, which may be complicated by **arrhythmias, endocarditis** or **heart failure.**

- **Musculoskeletal manifestations:** often the first sign of the disease and may include dolichostenomelia (excessive length of the extremities), high waist → upper segment / lower segment ratio, arachnodactyly, joint hypermobility, scoliotic deformities, acetabular prominence, thoracic deformity (pectus carinatum or pectus excavatum), kyphoscoliosis, ligament hyperlaxity, dolichocephaly in the antero-posterior axis, malignancy or malignant hypoplasia.
- **Ophthalmic manifestations:** result in axial myopia, which can lead to retinal detachment and lens dislocation (**ectopia or dislocation** are characteristic signs). Eye complications, especially **lens ectopy,** can lead to blindness. It can also be associated with cataracts, glaucoma or strabismus.
- There may also occur: **skin signs (stretch marks),** a risk of **pneumothorax and dural ectasia, hemivertebrae, diaphragmatic hernia, sleep apnea.**

GENETICAL ASPECTS

- → In the vast majority of cases, Marfan syndrome is caused by mutations in the **FBN1 gene (15q21.1),** which encodes **fibrillin-1**, a protein essential for connective tissue.
- Granite forms have been identified that are secondary to mutations in the **TGFBR2 gene** located on chromosome 3, which encodes a TGF-beta receptor.
- Genetic counseling: Transmission is **autosomal dominant.** An affected person has a **50%** chance of transmitting the mutation responsible for the disease. Some sporadic cases have also been reported ("de novo" mutations -1/4 of cases).

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DIAGNOSIS

→ **Diagnostic methods:** The diagnosis is based on clinical signs and family history. However, as a result of the variable clinical picture, the diagnosis may be difficult to establish. To facilitate the diagnosis, international diagnostic criteria (**Ghent criteria**) have been established based on major and / or minor clinical signs.

→ **Antenatal diagnosis:** Prenatal genetic diagnosis is possible for families in which the causal mutation has been identified.

TREATMENT

→ The approach must be **multidisciplinary**, with various interdisciplinary consultations: cardiology, genetics, rheumatology, orthopedics, ophthalmology, pediatrics, radiology.

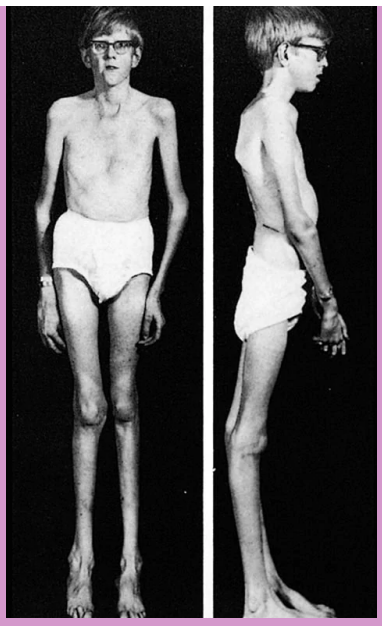
→ Management should aim to limit aortic dilation (beta-blockers and a reduction in sports activities) and periodically monitor the aorta (annual echocardiography, angiography-MRI) to allow surgery on the aortic root before dissection.

→ Surgery may be performed for skeletal abnormalities (stabilization of the spine in case of scoliosis or correction of thoracic deformities) and for ocular abnormalities (laser treatment or replacement of the dislocated lens with an artificial one). Treatment is otherwise symptomatic.

→ Physio kinesiotherapy may be helpful.

PROGNOSIS

→ The prognosis depends on the degree of aortic involvement. From the 3rd decade of life, cardiovascular damage becomes a vital danger. With regular monitoring and management, patients now have a life expectancy close to that of the general population. In the last 30 years, life expectancy has increased over 30 years - the average life expectancy of 43 years for men and 46 years for women.



Marfanoid phenotype: tall stature, dolichostenomelia, kyphoscoliosis

https://www.merckmanuals.com/professional/professional/multimedia/v1093814

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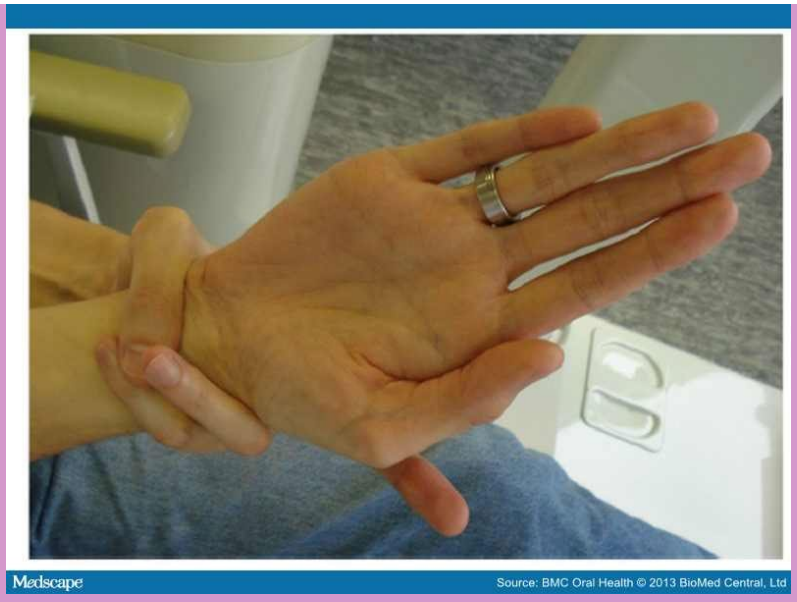
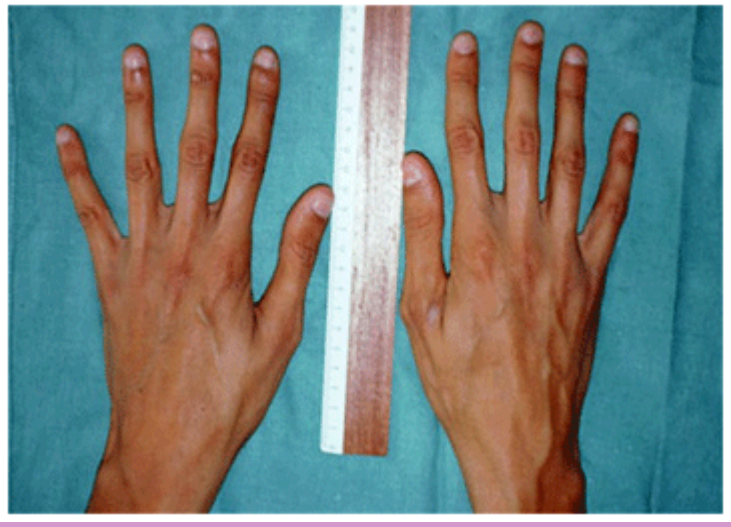


Walker positive sign

Steinberg positive sign

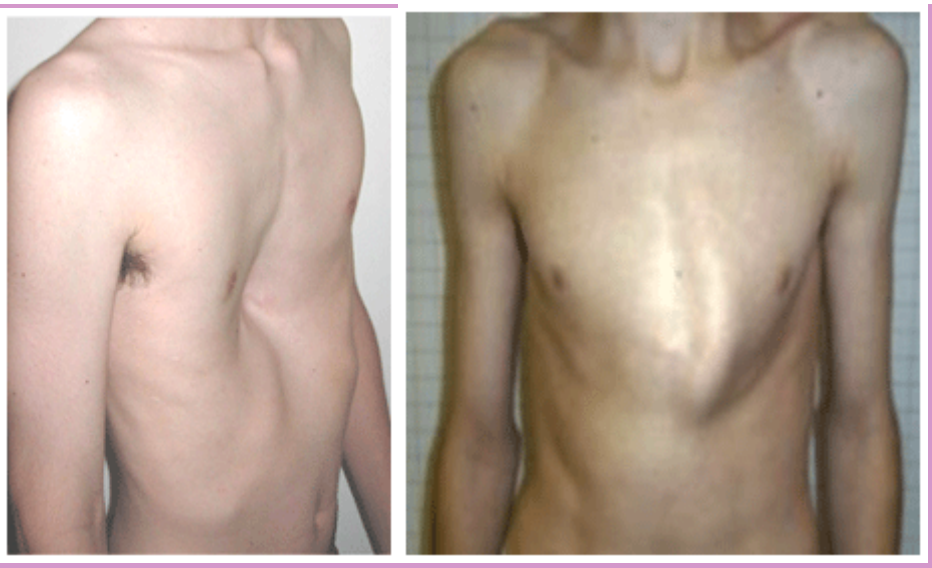
Source: https://emedicine.medscape.com/article/946315-overview

Translation from Romanian



Arachnodactyly

Source: https://www.e-rheumatology.gr/scientific-articles/syndromo-marfan-0



Pectus excavatum/pectus carinatum

Source: https://www.e-rheumatology.gr/scientific-articles/syndromo-marfan-0

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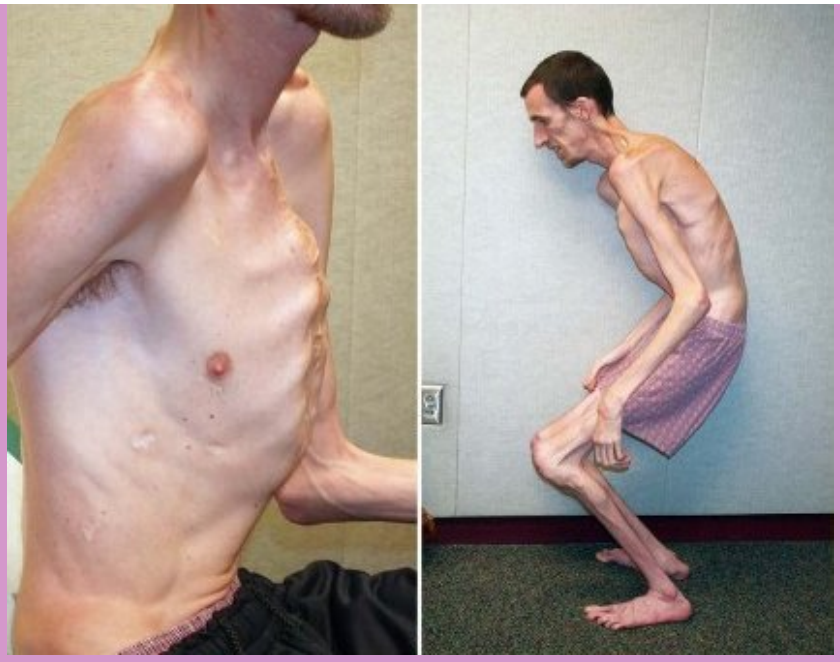

Marfanoid phenotype; pectus carinatum; dolichostenomelia; kyphoscoliosis

Characteristic facies for Marfan Syndrome: dolichocephaly, malaria hypoplasia, enophthalmia, retrognathia and antimongoloid eyelid slits

Source: https://emedicine.medscape.com/article/946315-overview

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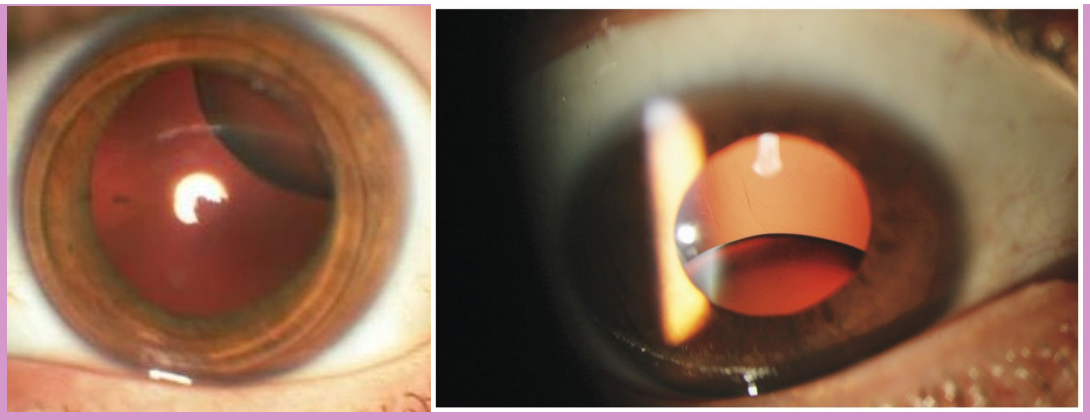
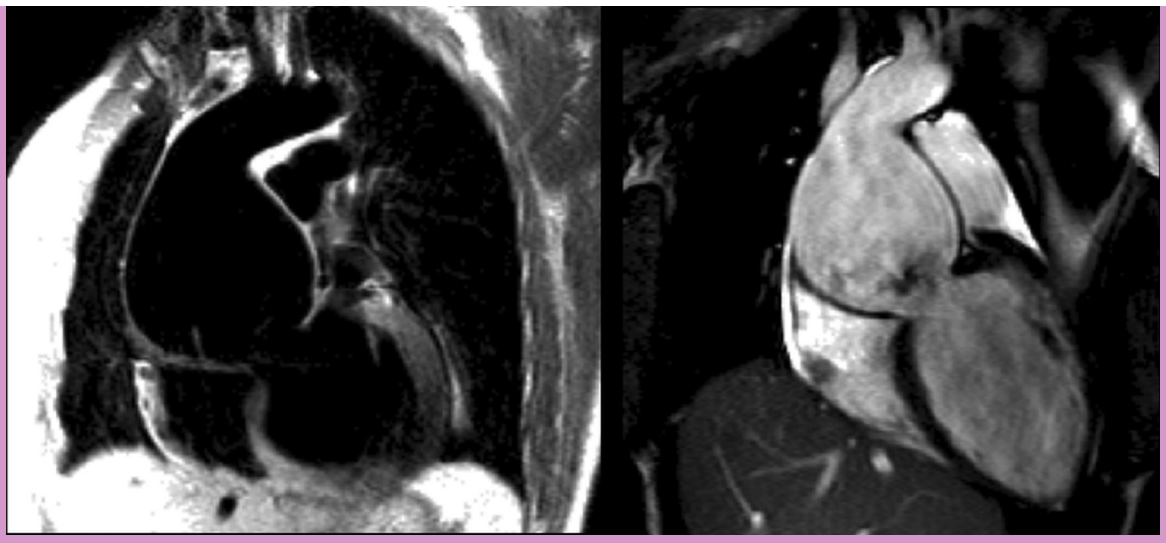


Ectopia lentis / lens dislocation

Sources: **http://www.mrcophth.com/cataract/ectopialentis.html** ;

https://www.nejm.org/doi/full/10.1056/NEJMicm1406002



Aortic root aneurysm in Marfan Syndrome

Source: https://heart.bmj.com/content/100/20/1571

Chart 1: Elements of the systemic score in Marfan Syndrome

Sign	Score (points)
Arachnodactyly - Wrist AND thumb - Wrist OR thumb sign	 3 1
Chest deformities - Pectus carinatum - Pectus excavatum or chest symmetry	 2 1
Deformities of the posterior bones of the leg Flat foot	2 1
Spontaneous pneumothorax	2

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Dural ectasia	2
Protrusio acetabuli	2
Upper / lower body ratio AND increase in arm extension / height ratio without significant scoliosis	1
Scoliosis or thoracolumbar kyphosis	1
Reduced elbow extension (≤ 170 degrees with maximum extension)	1
Facial features: at least 3 out of 5 1. Dolicocephaly 2. Enophthalmia 3. Oblique eyelid slits down 4. Malaria hypoplasia 5. Retrognathia	1
Stretch marks	1
Myopia more than 3 diopters	1
Mitral valve prolapse	1

Chart 2 : Revised Ghent Criteria for the Diagnosis of Marfan Syndrome

In the absence of the family history of Marfan syndrome	**When the family history is positive for Marfan syndrome**
Score 7 of the aortic root diameter ≥ 2 or aortic dissection AND one of: • Crystalline subluxation • FBN1 pathogenic mutation • Systemic score ≥ 7 Ectopia lentis AND pathogenic mutation in a patient with aortic aneurysm	Any of the following: • Crystalline subluxation • Systemic score ≥ 7 • Score 7 of the aortic root diameter ≥ 2 to those over 20 years of age, ≥ 3 to those under the age of 20 years, OR aortic dissection

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I, BURA TEODORA - NATALIA, certified interpreter and translator for English, by virtue of the authorization no. 35530/20.03.2013, issued by the Ministry of Justice of Romania, hereby certify the accuracy of the translation from Romanian into English.

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