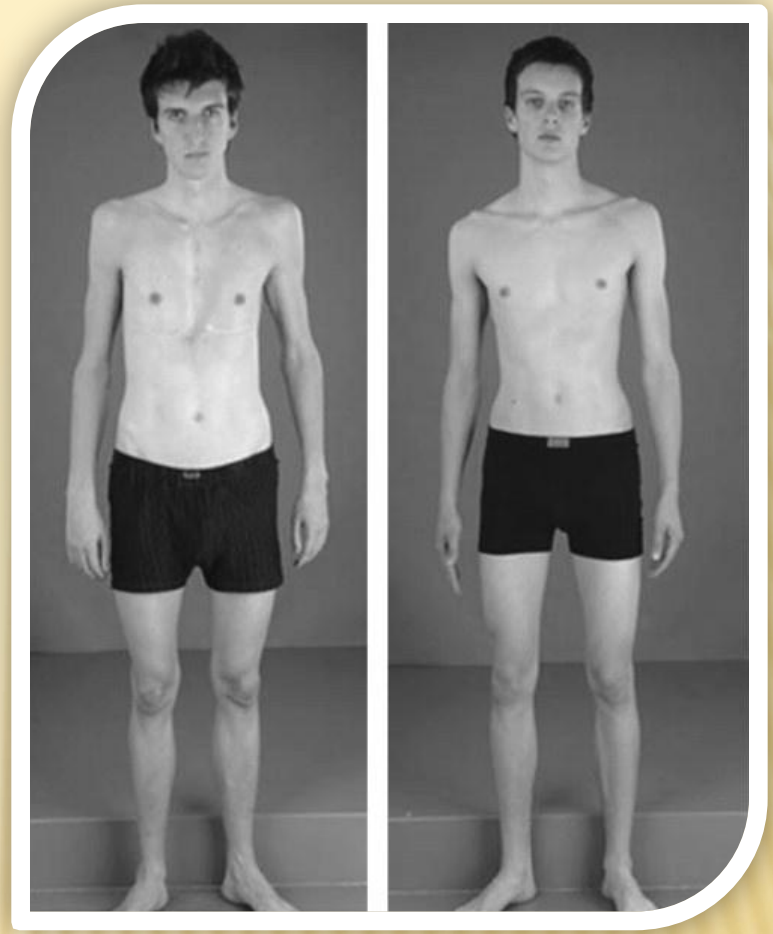


Vadym Kopko

# MARFAN SYNDROM



# WHAT IS IT?

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- ❑ Marfan syndrome (also called Marfan's syndrome) is a genetic disorder of the connective tissue. People with Marfan tend to be unusually tall, with long limbs and long, thin fingers.
- ❑ The syndrome is inherited as a dominant trait, carried by the gene FBN1, which encodes the connective protein fibrillin-1. People have a pair of FBN1 genes. Because it is dominant, people who have inherited one affected FBN1 gene from either parent will have Marfan syndrome.
- ❑ Marfan syndrome has a range of expressions, from mild to severe. The most serious complications are defects of the heart valves and aorta. It may also affect the lungs, the eyes, the dural sac surrounding the spinal cord, the skeleton and the hard palate.
- ❑ In addition to being a connective protein that forms the structural support for tissues outside the cell, the normal fibrillin-1 protein binds to another protein, transforming growth factor beta (TGF- $\beta$ ). TGF- $\beta$  has deleterious effects on vascular smooth muscle development and the integrity of the extracellular matrix. Researchers now believe, secondary to mutated fibrillin, excessive TGF- $\beta$  at the lungs, heart valves, and aorta weakens the tissues and causes the features of Marfan syndrome. Since angiotensin II receptor antagonists (ARBs) also reduce TGF- $\beta$ , ARBs (losartan, etc.) have been tested in a small sample of young, severely affected Marfan syndrome patients. In some patients, the growth of the aorta was indeed reduced.
- ❑ Marfan syndrome is named after Antoine Marfan, the French pediatrician who first described the condition in 1896. The gene linked to the disease was first identified by Hal Dietz and Francesco Ramirez in 1991.

# SYMPTOMS

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- More than 30 different signs and symptoms are variably associated with Marfan syndrome. The most prominent of these, affecting the skeletal system, are found in numerous other diseases (see Differential Diagnosis, below). Thus, it is not possible to make a diagnosis of Marfan syndrome simply by the person's appearance. Instead, distinguishing Marfan syndrome from other "marfanoid" syndromes (without recourse to DNA testing) requires the assessment of non-skeletal clinical and laboratory findings, especially of the eyes, aorta, and heart. Complicating the physical assessment of such persons, considerable clinical variability occurs within families carrying an identical DNA variant.

# FREQUENCY IN POPULATION

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- Contributors to public perception of Marfan syndrome include Flo Hyman, an Olympic silver medalist in Women's Volleyball (1984) who died suddenly at a match from an aortic dissection; Jonathan Larson, the author and composer of Rent, who died from an aortic dissection the day before the off-Broadway opening of Rent; and Vincent Schiavelli, an actor and spokesperson for the National Marfan Foundation.
- Musicians and composers Niccolò Paganini, Sergei Rachmaninoff, and Robert Johnson are thought to have had the disease. Bradford Cox of the indie rock band Deerhunter has openly discussed having Marfan syndrome and its effects on his self-perception and confidence. Based primarily on skeletal findings, Abraham Lincoln was once thought to have had Marfan syndrome, but recent work all but rules this out, suggesting that he instead had the disease Multiple endocrine neoplasia type 2B, which mimics the skeletal features of Marfan syndrome (see: Medical and mental health of Abraham Lincoln).
- Philip Roth's novel *I Married a Communist* focuses on a radio host called Ira Ringold who suffers from, and eventually dies from the condition

# INHERITANCE PATTERNS

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- ▣ Overall odds of inheritance: Usually inherited from one parent who has Marfan syndrome; see inheritance of autosomal dominant diseases.
- ▣ Sibling of diseased child odds of inheriting disease: Usually 50% for autosomal dominant diseases.
- ▣ Overall odds of inheriting from mother: Usually 50% for autosomal dominant diseases.
- ▣ Overall odds of inheriting from father: Usually 50% for autosomal dominant diseases.
- ▣ Mother to son inheritance odds: Usually 50% for autosomal dominant diseases.
- ▣ Father to son inheritance odds: Usually 50% for autosomal dominant diseases.
- ▣ Mother to daughter inheritance odds: Usually 50% for autosomal dominant diseases.
- ▣ Father to daughter inheritance odds: Usually 50% for autosomal dominant diseases.
- ▣ Inheritance from one diseased parent odds: Usually 50% for autosomal dominant diseases.
- ▣ Inheritance from two diseased parents odds: Usually 75% (50% disease, 25% double dominant) for autosomal dominant diseases.

# TREATMENS

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- Aortic dilation, or aortic aneurysm, is the most common and serious heart problem linked to Marfan syndrome. In this condition, the aorta—the main artery that carries oxygen-rich blood to your body—stretches and grows weak.
- Medicines are used to try to slow the rate of aortic dilation. Surgery is used to replace the dilated segment of aorta before it tears.
- If you have Marfan syndrome, you'll need routine care and tests to check your heart valves and aorta.