

An 11-year-old boy is brought to the physician for evaluation of scoliosis. His mother noticed that he always seems to be leaning even when he tries to sit or stand upright. The boy has a history of myopia and upward lens dislocation for which he wears corrective glasses. He otherwise has been healthy and doing well in school. His father had scoliosis and vision problems and died from "heart problems" last year. Physical examination shows a boy with a long face, high arched palate with crowded teeth, and upward dislocation of the lens. He has a tall stature for his age; long arms and legs with minimal subcutaneous fat; long, thin fingers; and a prominent sternum. Joint hypermobility, skin hyperelasticity, and 15 degrees of thoracic scoliosis are seen. A diastolic murmur is heard in the aortic area. Which of the following is the most likely etiology of this patient's condition?

- ☐ A. Cystathionine synthase deficiency
- ☐ B. Defective collagen production
- ☐ C. Mutation of the fibrillin-1 gene
- ☐ D. Mutation of the fibrillin-2 gene
- ☐ E. Nondisjunction resulting in an extra X chromosome

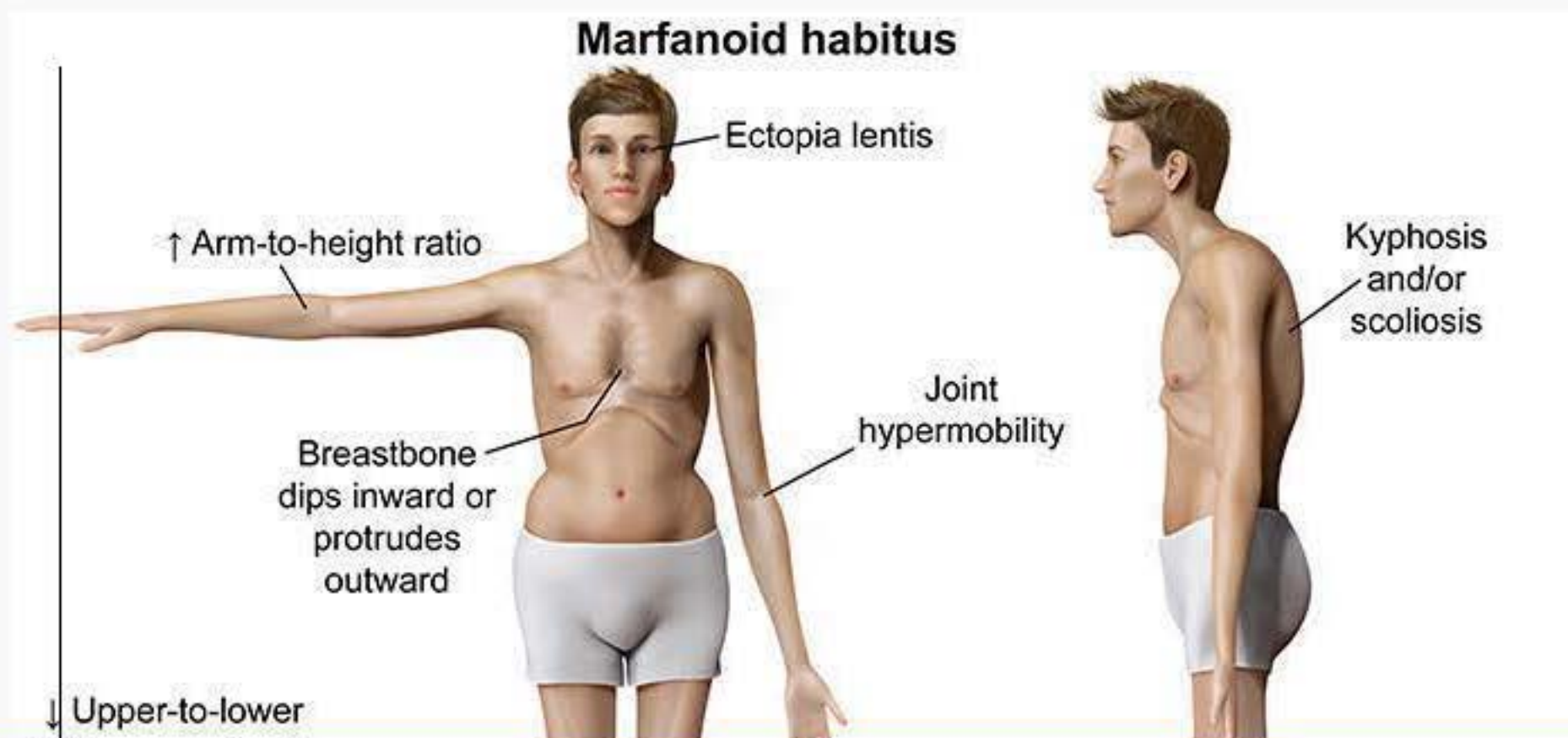
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- ☐ A. Cystathionine synthase deficiency [4%]
- ☐ B. Defective collagen production [11%]
- ☒ C. Mutation of the fibrillin-1 gene [80%]
- ☐ D. Mutation of the fibrillin-2 gene [4%]
- ☐ E. Nondisjunction resulting in an extra X chromosome [1%]

[Proceed to Next Item](#)**Explanation:**

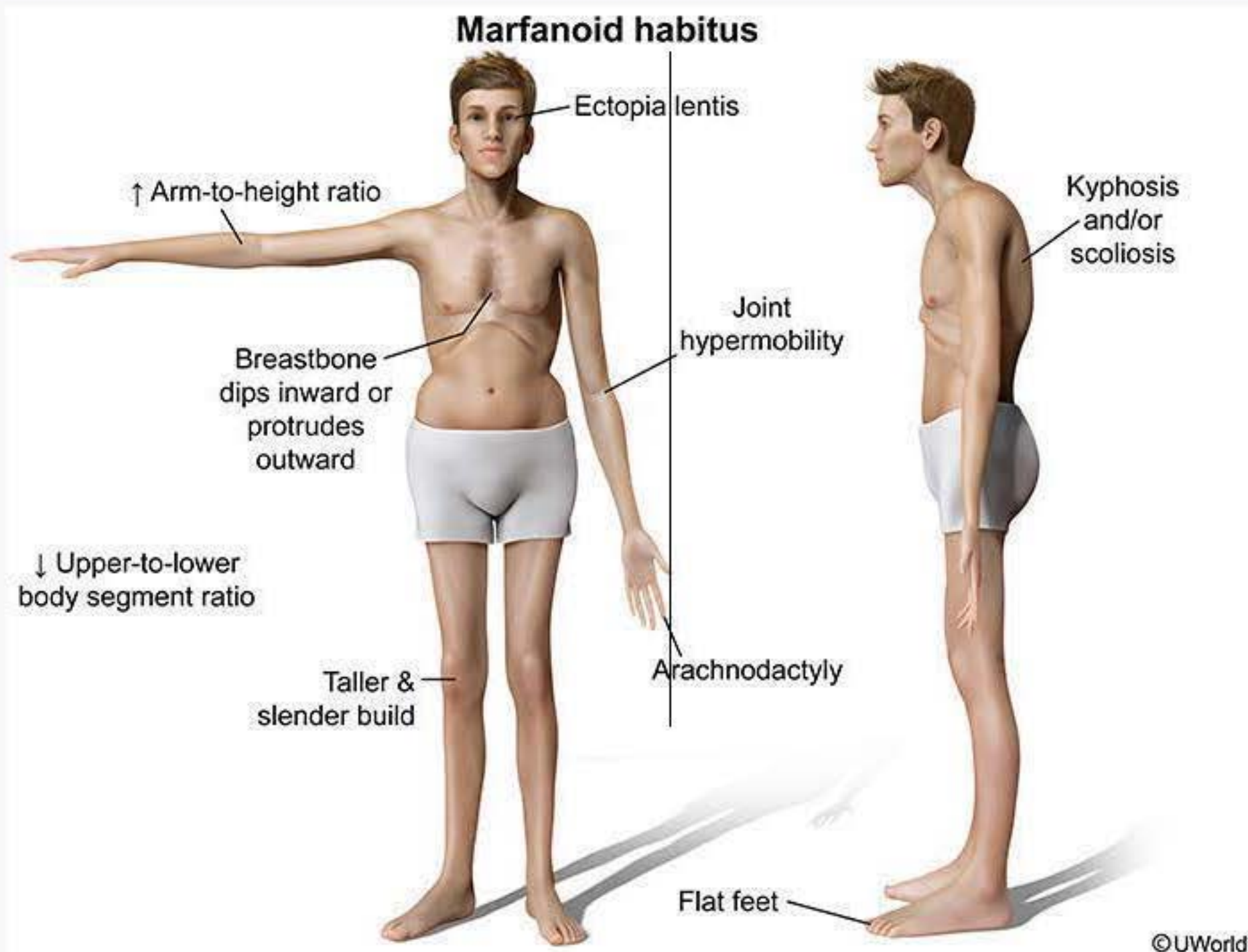
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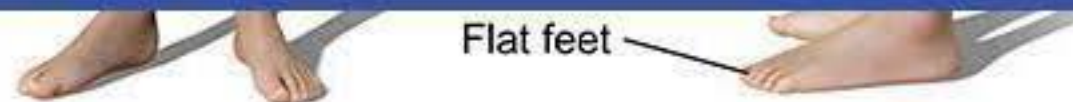
Explanation:

User Id: [REDACTED]



This patient's family history and physical appearance are very characteristic of Marfan syndrome. Marfan syndrome is an autosomal dominant disorder of the fibrillin-1 gene that results in systemic weakening of connective tissue. Classic skeletal manifestations include **joint hypermobility**, skin hyperelasticity, long fingers (**arachnodactyly** ["thumb sign"]), **pectus excavatum**, and **scoliosis/kyphosis**. The face is long, the palate has a high arch, and the teeth are crowded. **Lens dislocation** (ectopia lentis), iridodonesis (a rapid contraction and dilation of the iris), and myopia (from elongation of the globe) are also typical.

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The most life-threatening finding in Marfan syndrome is **aortic root dilation**. The diastolic murmur in this patient reflects **aortic regurgitation**. The syndrome requires close monitoring with echocardiography for the development of **aneurysms** and **aortic arch dissection**. Mitral valve prolapse is also common and manifests as a mid-systolic click and late systolic murmur. First-degree relatives should undergo genetic testing.

(Choice A) Homocystinuria is an autosomal recessive disorder that results from deficiency of cystathionine synthase, an enzyme involved in the metabolism of methionine. These patients share many features of Marfan syndrome (eg, pectus deformity, tall stature, arachnodactyly). However, they usually have a fair complexion, thromboembolic events, and intellectual disability. The other main differentiating feature is lens dislocation in homocystinuria that is downward rather than upward.

(Choice B) Ehlers-Danlos syndrome is a collagen disorder characterized by scoliosis, joint laxity, and aortic dilation. Patients with this disorder do not have the disproportionately tall stature, lens dislocation, or pectus carinatum seen in Marfan syndrome.

(Choice D) Congenital contractural arachnodactyly is an autosomal dominant condition resulting from mutations of the fibrillin-2 gene. These patients have tall stature, arachnodactyly, and multiple contractures involving large joints. Ocular and cardiovascular symptoms are not present in congenital contractural arachnodactyly. In addition, patients with Marfan syndrome do not have joint contractures.

(Choice E) A tall and slender stature, but not connective tissue problems, is seen in Klinefelter syndrome.

Educational objective:

Marfan syndrome is an autosomal dominant disorder that results from mutations of the fibrillin-1 gene. Affected patients have tall stature; long, thin extremities; arachnodactyly; joint hypermobility; upward lens dislocation; and aortic root dilation.

include **joint hypermobility**, skin hyperelasticity, long fingers (**arachnodactyly** ["**thumb sign**"]), **pectus excavatum**, and **scoliosis/kyphosis**. The face is long, the palate has a high arch, and the teeth are crowded. **Lens dislocation** (ectopia lentis), iridodonesis (a rapid contraction and dilation of the iris), and myopia (from elongation of the globe) are also typical.

The most life-threatening finding in Marfan syndrome is **aortic root dilation**. The diastolic murmur in this patient reflects **aortic regurgitation**. The syndrome requires close monitoring with echocardiography for the development of **aneurysms** and **aortic arch dissection**. Mitral valve prolapse is also common and manifests as a mid-systolic click and late systolic murmur. First-degree relatives should undergo genetic testing.

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Marfan syndrome is an autosomal dominant disorder that results from mutations of the fibrillin-1 gene. Affected patients have tall stature; long, thin extremities; arachnodactyly; joint hypermobility; upward lens dislocation; and aortic root dilation.

References:

1. **Health supervision for children with Marfan syndrome.**

Media Exhibit

syndrome

Thumb sign



Arachnodactyly and loose joints allow the distal phalanx to protrude beyond the ulnar side of a clenched fist

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Media Exhibit

aortic aneurysms

Ascending
aortic aneurysm



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