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Health Supervision for Children With Marfan Syndrome

Brad T. Tinkle, MD; Howard M. Saal, MD; the COMMITTEE ON GENETICS; Robert A. Saul, MD; Stephen R. Braddock, MD; Emily Chen, MD; Debra L. Freedenberg, MD; Marilyn C. Jones, MD; James M. Perrin, MD; Beth Anne Tarini, MD

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Marfan syndrome is a systemic, heritable connective tissue disorder that affects many different organ systems and is best managed by using a multidisciplinary approach. The guidance in this report is designed to assist the pediatrician in recognizing the features of Marfan syndrome as well as caring for the individual with this disorder.

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Introduction

Marfan syndrome is a heritable, multisystem disorder of connective tissue with extensive clinical variability. It is a relatively common condition, with approximately 1 in 5000 people affected.¹ Cardinal features involve the ocular, musculoskeletal, and cardiovascular systems. Because of the high degree of variability of this disorder, many of these clinical features can be present at birth or can manifest later in childhood or even adulthood.

Marfan syndrome is an autosomal dominant disorder mainly caused by defects in *FBN1*, the gene that codes for the protein fibrillin, although patients with mutations in other genes, including *TGFBR1* and *TGFBR2*, have also been reported, albeit rarely.² Mutations in *FBN1* are associated with a wide phenotypic spectrum ranging from classic features of Marfan syndrome presenting in childhood and early adulthood to severe neonatal presentation with rapidly progressive disease. At the other end of the spectrum, isolated phenotypic features, such as ectopia lentis or skeletal manifestations alone, may be the only presenting signs. Mutations in *FBN1* are found in up to 95% of those meeting diagnostic criteria.^{3,4} However, the diagnosis of Marfan syndrome is clinically based on well-defined criteria (revised Ghent diagnostic criteria [[Tables 1](#) and [2](#)]) and does not include the whole spectrum of *FBN1*-related disorders, especially the milder, isolated features.⁵ Thus, genetic testing of *FBN1* is best reserved for those patients in whom there is a strong clinical suspicion of Marfan syndrome, including those with the "emerging" phenotype, using established guidelines of the interpretation of such results. Because many of the more specific clinical features are age dependent (eg, ectopia lentis, aortic dilation, dural ectasia, protrusio acetabuli), children and adolescents may not fulfill formal diagnostic criteria and are often described as having "potential" Marfan syndrome. Younger patients at risk for Marfan syndrome on the basis of clinical features or a positive family history should be evaluated periodically (eg, at 5, 10, 15, and 18 years of age) in lieu of genetic testing.

TABLE 1

Revised Ghent Diagnostic Criteria for Marfan Syndrome

| |
|---|
| Diagnosis of definitive Marfan syndrome (any of the following) |
| ¥ Aortic root ³ 2 z score and ectopia lentis |
| ¥ Aortic root ³ 2 z score and <i>FBN1</i> mutation |
| ¥ Aortic root ³ 2 z score and systemic score ³ 7 |
| ¥ Ectopia lentis and <i>FBN1</i> mutation known to be associated with Marfan syndrome |
| ¥ Positive family history of Marfan syndrome and ectopia lentis |
| ¥ Positive family history of Marfan syndrome and systemic score ³ 7 |
| ¥ Positive family history of Marfan syndrome and aortic root ³ 3 z score in those <20 y of age or ³ 2 z score in those >20 y of age |
| Diagnosis of potential Marfan syndrome |
| ¥ <i>FBN1</i> mutation with aortic root with a z score <3 in those <20 y of age |

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TABLE 2

Systemic Scoring System for the Revised Ghent Diagnostic Criteria for Marfan Syndrome (Shown in Table 1)

| Feature | Value |
|--|-------|
| Wrist <i>and</i> thumb sign | 3 |
| Wrist <i>or</i> thumb sign | 1 |
| Pectus carinatum | 2 |
| Pectus excavatum or chest asymmetry | 1 |
| Hindfoot deformity (eg, valgus) | 2 |
| Pes planus | 1 |
| Pneumothorax | 2 |
| Dural ectasia | 2 |
| Protrusio acetabulae | 2 |
| Reduced upper-to-lower segment ratio <i>and</i> increased arm-span-to-height ratio | 1 |
| | |

| | |
|---|---|
| Scoliosis or thoracolumbar kyphosis | 1 |
| Reduced elbow extension | 1 |
| Craniofacial features: 3 of the following: dolichocephaly, downward-slanting palpebral fissures, enophthalmos, retrognathia, and malar hypoplasia | 1 |
| Skin striae | 1 |
| Myopia | 1 |
| Mitral valve prolapse | 1 |

Adapted from Loeys et al.³ Z score calculations are based on Roman et al.³⁸

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Many features of Marfan syndrome are seen in isolation as well as in other genetic syndromes ([Table 3](#)).⁶ Diagnosis should be clearly established when possible. For those suspected to have Marfan syndrome based on clinical grounds after physical, cardiac, and ophthalmic evaluation but who may not meet full clinical criteria, one can consider *FBN1* testing.⁷

TABLE 3

Differential Diagnoses: Syndromes With Overlapping Features of Marfan Syndrome

| Syndrome | Manifestations | Genetic Etiology |
|---|--|-----------------------|
| Mitral valve prolapse syndrome | Mitral valve prolapse; skeletal manifestations as seen in Marfan syndrome | <i>FBN1</i> (in some) |
| MASS phenotype | Mitral valve prolapse; myopia; nonprogressive aortic dilation; nonspecific skin and skeletal features | <i>FBN1</i> |
| Familial ectopia lentis | Eye and skeletal findings of Marfan syndrome | <i>FBN1</i> (in some) |
| Shprintzen-Goldberg syndrome | Skeletal and cardiac findings of Marfan syndrome; craniosynostosis; hypertelorism; proptosis; abdominal hernias; joint laxity; developmental delay/intellectual disability | <i>FBN1</i> (in some) |
| Weill-Marchesani syndrome (autosomal dominant form) | Ectopia lentis; short stature; brachydactyly; characteristic facial features | <i>FBN1</i> |
| Loeys-Dietz | Skeletal and cardiovascular features of Marfan syndrome; no ectopia lentis; aggressive dilation of large- | <i>TGFBR1</i> |

| | | |
|---|--|----------------|
| syndrome | and medium-sized arteries; most common and unique features include hypertelorism, bifid uvula/cleft palate, blue sclerae, developmental delays, hydrocephalus, translucent skin, arterial tortuosity, and craniosynostosis | <i>TGFBR2</i> |
| Congenital contractural arachnodactyly | Marfan-like skeletal features; "crumpled" ears; contractures of the knees, ankles, and digits at birth; progressive kyphoscoliosis; arachnodactyly; cardiac valvular anomalies | <i>FBN2</i> |
| Familial thoracic aortic aneurysm | Dilation of the aorta and dissections either at the level of the sinuses of Valsalva or the ascending thoracic aorta without the other phenotypic features of Marfan syndrome | Heterogeneous |
| Ehlers-Danlos syndrome, vascular type | Thin skin with visible veins; easy bruising; small joint laxity; rupture of hollow organs as well as medium- and large-size arteries | <i>COL3A1</i> |
| | | <i>COL3A2</i> |
| Ehlers-Danlos syndrome, kyphoscoliotic form (type VI) | Marfanoid body habitus; kyphoscoliosis; joint laxity; mitral valve prolapse; hypotonia; blue sclerae; ocular fragility; at risk for rupture of medium-sized arteries | <i>FLOD</i> |
| | | <i>ZNF469</i> |
| Homocystinuria | Ectopia lentis; skeletal abnormalities such as those seen in Marfan syndrome; variable cognitive impairment; tendency for thrombotic events | <i>CBS</i> |
| Stickler syndrome | Severe myopia; retinal detachment; hearing loss; midface hypoplasia; cleft palate; spondyloepiphyseal dysplasia | <i>COL2A1</i> |
| | | <i>COL11A1</i> |
| | | <i>COL11A2</i> |
| | | <i>COL9A1</i> |
| Fragile X syndrome | Often tall; long face; joint laxity; mild dilation of the aorta; mitral valve prolapse; pectus excavatum; variable intellectual disability | <i>FMR1</i> |

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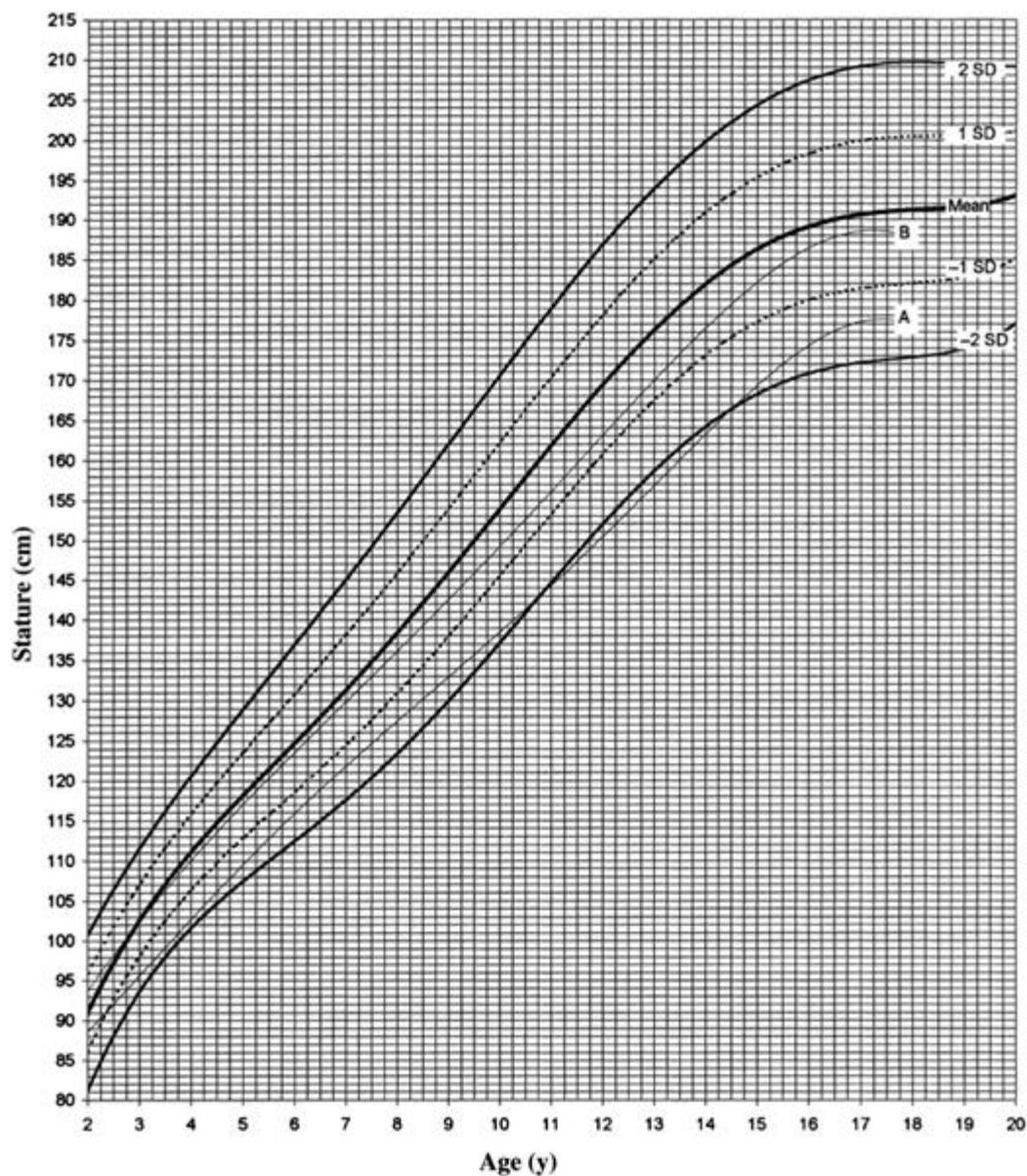
Approximately one-quarter of cases occur as a result of a new mutation, with the remainder inherited from an affected parent. Because of the broad phenotypic variability, some parents will not be readily recognized as having Marfan syndrome.⁸ In such cases, both parents and at-risk first-degree relatives should have physical, ophthalmologic, and cardiac evaluation as well, with consideration of genetic testing.

Growth and Development

Overall growth is characterized by excessive linear growth of the long bones. Typically, most individuals with Marfan syndrome are tall for age (**Figs 1** and **2**), but it is important to note that not all affected individuals are tall by population

standards; they are typically taller than predicted for their family (excluding others with Marfan syndrome).⁹ Mean final height was 191.3 ± 9 cm (75 in) for males and 175.4 ± 8.2 cm (69 in) for females.

FIGURE 1



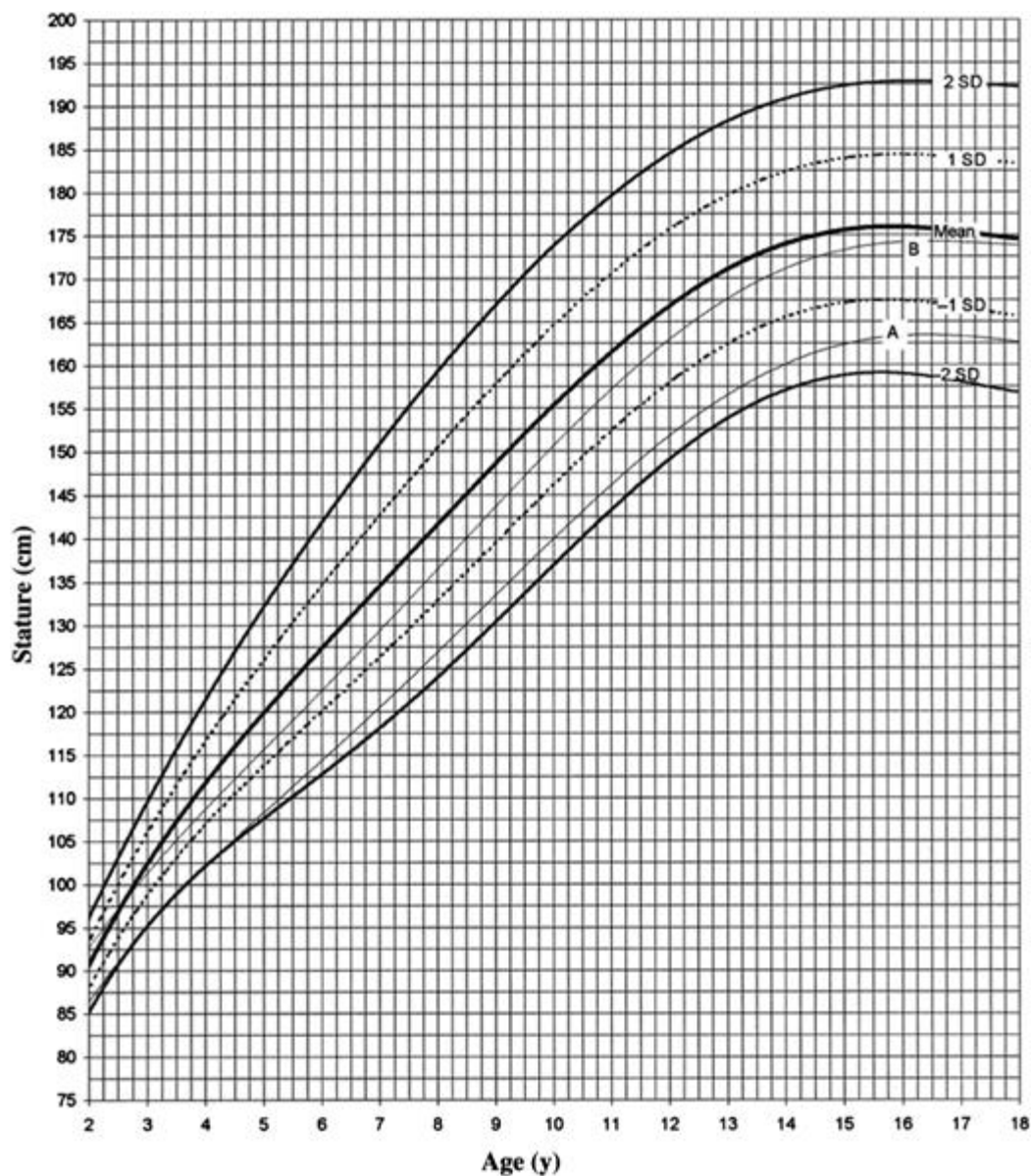
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Growth curves for males in Marfan syndrome. (A) 50th percentile and (B) 95th percentile for the general population used for comparison. Reprinted with permission from Erkula G, Jones KB, Sponseller PD, Dietz HC, Pyeritz RE. Growth and maturation in Marfan syndrome. *Am J Med Genet.*

2002;109(2):103.⁹

FIGURE 2



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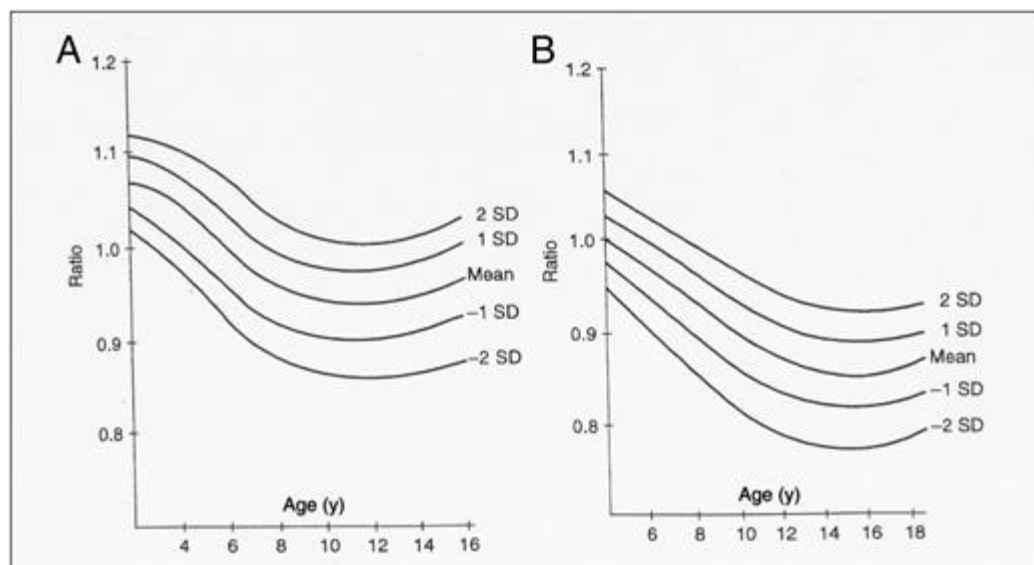
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Growth curves for females in Marfan syndrome. (A) 50th percentile and (B) 95th percentile for the general population used for comparison. Reprinted with permission from Erkula G, Jones KB, Sponseller PD, Dietz HC, Pyeritz RE. Growth and maturation in Marfan syndrome. *Am J Med Genet.* 2002;109(2):104.⁹

The growth of the tubular bones is accelerated in Marfan syndrome, resulting in disproportionate features. The extremities are often disproportionately long in comparison with the trunk (dolichostenomelia), altering the upper-to-lower segment and the arm-span-to-height ratios. The arm-span-to-height ratio is relatively fixed during childhood, but the upper-to-lower segment ratio changes during growth ([Fig 3](#)). Use of such measurements should take into account

racial, gender, and age differences. Similarly, the tubular bones of the hand and fingers are elongated, but the palm is not proportionately wider, resulting in relative arachnodactyly as measured by the thumb and wrist signs ([Fig 4](#)).

FIGURE 3

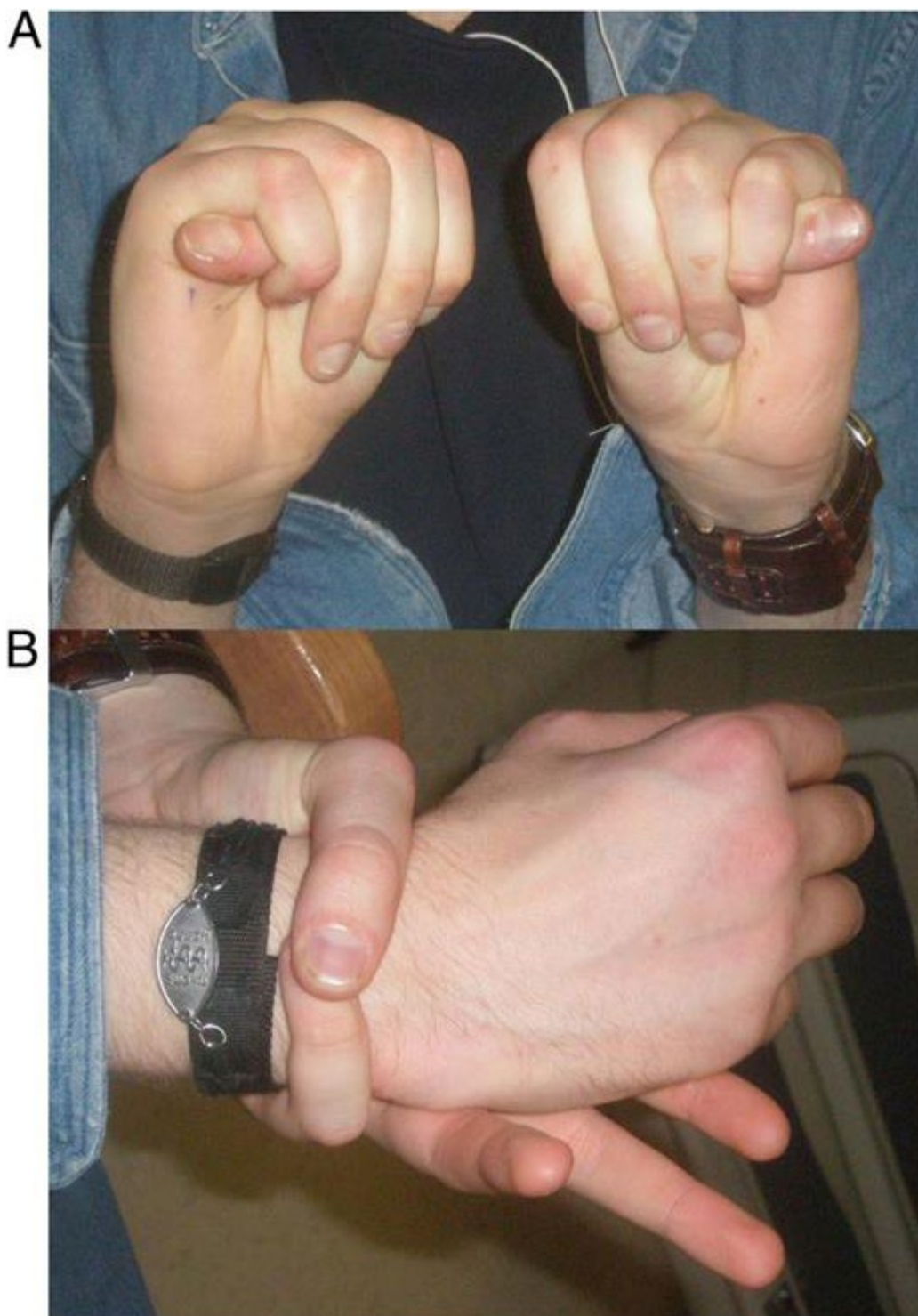


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Normative upper-to-lower segment ratios for (A) white and (B) African-American subjects. Reprinted with permission from McKusick VA. *Heritable Disorders of Connective Tissue*. Philadelphia, PA: Mosby; 1972.

FIGURE 4



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(A) Positive thumb sign with the thumbnail extending past the ulnar side of the hand and (B) positive wrist sign with the overlap of the nail beds of the thumb and fifth finger.

Excessive growth in Marfan syndrome is attributable, in part, to a peak growth velocity that typically occurs as much as 2 years earlier than the general population.⁹ Hormonal therapy to limit adult height is rarely used in males. Complications can include accelerated growth, early puberty, and the undesirable consequences of associated increased blood

pressure, which may increase the progression of the aortic dilation. Prepubertal females have been treated with high-dose estrogen therapy and progesterone to reduce final adult height in the past; however, this treatment remains controversial in both its psychosocial and medical benefits.¹⁰

Lean muscle mass is also affected. Individuals with Marfan syndrome often show a paucity of muscle mass and fat stores despite adequate caloric intake. Weight is often below the 50th percentile for age.⁹

Cognitive ability in patients with Marfan syndrome is usually within the typical range for the general population. However, poor vision and underlying medical problems may interfere with learning. Similarly, many patients report chronic fatigue, which may affect education and can manifest as inattention or poor concentration.¹¹ The etiology of the fatigue is likely heterogeneous, in part because of the underlying chronic condition, medications such as β -blockers, sleep disturbance (eg, sleep apnea), and/or orthostatic intolerance.¹²

Skeletal

Skeletal system involvement in Marfan syndrome is characterized by bone overgrowth. Such overgrowth may be noticeable at birth or can develop in young children, with a tendency to progress more rapidly during periods of rapid growth, necessitating close monitoring at such times (Table 4).

TABLE 4

Anticipatory Guidance in Marfan Syndrome

| Option | At Diagnosis | 0Ð12 mo | 1Ð5 y | 6Ð12 y ^a | 13Ð18 y ^a | 19Ð22 y |
|----------------------------------|--------------|--------------|------------|---------------------|----------------------|------------------|
| Cardiac examination ^b | Ã | Each visit | Each visit | Each visit | Yearly | Yearly |
| Echocardiogram | Ã | As indicated | Yearly | Yearly | Yearly | Yearly |
| Ocular (ophthalmology) | Ã | | Yearly | Yearly | Yearly | Yearly |
| Musculoskeletal ^b | | | | | | |
| Scoliosis clinical examination | Ã | Each visit | Yearly | Every 6 mo | Every 6 mo | Yearly |
| Joint laxity | Ã | Each visit | Yearly | Every 6 mo | Every 6 mo | |
| Pectus deformity | Ã | Each visit | Yearly | Every 6 mo | Every 6 mo | |
| Bone age | | | | Ã ^c | | |
| Review diagnosis | Ã | PRN | PRN | PRN ^d | PRN ^d | PRN ^d |
| Examine family members | Ã | PRN | PRN | PRN | PRN | PRN |

| | | | | | | |
|---------------------------|---|-----|-----|-----|----------------|------------------|
| Support group information | Ä | PRN | PRN | PRN | PRN | PRN |
| Genetic counseling | Ä | | | | Ä ^e | Ä ^e |
| Lifestyle ^f | | | | Ä | Ä | Ä |
| Transition | | | | | Discuss plans | Begin transition |

a b c d e f

Many systems should be reviewed regularly at developmentally appropriate stages. PRN, as needed.

If abnormal results on examination, refer for further evaluation. Follow-up evaluations as indicated. Periods of rapid growth require closer supervision.

Bone age determination in preadolescence. If large discrepancy between bone age and height age, hormonal therapy should be considered.



Review symptoms of potential catastrophic events such as aortic dissection, vision changes, and pneumothorax.

Review physical activity restrictions/lifestyle modifications. Discuss reproductive and pregnancy risks.

Overgrowth of the ribs can push the sternum inward (pectus excavatum) or outward (pectus carinatum). Nearly two-thirds of patients with Marfan syndrome will develop pectus excavatum, which is often perceived as a disturbing physical feature by teenagers.¹³ The pectus deformity can be severe and, in extreme circumstances, can interfere with pulmonary functioning, warranting surgical intervention.¹⁴ Pectus excavatum may also have a detrimental effect on cardiac function, especially during submaximal exercising¹⁵ and is often repaired before cardiac surgery for aortic root replacement. Pectus deformity is often present before 10 years of age but may worsen during an adolescent growth spurt.

Scoliosis is seen in slightly more than one-half of individuals with Marfan syndrome and can be mild to severe as well as atypically progressive.^{16 17} Close monitoring by using the forward-bending test at yearly intervals and management by an orthopedist is preferred because surgical stabilization of the spine may be required.¹⁸ Bracing has a low success rate if the curves are greater than 35° to 40° but may have some preventive value for smaller curves. Those with spinal curvatures less than 30° have an excellent long-term prognosis. Marked progression is often seen by those with spinal curvatures greater than 50°. The progression of scoliosis can occur well into adulthood. Thoracic kyphosis is also common and can be postural or a further complication of bony overgrowth and ligamentous laxity (eg, kyphoscoliosis). Postural education and joint stabilization with core strengthening may be of benefit but are unproven for the treatment of scoliosis in this population. Untreated spinal deformities can lead to chronic back pain and restrictive lung disease. Spinal deformity correction is more prone to complications than in idiopathic deformity and should be performed by those with some experience in treating patients with Marfan syndrome.¹⁹

The acetabulum of the hip can be abnormally deep (protrusio acetabuli) in some patients with Marfan syndrome and can lead to pelvic or upper leg pain. Protrusio acetabuli is seen commonly in Marfan syndrome²⁰; however, it is not unique to this condition and is seen in a number of infectious, inflammatory, metabolic, genetic, neoplastic, and traumatic conditions.²¹ In Marfan syndrome, the protrusio acetabuli is often asymptomatic, and surgical intervention is rarely indicated.²²

Some people with Marfan syndrome will show reduced mobility of the elbow, but other joints may demonstrate ligamentous laxity. Joint laxity may be more significant in young patients but rarely leads to motor delays. True joint dislocations are rare. Joint laxity can lead to muscle fatigue and overuse pain/injury.²³ More typically, such individuals demonstrate poor writing skills and complain of hand pain/fatigue with prolonged use. Physical and/or occupational therapy can address these joint laxity issues by using joint stabilization exercises, postural support, education, alternative strategies (eg, use of a laptop for taking notes), and bracing/resting splints if necessary.

Inward rotation of the medial aspect of the ankle can result in pes planus (**Fig 5**). This condition may lead to foot, ankle, knee, hip, and/or low back pain.²⁴ Some patients will benefit from the use of shoe orthoses, such as an arch support and more supportive shoes. Surgical intervention is rarely indicated or fully successful. Others will have highly arched feet but have little or no symptoms.

FIGURE 5

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Elongated feet with collapse of the medial arch resulting in pes planus.

The facial features of Marfan syndrome include a long and narrow face with deeply set eyes (enophthalmos), downward slanting of the eyes, flat cheek bones (malar hypoplasia), and a small chin (micrognathia) (**Fig 6**). However, facial features are often highly variable and may change with age. In addition, these facial features are not highly sensitive for the presence of Marfan syndrome.²⁵ The palate is often highly arched and narrowed (**Fig 7**).

FIGURE 6



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Facial features of Marfan syndrome are highly variable, ranging from subtle findings to more classic facial features. Photo consents for publication on file.

FIGURE 7



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High arched (steep) palate.

Decreased bone density has been documented in the lumbar and hip regions in patients with Marfan syndrome.^{26 27}

The etiology of this bone loss remains speculative, but no significant increase in bone fracture rates has been seen.²⁸

Ocular

Myopia is the most common ocular feature and often progresses rapidly during childhood.²⁹ Displacement of the lens (ectopia lentis) is a hallmark feature of Marfan syndrome but is only seen in 1 or both eyes in approximately 60% of affected individuals.³⁰ It is often the presenting feature and occurs much more commonly before 10 years of age. This finding is most reliably diagnosed according to a slit-lamp examination after full pupillary dilation.

The globe is often elongated, and the cornea may be flat or even cone-shaped (keratoconus). People with Marfan syndrome are at increased risk of retinal detachment, glaucoma, and early cataract formation, typically in adulthood. Flashes of light (photopsia) and new floaters are symptoms of posterior vitreous detachment, which may precede retinal detachment.^{31,32} Retinal detachment should be considered in any patient with acute onset of visual symptoms, and these patients should be evaluated and treated emergently. Most retinal detachments can be repaired successfully, but the key to optimum visual recovery is prompt diagnosis and treatment.

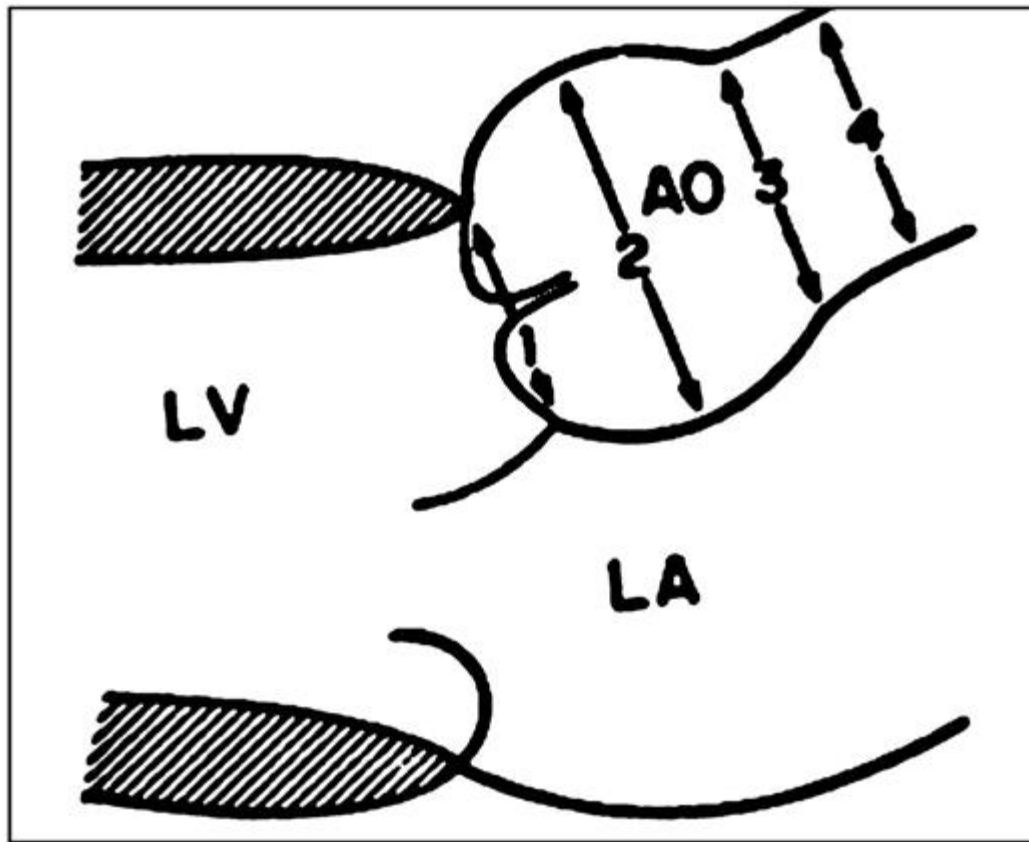
Affected individuals should be followed up closely by an ophthalmologist familiar with Marfan syndrome at least yearly with slit lamp examinations for lens subluxation and evaluations for glaucoma and cataracts. Most often, eye problems can be controlled adequately with corrective lenses alone. Careful and aggressive refraction and visual correction are mandatory in young children at risk for amblyopia. Lens dislocation can present a clinical challenge. Typically, the lens will sublux superiorly with Marfan syndrome. If the lens is subluxed but still within the visual axis, substantial lenticular astigmatism may result, which can require powerful astigmatic spectacle correction. If the lens edge has subluxed at or beyond the center of the visual axis, aphakic spectacle or contact lens correction may improve vision. If there is sufficient optical distortion from lens subluxation, surgical removal of the lens (aphakia) or lens replacement (pseudophakia) may be the treatment of choice.³³ Because of inherently weak zonular support for the Marfan lens, pseudophakia may require supplemental means of attachment to affix the intraocular lens. Although this procedure is currently considered safe when performed in specialized centers, major complications, including retinal detachment, can occur. The long-term stability and safety of sew-in intraocular lenses are unknown. Zonular weakness in Marfan syndrome may also result in complete lens subluxation into the vitreous or result in prolapse of the lens into the anterior chamber of the eye, which may necessitate surgical removal. Corneal refractive surgery for myopia is generally contraindicated in individuals with Marfan syndrome, given the risk of additional eye complications.

Cardiovascular

The cardiovascular system is the major source of morbidity and mortality in Marfan syndrome. Cardiovascular manifestations include dilation of the aorta, aortic valve insufficiency, a predisposition for aortic tear and rupture, mitral valve prolapse with or without regurgitation, tricuspid valve prolapse, and enlargement of the proximal pulmonary artery.³⁴

The aortic dilation in Marfan syndrome tends to progress over time, with the vast majority of cases becoming evident before 18 years of age. The dilation typically is at the level of the sinuses of Valsalva, but dilation of any part of the aorta can be seen in these patients (**Fig 8**). Histologic examination reveals elastic fiber fragmentation with total loss of elastin content and accumulation of amorphous matrix components in the aortic media. This cystic medial necrosis does not distinguish Marfan syndrome from other causes of aortic aneurysm and, therefore, is only a description, not a pathognomonic feature.

FIGURE 8


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Dilation at the level of the aortic root as seen in Marfan syndrome. 1, aortic valve annulus; 2, aortic root (sinuses of Valsalva); 3, sinotubular junction; 4, ascending aorta; AO, aorta; LA, left atrium; LV, left ventricle. Rights to be retained by author (B.T.T.).

The age of onset and rate of progression of aortic dilation are highly variable. As the aneurysm enlarges, the aortic annulus can be overstretched, leading to secondary aortic regurgitation. Valvular dysfunction can lead to volume overload with secondary left ventricular dilation and heart failure. Indeed, mitral valve prolapse with congestive heart failure is the leading cause of cardiovascular morbidity and mortality in young children with Marfan syndrome.³⁵

A significant risk of aortic dissection or rupture occurs when the maximal aortic dimension reaches approximately 5.0 cm in adults, although rupture at 4.5 cm has been documented among women.³⁶ Fortunately, aortic dissection is exceedingly rare in early childhood. Acute aortic dissection usually presents as severe chest pain but can also include pallor, pulselessness, paresthesia, and paralysis. Asymmetric blood pressure may also be a sign of dissection.

All individuals with a diagnosis of Marfan syndrome should be followed up by a cardiologist familiar with Marfan

syndrome. An echocardiogram should be obtained at diagnosis. A subsequent echocardiogram is often desired in 6 months to assess the rate of progression.³⁷ Yearly echocardiograms are sufficient when aortic dimensions are small (<4.5 cm in adults) and rates of aortic dilation are low (<0.5 cm per year). Aortic root measurements should be interpreted on the basis of normal values for age and body size.³⁸ Nomograms are available through the National Marfan Foundation (<http://www.marfan.org/marfan/2576/Aortic-Root-Dilatation-Nomogram>). More frequent evaluations are indicated when the aortic root diameter exceeds 4.5 cm in adults, when the rate of aortic dilation exceeds 0.5 cm per year, or with the onset of significant valvular or ventricular dysfunction. Aortic root dimensions can also be determined by using computed tomography angiography or magnetic resonance angiography, and they potentially have the benefit of evaluating beyond the aortic root. Because aortic dilation can occur at any age, lifelong monitoring is warranted.

Medications that reduce hemodynamic stress on the aortic wall, such as β -blockers, are often prescribed.³⁷ Therapy should be considered at the time of diagnosis at any age or on appreciation of progressive aortic root dilation, even in the absence of a definitive diagnosis.³⁹ The dose needs to be titrated to effect, keeping heart rate after submaximal exercise or agitation less than 110 beats per minute in young children or less than 100 beats per minute in older children or adults. In patients who cannot tolerate β -blockers (eg, individuals with asthma, depression, fatigue), verapamil is commonly used,⁴⁰ although recently, concerns have been raised about calcium channel blockers and an increased risk of aortic complications.⁴¹ Currently, randomized controlled trials are underway evaluating the response to the angiotensin receptor blocker losartan, in response to earlier mouse model work⁴² and a small cohort study.⁴³ If congestive heart failure is present as a result of valvular dysfunction, afterload-reducing agents (in combination with a β -blocker) can improve cardiovascular function, but surgical intervention may be warranted.

Surgical repair of the aorta is indicated once: (1) the maximal aortic root measurement exceeds 5.0 cm; (2) the rate of increase of the aortic diameter approaches 1.0 cm per year; or (3) there is progressive aortic regurgitation.⁴⁴ More aggressive therapy may be indicated in individuals with a family history of early aortic dissection. Many individuals can receive a valve-sparing procedure that precludes the need for chronic anticoagulation therapy.^{45,46} Children run the highest risk of requiring repeated cardiac operations, such as valve replacement.⁴⁷

Aortic dilation can also be seen in the descending aorta, although typically at later ages. All people with Marfan syndrome should begin intermittent surveillance of the entire aorta with computed tomography angiography or magnetic resonance angiography scans in young adulthood.^{48,49} Such imaging should also be performed at least annually in anyone with a history of aortic root replacement or dissection.

Participation in contact sports, competitive sports, and isometric exercise should be restricted.⁵⁰ However, all people with Marfan syndrome can and should remain active, with aerobic activities performed in moderation.

Agents that stimulate the cardiovascular system, including routine use of decongestants, should be avoided. Caffeine can aggravate a tendency for arrhythmia. The use of psychostimulant medications for chronic fatigue or attention-deficit/hyperactivity disorder should be used with caution and be approved by the cardiologist.

Subacute bacterial endocarditis prophylaxis may be indicated for dental work or other procedures expected to contaminate the bloodstream with bacteria in the presence of significant valvular insufficiency. With proper management, the life expectancy of someone with Marfan syndrome approximates that of the general population.^{51 52}

Pulmonary Airway

Pulmonary issues encountered in Marfan syndrome include spontaneous pneumothorax, reduced pulmonary reserve, and sleep apnea. In neonatal Marfan syndrome, an emphysematous lung disease is uniformly present and also occurs in approximately 10% to 15% of those with classic Marfan syndrome.

Lung bullae, which develop in 4% to 15% of patients with Marfan syndrome, can develop anywhere on the surface of the lungs but especially in the upper lobes.⁵³ Such bullae (or blebs) can predispose to spontaneous pneumothorax. Symptoms of pneumothorax include sudden onset of chest pain, dyspnea, and/or cyanosis. Breathing against resistance (eg, playing a brass instrument), scuba diving, or high-altitude sports (eg, skydiving, mountaineering) should be avoided, especially among those with a family history of spontaneous pneumothorax. Those with recurrent pneumothorax may require chemical or surgical pleurodesis or surgical resection of pulmonary blebs.

A restrictive lung disease pattern with increased total and residual lung volume as well as exercise intolerance is typically seen in the majority of those affected.⁵⁴ Often, this pattern is related to pectus deformity, chest wall asymmetry, and/or scoliosis. Surgical repair of severe pectus excavatum or scoliosis may improve overall pulmonary lung function. Pulmonary function tests should be performed in any patient with pulmonary complaints or significant pectus deformity and can be monitored after surgical repair.

Obstructive sleep apnea is commonly seen in patients with Marfan syndrome.⁵⁵ Increased nasal resistance attributable to craniofacial abnormalities, such as a high arched palate, micrognathia with possible glossoptosis, and laryngotracheomalacia, can cause difficulty with intubation/anesthesia as well as significant upper airway resistance.⁵⁶ Sleep apnea is underappreciated among adolescents and young adults with Marfan syndrome. Symptoms commonly seen in Marfan syndrome that may be partially attributable to sleep apnea include fatigue and loss of energy as well as impaired memory and cognition. Symptoms of sleep dysfunction, such as fatigue, decreased sleep duration, nonrestorative sleep, and snoring, should be reviewed at each visit. A formal sleep evaluation should be considered in such cases.

Integument

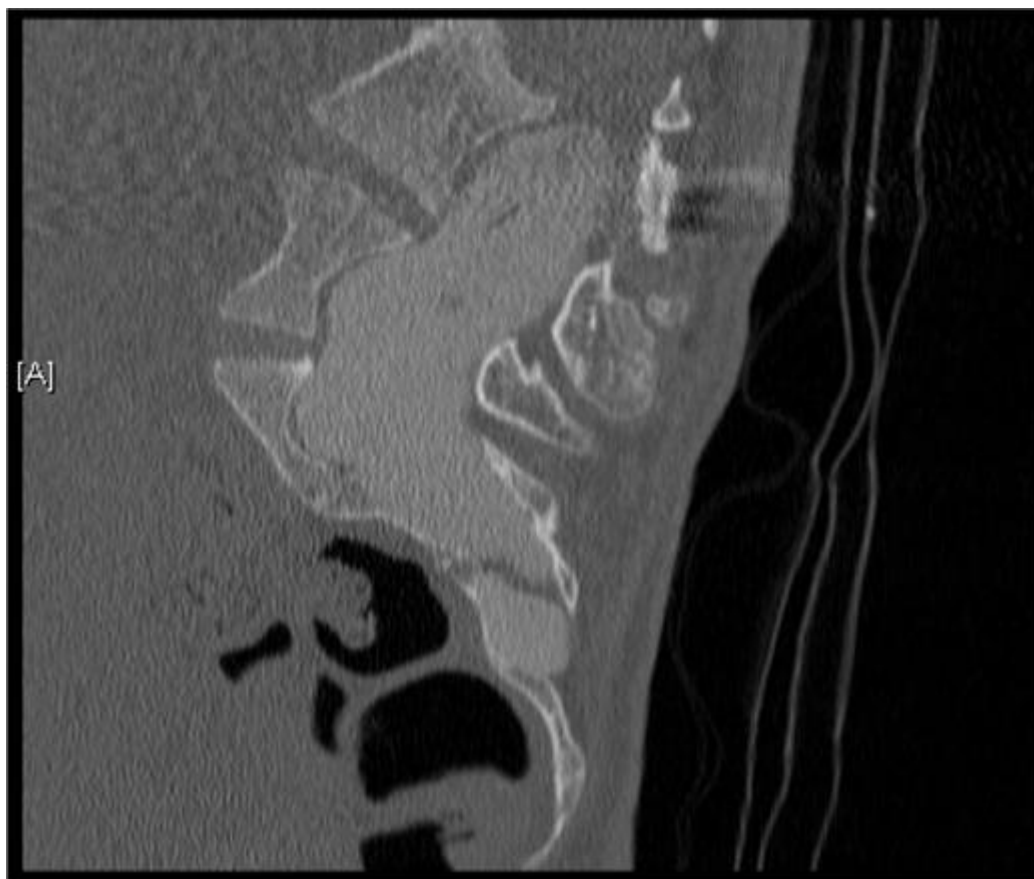
Approximately two-thirds of people with Marfan syndrome develop stretch marks of the skin.⁵⁷ Often, these are located across the lower back as well as the inguinal and axillary regions. These stretch marks are signs of rapid growth and are usually perpendicular to the axes of growth.

Because of the defect in connective tissue, individuals with Marfan syndrome are also at risk for hernias. Many will have inguinal herniation that will require surgical repair. However, recurrent hernias or hernias at the site of surgical incisions are a more distinctive hallmark of a connective tissue disorder, such as Marfan syndrome. Primary hernia repair should use a synthetic mesh (or similar artificial construct) in all known or suspected cases of Marfan syndrome to minimize the risk of recurrence.

Dural Ectasia

Most individuals with Marfan syndrome often develop stretching of the dural sac in the dependent lumbosacral region, resulting in dural ectasia (**Fig 9**).⁵⁸ This development can lead to bony erosion and nerve entrapment. Symptoms can include pain in the lower back, hip/pelvic region, and proximal leg, as well as weakness/numbness above and below the knees.⁵⁹ However, in most patients, the dural ectasia is asymptomatic.⁶⁰

FIGURE 9



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Dural ectasia of the lumbar spinal canal. MRI appearance of the dilated dural sac, which can erode the bone and entrap nerves.

Excessive accumulation or leakage of cerebrospinal fluid from the dural sac can cause postural hypotension and low-pressure headaches.^{61,62} Damage of the dura from spinal taps or epidurals may not sufficiently heal, causing leakage, which also predisposes the patient to postural headaches. In severe cases of dural ectasia, spinal shunting and/or medication can be used. Complications after surgical repair of the dura include cerebrospinal fluid leakage and recurrence. Detection of dural ectasia can be performed using either MRI or computed tomography scan.

Dental

People with Marfan syndrome typically have oromaxillofacial anomalies. Most have an elongated face, malar hypoplasia, high-arched palate, and micrognathia. Often, these anomalies will cause significant dental crowding and malalignment. Routine dental care is recommended; however, many individuals with Marfan syndrome require orthodontia for proper occlusion as well as appearance. Oral and maxillofacial interventions may also be indicated, such as palatal expansion and/or mandibular distraction.

Physical Activity

Although all children are encouraged to participate in physical activity for overall health, skill development, coordination, musculoskeletal health, and socialization, individuals with Marfan syndrome are at significant risk of physical injury and medical complications. Of concern are activities including contact sports and activities involving burst exertion (eg, sprinting) and intense static (isometric) exertion, such as weight lifting.⁶³ In general, patients with Marfan syndrome without aortic dilation or significant mitral valve regurgitation are encouraged to participate in competitive and noncompetitive (recreational) activities, but this action is still limited by the intensity level of the activity and the individual.⁵⁰ Sports in which ocular trauma is likely, such as boxing or full-contact karate, should be discouraged. Participation in any activity should be evaluated and discussed before initiation of that activity. Activities of most concern include basketball, body building/weight lifting, hockey, running, skiing, racquetball, surfing, scuba diving, and rock climbing. More acceptable alternatives include modest hiking, stationary cycling, bowling, golf, skating, snorkeling, and brisk walking. Caution is needed for patients with low blood pressure and orthostatic intolerance, including those receiving β -blocker therapy, who may be more susceptible to easy fatigue, near-syncopal/syncopal episodes, and falls.¹²

Psychosocial

Marfan syndrome affects each individual differently. Marfan syndrome has a significant effect on daily activities and perceived quality of life. However, in 2 small series, most affected individuals older than 13 years reported a positive general self-image.^{64 65}

Many of those affected by Marfan syndrome benefit from networking and peer relationships. The National Marfan Foundation (www.marfan.org) is an excellent US resource for connections as well as medical advice. Most countries have similar organizations.

Transition/Medical Home

Because Marfan syndrome can affect the very young and continues throughout a patient's lifetime, it is important that people with Marfan syndrome be recognized and have a medical home. Affected people are often followed up by cardiologists, ophthalmologists, and orthopedists.⁶⁶ Care needs to be coordinated among the various specialties, with a special focus on the period of transition from adolescence to adulthood.

Pregnancy

Pregnancy can lead to significant medical complications for women with Marfan syndrome and should be approached with careful deliberation.⁶⁷ If the aortic root exceeds 4.0 cm, complications can include rapid progression of aortic root enlargement and/or aortic dissection or rupture during pregnancy, delivery, and in the postpartum period. Women whose aorta is greater than 4.5 cm or who previously had an aortic dissection/rupture are at substantially higher risk.⁶⁸ Women with aortic dimensions greater than 5.0 cm are at significant risk for aortic rupture, and pregnancy should be delayed if possible until after definitive treatment of the aorta has been completed. If already pregnant, consideration of immediate aortic replacement, early delivery, or termination of the pregnancy should be considered, given the potentially severe consequences.

A higher-than-expected rate of spontaneous abortion has been reported in women with Marfan syndrome, although the etiology is unknown.⁶⁹ In addition, women with Marfan syndrome experience a higher rate of preterm deliveries, premature rupture of membranes, and increased mortality of their offspring.^{69 70} Dural ectasia should be considered in any affected individual, and avoidance of spinal anesthesia may be necessary. Epidural anesthesia is safe for most women with Marfan syndrome, although it is not advised for those with moderately severe dural ectasia. General anesthesia has the benefit of avoiding complication of spinal anesthesia with dural ectasia and less stress on the aorta during delivery. Optimally, pregnancy should be considered after appropriate counseling from a geneticist or a cardiologist familiar with Marfan syndrome, a genetic counselor, and a perinatologist.

Prenatal

The pediatrician is sometimes called on to counsel a family prenatally with regard to Marfan syndrome. The pediatrician may have been previously involved with this family through care of siblings or one of the expectant parents. Families may also seek pediatric advice in the care and management of a fetus at risk. This management may involve a few different scenarios.

1. The pediatrician may be asked about the risk to a child of a parent with Marfan syndrome. The risk of inheriting the genetic defect in Marfan syndrome is 50%, consistent with autosomal dominant inheritance. Often, expectant parents are concerned about the severity of the disorder in the next generation. Variability of the Marfan phenotype is extensive but is more similar among affected family members, suggesting that the genetic defect is largely responsible for the phenotype. Most people with classic Marfan syndrome do not have children with a much more severe phenotype, such as neonatal Marfan syndrome.⁷¹ One should also be aware of the consequences that may affect the pregnancy outcome for women with Marfan syndrome. As mentioned previously, women with an aortic root greater than 4.5 cm in diameter should avoid pregnancy or undergo elective aortic grafting before becoming pregnant.⁷² Aortic dissection or rupture has occurred in women with an aorta less than 5.0 cm, which may result in significant morbidity and mortality of the fetus/infant and the expectant mother.
2. Parents of a child with Marfan syndrome may ask about recurrence risk of Marfan syndrome in subsequent pregnancies. This issue may best be explained by a geneticist. In short, 1 of the parents may either be unrecognized as having Marfan syndrome (therefore, recurrence risk is 50%) or both parents may be unaffected and, therefore, carry only a slight chance of having a low level of germline mosaicism (with anticipated recurrence risk of 2%–3%). Because of a high occurrence of unrecognized Marfan syndrome in parents of a child with Marfan syndrome, it is advisable for both parents to undergo further evaluation to establish their own personal risk as well as the risk for subsequent pregnancies.
3. An expectant couple may have a fetus with concerning features of neonatal Marfan syndrome discovered through prenatal ultrasonography or even fetal MRI. Ultrasonographic findings may include unusually long limbs and congenital heart disease and are often detected in the third trimester.⁷³ Genetic testing for *FBN1* mutations by using amniocentesis may be helpful to confirm the diagnosis of Marfan syndrome and to reveal specific mutations in *FBN1* that may be more typically associated with neonatal Marfan syndrome and, therefore, reduced survivability.

Neonatal Marfan Syndrome

Neonatal Marfan syndrome is the most severe disorder attributable to a fibrillinopathy. Features overlap significantly with classic Marfan syndrome but are more severe. Infants with neonatal Marfan syndrome are long with simple/crumpled ears, aged-appearing face, enlarged corneas, ectopia lentis, chest deformity, large feet, arachnodactyly, and contractures.⁷⁴ Respiratory insufficiency is common as a result of an abnormally pliant chest wall and emphysematous changes in the lungs. Cardiac abnormalities are severe and include polyvalvular dysplasia and aortic dilation. Mortality is

high within the first year of life because of cardiac failure secondary to severe mitral valve regurgitation. Almost all cases of neonatal Marfan syndrome are sporadic and are associated with mutations clustering within exons 24 through 32 of *FBN1*.

Support Groups

National Marfan Foundation

22 Manhasset Ave,

Port Washington, NY 11050

Phone: 1-800-8-MARFAN ext 10 (1-800-862-7326); 1-516-883-8712

Fax: 1-516-883-8040

E-mail: staff@marfan.org

Web site: www.marfan.org

Canadian Marfan Association

Centre Plaza Postal Outlet

128 Queen St South

PO Box 42257

Mississauga, ONT, L5M4Z0, Canada

Phone: 866-722-1722 (toll-free); 905-826-3223

Fax: 905-826-2125

E-mail: info@marfan.ca

Web site: www.marfan.ca

Marfan Association UK

Rochester House

5 Aldershot Rd

Fleet, Hampshire

GU51 3NG, England

Phone: (0) 1252 810472

E-mail: support@marfan.org.uk

Web site: www.marfan.org.uk

Lead Authors

Brad T. Tinkle, MD, PhD

Howard M. Saal, MD

Committee on Genetics, 2011–2012

Robert A. Saul, MD, Chairperson

Stephen R. Braddock, MD

Emily Chen, MD, PhD

Debra L. Freedenberg, MD

Marilyn C. Jones, MD

James M. Perrin, MD

Beth Anne Tarini, MD

Former Committee on Genetics Members

Howard M. Saal, MD, Contributor

Brad T. Tinkle, MD, PhD

Liaisons

Sara Copeland, MD Ñ *Maternal and Child Health Bureau/Health Resources and Services Administration*

Katrina M. Dipple, MD, PhD Ñ *American College of Medical Genetics*

W. Allen Hogge, MD Ñ *American Congress of Obstetricians and Gynecologists*

Melissa A. Parisi, MD, PhD Ñ *Eunice Kennedy Shriver National Institute of Child Health and Human Development*

Stuart K. Shapira, MD, PhD Ñ *Centers for Disease Control and Prevention*

Staff

Paul Spire

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The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

All clinical reports from the American Academy of Pediatrics automatically expire 5 years after publication unless reaffirmed, revised, or retired at or before that time.

References

1 Dietz HC, Loeys B, Carta L, Ramirez F. Recent progress towards a molecular understanding of Marfan syndrome. *Am J Med Genet C Semin Med Genet.* 2005;139C(1):4Ð9[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

2 Dean JC. Marfan syndrome: clinical diagnosis and management. *Eur J Hum Genet.* 2007;15(7):724Ð733 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

3 Loeys BL, Dietz HC, Braverman AC, et al. The revised Ghent nosology for the Marfan syndrome. *J Med Genet.* 2010;47(7):476Ð485[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

4 Attanasio M, Lapini I, Evangelisti L, et al. FBN1 mutation screening of patients with Marfan syndrome and related disorders: detection of 46 novel FBN1 mutations. *Clin Genet.* 2008;74(1):39Ð46[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

5 Loeys B, De Backer J, Van Acker P, et al. Comprehensive molecular screening of the FBN1 gene favors locus homogeneity of classical Marfan syndrome. *Hum Mutat.* 2004;24(2):140E146[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

6 Rybczynski M, Bernhardt AM, Rehder U, et al. The spectrum of syndromes and manifestations in individuals screened for suspected Marfan syndrome. *Am J Med Genet A.* 2008;146A(24):3157E3166[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

7 Faivre L, Masurel-Paulet A, Collod-Bęroud G, et al. Clinical and molecular study of 320 children with Marfan syndrome and related type I fibrillinopathies in a series of 1009 probands with pathogenic FBN1 mutations. *Pediatrics.* 2009;123(1):391E398[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

8 Summers KM, West JA, Peterson MM, Stark D, McGill JJ, West MJ. Challenges in the diagnosis of Marfan syndrome. *Med J Aust.* 2006;184(12):627E631[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

9 Erkula G, Jones KB, Sponseller PD, Dietz HC, Pyeritz RE. Growth and maturation in Marfan syndrome. *Am J Med Genet.* 2002;109(2):100E115[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

10 Lee JM, Howell JD. Tall girls: the social shaping of a medical therapy. *Arch Pediatr Adolesc Med.* 2006;160(10):1035E1039[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

11 Rand-Hendriksen S, Sęrensen I, Holmstręm H, Andersson S, Finset A. Fatigue, cognitive functioning and psychological distress in Marfan syndrome, a pilot study. *Psychol Health Med.* 2007;12(3):305E313[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

12 van Dijk N, Boer MC, Mulder BJ, van Montfrans GA, Wieling W. Is fatigue in Marfan syndrome related to orthostatic intolerance? *Clin Auton Res.* 2008;18(4):187E193[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

13 Scherer LR, Am PH, Dressel DA, Pyeritz RM, Haller JA Jr. Surgical management of children and young adults with Marfan syndrome and pectus excavatum. *J Pediatr Surg.* 1988;23(12):1169E1172[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

14 Lawson ML, Mellins RB, Paulson JF, et al. Increasing severity of pectus excavatum is associated with reduced pulmonary function. *J Pediatr.* 2011;159(2):256.e2E261.e2

15 Lesbo M, Tang M, Nielsen HH, et al. Compromised cardiac function in exercising teenagers with pectus excavatum. *Interact Cardiovasc Thorac Surg.* 2011;13(4):377E380[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

16 Sponseller PD, Hobbs W, Riley LH III, Pyeritz RE. The thoracolumbar spine in Marfan syndrome. *J Bone Joint Surg Am*. 1995;77(6):867-876 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

17 Glard Y, Launay F, Edgard-Rosa G, Collignon P, Jouve JL, Bollini G. Scoliotic curve patterns in patients with Marfan syndrome. *J Child Orthop*. 2008;2(3):211-216 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

18 Di Silvestre M, Gregg T, Giacomini S, Cioni A, Bakaloudis G, Lolli F, Parisini P. Surgical treatment for scoliosis in Marfan syndrome. *Spine (Phila Pa 1976)*. 2005;30(20):E597-E604

19 Shirley ED, Sponseller PD. Marfan syndrome. *J Am Acad Orthop Surg*. 2009;17(9):572-581 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

20 Lundby R, Kirkhus E, Rand-Hendriksen S, Hald J, Pripp AH, Smith HJ. CT of the hips in the investigation of protrusio acetabuli in Marfan syndrome. A case control study. *Eur Radiol*. 2011;21(7):1485-1491 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

21 Dunlop CC, Jones CW, Maffulli N. Protrusio acetabuli. *Bull Hosp Jt Dis*. 2005;62(3-4):105-114

22 Sponseller PD, Jones KB, Ahn NU, Erkula G, Foran JR, Dietz HC III. Protrusio acetabuli in Marfan syndrome: age-related prevalence and associated hip function. *J Bone Joint Surg Am*. 2006;88(3):486-495 [[PubMed](#)]

[Google Scholar](#)

23 Bird HA. Joint hypermobility. *Musculoskelet Care*. 2007;5(1):4-19 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

24 Dietz HC. Marfan syndrome. In: Pagon RA, Adam MP, Bird TD, et al, eds. *GeneReviews*. Seattle, WA: University of Washington; 1993-2013. Available at: www.ncbi.nlm.nih.gov/books/NBK1335/. Accessed August 18, 2013

25 Ting BL, Mathur D, Loeys BL, Dietz HC III, Sponseller PD. The diagnostic value of the facial features of Marfan syndrome. *J Child Orthop*. 2010;4(6):545-551 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

26 Giampietro PF, Peterson M, Schneider R, et al. Assessment of bone mineral density in adults and children with Marfan syndrome. *Osteoporos Int*. 2003;14(7):559-563 [[PubMed](#)]

[Google Scholar](#)

27 Moura B, Tubach F, Sulpice M, et al Multidisciplinary Marfan Syndrome Clinic Group. Bone mineral density in Marfan syndrome. A large case-control study. *Joint Bone Spine*. 2006;73(6):733-735 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

28 Giampietro PF, Peterson MG, Schneider R, et al. Bone mineral density determinations by dual-energy x-ray absorptiometry in the management of patients with Marfan syndrome—some factors which affect the

measurement. *HSS J*. 2007;3(1):89Ð92[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

29 Nemet AY, Assia EI, Apple DJ, Barequet IS. Current concepts of ocular manifestations in Marfan syndrome. *Surv Ophthalmol*. 2006;51(6):561Ð575[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

30 Maumenee IH. The eye in the Marfan syndrome. *Trans Am Ophthalmol Soc*. 1981;79:684Ð733[[PubMed](#)]

[Google Scholar](#)

31 Kang HK, Luff AJ. Management of retinal detachment: a guide for non-ophthalmologists. *BMJ*. 2008;336(7655):1235Ð1240[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

32 Hollands H, Johnson D, Brox AC, Almeida D, Simel DL, Sharma S. Acute-onset floaters and flashes: is this patient at risk for retinal detachment? *JAMA*. 2009;302(20):2243Ð2249[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

33 Morrison D, Sternberg P, Donahue S. Anterior chamber intraocular lens (ACIOL) placement after pars plana lensectomy in pediatric Marfan syndrome. *J AAPOS*. 2005;9(3):240Ð242[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

34 Stuart AG, Williams A. Marfan's syndrome and the heart. *Arch Dis Child*. 2007;92(4):351Ð356[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

35 Sisk HE, Zahka KG, Pyeritz RE. The Marfan syndrome in early childhood: analysis of 15 patients diagnosed at less than 4 years of age. *Am J Cardiol*. 1983;52(3):353Ð358[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

36 Meijboom LJ, Timmermans J, Zwinderman AH, Engelfriet PM, Mulder BJ. Aortic root growth in men and women with the Marfan's syndrome. *Am J Cardiol*. 2005;96(10):1441Ð1444[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

37 Cañadas V, Vilacosta I, Bruna I, Fuster V. Marfan syndrome. Part 2: treatment and management of patients. *Nat Rev Cardiol*. 2010;7(5):266Ð276[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

38 Roman MJ, Devereux RB, Kramer-Fox R, O'Loughlin J. Two-dimensional echocardiographic aortic root dimensions in normal children and adults. *Am J Cardiol*. 1989;64(8):507Ð512[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

39 Sharkey AM. Cardiovascular management of Marfan syndrome in the young. *Curr Treat Options Cardiovasc Med*. 2006;8(5):396Ð402[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

40 Rossi-Foulkes R, Roman MJ, Rosen SE, et al. Phenotypic features and impact of beta blocker or calcium antagonist therapy on aortic lumen size in the Marfan syndrome. *Am J Cardiol*. 1999;83(9):1364-1368 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

41 Kroner BL, Tolunay HE, Basson CT, et al. The National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC): results from phase I and scientific opportunities in phase II. *Am Heart J*. 2009;162(4):627.e1-632.e1

42 Habashi JP, Judge DP, Holm TM, et al. Losartan, an AT1 antagonist, prevents aortic aneurysm in a mouse model of Marfan syndrome. *Science*. 2006;312(5770):117-121 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

43 Brooke BS, Habashi JP, Judge DP, Patel N, Loeys B, Dietz HC III. Angiotensin II blockade and aortic-root dilation in Marfan's syndrome. *N Engl J Med*. 2008;358(26):2787-2795 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

44 Gott VL, Cameron DE, Alejo DE, et al. Aortic root replacement in 271 Marfan patients: a 24-year experience. *Ann Thorac Surg*. 2002;73(2):438-443 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

45 Settepani F, Szeto WY, Pacini D, et al. Reimplantation valve-sparing aortic root replacement in Marfan syndrome using the Valsalva conduit: an intercontinental multicenter study. *Ann Thorac Surg*. 2007;83(2):S769-S773, discussion S785-S790 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

46 Cameron DE, Alejo DE, Patel ND, et al. Aortic root replacement in 372 Marfan patients: evolution of operative repair over 30 years. *Ann Thorac Surg*. 2009;87(5):1344-1349, discussion 1349-1350 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

47 Gillinov AM, Zehr KJ, Redmond JM, et al. Cardiac operations in children with Marfan's syndrome: indications and results. *Ann Thorac Surg*. 1997;64(4):1140-1144, discussion 1144-1145 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

48 Finkbohner R, Johnston D, Crawford ES, Coselli J, Milewicz DM. Marfan syndrome. Long-term survival and complications after aortic aneurysm repair. *Circulation*. 1995;91(3):728-733 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

49 Yetman AT, Roosevelt GE, Veit N, Everitt MD. Distal aortic and peripheral arterial aneurysms in patients with Marfan syndrome. *J Am Coll Cardiol*. 2011;58(24):2544-2545 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

50 Pelliccia A, Zipes DP, Maron BJ. Bethesda Conference #36 and the European Society of Cardiology Consensus Recommendations revisited a comparison of U.S. and European criteria for eligibility and disqualification of competitive athletes with cardiovascular abnormalities. *J Am Coll Cardiol*. 2008;52(24):1990-1996 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

51 Silverman DI, Burton KJ, Gray J, et al. Life expectancy in the Marfan syndrome. *Am J Cardiol*. 1995;75(2):157-160 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

52 Gray JR, Bridges AB, West RR, et al. Life expectancy in British Marfan syndrome populations. *Clin Genet*. 1998;54(2):124-128 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

53 Wood JR, Bellamy D, Child AH, Citron KM. Pulmonary disease in patients with Marfan syndrome. *Thorax*. 1984;39(10):780-784 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

54 Giske L, Stanghelle JK, Rand-Hendriksen S, Strøm V, Wilhelmsen JE, Røge C. Pulmonary function, working capacity and strength in young adults with Marfan syndrome. *J Rehabil Med*. 2003;35(5):221-228 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

55 Kohler M, Blair E, Risby P, et al. The prevalence of obstructive sleep apnoea and its association with aortic dilatation in Marfan's syndrome. *Thorax*. 2009;64(2):162-166 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

56 Cistulli PA, Gotsopoulos H, Sullivan CE. Relationship between craniofacial abnormalities and sleep-disordered breathing in Marfan's syndrome. *Chest*. 2001;120(5):1455-1460 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

57 Cohen PR, Schneiderman P. Clinical manifestations of the Marfan syndrome. *Int J Dermatol*. 1989;28(5):291-299 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

58 Rand-Hendriksen S, Lundby R, Tjeldhom L, et al. Prevalence data on all Ghent features in a cross-sectional study of 87 adults with proven Marfan syndrome. *Eur J Hum Genet*. 2009;17(10):1222-1230 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

59 Foran JR, Pyeritz RE, Dietz HC, Sponseller PD. Characterization of the symptoms associated with dural ectasia in the Marfan patient. *Am J Med Genet A*. 2005;134A(1):58-65 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

60 Nallamshetty L, Ahn NU, Ahn UM, et al. Dural ectasia and back pain: review of the literature and case report. *J Spinal Disord Tech*. 2002;15(4):326-329 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

61 Milledge JT, Ades LC, Cooper MG, Jaumees A, Onikul E. Severe spontaneous intracranial hypotension and Marfan syndrome in an adolescent. *J Paediatr Child Health*. 2005;41(1-2):68-71 [[PubMed](#)]

[Google Scholar](#)

62 Rosser T, Finkel J, Vezina G, Majd M. Postural headache in a child with Marfan syndrome: case report and review of the literature. *J Child Neurol*. 2005;20(2):153-155[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

63 Maron BJ, Chaitman BR, Ackerman MJ, et al Working Groups of the American Heart Association Committee on Exercise, Cardiac Rehabilitation, and Prevention Councils on Clinical Cardiology and Cardiovascular Disease in the Young. Recommendations for physical activity and recreational sports participation for young patients with genetic cardiovascular diseases. *Circulation*. 2004;109(22):2807-2816[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

64 De Bie S, De Paepe A, Delvaux I, Davies S, Hennekam RC. Marfan syndrome in Europe. *Community Genet*. 2004;7(4):216-225[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

65 Fusar-Poli P, Klersy C, Stramesi F, Callegari A, Arbustini E, Politi P. Determinants of quality of life in Marfan syndrome. *Psychosomatics*. 2008;49(3):243-248[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

66 Raanani E, Ghosh P. The multidisciplinary approach to the Marfan patient. *Isr Med Assoc J*. 2008;10(3):171-174[[PubMed](#)]

[Google Scholar](#)

67 Goland S, Barakat M, Khatri N, Elkayam U. Pregnancy in Marfan syndrome: maternal and fetal risk and recommendations for patient assessment and management. *Cardiol Rev*. 2009;17(6):253-262[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

68 Meijboom LJ, Vos FE, Timmermans J, Boers GH, Zwinderman AH, Mulder BJ. Pregnancy and aortic root growth in the Marfan syndrome: a prospective study. *Eur Heart J*. 2005;26(9):914-920[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

69 Anum EA, Hill LD, Pandya A, Strauss JF III. Connective tissue and related disorders and preterm birth: clues to genes contributing to prematurity. *Placenta*. 2009;30(3):207-215[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

70 Meijboom LJ, Drenthen W, Pieper PG, et al ZAHARA investigators. Obstetric complications in Marfan syndrome. *Int J Cardiol*. 2006;110(1):53-59[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

71 Tekin M, Cengiz FB, Ayberkin E, et al. Familial neonatal Marfan syndrome due to parental mosaicism of a missense mutation in the FBN1 gene. *Am J Med Genet A*. 2007;143A(8):875-880[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

72 Volach V, Elami A, Gilon D, Pollak A, Ginosar Y, Ezra Y. Pregnancy in Marfan syndrome after aortic root replacement: a case report and review of the literature. *Congenit Heart Dis*. 2006;1(4):184-188[[PubMed](#)]

[Google Scholar](#) [Crossref](#)

73 Burke LW, Pyeritz RE. Prenatal diagnosis of connective tissue disorders. In: Milunsky A, ed. *Genetic Disorders and the Fetus: Diagnosis, Prevention and Treatment*. 4th ed. Baltimore, MD: Johns Hopkins University Press; 1998:612D634

[Google Scholar](#)

74 Sutherell J, Zarate Y, Tinkle BT, et al. Novel fibrillin 1 mutation in a case of neonatal Marfan syndrome: the increasing importance of early recognition. *Congenit Heart Dis*. 2007;2(5):342D346 [[PubMed](#)]

[Google Scholar](#) [Crossref](#)

75 Geva T, Sanders SP, Diogenes MS, Rockenmacher S, Van Praagh R. Two-dimensional and Doppler echocardiographic and pathologic characteristics of the infantile Marfan syndrome. *Am J Cardiol*. 1990;65(18):1230D1237 [[PubMed](#)]

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