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. 

**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.
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. 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). Mean final height was 191.3 ± 9 cm (75 in) for males and 175.4 ± 8.2 cm (69 in) for females.

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).

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. 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.

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.

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. 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.

### TABLE 1 Revised Ghent Diagnostic Criteria for Marfan Syndrome

<table>
<thead>
<tr>
<th>Diagnosis of definitive Marfan syndrome (any of the following)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Aortic root ≥ z score and ectopia lentis</td>
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<tr>
<td>- Aortic root ≥ z score and FBN1 mutation</td>
</tr>
<tr>
<td>- Aortic root ≥ z score and systemic score ≥ 7</td>
</tr>
<tr>
<td>- Ectopia lentis and FBN1 mutation known to be associated with Marfan syndrome</td>
</tr>
<tr>
<td>- Positive family history of Marfan syndrome and ectopia lentis</td>
</tr>
<tr>
<td>- Positive family history of Marfan syndrome and systemic score ≥ 7</td>
</tr>
<tr>
<td>- Positive family history of Marfan syndrome and aortic root ≥ z score in those &lt;20 y of age or ≥ 2 z score in those &gt;20 y of age</td>
</tr>
</tbody>
</table>

Diagnosis of potential Marfan syndrome

- FBN1 mutation with aortic root with a z score <3 in those <20 y of age

Many features of Marfan syndrome are seen in isolation as well as in other genetic syndromes (Table 3). 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.

### TABLE 2 Systemic Scoring System for the Revised Ghent Diagnostic Criteria for Marfan Syndrome (Shown in Table 1)

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist and thumb sign</td>
<td>3</td>
</tr>
<tr>
<td>Wrist or thumb sign</td>
<td>1</td>
</tr>
<tr>
<td>Pectus carinatum</td>
<td>2</td>
</tr>
<tr>
<td>Pectus excavatum or chest asymmetry</td>
<td>1</td>
</tr>
<tr>
<td>Hindfoot deformity (eg, valgus)</td>
<td>2</td>
</tr>
<tr>
<td>Pes planus</td>
<td>1</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2</td>
</tr>
<tr>
<td>Dural ectasia</td>
<td>2</td>
</tr>
<tr>
<td>Protrusio acetabulæ</td>
<td>2</td>
</tr>
<tr>
<td>Reduced upper-to-lower segment ratio and increased arm-span-to-height ratio</td>
<td>1</td>
</tr>
<tr>
<td>Scoliosis or thoracolumbar kyphosis</td>
<td>1</td>
</tr>
<tr>
<td>Reduced elbow extension</td>
<td>1</td>
</tr>
<tr>
<td>Craniofacial features: 3 of the following—dolichocephaly, downward-slanting palpebral fissures, enophthalmos, retrognathia, and malar hypoplasia</td>
<td>1</td>
</tr>
<tr>
<td>Skin striae</td>
<td>1</td>
</tr>
<tr>
<td>Myopia</td>
<td>1</td>
</tr>
<tr>
<td>Mitral valve prolapse</td>
<td>1</td>
</tr>
</tbody>
</table>

Adapted from Leys et al. Z score calculations are based on Roman et al.

### 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). Overgrowth of the ribs can push the sternum inward (pectus excavatum) or outward (pectus carinatum). Nearly two-thirds of patients with Marfan syndrome show a paucity of muscle mass and fat stores despite adequate caloric intake. Weight is often below the 50th percentile for age.
syndrome will develop pectus excavatum, which is often perceived as a disturbing physical feature by teenagers.\textsuperscript{13} The pectus deformity can be severe and, in extreme circumstances, can interfere with pulmonary functioning, warranting surgical intervention.\textsuperscript{14} Pectus excavatum may also have a detrimental effect on cardiac function, especially during submaximal exercising\textsuperscript{15} 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 syndrome\textsuperscript{20};
however, it is not unique to this condition and is seen in a number of infectious, inflammatory, metabolic, genetic, neoplastic, and traumatic conditions. In Marfan syndrome, the protrusio acetabuli is often asymptomatic, and surgical intervention is rarely indicated. 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. 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. 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.

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. The palate is often highly arched and narrowed (Fig 7).

Decreased bone density has been documented in the lumbar and hip regions in patients with Marfan syndrome. The etiology of this bone loss remains speculative, but no significant increase in bone fracture rates has been seen.

**OCULAR**

Myopia is the most common ocular feature and often progresses rapidly during childhood. 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. 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. 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.

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. 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. The age of onset and rate of progression of aortic dilation are highly variable. As the aneurysm enlarges, the aortic anulus may 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.

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. 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. 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. 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. 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. 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

FIGURE 6
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
High arched (“steepled”) palate.
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 work[42] 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. 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. Increased nasal resistance attributable to craniofacial abnormalities, such as a high arched palate, micrognathia with possible glossopaties, such as a 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. 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. 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.

**INTEGUMENT**

Approximately two-thirds of people with Marfan syndrome develop stretch marks of the skin. 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.
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 complications for women with Marfan syndrome and should be approached with careful deliberation.67 If the aortic root is 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 or 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. 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. Respiratory insufficiency is common as a result of an abnormally pliant chest wall and emotional 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
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