Genetics	Marfan syndrome

REFERRAL GUIDELINE

Guidelines Referenced	1. http://pediatrics.aappublications.org/content/pediatrics/132/4/e1059.full.pdf 2. http://diagnosticcriteria.org/marfan/reprints/Loeys-2010-JMedGenet-47-p476-485.pdf 3. https://www.uptodate.com/contents/management-of-marfan-syndrome-and-related-disorders 4. http://www.marfan.org
Background	Marfan syndrome is an autosomal dominant, multisystem disorder of connective tissue with extensive clinical variability. It is a relatively common condition, with approximately 1 in 5000 people affected. 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 (1). Marfan syndrome is caused by defects in *FBN1*, the gene that codes for the protein fibrillin 1. Approximately one-quarter of cases occur as a result of a new mutation, with the remainder inherited from an affected parent (1). The diagnosis of Marfan syndrome is clinically based on well-defined criteria (revised Ghent diagnostic criteria), and should be clearly established when possible. Since many of the more specific clinical features are age dependent, children and adolescents may not fulfill formal diagnostic criteria at the time of their initial evaluation (2). Genetic testing for Marfan syndrome is available but is not required to make the diagnosis. However, it can be performed to confirm the clinical suspicion. **Revised Ghent diagnostic criteria (2)** The diagnosis can be made when 1 of the following 4 scenarios are present: 1. The presence of aortic root dilation (>2SD above the mean for BSA) or dissection and ectopia lentis (lens dislocation). 2. The presence of aortic root dilation (>2SD above the mean for BSA) or dissection and the identification of a pathologic mutation in the fibrillin 1 gene. 3. The presence of ectopia lentis and the identification of a pathologic fibrillin 1 mutation. 4. The presence of aortic root dilation (>2SD above the mean for BSA) or dissection and the presence of systemic findings with a score equal to or greater to 7 points (and other overlapping connective tissue disorders have been considered and ruled out). The systemic scoring system is as follows: • Wrist AND thumb sign [3pts]; wrist OR thumb sign [1pt] • Pectus carinatum deformity [2pts]; pectus excavatum or chest asymmetry [1pt] • Hind foot deformity [2pts]; plain pes planus [1pt] • Pneumothorax [2pts] • Dural ectasia [2pts] • Protrusio acetabuli [2pts] • Reduced upper segment/lower segment ratio and increased arm-height ratio and no severe scoliosis [1pt] • Scoliosis (>20°) or thoracolumbar kyphosis [1pt] • Reduced elbow extension [1pt] • Facial features (3/5) [1pt] (dolichocephaly, enophthalmos, down-slanting palpebral fissures, malar hypoplasia, retrognathia). • Skin striae [1pt] • Myopia greater than 3 diopters [1pt] • Mitral valve prolapse (all types) [1pt]

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Initial Evaluation	**Medical history:** • For new patients to primary care: collect any previous diagnostic info including a known diagnosis of Marfan syndrome and/or results of a pathogenic fibrillin 1 mutation • Dilation or dissection of the aorta • Dislocated lenses of the eyes • Tall stature **Physical exam:** • Growth parameters • Skeletal, skin, and facial features per the revised Ghent criteria **Family history:** • Known diagnosis of Marfan syndrome and/or a pathogenic fibrillin 1 mutation • Dilation or dissection of the aorta • Dislocated lenses of the eyes • Tall stature • Sudden death of unknown cause
Pre-Visit Work Up	• Referral to cardiology with echocardiogram • Referral to ophthalmology

When to Refer	• New patients with h/o either Marfan syndrome dx and/or a pathogenic fibrillin 1 mutation
	• Meets the Ghent criteria:
	  ○ Aortic root dilation with a Z-score greater than 2
	  ○ Lens dislocation
	  ○ Systemic features score of 7 or greater
	• Family history of Marfan syndrome
	• Questions regarding a referral: please phone 828-213-0022 (between 8a-5p) or 828-213-1111 and ask for the geneticist on call

Co-management Strategy (as appropriate)	**Specialist scope of care** If diagnosis of Marfan syndrome is not known: • Initial evaluation with appropriate studies and referrals as needed to establish a dx. • Other referrals as needed depending on the patient's clinical features. • Follow up will depend on various factors (i.e., age, complexity); Q1-3 years or as needed. If diagnosis of Marfan syndrome is known: • Initial evaluation with studies and referrals as needed depending on the patient's clinical features. Follow up will depend on various factors (i.e., age, complexity); Q1-3 years or as needed.
	Primary care scope of care If known diagnosis of Marfan syndrome: • Ensure appropriate care with recommended specialists (cardiology, ophthalmology, orthopedics and other specialists as needed). • Individuals with Marfan syndrome should avoid contact and/or competitive sports, isometric exercise, and agents that stimulate the cardiovascular system (e.g., decongestants and caffeine). If patient determined not to have Marfan syndrome: Routine care based on the patient's specific medical needs. Refer back to Genetics if new concerns.
Return to Primary Care	Every patient will be returned to their primary care physician after their genetics evaluation, with recommendations made depending on the patient's clinical findings.