Marfan 101:
Understanding the Basics

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Objectives

- Learn about Marfan syndrome including what causes this condition, who is affected, and what are common signs
- Consider related disorders with findings that may overlap with Marfan syndrome
- Discuss how Marfan syndrome is diagnosed and common tests to expect when undergoing evaluation
- Briefly review recommended management

Marfan Syndrome

- **Genetic disorder** that affects the body's connective tissue

- What is **"connective tissue"?**
  - A substance made up of proteins that is found throughout our bodies and holds our cells, organs and tissues together
  - *Fibrillin-1* is the protein specifically affected in Marfan syndrome
  - Defects in the gene which makes *fibrillin-1* cause an increase in *transforming growth factor beta* or *TGF-β*, which causes problems with connective tissue throughout the body

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Marfan Syndrome

- **Prevalence**: 1 per 5000 individuals
  - Males = females
  - All races and ethnic groups equally affected
- **Inherited condition** with autosomal dominant transmission
  - 50% chance that a person with MFS will pass along the mutation each time they have a child
  - 25% *spontaneous* mutations which occur for the first time in a family

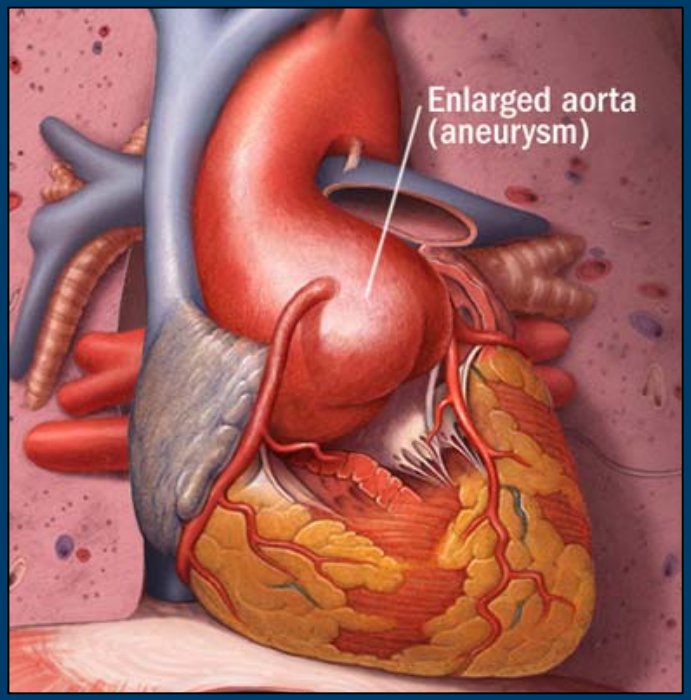
What are the signs of Marfan syndrome?

- Features may be present at birth or may develop and worsen with increasing age
- **Variable expression** means that every individual is affected differently
- **Affected systems** may include:
  - Heart and blood vessels
  - Bones and joints
  - Eyes
  - Lungs
  - Skin
  - Spinal cord

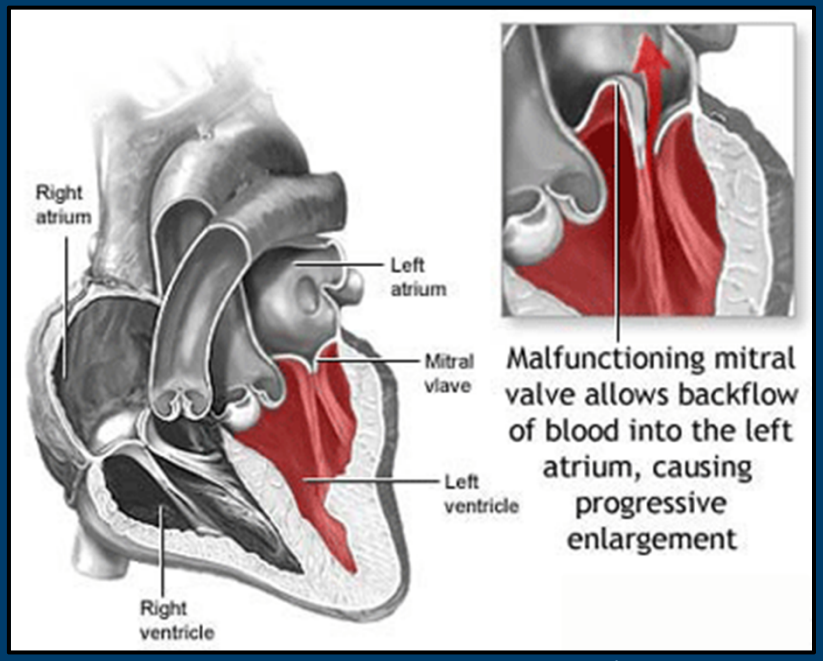
Disorders related to Marfan syndrome

- Involve the connective tissue and may have overlapping findings
- May also have progressive enlargement of the aorta
- Some **related disorders** include:
  - Loeys-Dietz syndrome (LDS)
  - Ehlers-Danlos syndrome (EDS)
  - Familial Thoracic Aortic Aneurysm and Dissection (FTAAD) syndrome

Heart and blood vessels



www.mayoclinic.org



www.heartsurgeons.com

Progressive aortic enlargement

- Aneurysm
- Aortic valve insufficiency
- Aortic dissection and/or rupture

Mitral valve prolapse

- “Floppy” valve
- Mitral insufficiency
- Abnormal heart rhythm

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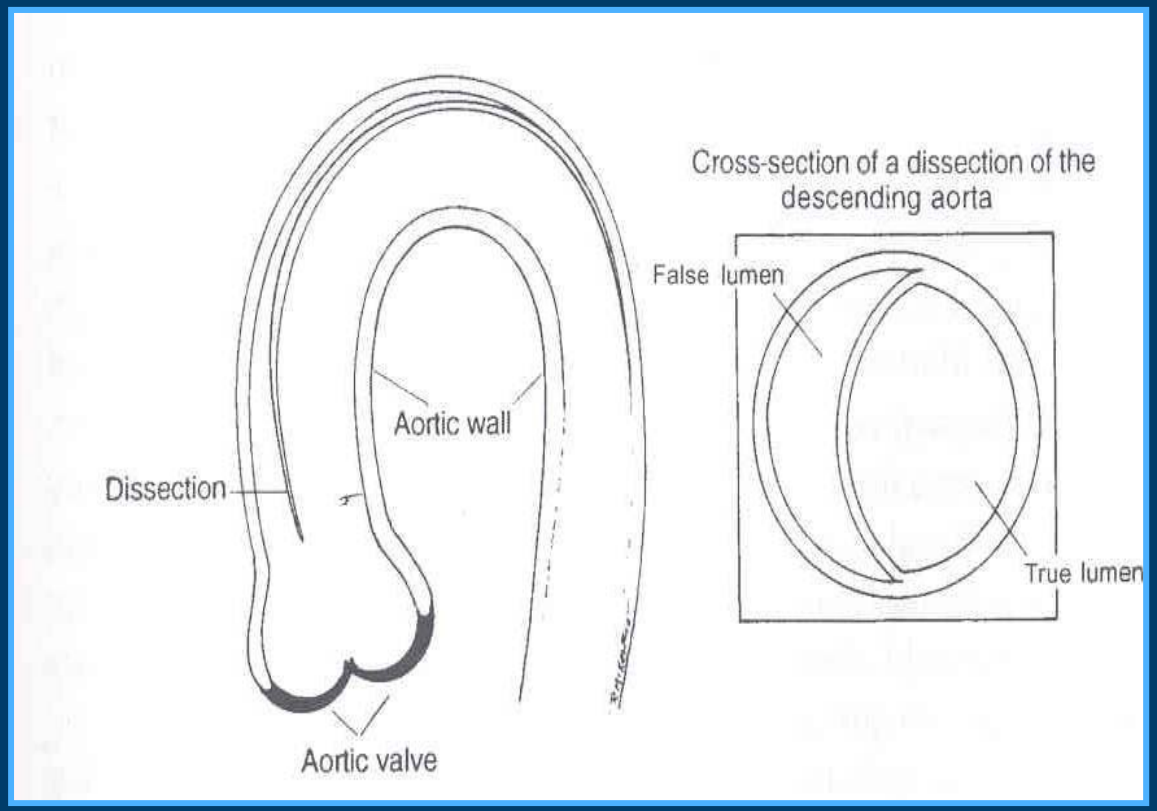
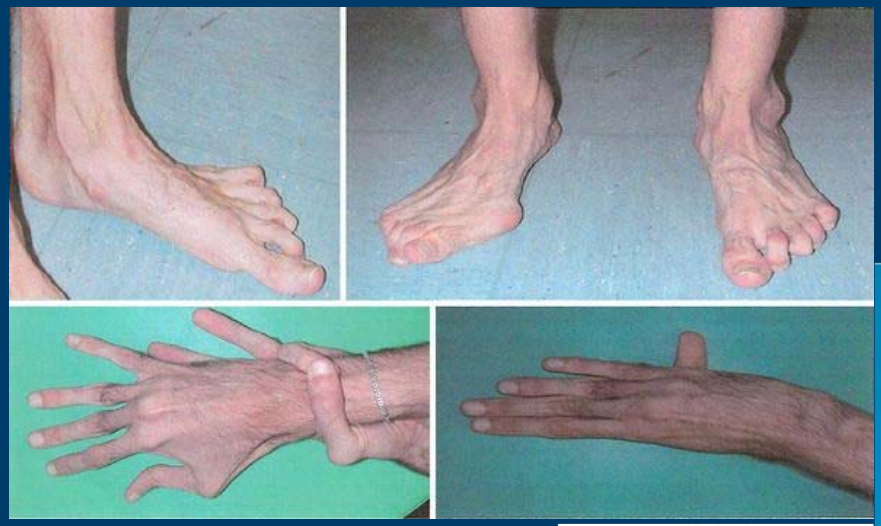
Aortic dissection

Associated with severe pain in anterior chest, back and/or neck



Potentially life-threatening emergency –
immediate medical evaluation should be pursued

Bones and joints



Flat feet
Hypermobile joints
Long fingers

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Chest wall abnormalities

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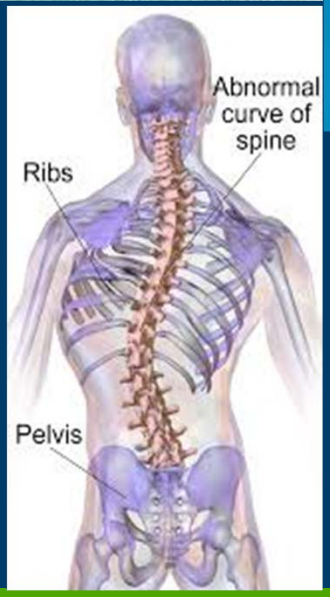

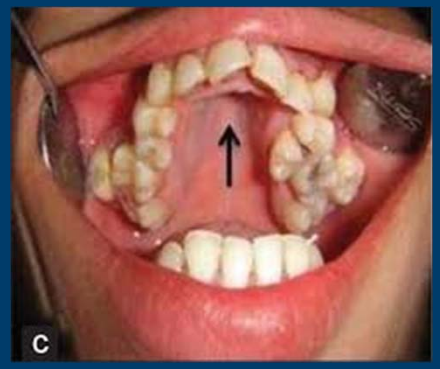

High arched palate
Dental crowding

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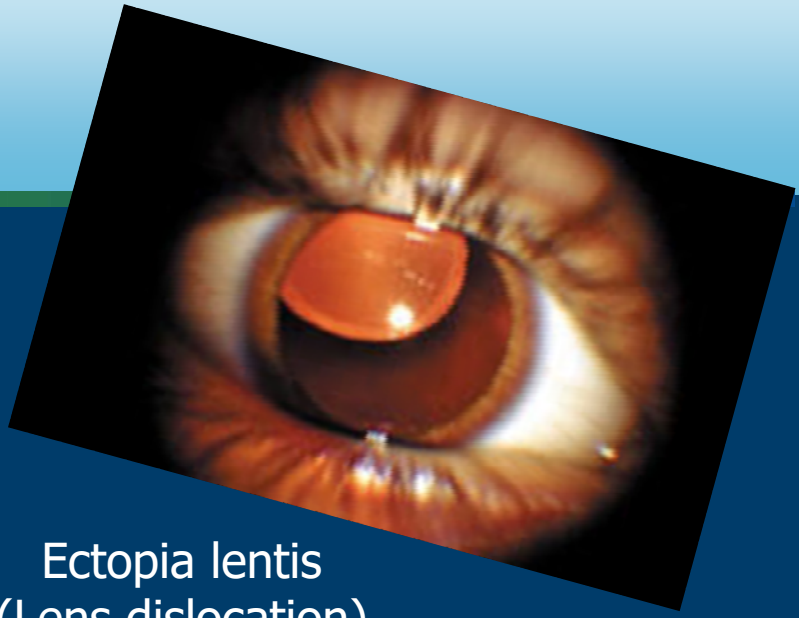
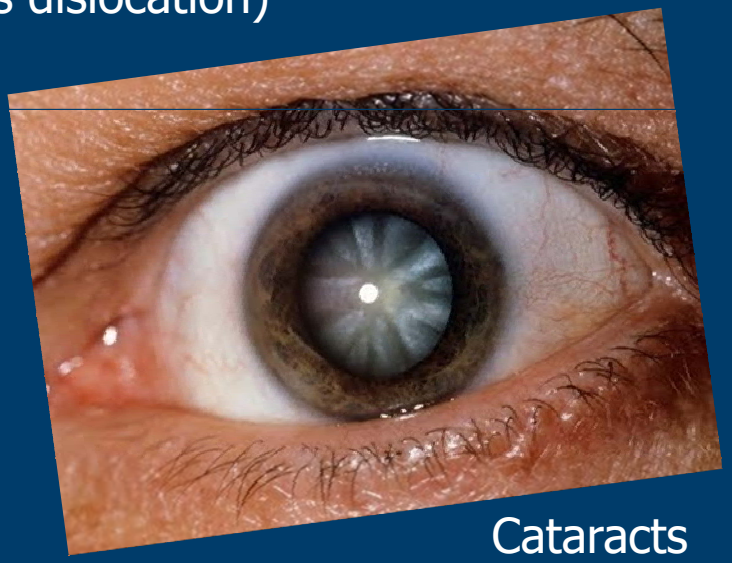
Ocular system

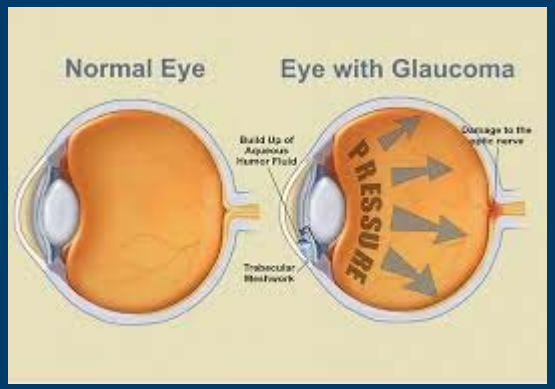
Myopia = nearsightedness



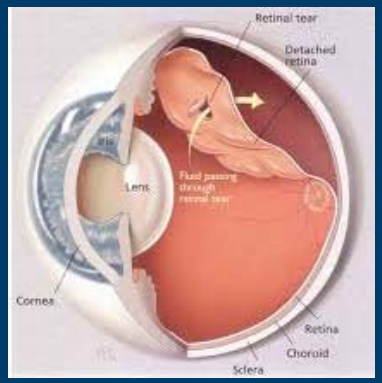
Ectopia lentis
(Lens dislocation)



Cataracts



Glaucoma



Retinal detachment

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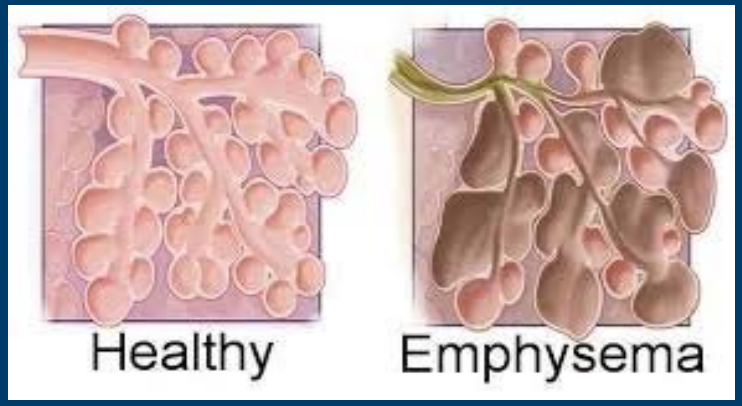
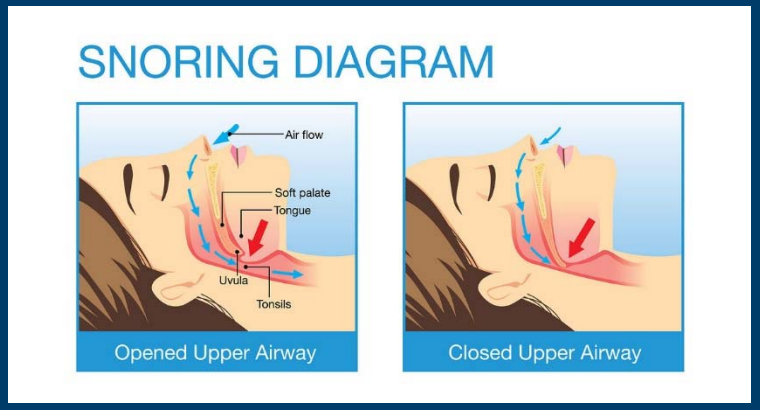
Pulmonary

Pneumothorax = sudden lung collapse

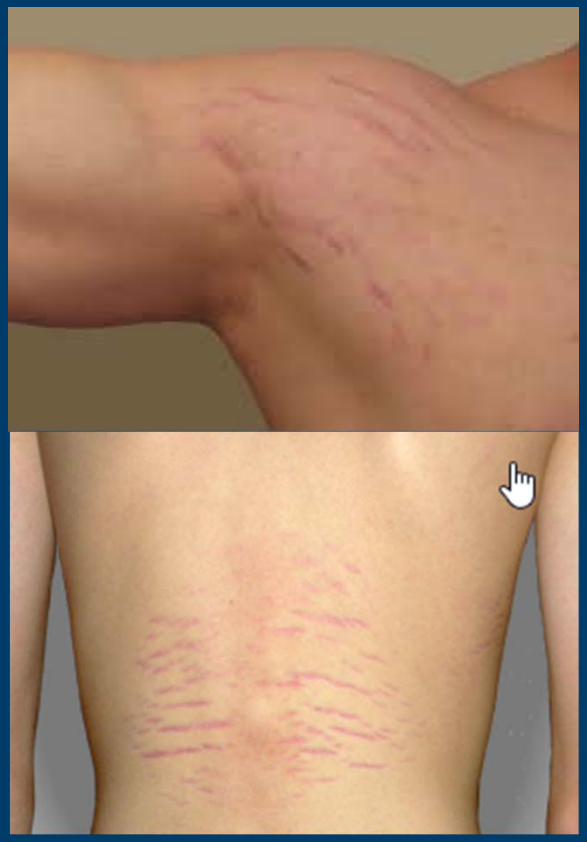


Emphysema

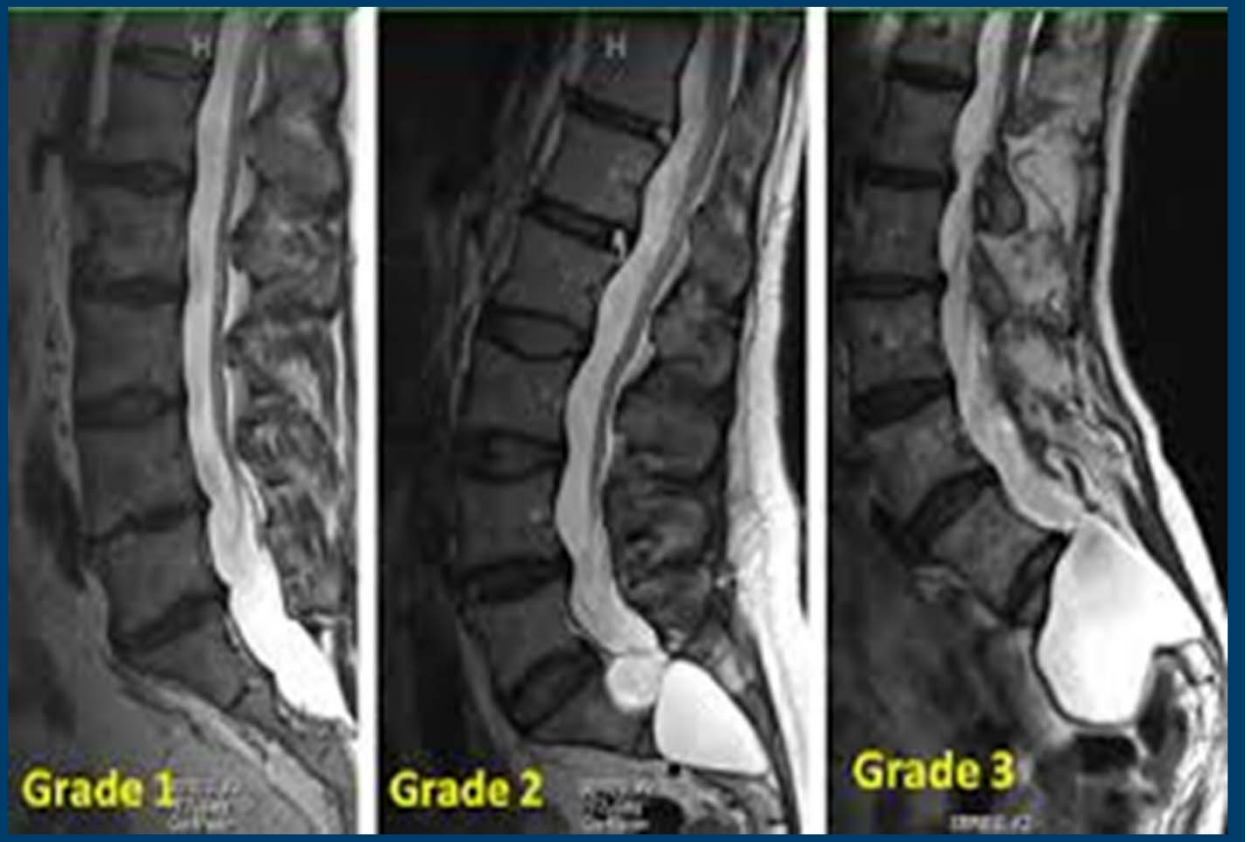


Sleep apnea

Other systems



Striae = stretch marks



Dural ectasia

Making the diagnosis: Early and accurate is essential!

- Seek a physician experienced in connective tissue disorders

- Exam should include:
  - Detailed medical and family history
  - Complete physical examination
  - Echocardiogram
  - Electrocardiogram
  - Eye exam, include slit lamp exam of lens
  - CT or MR may be necessary to evaluate the spine
  - Genetic testing may help confirm or rule out a diagnosis of Marfan syndrome in family members at risk

Aortic dilation – a key feature of diagnosis

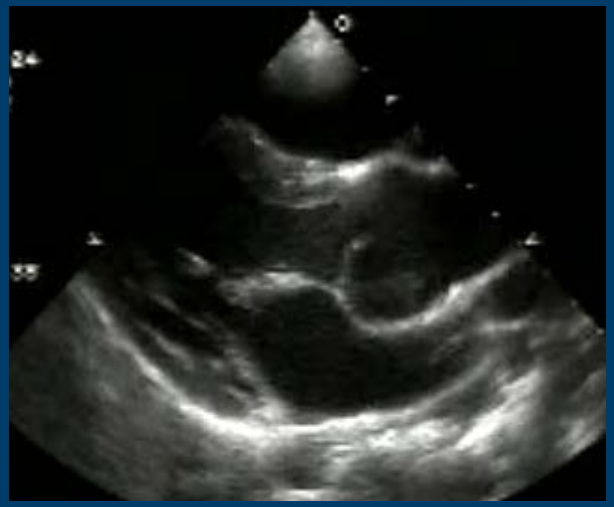
The Revised Ghent Criteria

- In the absence of family history:
  - Aortic dilation AND ectopia lentis
  - Aortic dilation AND *FBN-1* mutation
  - Aortic dilation AND systemic findings (≥7)
- In the presence of family history:
  - Ectopia lentis
  - Systemic findings (≥7 pts)
  - Aortic dilation (Z ≥ 2 above 20 yrs old, ≥3 below 20 yrs old)

Loeys B, et al, J Med Genet 2010, 47: 476-485

Cardiovascular surveillance

- Initial echo with f/u echo within 6 mos
  If dimensions are stable, echo annually
- More frequent imaging indicated if:
  - Aortic root > 4.5 cm
  - Rate of aortic root dilation > 0.5 cm/year
  - Progressive aortic regurgitation



- Intermittent CT or MR in young adulthood
- At least annual CT or MR s/p aortic root replacement or dissection

Management

- Exercise restriction
- Medical management is aimed a slowing aortic growth
  - Beta blockers (*propranolol, atenolol, metoprolol*)
  - Angiotensin II receptor blockers (*losartan, irbesartan*)
  - ACE inhibitors (*enalapril, lisinopril*)
- Surgical intervention when needed
- Supportive services

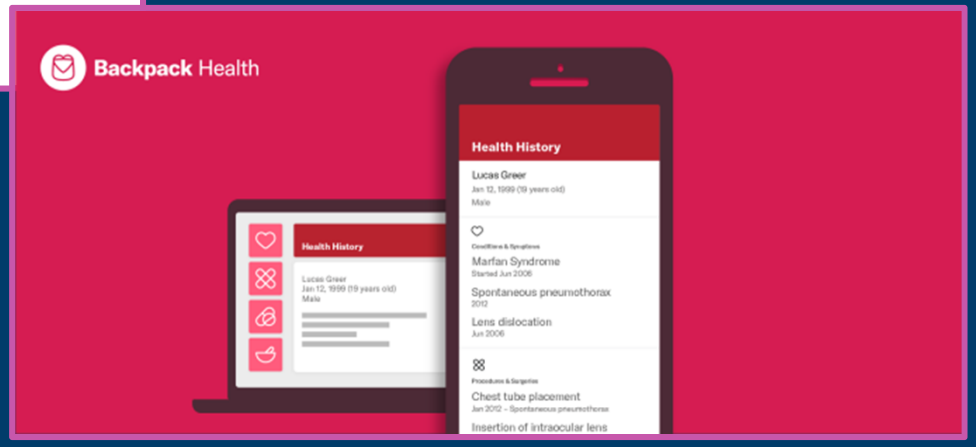
Summary…

- Marfan syndrome is a genetic disorder of the connective tissue, which primarily affects the ocular, musculoskeletal and cardiovascular system.
- Cardiovascular complications in Marfan syndrome, as well as in related disorders may be life-threatening, and therefore early and accurate diagnosis is essential.
- Regular surveillance, medical therapy and surgical intervention if needed can improve long-term outcomes and save lives.

Sharing health information

Medical alert bracelets

Key to improving outcomes when time is of the essence



Backpack Health App

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