Respiratory Disorders in MARFAN SYNDROME

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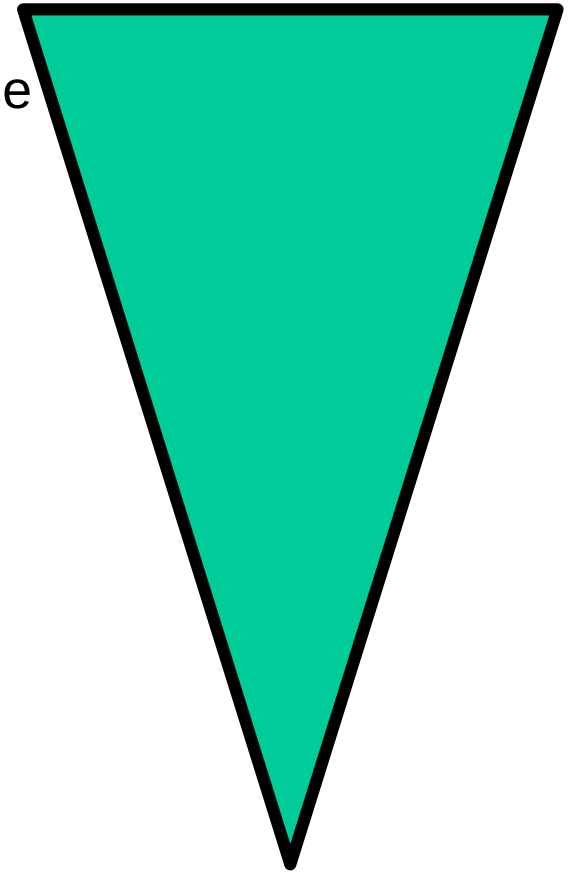
Shortness of Breath in MFS: Three Possibilities

HEART

Valvular heart disease

Arrhythmias

Cardiomyopathy



LUNGS

Chest wall deformities

Respiratory Muscle Weakness

Enlarged airspaces(emphysema)

Pneumothorax

Sleep apnea syndrome

Asthma

Pulmonary hypertension

DECONDITIONING

Why are there lung problems in MFS?

Fibrillin-1 is expressed in the lung.

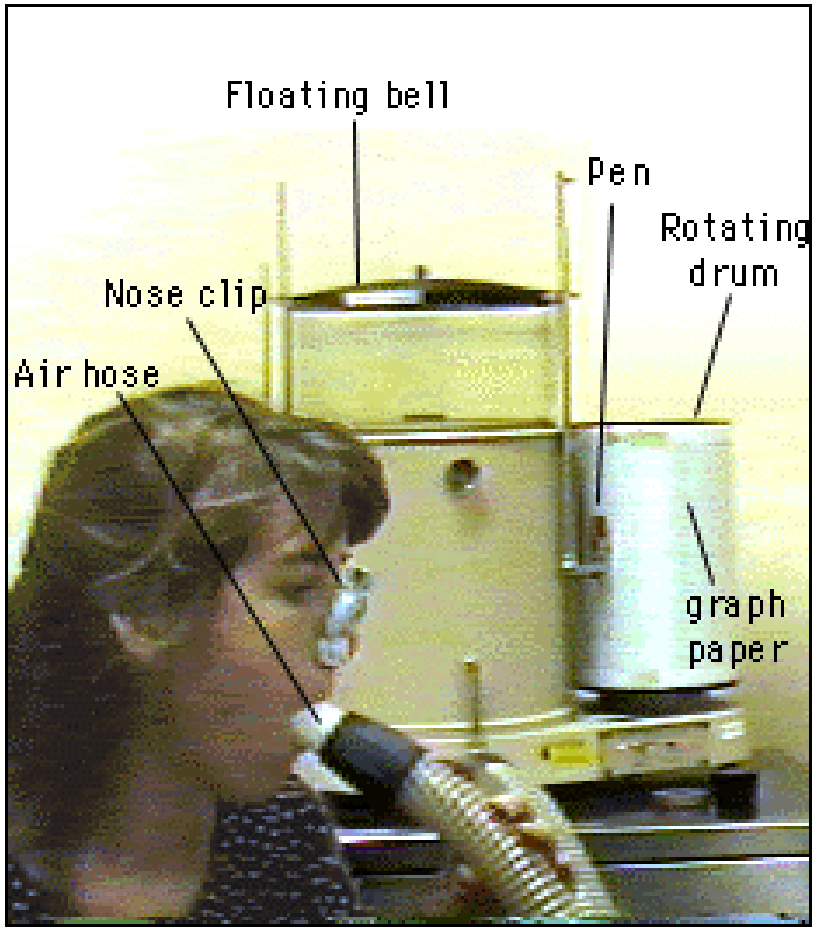
Fibrillin-1 is associated with elastin and connective tissue.

- **Candidate diseases**
  - Emphysema (elastin/developmental)
  - Pneumothorax (elastin/developmental)
  - Sleep apnea (connective tissue)
  - Lung musculoskeletal impairment (connective tissue

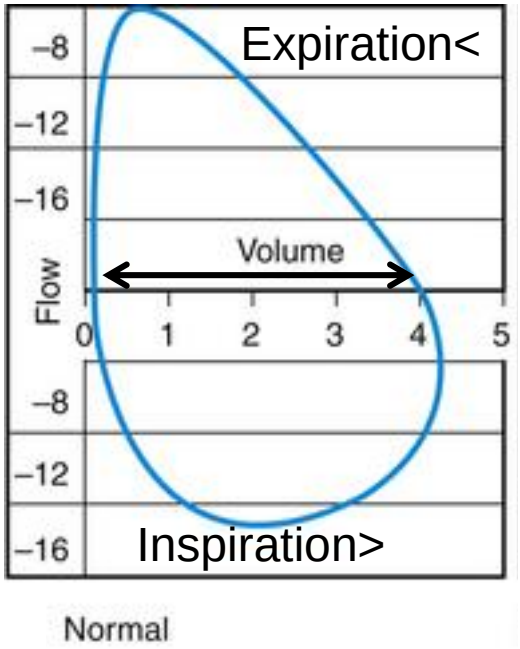
Restrictive Lung Disease

- >50% of pts with Marfan Syndrome
- Musculoskeletal abnormalities of the chest
- Cannot expand the chest fully
- Symptoms:
  - Shortness of breath with exertion
  - Cyanosis, Heart strain

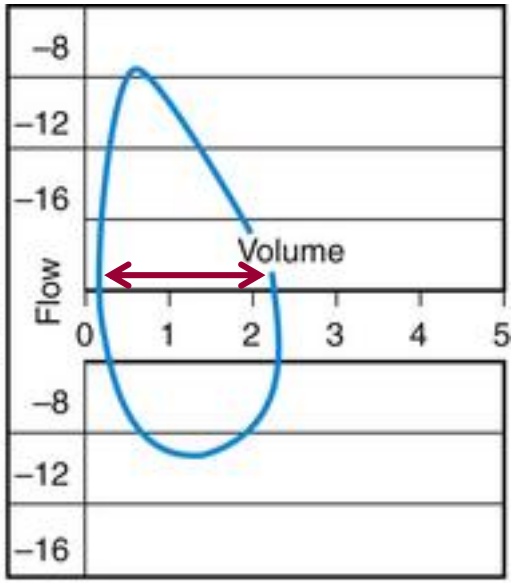
Spirometry
Pulmonary Function Testing (PFTs)



Restrictive Lung Disease- Lung Function



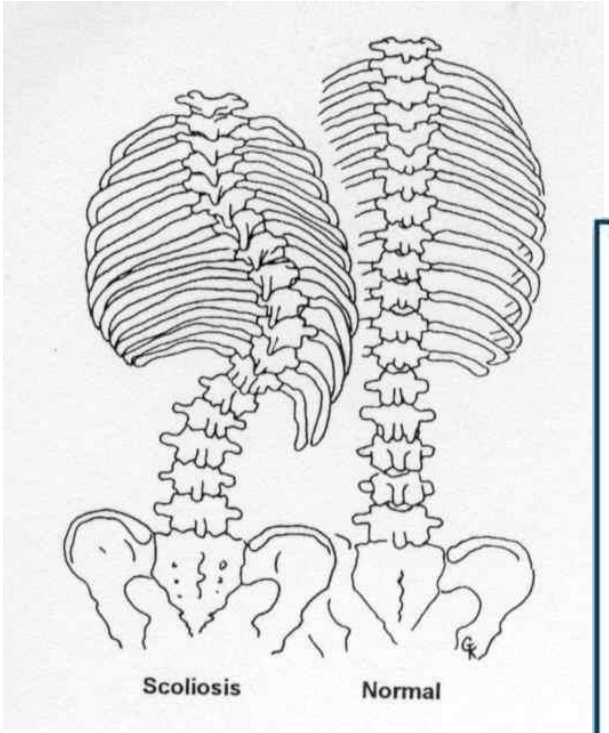
Normal



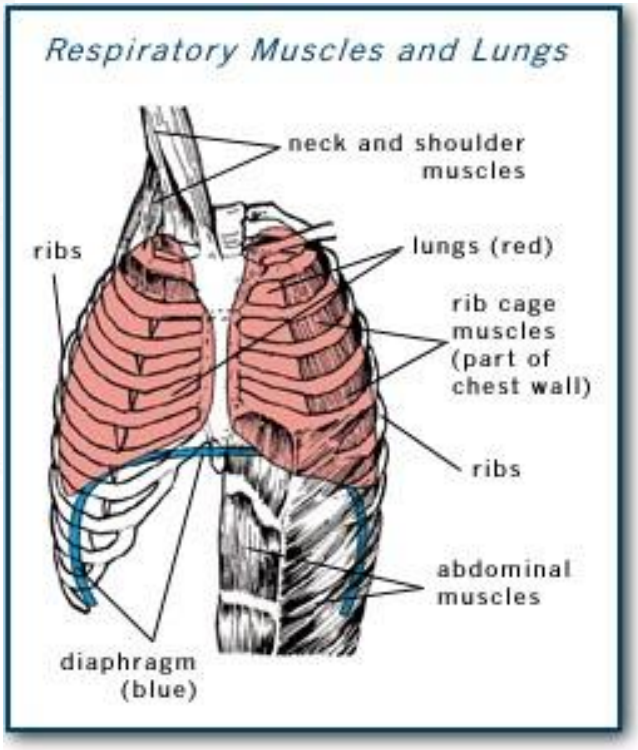
Restrictive

Reduction in Lung Capacity!

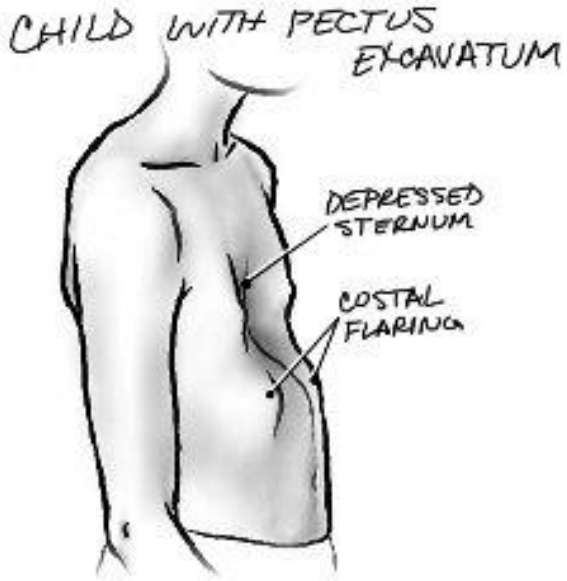
Skeletal Abnormalities and Restrictive Lung Disease-MFS



Scoliosis



Respiratory Muscle Weakness



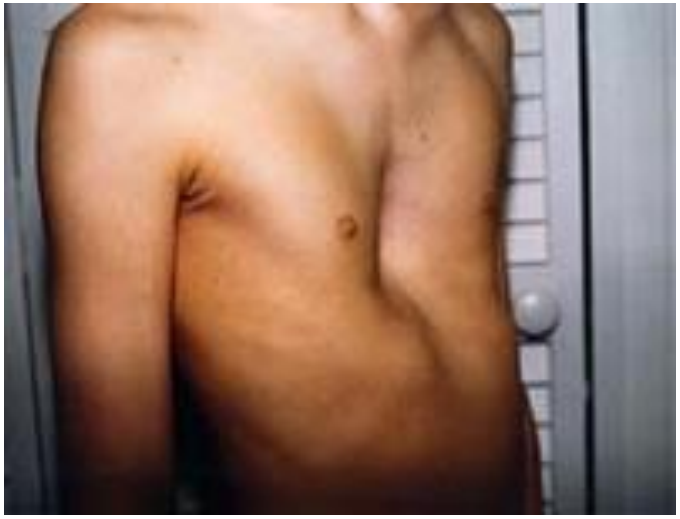
Pectus Abnormality

Neuromuscular disorders and Restrictive Lung Disease

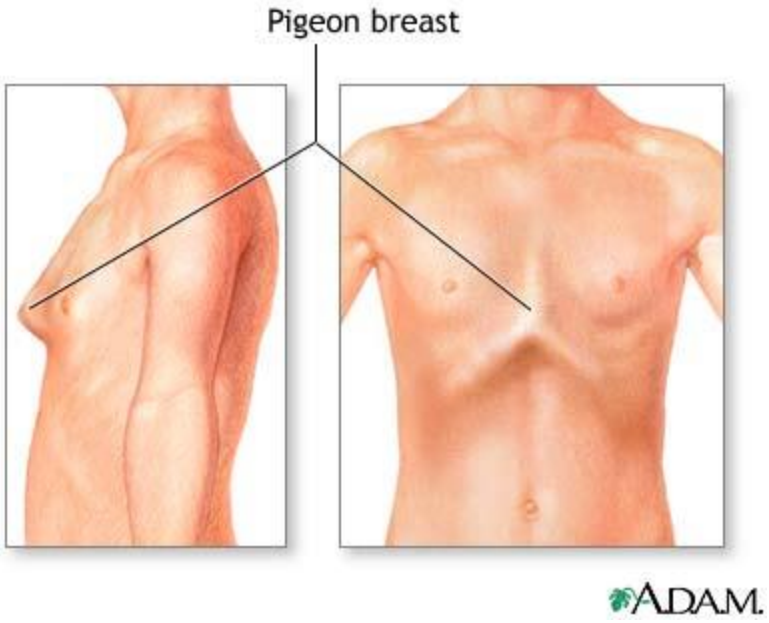
- Marfan Syndrome can be associated with skeletal muscle weakness.
- Weak respiratory muscles can lead to reduced lung capacity→Restriction
- Diagnosis: Pulmonary Function Tests which include Maximal Inspiratory and Expiratory Pressures.
- Treatment: Pulmonary Rehabilitation, Ventilatory Support

Pectus Abnormalities

Pectus Excavatum



Pectus Carinatum



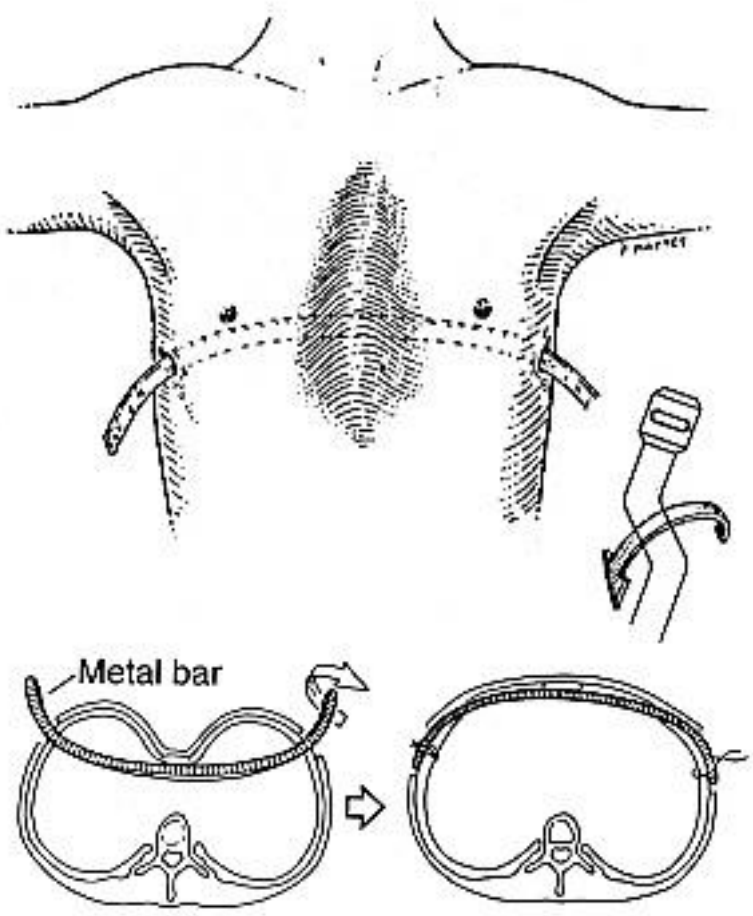
Present in two-thirds of patients with Marfan Syndrome

Natural History
Pectus Abnormalities

- Typically benign, but few studies. Modest reduction in lung function.
- Evidence or potential for respiratory dysfunction is often the stated reason for early repair of severe defects, although **cosmesis is typically of greater concern**.

Treatment of Pectus Abnormalities

NUSS PROCEDURE



Advantages

--Easier

--Shorter

--Fewer complications

--21 yr f/u—good anatomic result, limited lung function data

Does correction of pectus deformities improve lung function?

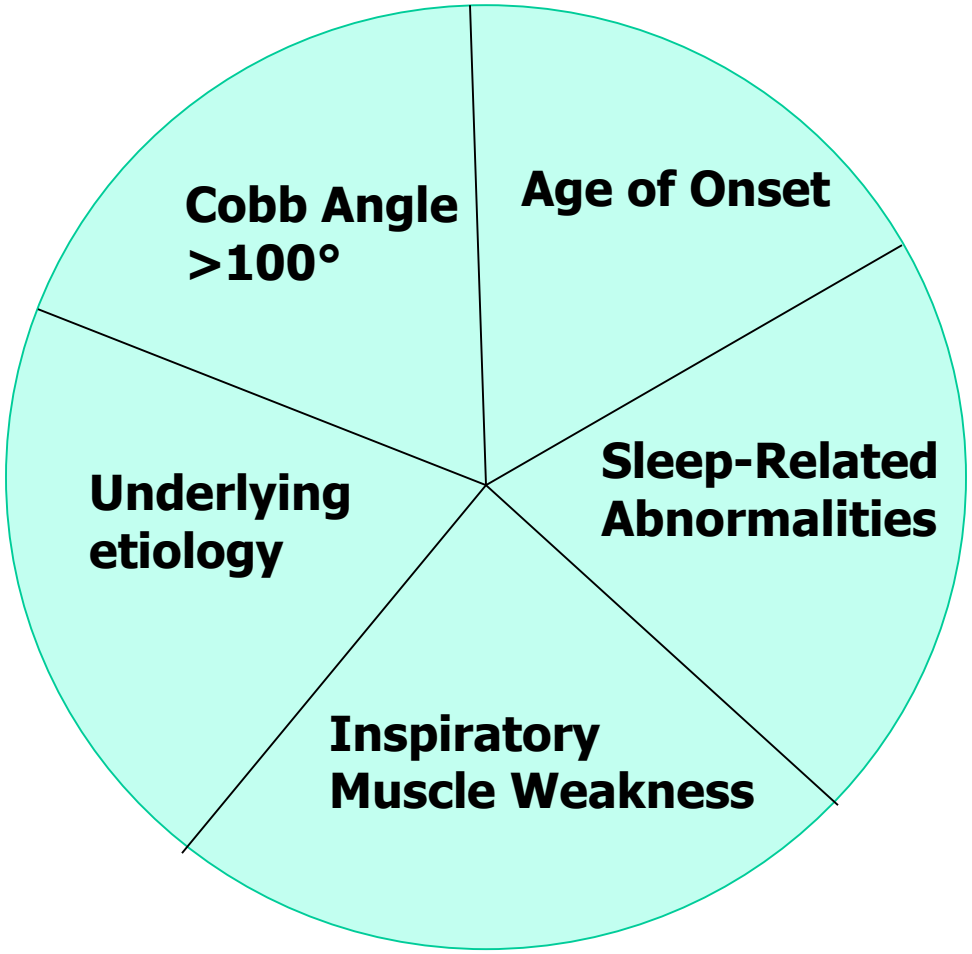
Probably NO.

Considerations:

--Complexity of chest wall defects, esp. if associated with scoliosis in persons with Marfan Syndrome may lead to more accelerated lung dysfunction without repair.

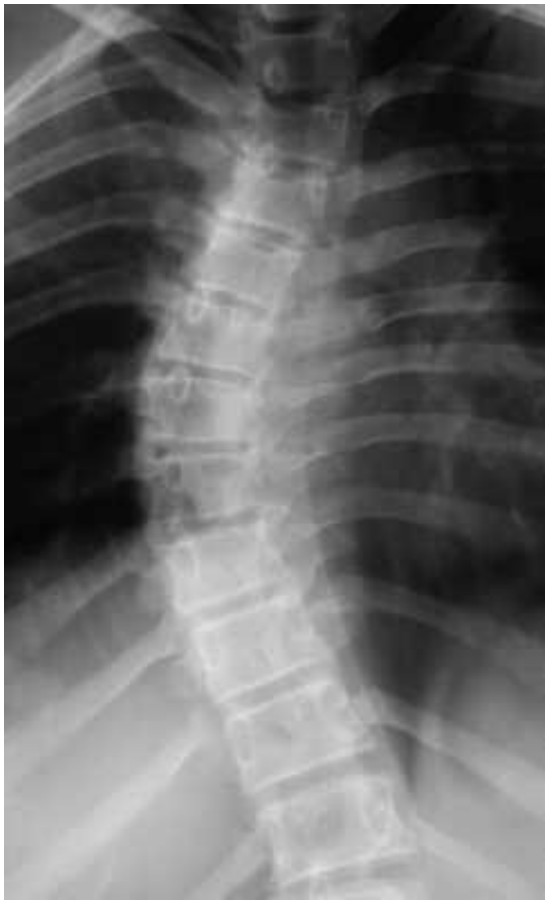
--Need for assessments of functional capacity: six minute walk tests, cardiopulmonary exercise testing.

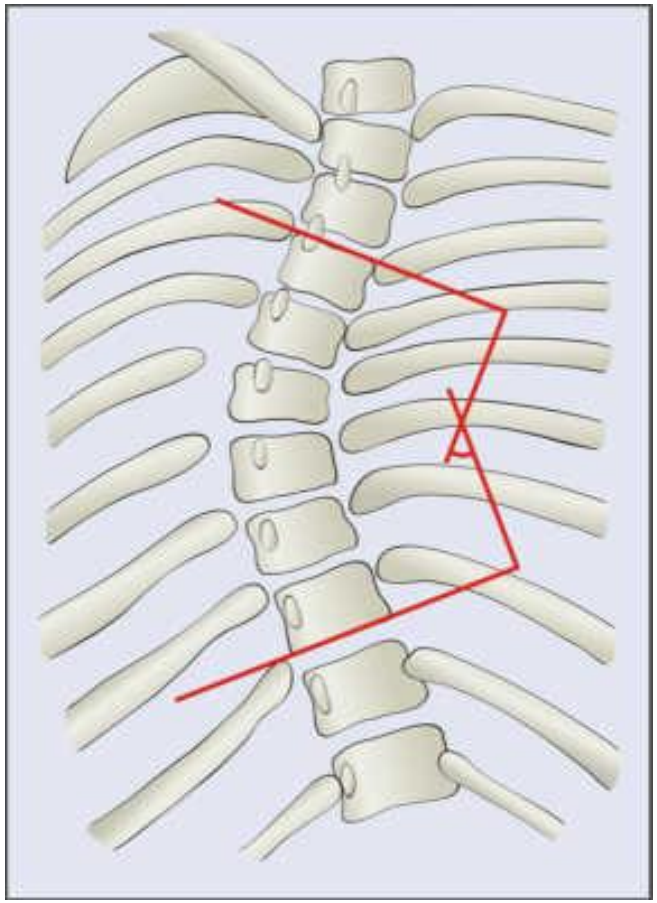
KyphoScoliosis-Factors Predisposing to Respiratory Insufficiency

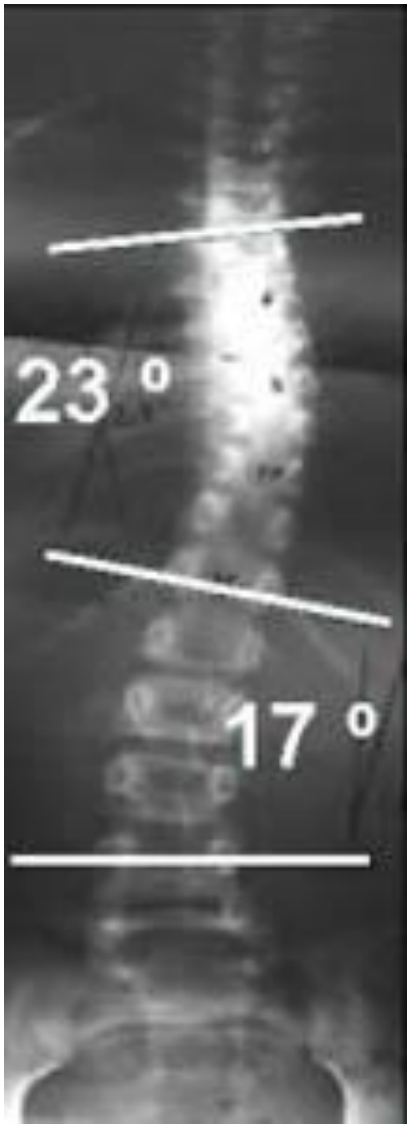


Modified from Fishman's Pulmonary Diseases and Disorders. 1999.

Cobb Angle-Scoliosis Severity







VC (% pred) = 87.6 - .338 X Cobb Angle

Thoracic curves worse than thoracolumbar curves!

Restrictive Lung Disease-Scoliosis Severity

Cobb Angle	Clinical Manifestations
<10°	Normal, no symptoms
>25°	Incr. pulmonary vascular pressures, no symptoms
>40°	Consider surgical intervention
>70°	Reduced lung volumes
>100°	Shortness of breath with activity
>120°	Chronic respiratory failure, oxygen supplementation, non-invasive ventilation

Koumbourlis, 2006 Pediatric Respiratory Reviews

Scoliosis-
Pulmonary Evaluation

Full PFTs (pulmonary function tests), with DLCO, MIP/MEP

SNIFF Fluoroscopy to assess diaphragmatic function

Six minute walk test

+/- Sleep study

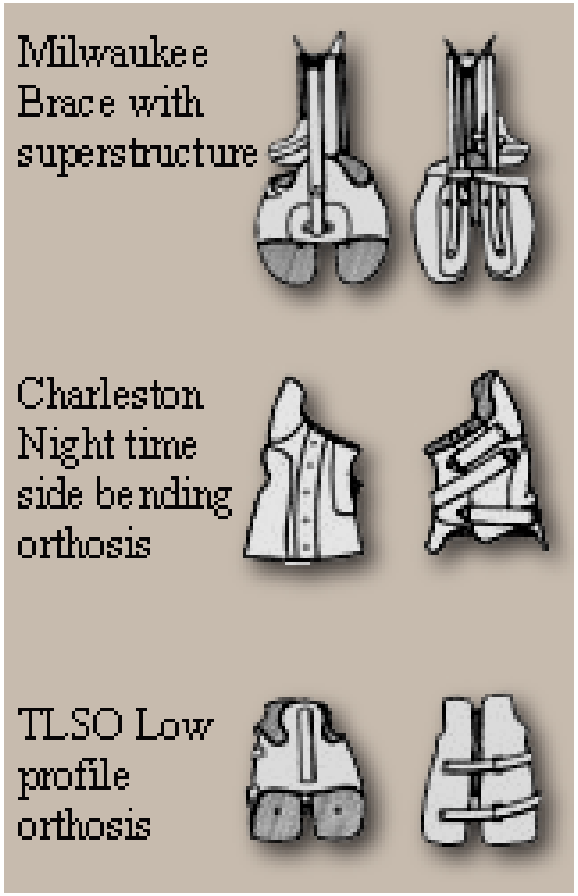
Scoliosis-Treatments

Observation

--q6months examination

--q12month spinal films

Cast/Bracing



Surgery

Rod placement +/- fusion

Growing rod placement

VEPTR

Spine staples

Magnetic rods (MCGRs)

Scoliosis-Treatments

Dual Goals of Intervention:

Prevent further structural deformity

Preserve or improve pulmonary function

BRACING

Progressive curvature <45°.

SURGERY

Progressive curvature despite bracing.

Cobb angle >70°

Respiratory failure

Restrictive Lung Disease-MFS

- **Pectus Deformities**
  - Surgical repair does not correct restriction.
  - Cosmesis should dictate repair unless severe deformity.
- **Neuromuscular Dz**
  - Pulmonary Rehabilitation
  - Ventilation strategies
- **Scoliosis**
  - Typically corrected early.
  - Progressive curvature without correction.
  - Pulmonary consequences without correction of severe thoracic deformity probably significant.

Restrictive Lung Disease

Respiratory Care

1. Noninvasive Positive Pressure Ventilation --May improve survival in selected pts; may improve dyspnea in less severe dz.
2. Pulmonary Rehabilitation —Improves lung volumes and exercise capacity. ?Role preop.
3. Supplemental Oxygen —If desaturation at rest or with activity
4. Bronchodilators if air trapping or wheezing.
5. +/- Airway clearance devices, Flutter valve

Restrictive Lung Disease-MFS

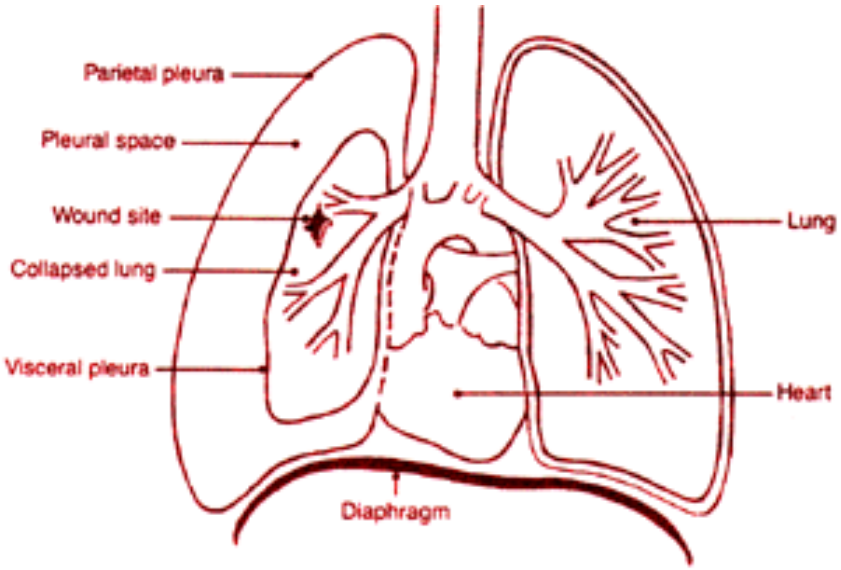
Take Home Messages

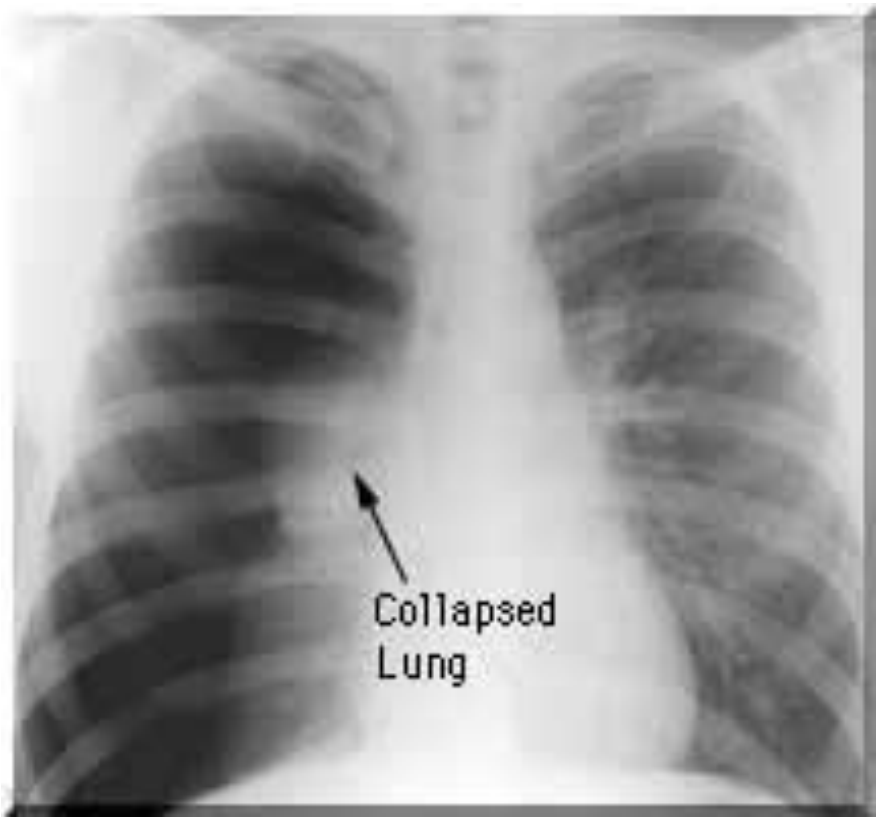
- Need serial pulmonary function tests to follow progression of pulmonary restriction. Functional assessment of value.
- Appropriate surgical intervention for scoliosis may prevent or delay further deterioration in lung function.
- Pectus repair should be driven by cosmesis unless complex chest wall deformity or significantly reduced lung function.

Marfan Syndrome and Pneumothorax

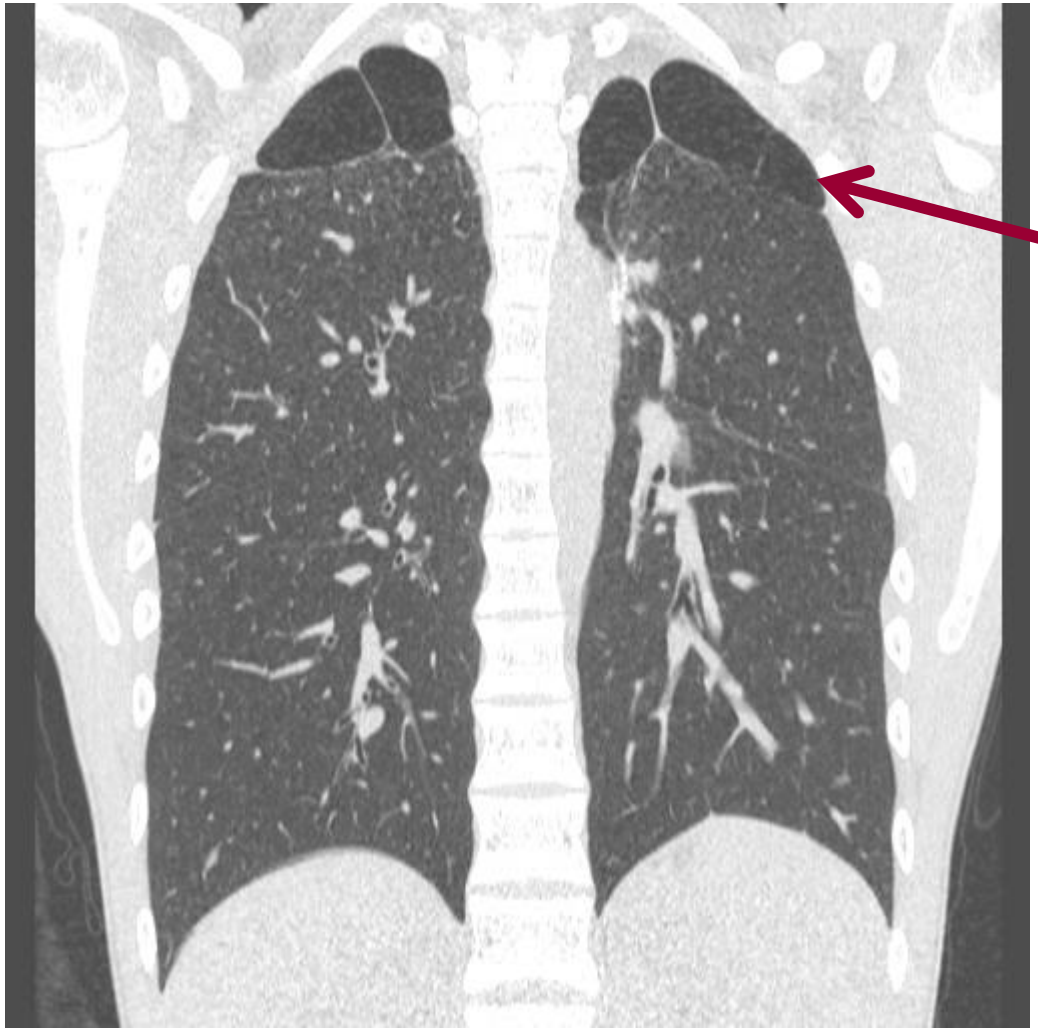
- What is pneumothorax?
  - "Lung collapse"; lung detaches from chest wall.
- What are the symptoms?
  - Acute onset of pleuritic chest pain, shortness of breath and dry cough.
- How is it diagnosed?
  - Chest Xray
  - CT Scan

Pneumothorax





18 yo man with MFS and recurrent bilateral pneumothoraces

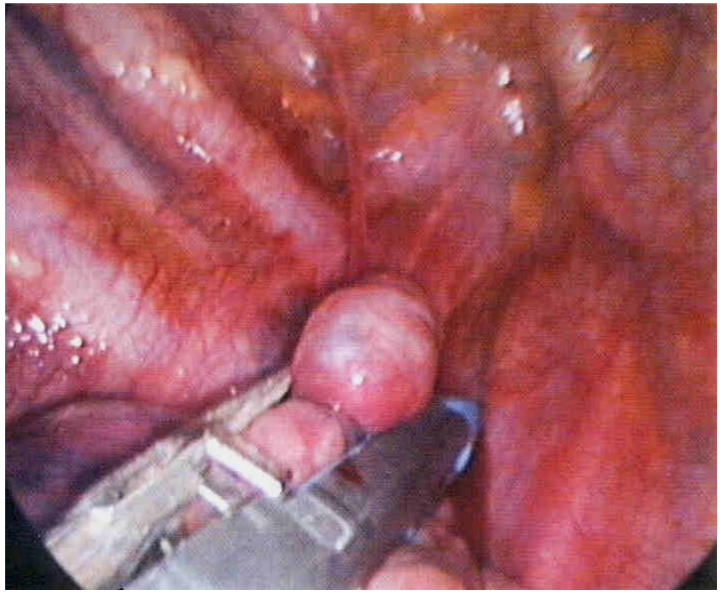


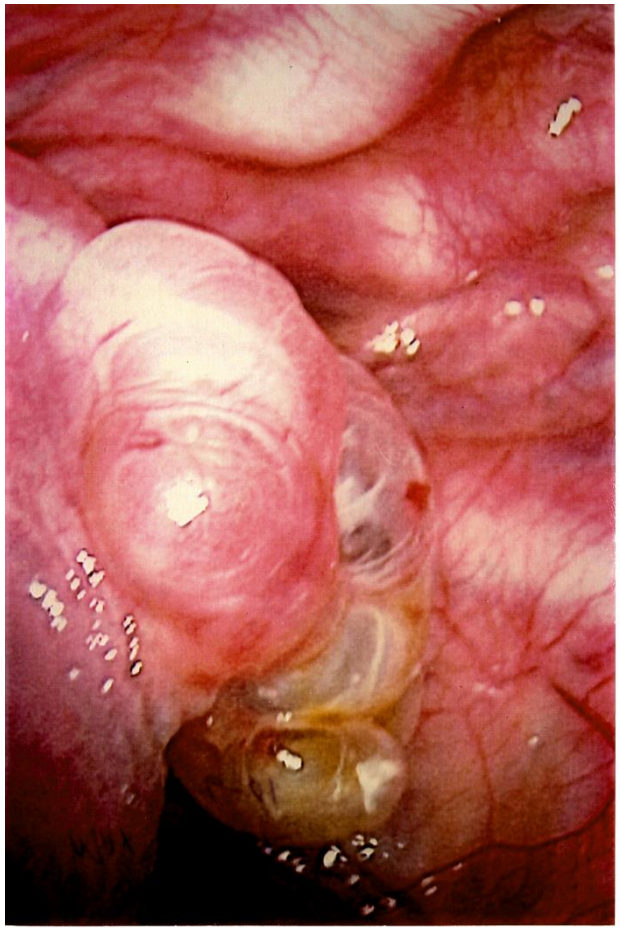
Apical blebs

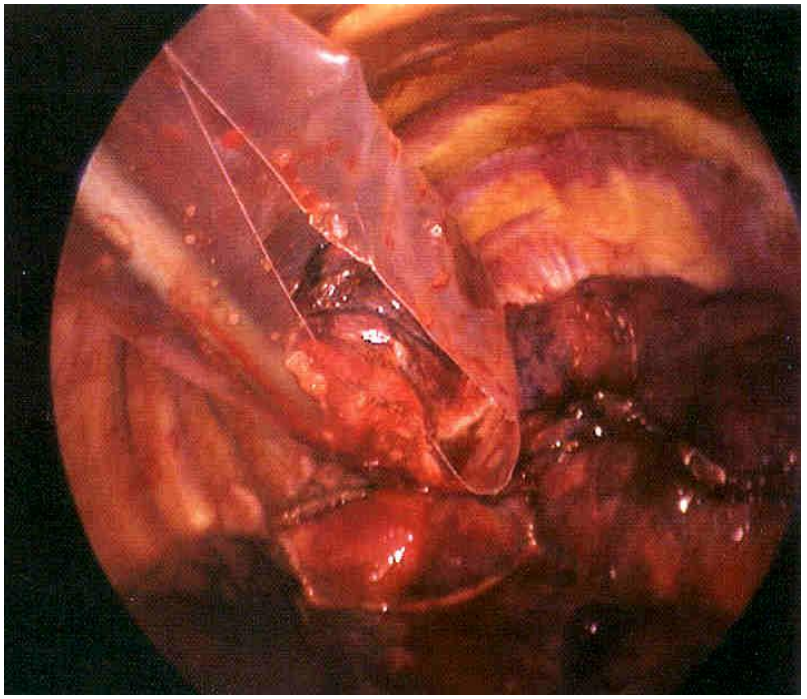
Pneumothorax--Treatment

- If small, hospitalization & supplemental oxygen.
- If moderate→large, chest tube placement for evacuation.
- If unresponsive to above or recurrent, pleurodesis is indicated. Mechanical better than chemical pleurodesis.
- Alternative to chest tube, Heimlich valve

Thoracoscopy







Pneumothorax - *Indications for Surgery*

(Bleb resection and mechanical pleurodesis)

- Massive air leak, poor re-expansion
- Recurrent pneumothorax
- Persistent air leak 7-10 days
- Simultaneous bilateral
- Hemopneumothorax
- Tension pneumothorax
- Large blebs/cysts

Pneumothorax--MFS

Take-Home Messages

- Pneumothorax is a common manifestation of Marfan Syndrome.
- If recurrent, pulmonary consultation should be obtained.
- Efforts at durable reexpansion should observe surgical considerations of eventual aortic repair. Mechanical pleurodesis preferred.

Emphysema in Marfan Syndrome

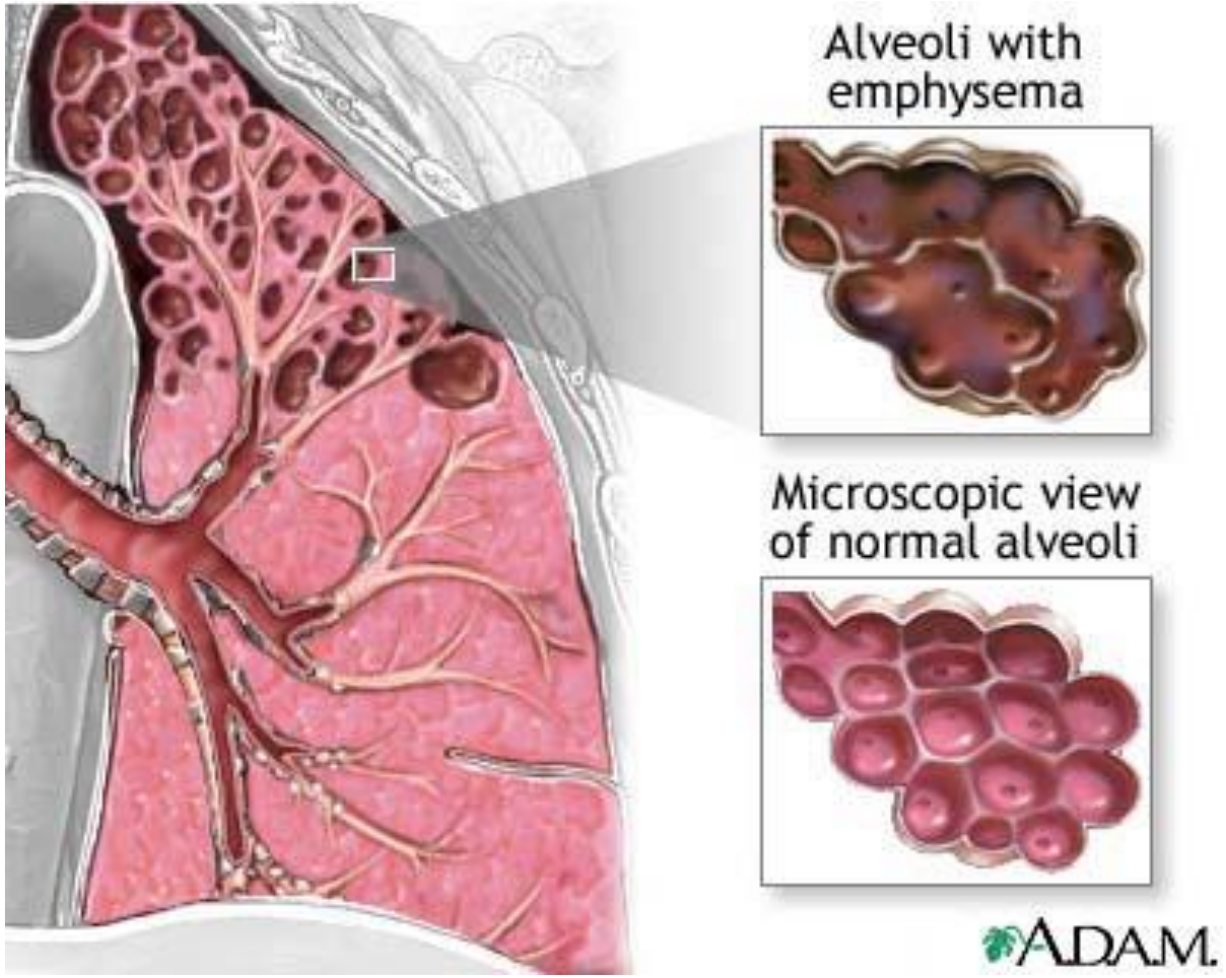
What is emphysema?

--Loss of alveolar walls (genetic and/or destructive)

--Enlargement of airspaces

--Airway obstruction/inflammation

Emphysema Findings—
Fewer alveoli
Irreversible



Emphysema--Symptoms

- Shortness of breath with activity
- Frequent bouts of “bronchitis”
  - Cough with green sputum
  - Chest congestion
  - After common cold or viral infection
- Low blood oxygen

Emphysema--Diagnosis

- Chest X-Ray
- Chest CT Scan, hi resolution scan
- Pulmonary Function Tests
- Arterial Blood Gas

Emphysema--Treatment

- Conventional
  - Bronchodilators
  - Inhaled Steroids
  - Oxygen, if necessary
  - Aggressive treatment of infections
  - Lung volume reduction surgery
- Experimental
  - Retinoic acid
  - Cytokine inhibition (Losartan)
  - Antioxidants

Emphysema--MFS

Take-Home Messages

- Emphysema is probably a sequelae of disturbances in lung development in Marfan patients.
- Symptoms of shortness of breath, recurrent bronchitis, pneumothorax should prompt evaluation by a lung specialist for emphysema and initiation of treatment.

Sleep Apnea

- Defn: Intermittent cessation of airflow at the nose and mouth during sleep.
- Affects ~2% middle-aged women, 4% middle aged men.
- Cause of excessive daytime sleepiness
- Obstructive—Can't breathe
- Central—Won't breathe

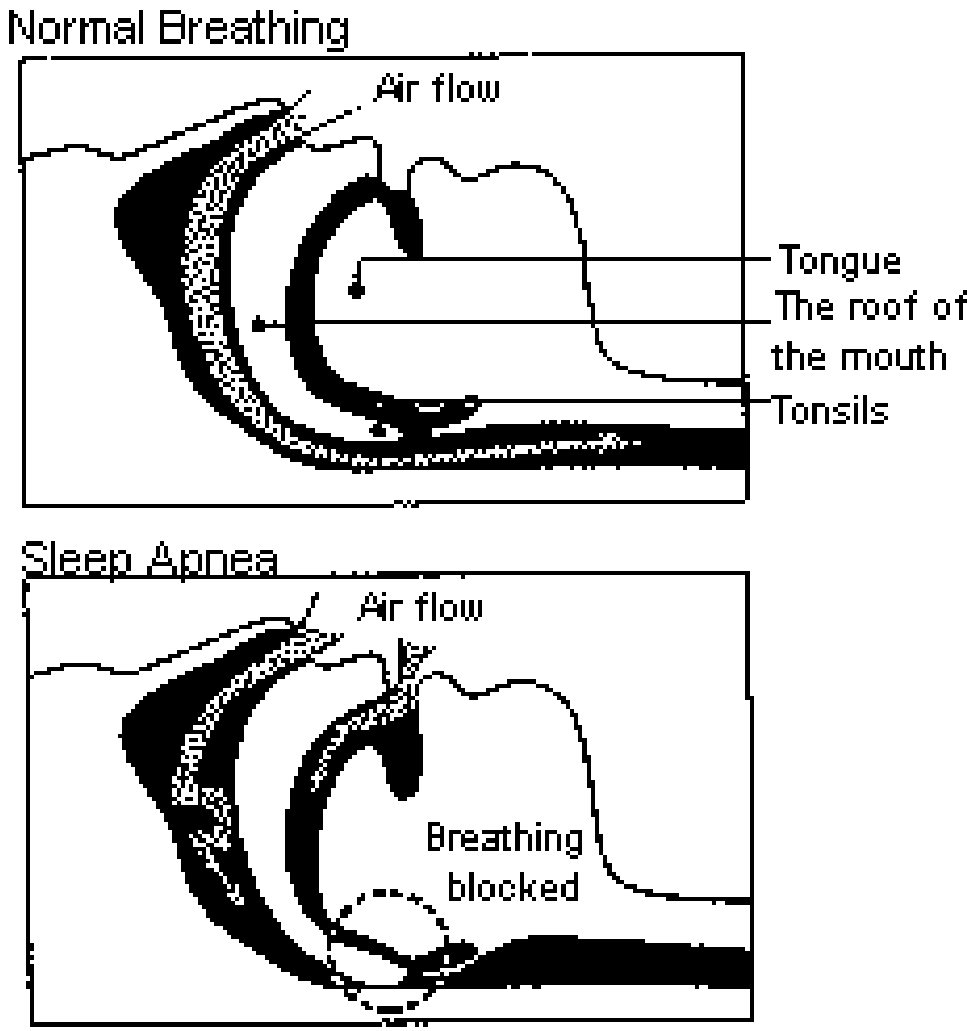

Normal Breathing
Air flow
Tongue
The roof of
the mouth
Tonsils
Sleep Apnea
Air flow
Breathing
blocked

Figure 3

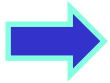
Sleep Apnea

- Common in general population (>15 million Americans)
- Potentially life-threatening w/ high clinical impact
  - Motor Vehicle Accidents
  - **Arrhythmias, heart attacks, aortic dissection**
  - Strokes
  - Reduced Productivity
  - Reduced quality of life

Nature of the Problem

- Recent studies have shown that up to 35% of patients with MFS have sleep apnea. (Control population-<5%)

Marfan Syndrome (Fibrillin-1 deficiency)

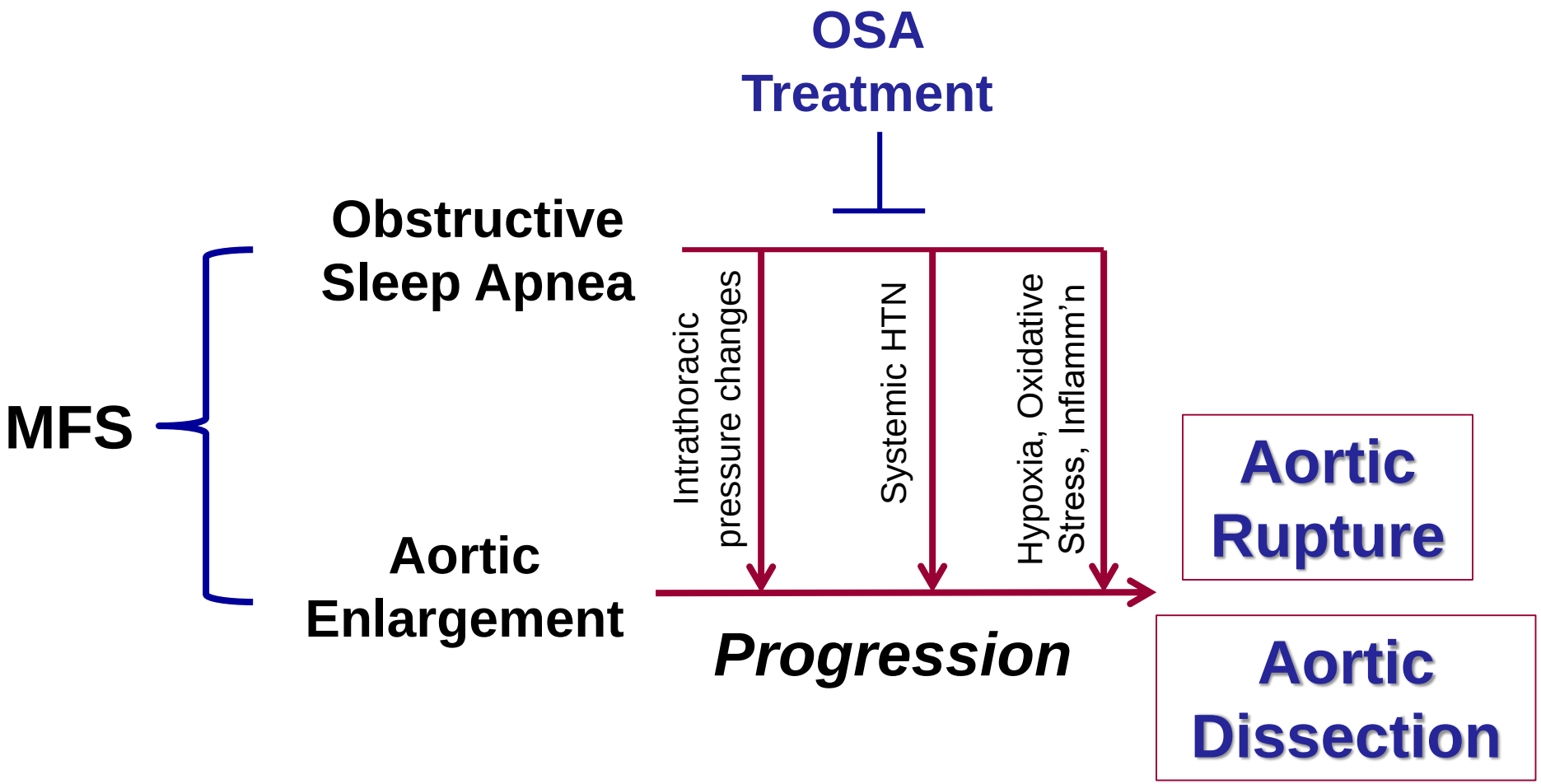


- **Craniofacial Dysmorphology**
- **Floppy upper airways**
- **Chest wall abnormalities**

- **SLEEP-DISORDERED BREATHING**
- **--Obstructive sleep apnea**
- **--Central sleep apnea**

Sleep Apnea-Aorta Connection

Proposed Paradigm



Sleep Apnea in Marfan Syndrome

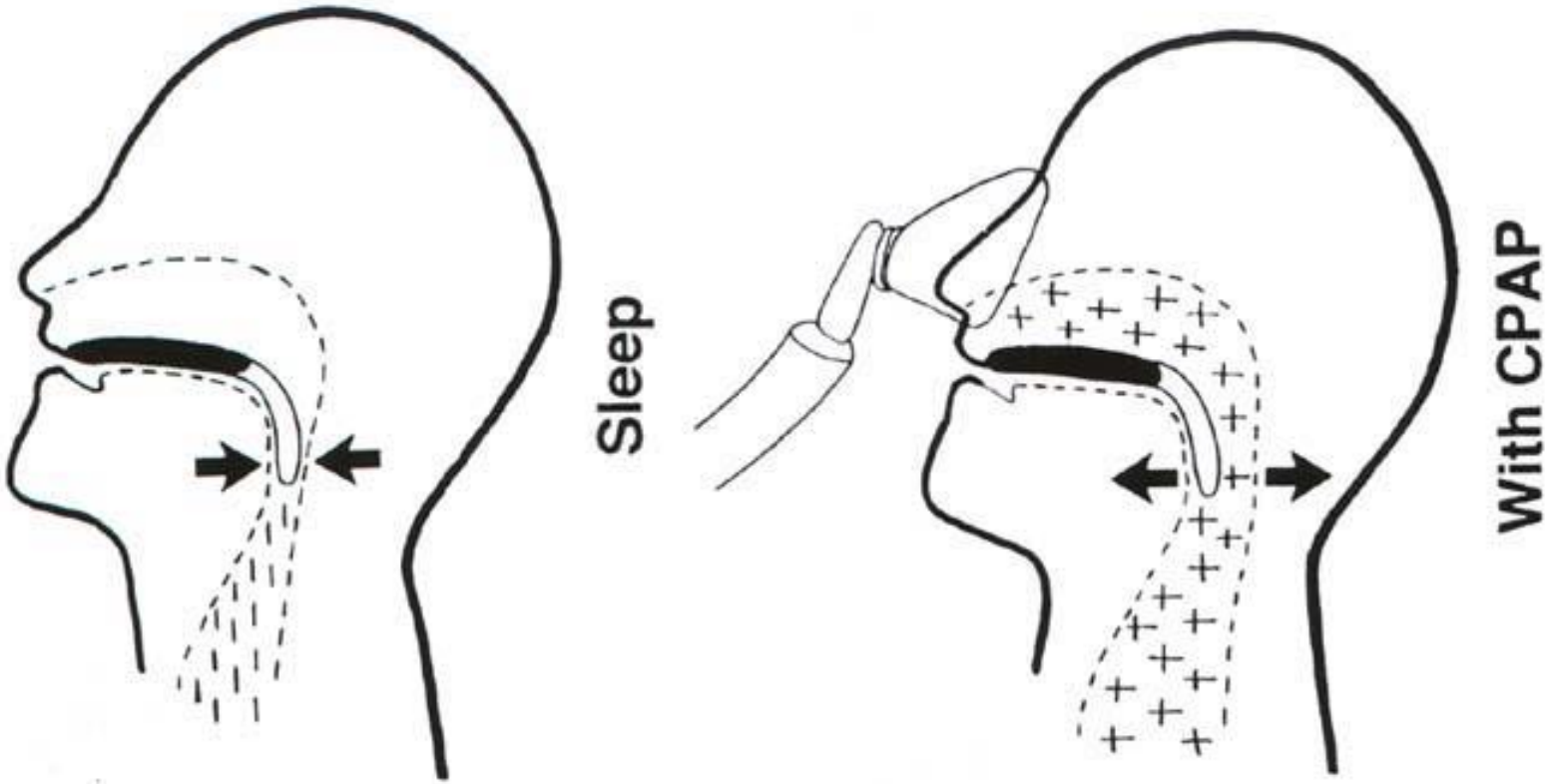
- Diagnosis:
  - Sleep Study
    - Brain activity, eye movements, muscle activity, airflow, oxygen levels
    - Awakenings—Apnea/hypopnea index, Abnl >5
    - Sleep latency—Abnl <5 minutes
  - Measurement of upper airway resistance during sleep

Sleep Apnea in Marfan Syndrome

Treatment

- Nasal CPAP
- +/- Supplemental oxygen
- If difficulty with CPAP mask fitting, consider
  - Mandibular advancement device
  - Oral appliance
- +/- Weight loss
- Drugs—Strong central component
- Rare—Surgery (uvulopalatoplasty, tracheostomy)

How does Nasal CPAP work?



Sleep Apnea Devices

Apnea Pillows

Nasal Mask

Dental Device

Full Face Mask

Sleep Apnea in Marfan Syndrome

Take-Home Messages

- Underdiagnosed in Marfan Syndrome
- All adult patients with Marfan Syndrome should be considered for screening, especially if sleep disturbances or severe chest wall deformity.