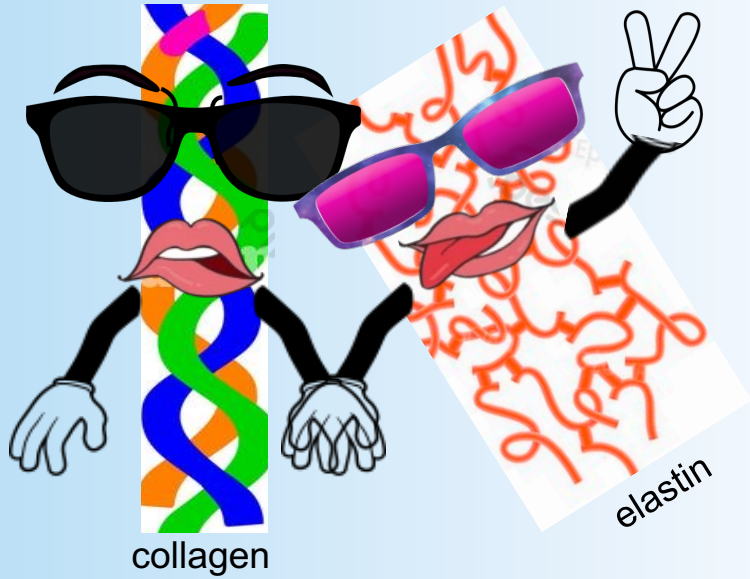
Fibrous proteins
Collagen and Elastin

By Michelle Kaminski

Fibrous Protein Basics

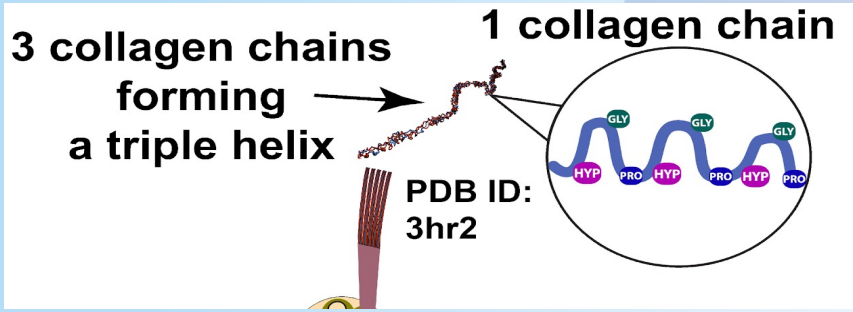
- Long chains of amino acids that have elongated and filamentous shape
- *High degree of Stability*
- Provides structural and tensile support
  - Usually in organs that need help resisting stretching or deformation
- Repetitive sequences
  - Collagen type 1 has glycine as every third A.A, glycine makes up about 1/3 of Collagen type 1 sequences

Our fine fibrous babes ;)



Collagen

- Repetitive sequences of glycine, proline, and lysine
- Enhances structural integrity
- Primarily produced by fibroblasts but also produced by osteoblasts and chondrocytes
- 3 alpha chains twisted into triple helix structure
  - Stabilized by hydrogen bonds
  - Aligned parallel with side chains pointing Towards the middle



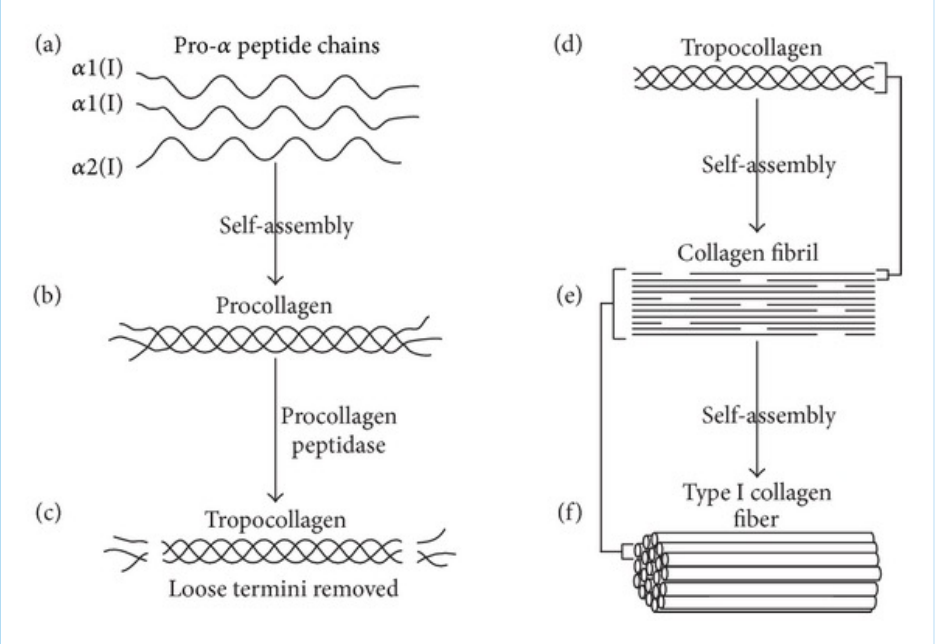
Collagen	Most abundant protein in the human body. Extensively modified by posttranslational modification. Organizes and strengthens extracellular matrix.	Be (So Totally) Cool, Read Books.
Type I	Most common (90%)—Bone (made by osteoblasts), Skin, Tendon, dentin, fascia, cornea, late wound repair.	Type I: bone. ↓ production in osteogenesis imperfecta type I.
Type II	Cartilage (including hyaline), vitreous body, nucleus pulposus.	Type II: cartwolage.
Type III	Reticulin—skin, blood vessels, uterus, fetal tissue, granulation tissue.	Type III: deficient in the uncommon, vascular type of Ehlers-Danlos syndrome (ThreE D).
Type IV	Basement membrane, basal lamina, lens.	Type IV: under the floor (basement membrane). Defective in Alport syndrome; targeted by autoantibodies in Goodpasture syndrome.

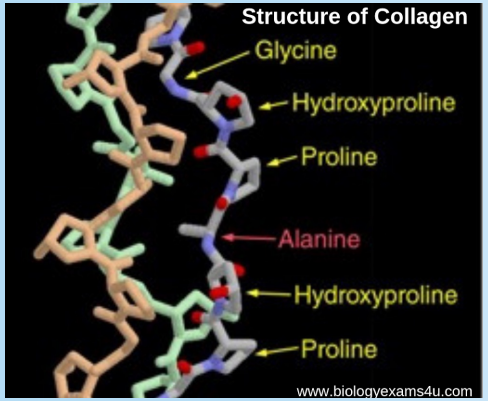
Type one got boned
Type two likes to chew car2lidge
Type three likes to get B.V. and babieS ;)
Type Four hides under the floor

studyaid

Collagen synthesis

1. Pro-Alpha chain is formed in R.E.R
2. Chain undergoes hydroxylation and glycosylation
    1. Hydroxylation: allows interaction between chains
    2. Glycosylation: prevents premature degradation
3. Chains then interact with each other forming alpha helix shape making procollagen



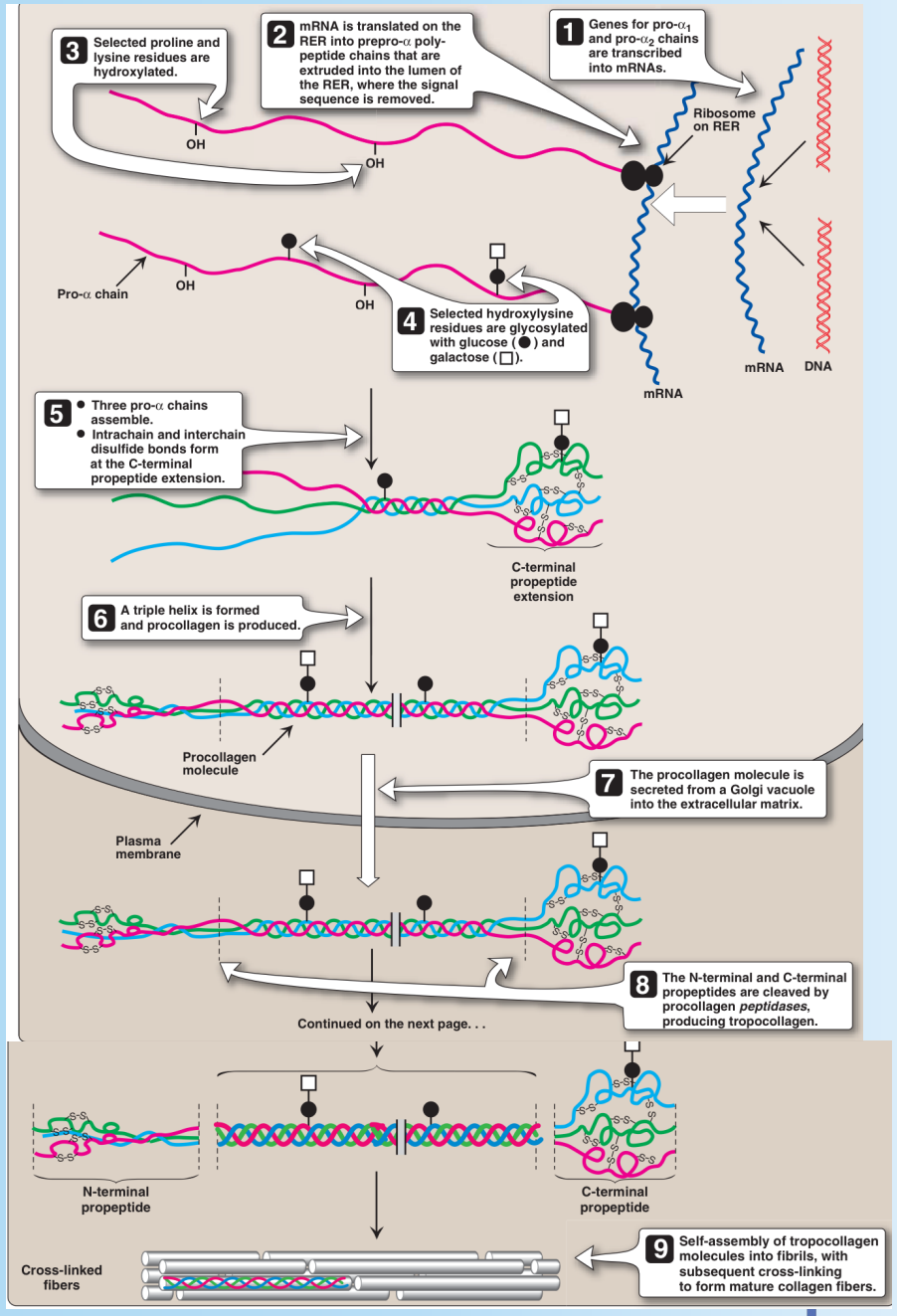


Collagen synthesis

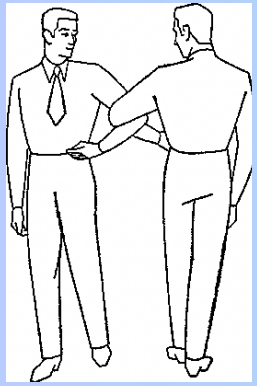
4. Procollagen gets transported in cell through RER→ Golgi → out of cell in vesicles
5. C and N terminals get chopped off = tropocollagen
6. Tropocollagen fibers interact and cross-link with other fibers with help of lysyl-oxidase

    Lysyl-oxidase uses copper as cofactor.

7. Collagen fibers are finally formed



Hydroxylation



Pro-alpha chain after getting hydroxylated

vs

Pro-alpha chains if they don't get hydroxylated

- Allows chains to become "sticky" and interact with each other
  - Stronger bonds are formed
- Prolyl hydroxylase + Lysyl hydroxylase
  - Need vitamin C as cofactor
  - Vitamin C deficiency = sCurvy
    - Cannot form proper collagen
    - weak or absent collagen proteins

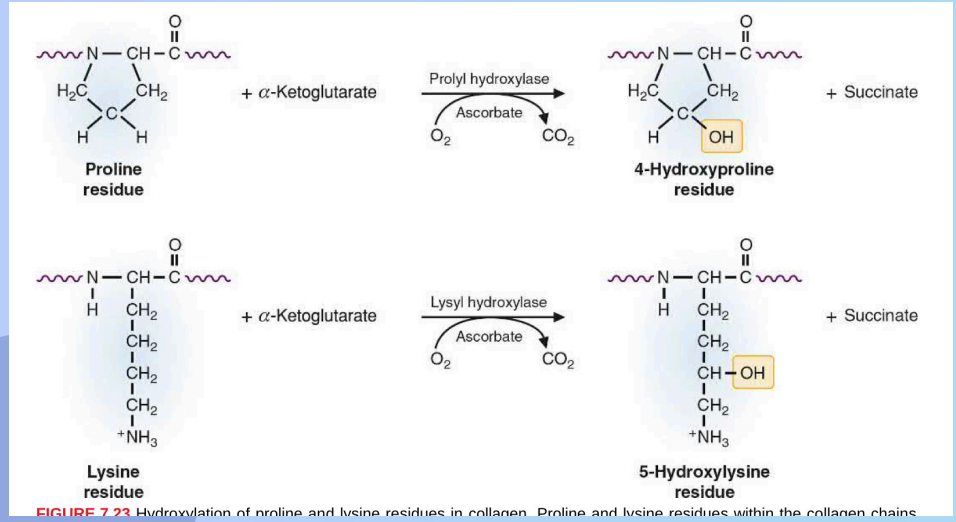
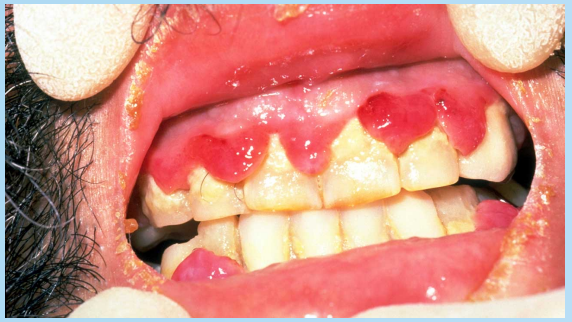
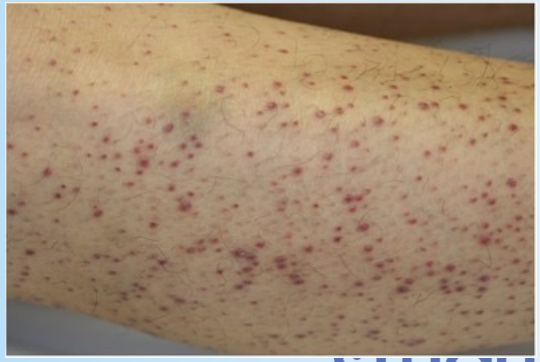
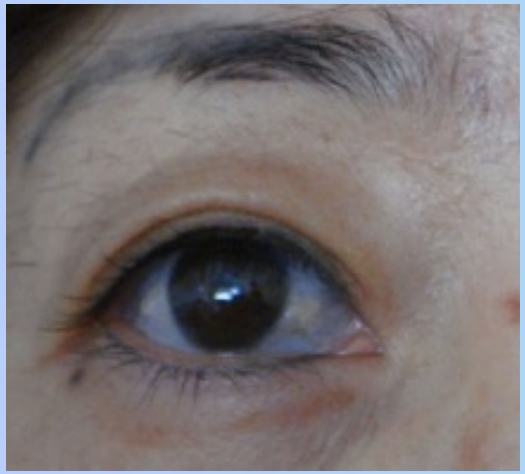


FIGURE 7.23 Hydroxylation of proline and lysine residues in collagen. Proline and lysine residues within the collagen chains

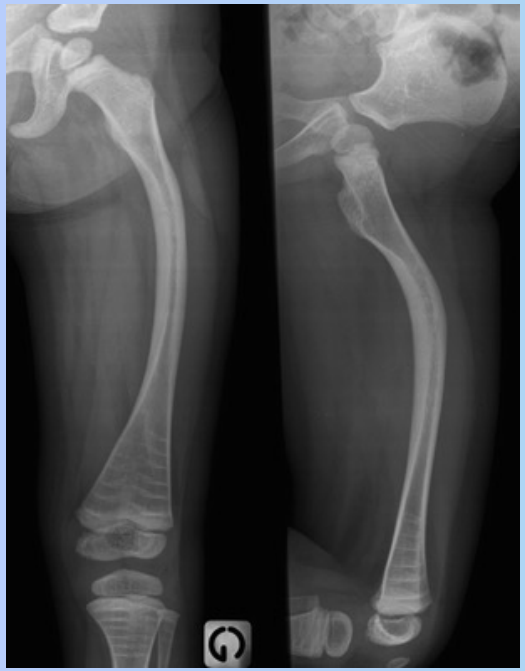




Bleeding gums and petechiae



Blue sclera



Bone Deformities

Osteogenesis Imperfecta

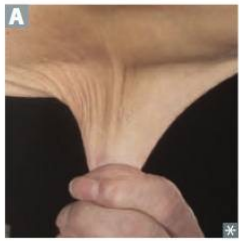
- Usually caused by reduction in synthesis of normal collagen type 1 or synthesis of mutated form of collagen type 1

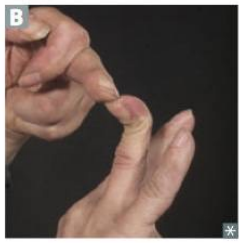
- Symptoms (OI patients can't BITE)
  - Frequent fractures
  - Bone Deformities
    - Bow legs
    - Scoliosis
    - Short stature
  - (I) Eye Deformities
    - Blue sclera
  - Teeth deformities
  - Ear – Hearing loss
    - Malformations of boney ear

- Patient will often be considered victim of abuse due to frequent fracture

Ehlers-Danlos + Menkes

Ehlers-Danlos syndrome





Faulty collagen synthesis causing hyperextensible skin A, hypermobile joints B, and tendency to bleed (easy bruising).

Multiple types. Inheritance and severity vary. Can be autosomal dominant or recessive. May be associated with joint dislocation, berry and aortic aneurysms, organ rupture.

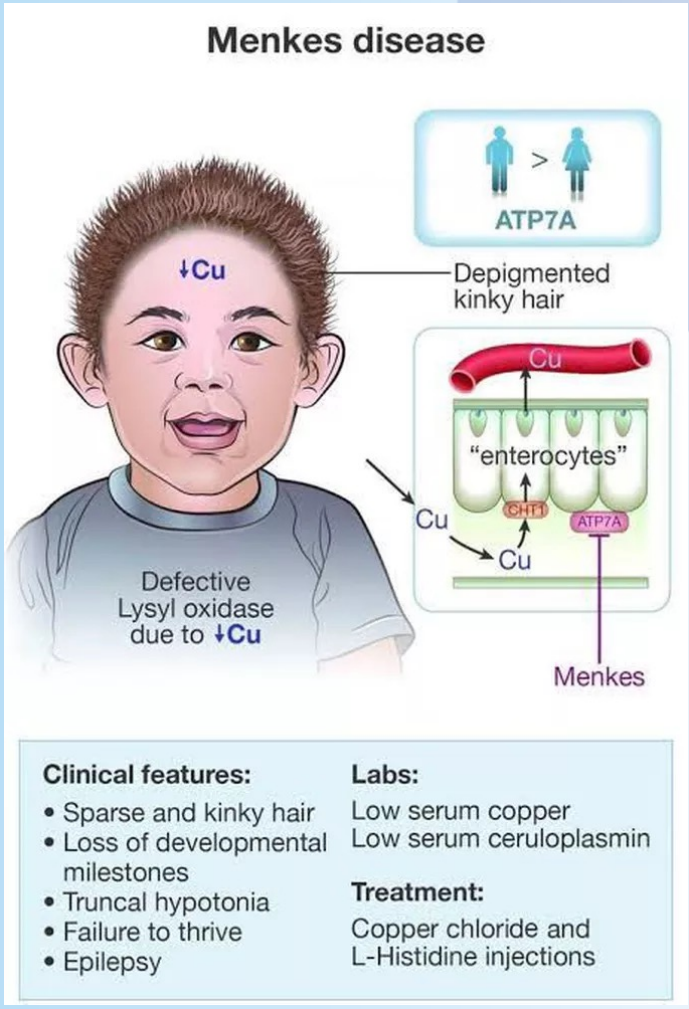
Hypermobility type (joint instability): most common type.

Classical type (joint and skin symptoms): caused by a mutation in type V collagen (eg, *COL5A1*, *COL5A2*).

Vascular type (fragile tissues including vessels [eg, aorta], muscles, and organs that are prone to rupture): deficient type III procollagen.

Menkes disease

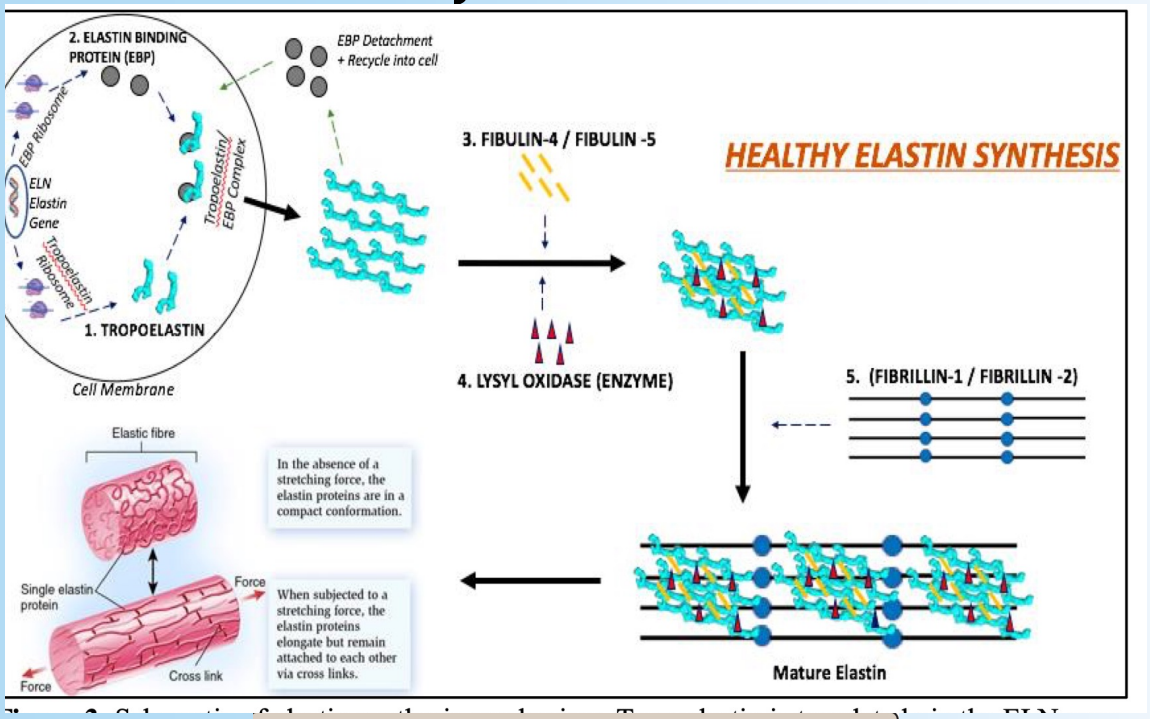
X-linked recessive connective tissue disease caused by impaired copper absorption and transport due to defective Menkes protein (ATP7A). Leads to ↓ activity of lysyl oxidase (copper is a necessary cofactor) → defective collagen. Results in brittle, "kinky" hair, growth retardation, and hypotonia.

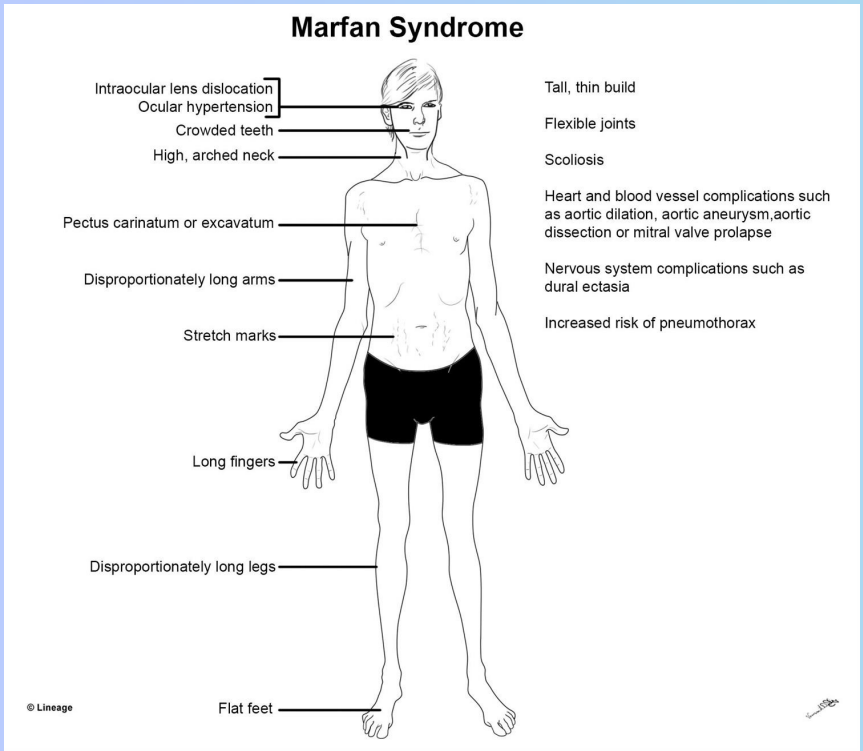


Elastin

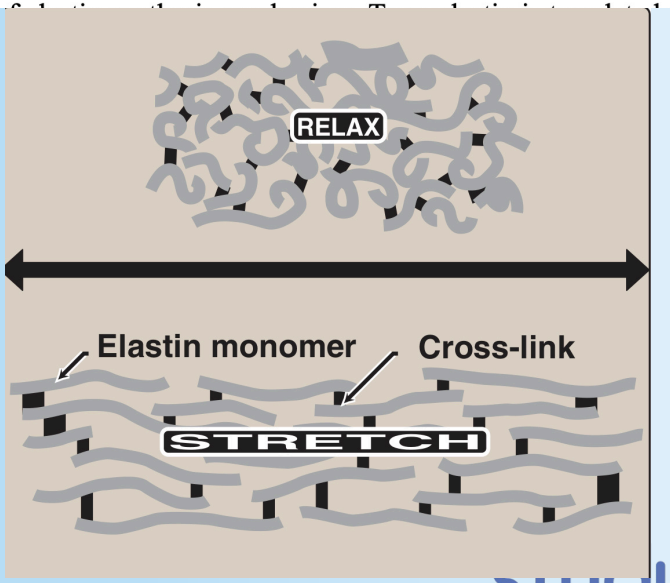
- Primary structure
  - Mostly composed of glycine and valine
- secondary structure
  - Predominantly amorphous structure
- Tough with high tensile strength
  - Found in lung alveoli, walls of large arteries, elastic ligaments

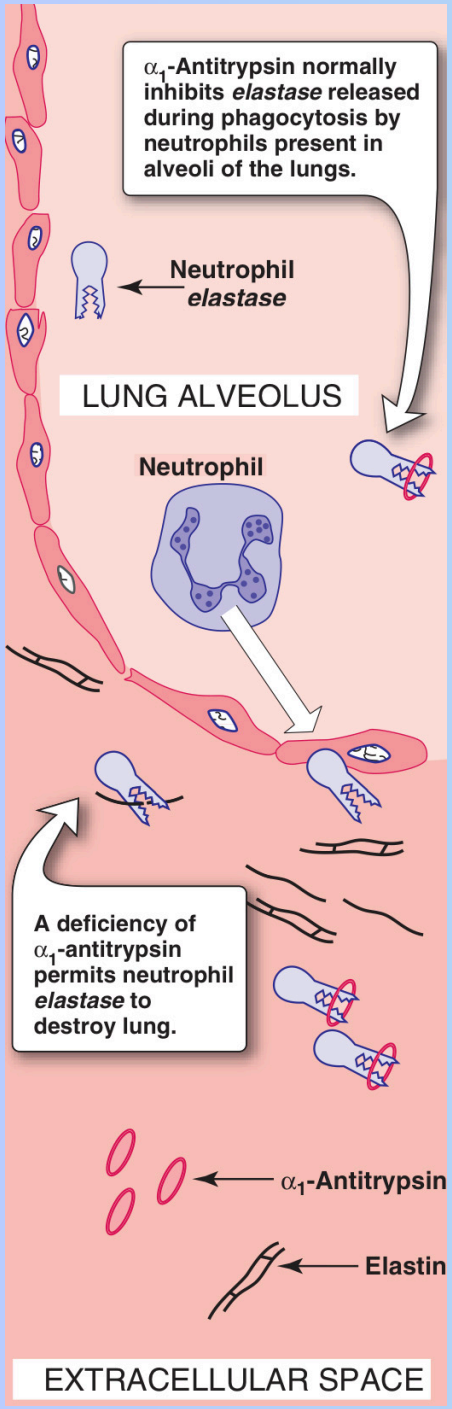
Synthesis





Marfan syndrome: mutation in fibrillin gene that will result in fibers that lack strength and elasticity





Elastin

- Elastase
  - Breaks down elastin
  - Released by neutrophils involved in phagocytosis
- Alpha-1 antitrypsin deficiency
  - Alpha-1 AT inhibits elastase
  - Deficiency in Aplha-1 AT results in destruction of alveolar walls
    - Normal Alveoli only exposed to small amounts of elastase since it can't regenerate
  - Approx. 2-5% of patients with emphysema are predisposed to Emphysema due to Alpha 1-AT deficiency

Copy participation link

1 Go to wooclap.com

2 Enter the event code in the top banner

Event code
GFRKNU

studyaid