

IV. CHAPTER SUMMARY

Collagen and elastin are fibrous proteins (Figure 4.15). Collagen molecules contain an abundance of **proline**, **lysine**, and **glycine**, the latter occurring at every third position in the primary structure. Collagen also contains **hydroxyproline**, **hydroxylysine**, and **glycosylated hydroxylysine**, each formed by posttranslational modification. Collagen molecules typically form **fibrils** containing a long, stiff, triple-stranded helical structure, in which three collagen polypeptide chains are wound around one another in a rope-like superhelix (**triple helix**). Other types of collagen form mesh-like networks. **Elastin** is a connective tissue protein with rubber-like properties in tissues such as the lung. **α_1 -Antitrypsin (AAT)**, produced primarily by the liver but also by monocytes and alveolar macrophages, prevents elastase-catalyzed degradation of elastin in the alveolar walls. A deficiency of AAT can cause **emphysema** and, in some cases, cirrhosis of the liver.

Study Questions

Choose the ONE best answer.

4.1 A 30-year-old woman of Northern European ancestry presents with progressive dyspnea (shortness of breath). She denies the use of cigarettes. Family history reveals that her sister also has problems with her lungs. Which one of the following etiologies most likely explains this patient's pulmonary symptoms?

- A. Deficiency in dietary vitamin C
- B. Deficiency of α_1 -antitrypsin
- C. Deficiency of prolyl hydroxylase
- D. Decreased elastase activity
- E. Increased collagenase activity

4.2 What is the differential basis of the liver and lung pathology seen in α_1 -antitrypsin deficiency?

4.3 A 7-month-old child "fell over" while crawling and now presents with a swollen leg. Imaging reveals a fracture of a bowed femur, secondary to minor trauma, and thin bones (see x-ray at right). Blue sclerae are also noted. At age 1 month, the infant had multiple fractures in various states of healing (right clavicle, right humerus, and right radius). A careful family history has ruled out nonaccidental trauma (child abuse) as a cause of the bone fractures. Which pairing of a defective (or deficient) molecule and the resulting pathology best fits this clinical description?



- A. Elastin and emphysema
- B. Fibrillin and Marfan disease
- C. Type I collagen and osteogenesis imperfecta (OI)
- D. Type V collagen and Ehlers-Danlos syndrome (EDS)
- E. Vitamin C and scurvy

4.4 How and why is proline hydroxylated in collagen?

Correct answer = B. α_1 -Antitrypsin (AAT) deficiency is a genetic disorder that can cause pulmonary damage and emphysema even in the absence of cigarette use. A deficiency of AAT permits increased elastase activity to destroy elastin in the alveolar walls. AAT deficiency should be suspected when chronic obstructive pulmonary disease develops in a patient younger than age 45 years who does not have a history of chronic bronchitis or tobacco use or when multiple family members develop obstructive lung disease at an early age. Choices A, C, and E refer to collagen, not elastin.

With α_1 -antitrypsin (AAT) deficiency, the cirrhosis that can result is due to polymerization and retention of AAT in the liver, its site of synthesis. The alveolar damage is due to the retention-based deficiency of AAT (a protease inhibitor) in the lung such that elastase (a protease) is unopposed.

Correct answer = C. The child most likely has osteogenesis imperfecta. Most cases arise from a defect in the genes encoding type I collagen. Bones in affected patients are thin, osteoporotic, often bowed, and extremely prone to fracture. Pulmonary problems are not seen in this child. Individuals with Marfan syndrome have impaired structural integrity of the skeleton, eyes, and cardiovascular system. Defects in type V collagen cause the classic form of EDS characterized by skin extensibility and fragility and joint hypermobility. Vitamin C deficiency is characterized by capillary fragility.

Proline is hydroxylated by prolyl hydroxylase, an enzyme of the rough endoplasmic reticulum that requires O_2 , Fe^{2+} , and vitamin C. Hydroxylation increases interchain hydrogen bond formation, strengthening the triple helix of collagen. Vitamin C deficiency impairs hydroxylation.