Alkaptonuria

It is a rare inherited genetic disorder in which body cannot process amino acids - phenylalanine and tyrosine.

→ It is caused by a mutation in HGD gene for enzyme homogentisate 1,2 - dioxygenase. (HGD)

→ If a person inherits an abnormal copy from both parents (recessive condition), the body accumulates an intermediate substance called homogentisic acid in blood and tissues.

→ It is excreted in urine, giving an unusual dark colour.

→ HG acid causes damage to cartilage, heart valves, leading to kidney stones, etc.

→ It is also called black urine disease and black bone disease.

Symptoms

→ Children or young adults are asymptomatic. as children or young adults.

→ Urine may turn brown or black.

→ Pigmentation may occur in cartilage of ear, sclera and corneal limbus of eye.

→ After the age of 30, people may feel pain in joints of spine, hips and knees.

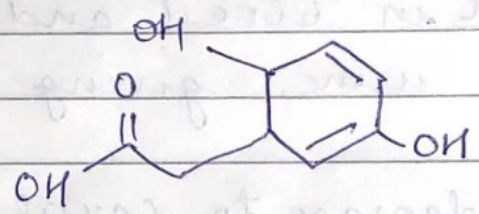
→ Bone mineral density is affected.

→ Increased risk of bone fractures.

Pathophysiology

→ All people carry two copies of gene HGD in their DNA, which contains genetic information to produce enzyme homogentisate 1, 2-dioxygenase (HGD) which is normally found
→ in many tissues of body.

In people with alkaptonuria, both copies of gene contain abnormalities due to which body cannot produce adequately functioning enzyme.



Homogentisic acid

→ Different mutations may affect the structure, function or solubility of enzyme.

→ In alkaptonuria, the HGD enzyme cannot metabolise homogentisic acid (generated from tyrosine) into 4-maleylacetoacetate.
→ Homogentisic acid levels in blood are 100-fold higher than would normally be expected.
→ It is converted to benzoquinone which forms polymers that resemble skin pigment melanin.

Diagnosis

It can be diagnosed by collecting urine for 24 hours and determining the amount of homogentisic acid by chromatography.

Treatment

- Large doses of Vitamin C.
- Herbicide Nitisinone