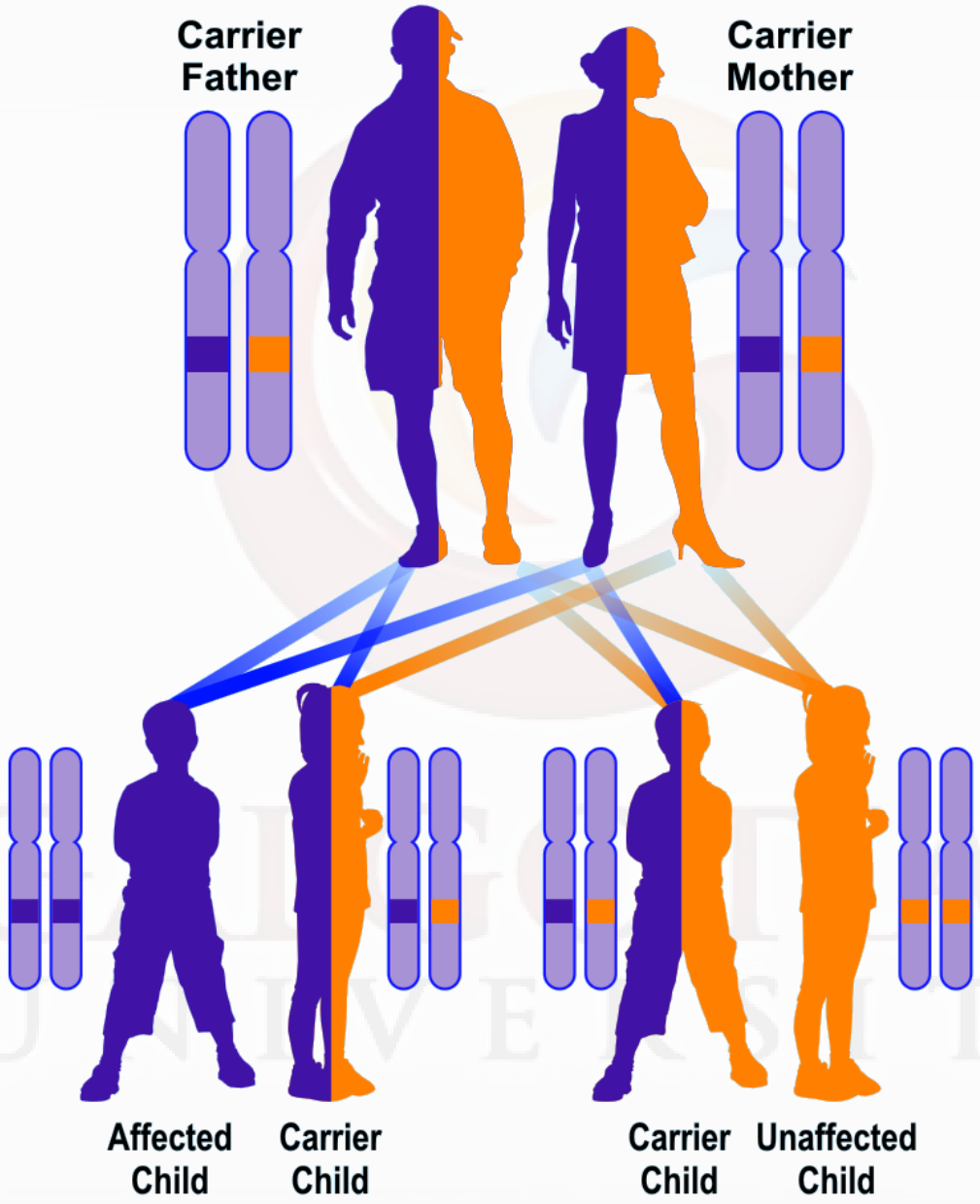
ALKAPTONURIA

Introduction

- Alkaptonuria is a rare inherited disorder.
- It occurs when mutation/defects enzyme called homogentisic dioxygenase (HGD).
- This enzyme is used to break down a toxic substance called homogentisic acid.
- Deficiency of this enzyme leads to homogentisic acid accumulation in the body.

- Is a rare disease also called black urine disease.
- is an inherited genetic disease of phenylalanine and tyrosine metabolism.
- Ochronosis, a buildup of dark pigment in connective tissues
- Estimated to occur in 1 of every 250-1 million live birth, Caused by a mutation on homogenitsate 1,2-dioxygenase (HGD) gene.
- Autosomally recessive condition i.e., both the parents must have the gene in order to pass the condition onto their progeny.

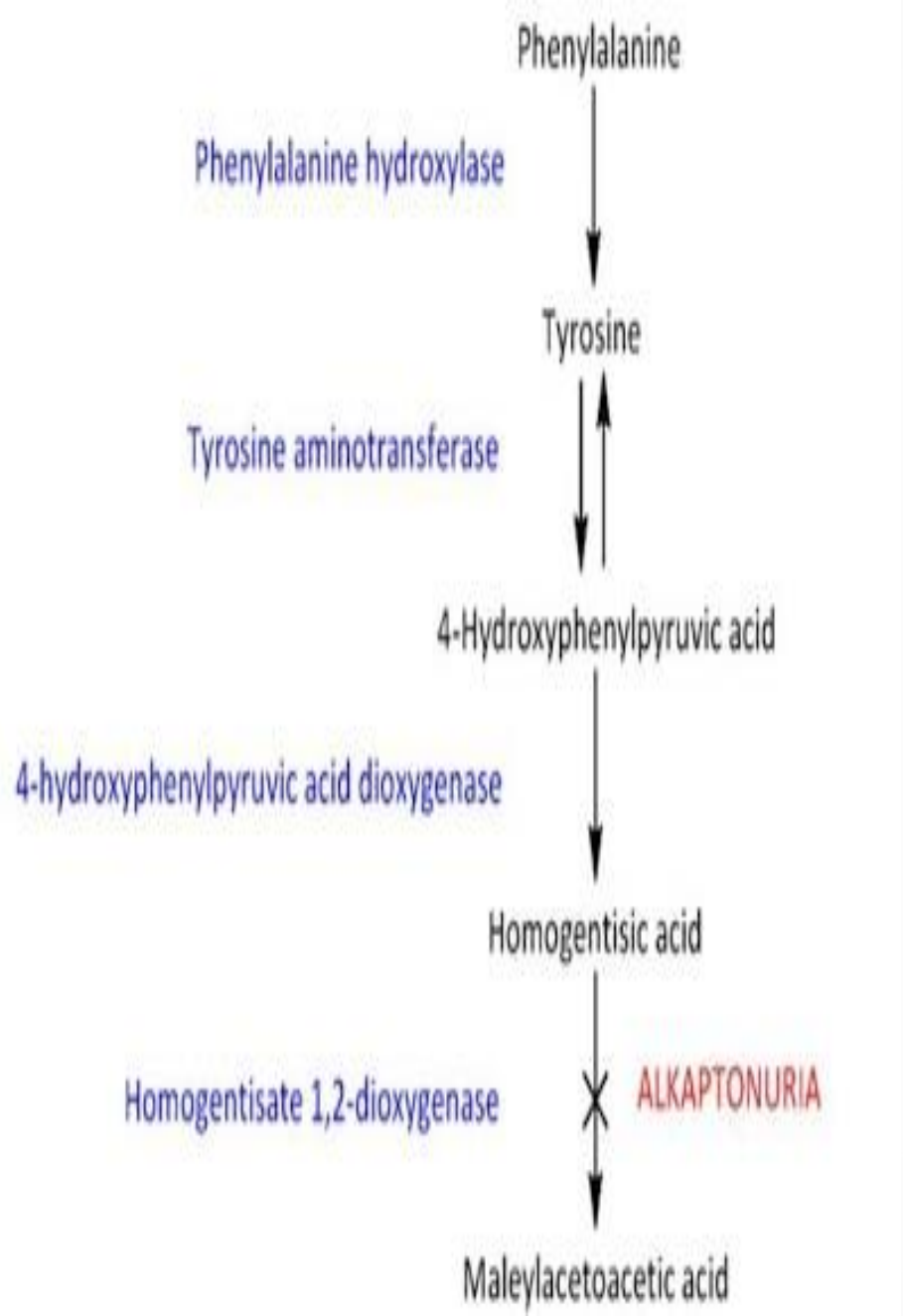
Autosomal Recessive



- Mutation or defect in HGD gene which causes lack of the enzyme homogentisate dioxygenase (HGD).

- This causes a build up of a homogentisic acid (HGA) in the bones, cartilage and urine.

- HGA is an intermediate in the degradation pathway of the amino acids (Phe & Tyr) to the Krebs cycle.



Mutation

- The gene defect makes the body unable to properly break down certain amino acids (tyrosine and phenylalanine)
- As a result, a substance called homogentisic acids builds up in the skin and other body tissues.
- The acid leaves the body through the urine. The urine turns brownish-black when it mixes with air.
- The build up of homogentisic acid causes bone and cartilage to become discolored and brittle.
- This typically leads to oestoarthritis, especially in spine and large joints.
- People with this disease have urine that turns dark brown or black when it's exposed to air.

Symptoms

- Urine in an infant's diaper may darken and can turn almost black after several hrs. However, many persons with this condition may not know they have it until mid-adulthood (around age 40), when joint and other problem occurs.
- Dark spots in the sclera (white) of eyes.
- Thickened and darkened cartilage in ears.
- Blue speckled discoloration of skin, particularly around sweat glands.
- Dark-colored sweat or sweat strains.
- Black earwax
- Kidney stones and prostate stones
- Arthritis (especially hip and knee joints)

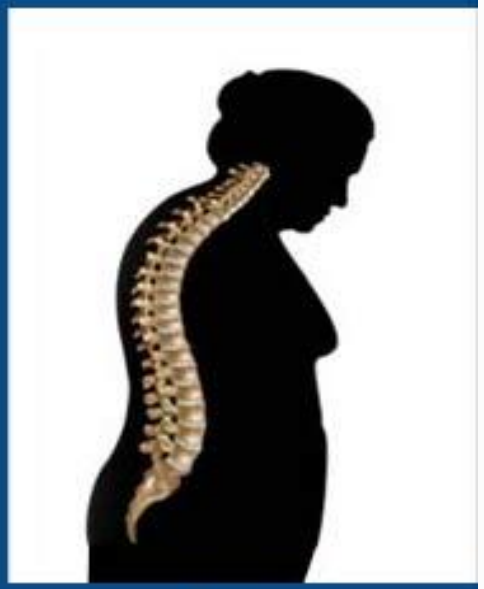
Symptoms & Signs of Alkaptonuria

Black colored urine

Ochronosis

Tendinitis

Kidney & prostate stones



Kyphosis or hunchback

source : wikipedia.org

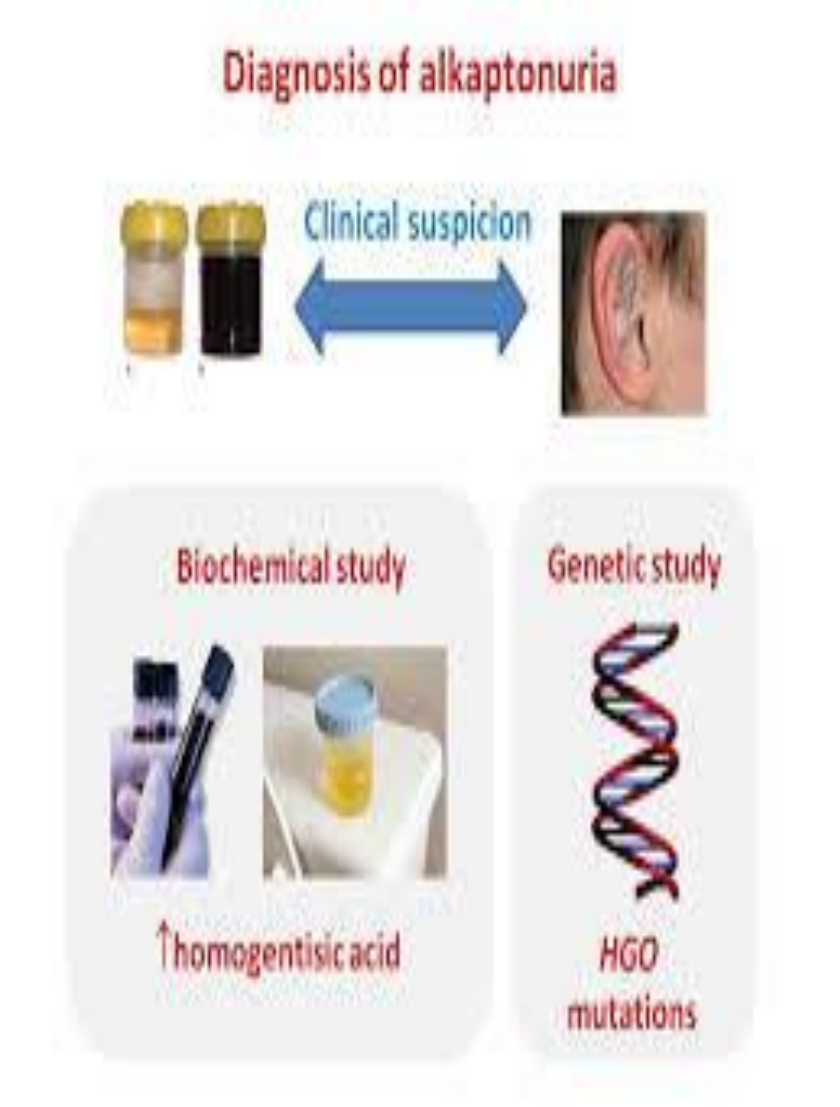
Diagnosis

- Urine test- addition of ferric chloride to the urine will change it's color to black.

  Gas chromatography to look for traces of HGA in urine.

- DNA testing- to check for mutated HGD gene. It is generally done by analyzing blood sample.

- Prenatal tests (amminocenteis or chronic villus sampling) can be done to screen a developing baby for this condition if the genetic charge has been identified.



Treatment

- The treatment of alkaptonuria is aimed at the specific symptoms.
- Activities that place significant physical stress to the spine and joints should be avoided.
- Patients receive anti-inflammatory medications or narcotics to treat joint plan.
- Physical and occupational therapy to maintain the strength and flexibility of muscles and joints.
- Some individuals require surgical intervention.

References

- Introne WJ, Gahl WA. Alkaptonuria. In: NORD Guide to Rare Disorders. Lippincott Williams & Wilkins. Philadelphia, PA. 2003:431.
- La Du BN. Alkaptonuria. In: Connective Tissue and Its Heritable Disorders. Molecular, Genetic, and Medical Aspects, 2nd ed, Royce PM, Steinmann B, editors. 2002 Wiley-Liss, New York, NY. pp.809-825.