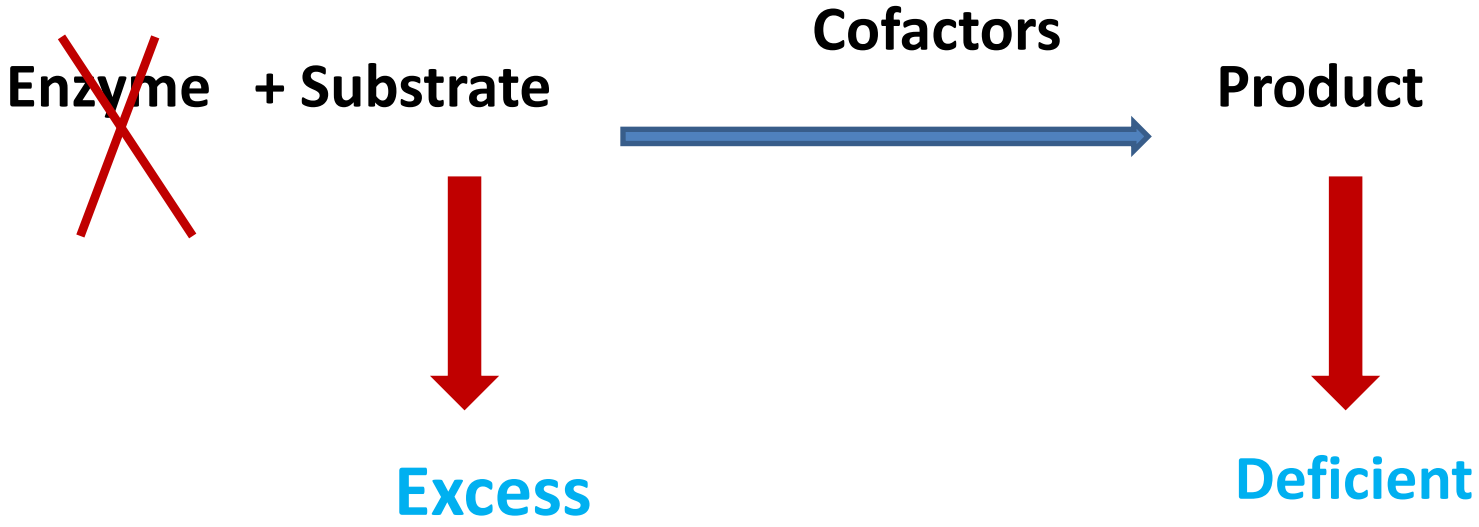
INBORN ERRORS OF AMINO ACIDS METABOLISM

TYROSINE METABOLISM

Inborn Error of Amino Acid Metabolism

Inborn Errors of aa Metabolism

- Caused by enzyme loss or deficiency due to gene loss or gene mutation

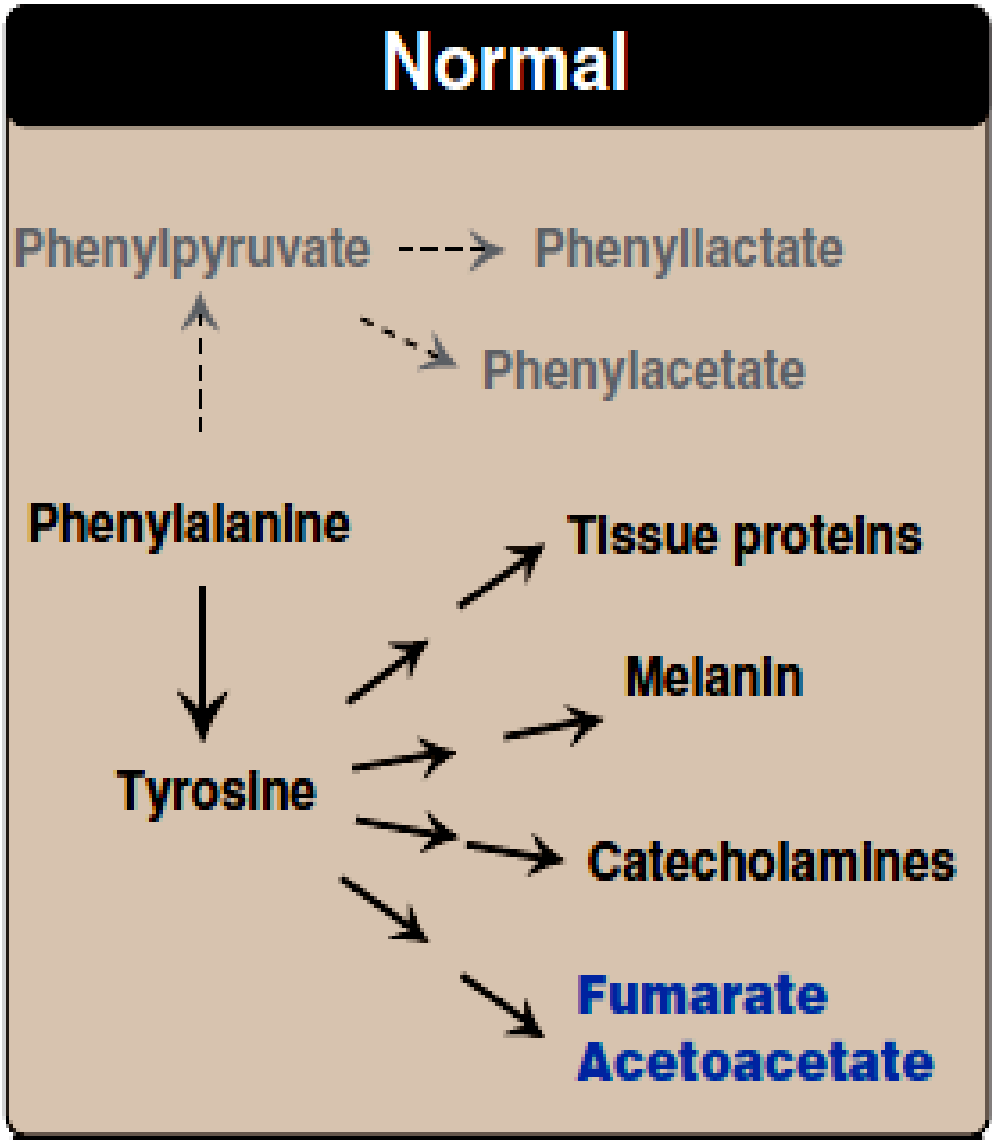


Tyrosine

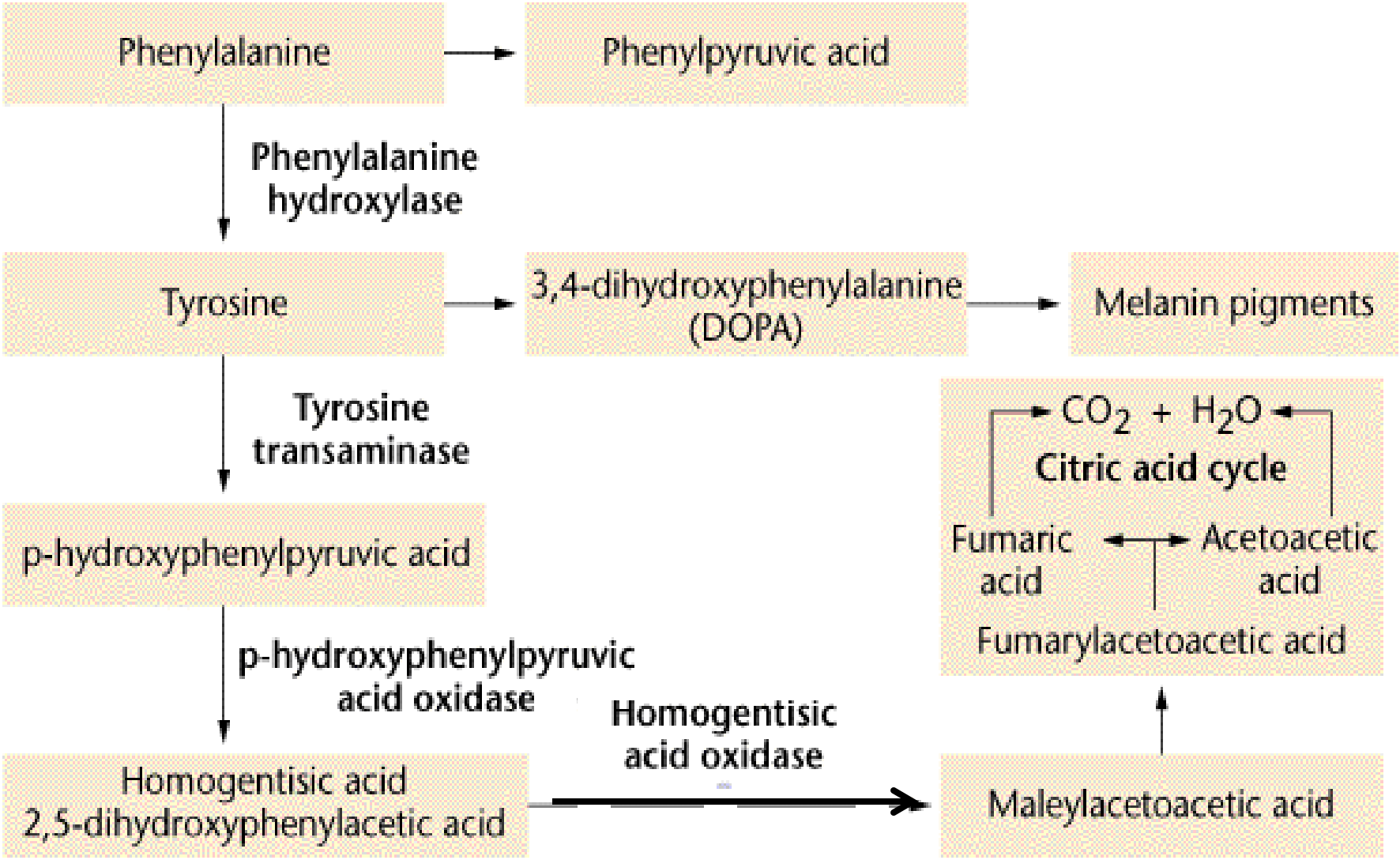
- Amino acid
- Rich food sources – eggs, cheese, turkey
- Can be synthesised in the body from phenylalanine (food sources - chicken, fish, cheese, beans, etc)



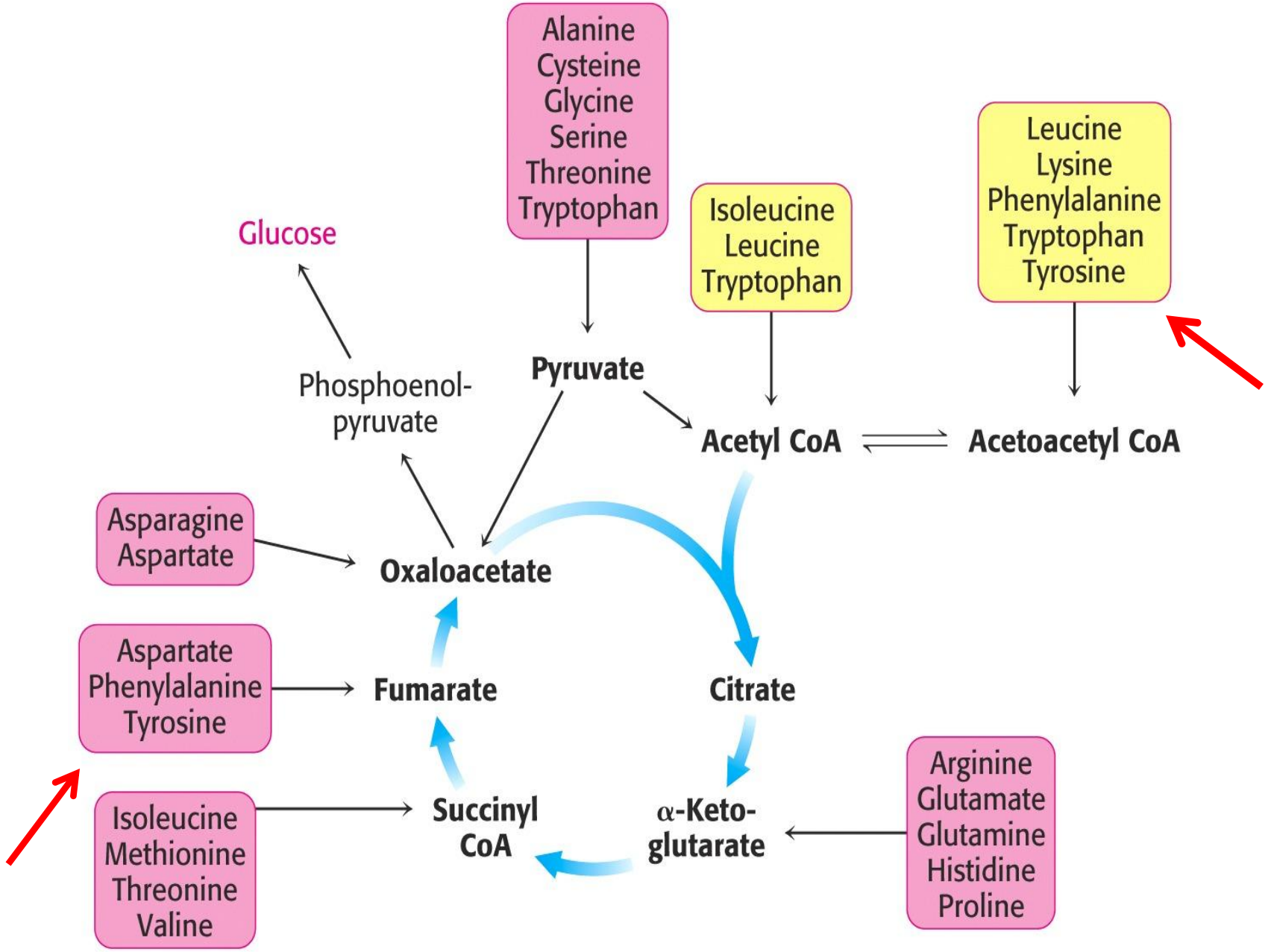
Degradation of TYROSINE & Aromatic Amino Acids

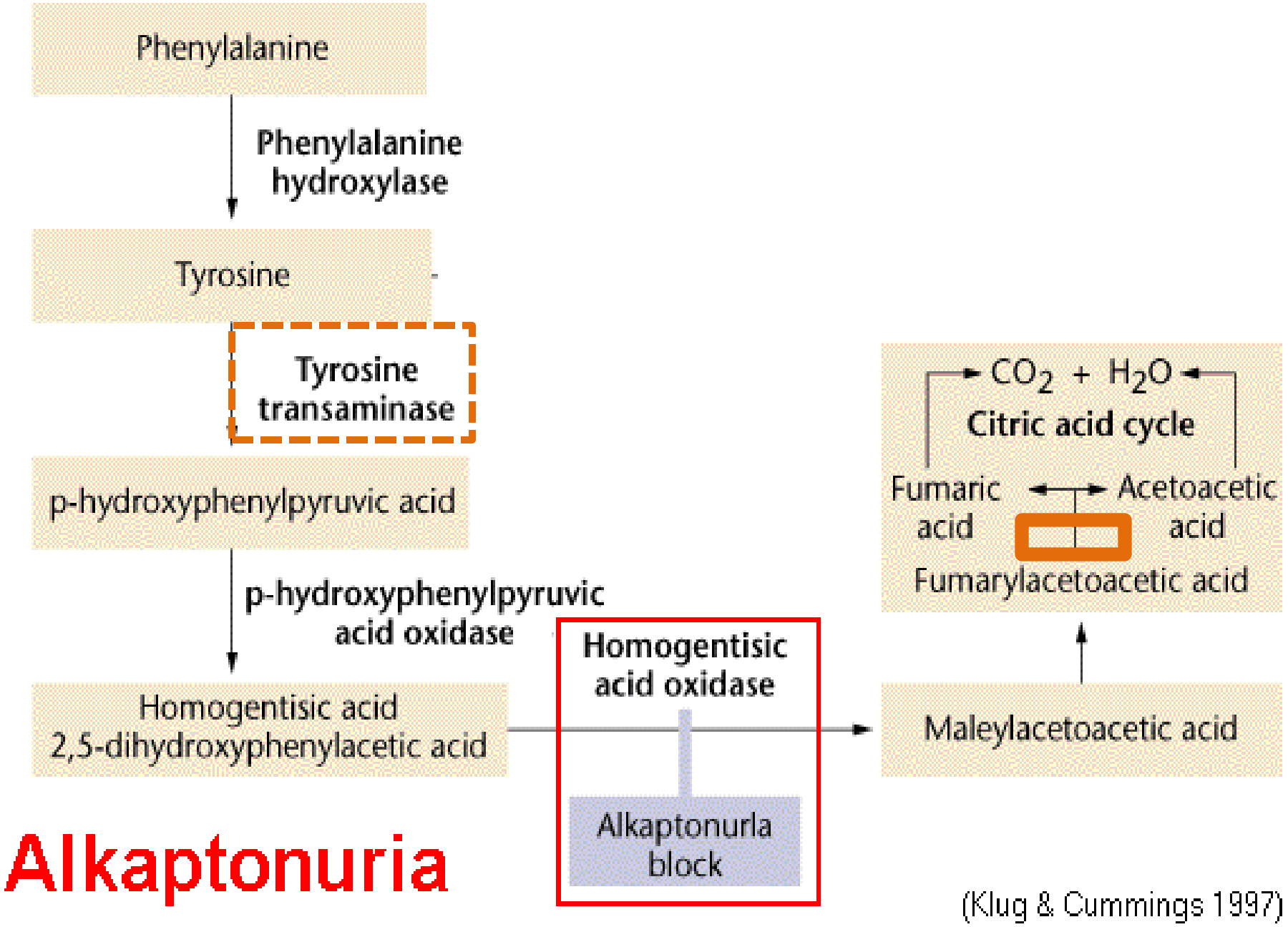


Tyrosine is a precursor for synthesis of melanins and of epinephrine and norepinephrine ***(catecholamines).***



(Klug & Cummings 1997)


Alanine
Cysteine
Glycine
Serine
Threonine
Tryptophan
Isoleucine
Leucine
Tryptophan
Leucine
Lysine
Phenylalanine
Tryptophan
Tyrosine
Glucose
Phosphoenol-
pyruvate
Pyruvate
Acetyl CoA
Acetoacetyl CoA
Asparagine
Aspartate
Oxaloacetate
Aspartate
Phenylalanine
Tyrosine
Fumarate
Citrate
Isoleucine
Methionine
Threonine
Valine
Succinyl
CoA
α-Keto-
glutarate
Arginine
Glutamate
Glutamine
Histidine
Proline



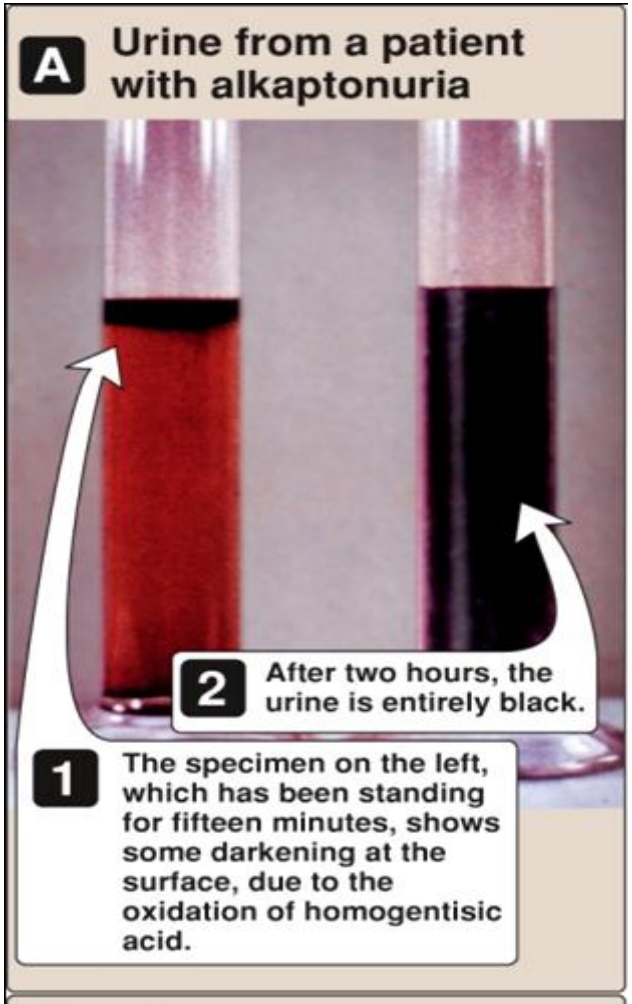
Alkaptonuria

(Klug & Cummings 1997)

HOMOGENTISATE OXIDASE DEFICIENCY (ALKAPTONURIA),

Alkaptonuria is a rare metabolic condition involving a deficiency in *homogentisic acid oxidase,* resulting in the accumulation of homogentisic acid. The condition has three characteristic symptoms:

1.homogentisic aciduria **(the patient's urine contains elevated levels of homogentisic acid, which is oxidized to a dark pigment on standing (Accumulation of homogentisic acid in the blood causes its excretion in urine, after which it gradually darkens upon exposure to air). Dark staining of the diapers sometimes can indicate the disease in infants, but usually no symptoms are present until later in life.**

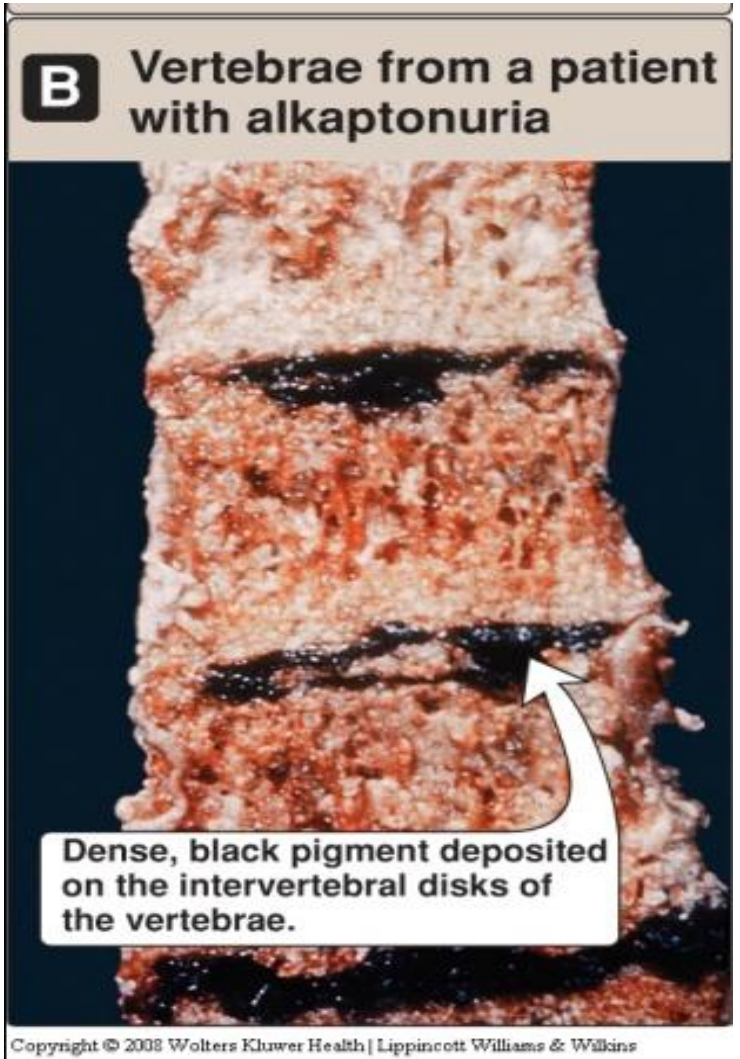


Homogentisate Oxidase Deficiency (Alcaptonuria),

2. large joint arthritis

Arthritis of the spine is a complication of alkaptonuria ochronosis .

Treatment is targeted to managing the symptoms.



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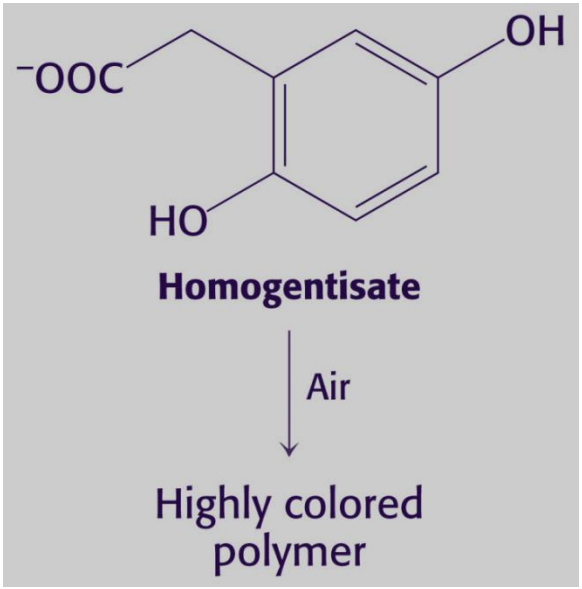
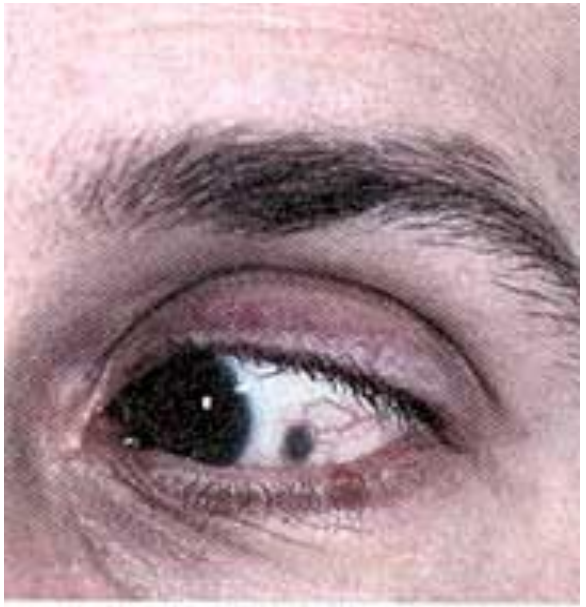
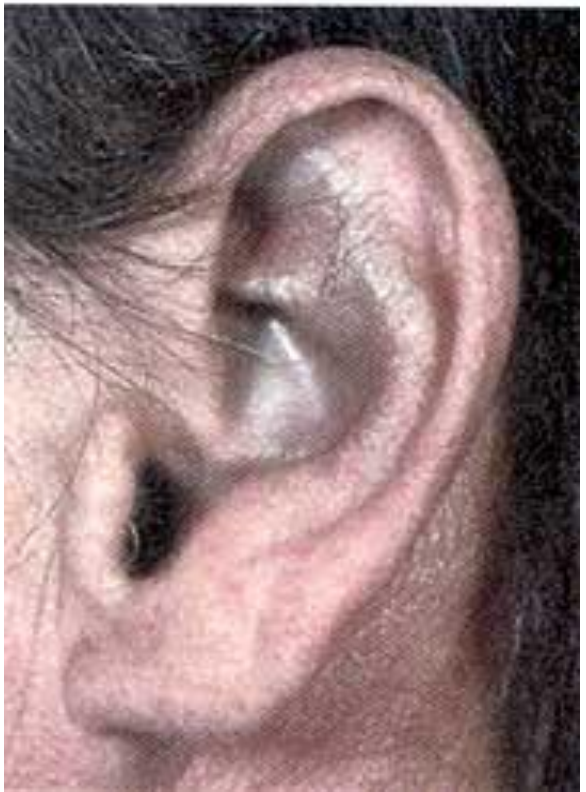
Homogentisate Oxidase Deficiency (Alkaptonuria),

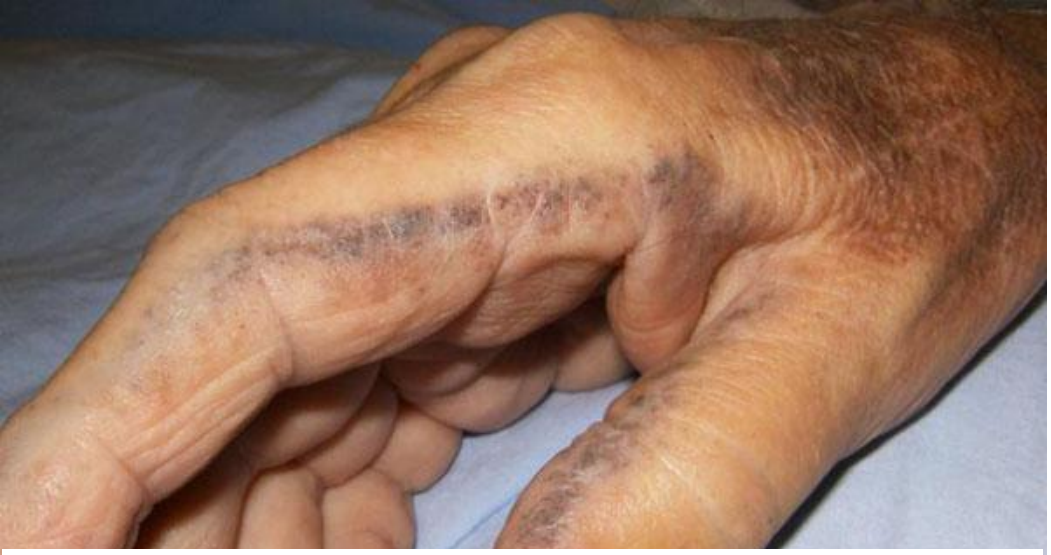
3. black ochronotic pigmentation of cartilage and collagenous tissue **(The dark pigment also accumulates over years in the cartilage (ochronosis) and may be seen in the sclera of the eye, in ear cartilage) .**
Patients with alkaptonuria are usually asymptomatic until about age 40.





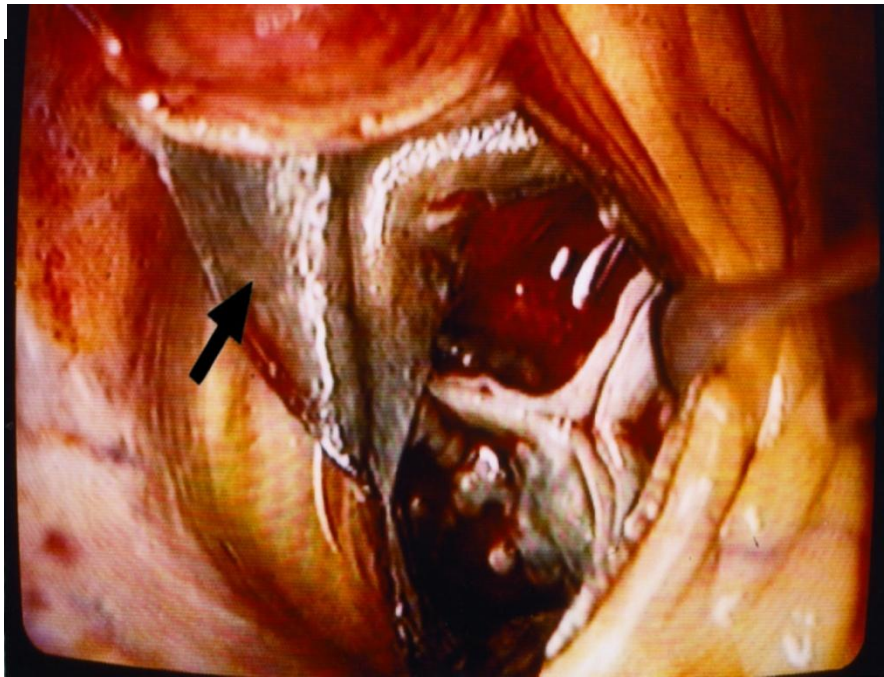


Alkaptonuria



Accumulation of oxidized homogentisic acid pigment in connective tissue (ochronosis)

Aortic valve stenosis in alcaptonuria



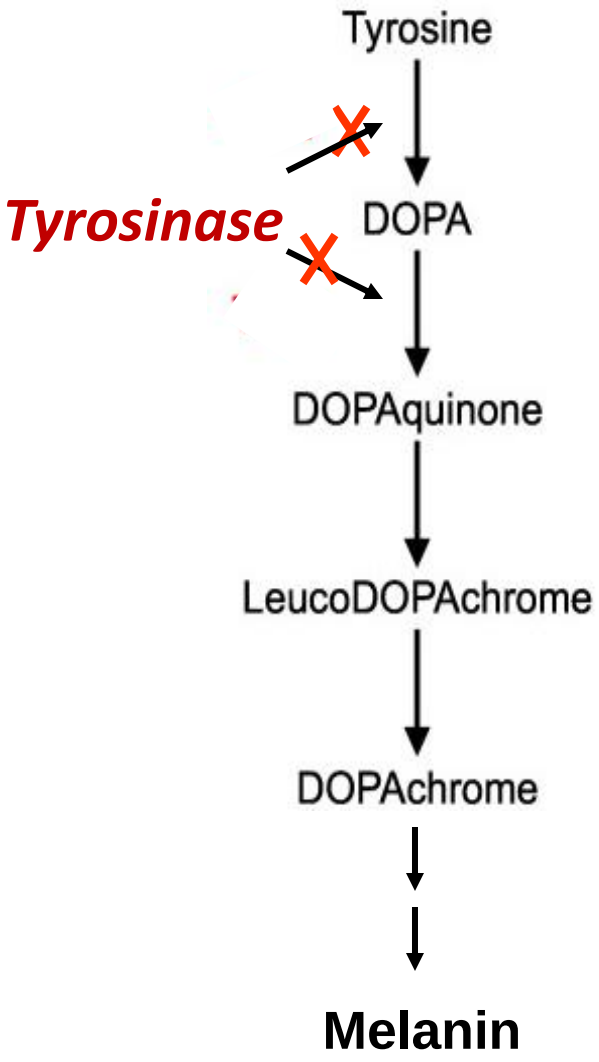
Treatment of Alkaptonuria

- Restricted intake of tyrosine and phenylalanine reduces homogentisic acid and dark pigmentation

Albinism

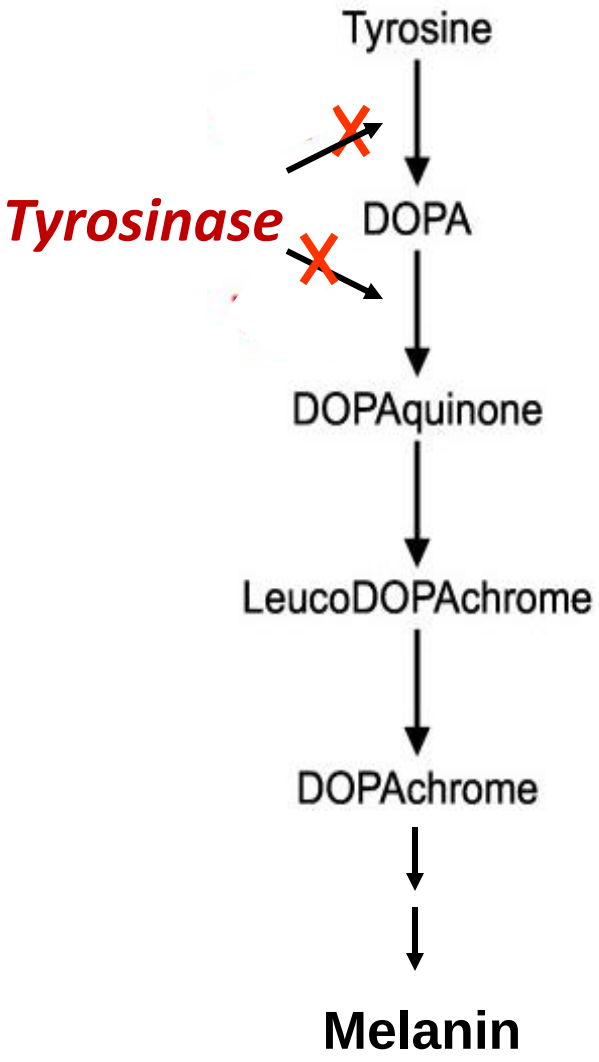
genetically determined lack or deficit of enzyme **tyrosinase**

Tyrosinase in melanocytes oxidises tyrosine to DOPA and DOPA-quinone



ALBINISM

Albinism refers to a group of conditions in which a defect in tyrosine metabolism results in a deficiency in the production of melanin. These defects result in the partial or full absence of pigment from the skin, hair, and eyes. Albinism appears in different forms, and it may be inherited by one of several modes: **autosomal recessive** (primary mode), **autosomal dominant,** or **X-linked**.



Albinism

Complete albinism (also called *tyrosinase-negative oculocutaneous albinism,* results from a deficiency of *tyrosinase,* causing a total absence of pigment from the hair, eyes, and skin It is the most severe form of the condition.

In addition to hypopigmentation, affected individuals have vision defects and photophobia (sunlight hurts their eyes). They are at increased risk for skin cancer.

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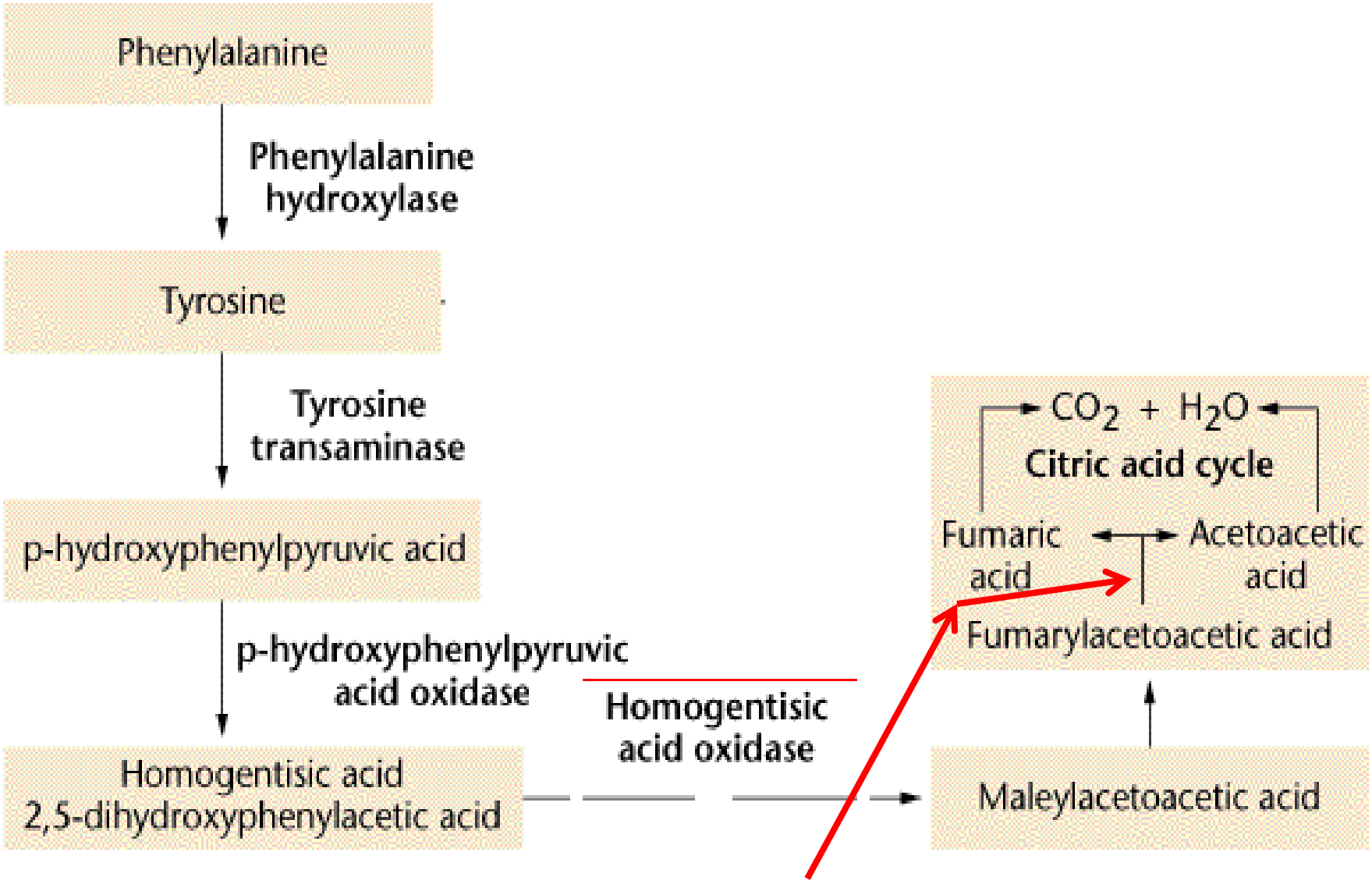
TYROSINEMIA

An extremely rare but treatable hereditary disorder.

When the body cannot break down tyrosine, high levels build up in the blood and form a toxic substance (known as succinylacetone) in the liver, kidneys, and central nervous system. This means that if tyrosinemia isn't treated, it may cause liver and kidney damage and brain-related problems, such as problems with learning.



A deficiency of the enzyme **fumarylacetoacetase** leads to an accumulation of the novel and extremely toxic compound succinylacetone

Tyrosinaemia type 1

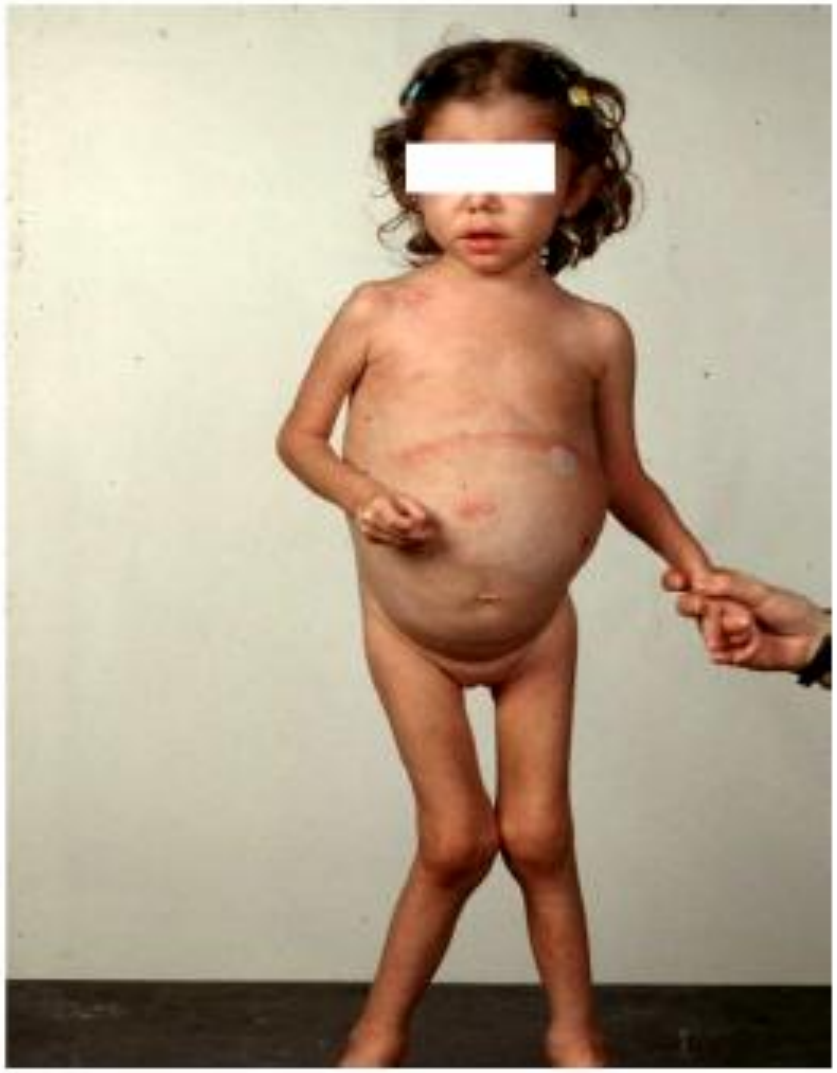
A deficiency of the enzyme fumarylacetoacetase leads to an accumulation of an extremely toxic compound succinylacetone . This is detected by urine organic acid analysis. Tyrosine concentrations in body fluids are also elevated but can be variable.

Affected children typically present with severe liver disease and **renal Fanconi syndrome**.

The drug ***NITISINONE*** inhibits an enzyme *(hydroxy phenylpyruvate dioxygenase)* higher in the pathway. This prevents the synthesis of succinylacetone and dramatically improves prognosis.

Patients continue to need dietary therapy to prevent tyrosine accumulation.

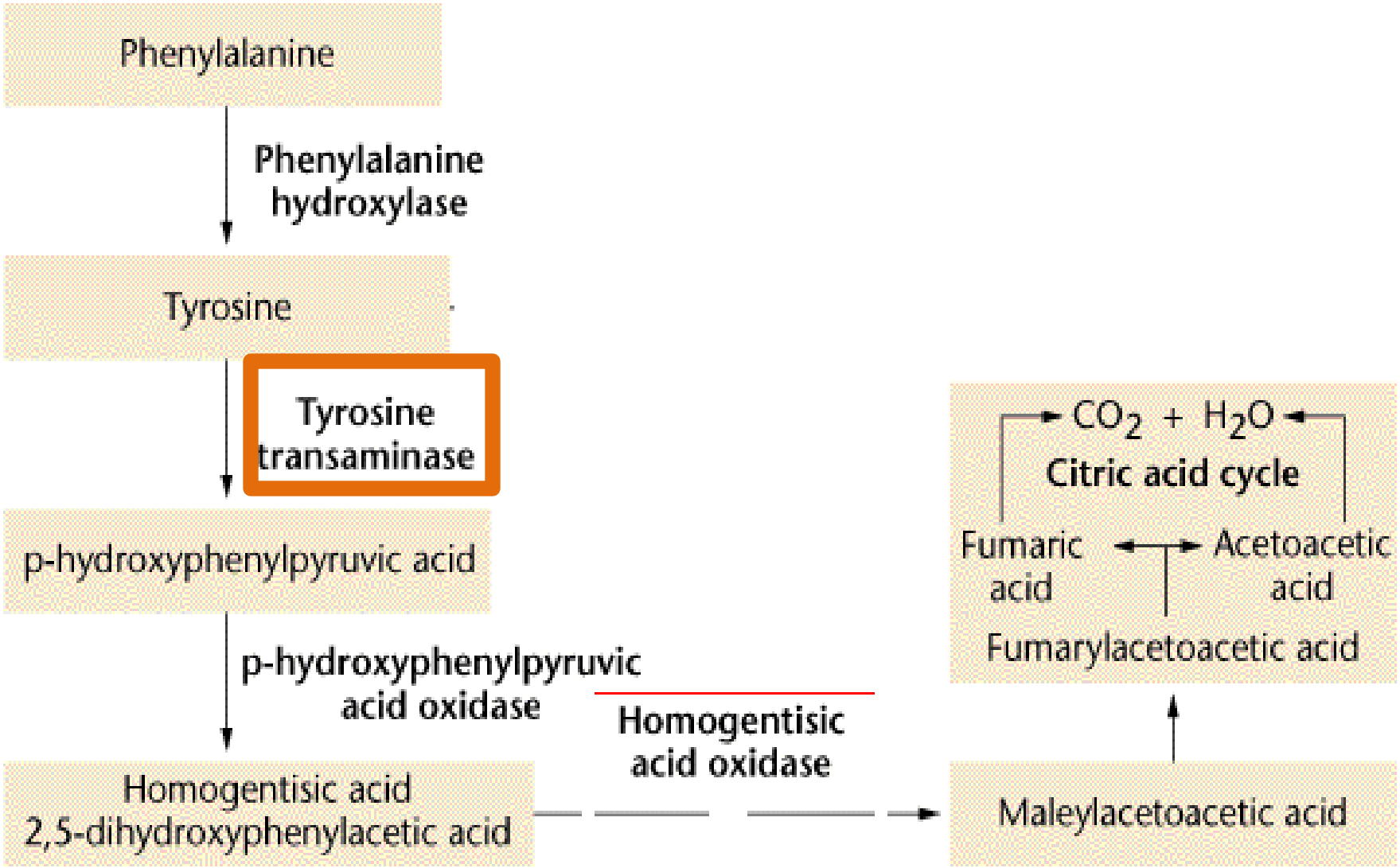
Tyrosinemia type I



- Fumarylacetoacetase deficiency
- Acute manifestation in infancy
- Hepatorenal involvement with acute hepatic dysfunction and Fanconi syndrome
- porfyric crises-abdominal cramps
- Chronic- ci heatis and ca in cirhosim
- Diet, nitisone, liver transplant

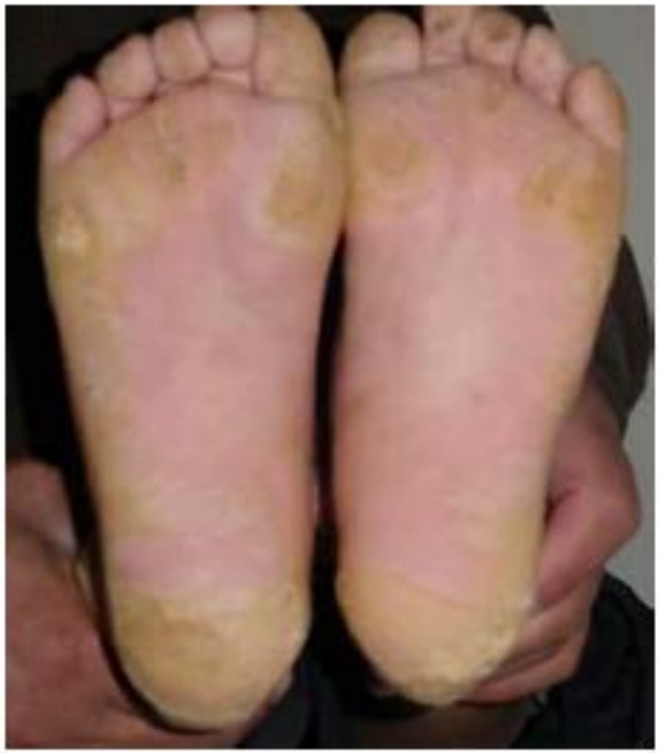
Tyrosinemia Type II

- Enzyme defect: Cytosolic tyrosine aminotransferase *(Tyrosine transaminase)*
- Clinical findings: Painful corneal lesions (lacrimation, photophobia, scars), mild mental retardation
- Diagnosis: High tyrosine and phenylalanine levels
- Therapy: Tyrosine and phenylalanine-restricted diet

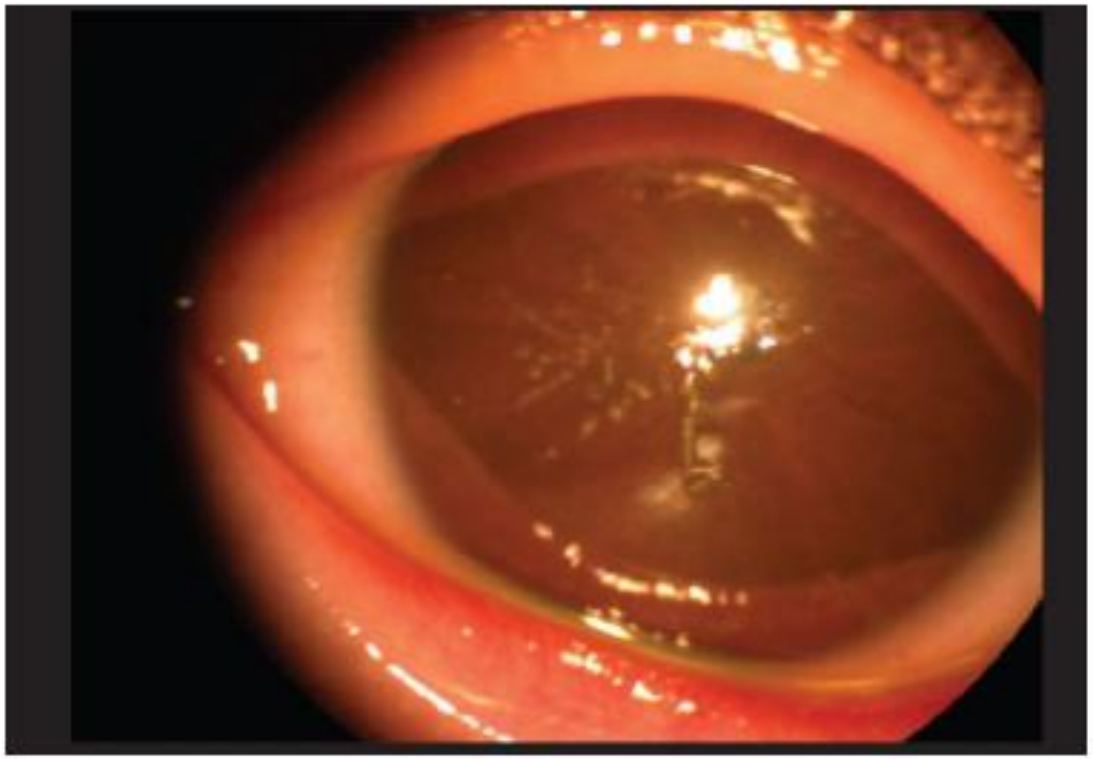


Tyrosinemia Type II -- A deficiency of the enzyme **TYROSINE TRANSAMINASE** leads to accumulation of Phenylalanine and Tyrosine

Tyrosinemia Type II



hyperkeratossi



herpetiformic keratitis

THANKS