Amino acids
part 2

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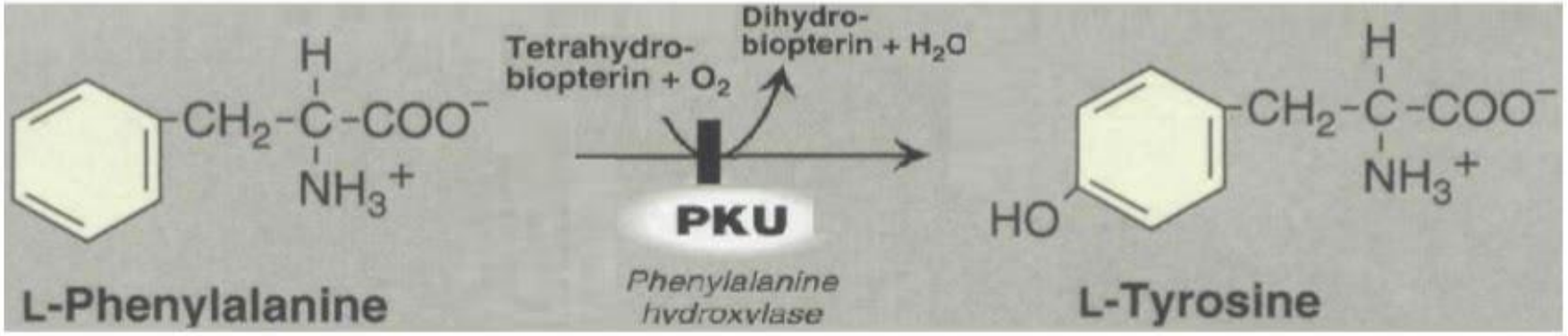
Phenylalanine

- is a ketogenic and glycogenic essential amino acid.
- **Functions:** phenylalanine is the precursor for Tyrosine.
- A. Phenylalanine can be converted to tyrosine mainly in liver as follows:



- B. This reaction needs phenylalanine hydroxylase enzyme and tetrahydrobiopterin as coenzyme. This results in the formation of dihydrobiopterin (DH B) which must be regenerated by dihydrobiopterin reductase enzyme

Phenylketonuria (PKU)

- Phenylketonuria (PKU) is a genetic disorder that is characterized by an inability of the body to metabolize phenylalanine, caused by a deficiency in Phenylalanine Hydroxylase (PAH) enzyme or The defect is due to deficiency of dihydrobiopterin reductase.an enzyme that catalyzes the regeneration of tetrahydrobiopterin (cofactor of PAH)
- 1. Classic phenylketonuria: Due to defect in phenylalanine hydroxylase. This is most common error.

- 2. Atypical phenylketonuria or hyperphenylalaninemia : Defect in dihydrobiopterin reductase

- Elevated brain phenylalanine and concomitant deficiencies of other amino acids lead to cerebral damage in early life.
- • **Symptoms** are mental retardation, failure to talk, seizures, fair hair and blue eyes due to deficiency of pigment melanin (hydroxylation of tyrosine by tyrosinase is inhibited by high levels of phenylalanine in PKU.

- **Diagnosis** may involve measuring the phenylalanine concentration in blood taken from a heel prick. The microbiological Guthrie test was used to assay phenylalanine, but now many laboratories use chromatography methods or tandem mass spectroscopy.

- **Treatment:**
- The aim of treatment is to lower plasma phenylalanine concentrations by giving a low-phenylalanine diet.
- dietary restriction should be life long
- the artificial sweetener aspartame is metabolized to phenylalanine.

tyrosine

- Tyrosine is a ketogenic and glycogenic non- essential amino acid.

Functions: Tyrosine is the precursor for:

- 1-Catecholamines.
- 2-Melanin pigments.
- 3-Thyroid hormones.

- **Catecholamines:**
- These are dopamine, norepinephrine and epinephrine.

- **Functions of catecholamines:**
- a) Neurotransmitters: Norepinephrine and dopamine act as neurotransmitters in the brain and at most sympathetic postganglionic endings.

- b) Regulation of metabolism: e.g.
- 1) Breakdown of glycogen (glycogenolysis) and lipids (lipolysis).

- 2) Increase of output of the heart and blood pressure.

- 3) Relaxation of smooth muscles of bronchi and intestine.

- **Melanin pigments:**
- **Synthesis of melanin:**
- In the skin, melanins are synthesized in melanocyte& (pigment forming cells) by tyrosine hydroxylase (tyrosinase) enzyme .

- **Functions of melanin:**
- a) Melanins are pigments present in many tissues particularly in the eye (iris), hair and skin.

- b) Melanins are synthesized to protect underlying cells from the harmful effects of sunlight.

THYROID HORMONES

FUNCTIONS OF THYROID HORMONES:

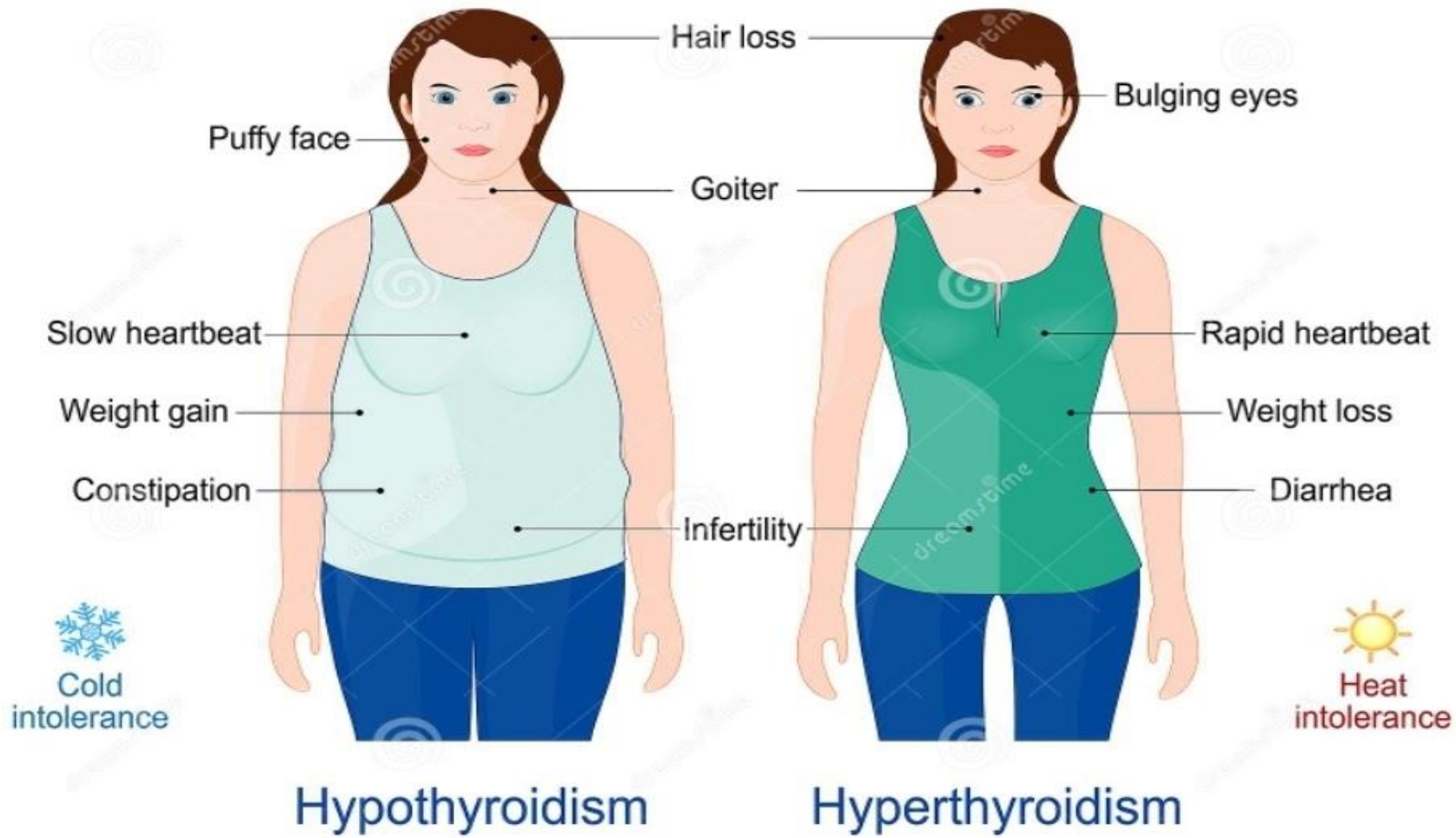
- a) They increase heat production and oxygen consumption in most tissues through stimulation of ATPase activity.

- b) They regulate the growth of long bones (together with growth hormone).

- c) They affect protein synthesis through stimulation of DNA in the nucleus of cells.

- d) They increase catecholamine effect.

Disorder of the thyroid gland



Disorders of tyrosine metabolism

- **Hereditary tyrosinemia (tyrosinosis):**
- Tyrosinemia is an error of metabolism, usually inborn, in which the body cannot effectively break down the amino acid tyrosine
- Forms of tyrosinemia: there are 3 types each one has specific enzyme defect and type 1 is more sever than the other types
- Tyrosinemia type I is a autosomal recessive genetic metabolic disorder characterized by lack of the enzyme fumarylacetoacetate hydrolase (FAH)
- Tyrosinaemia presents with renal tubular dysfunction, hypoglycaemia and severe liver disease

- **Alkaptonuria:**

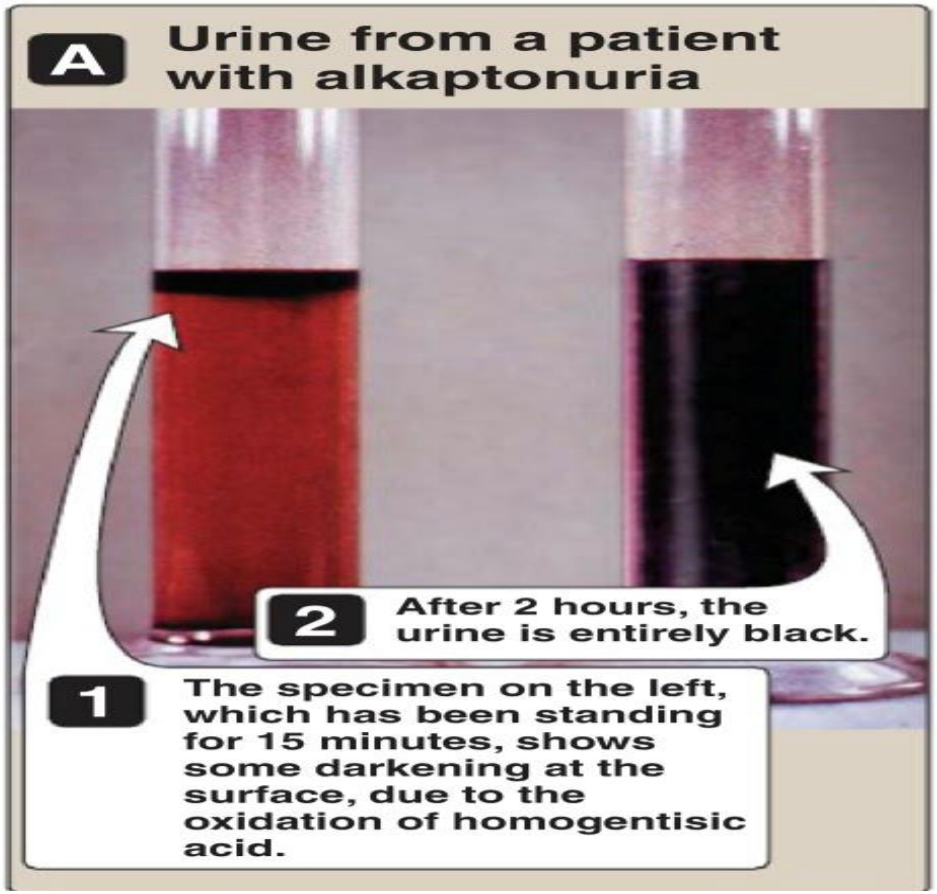
- disease resulting from deficiency of homogentisate oxidase enzyme.

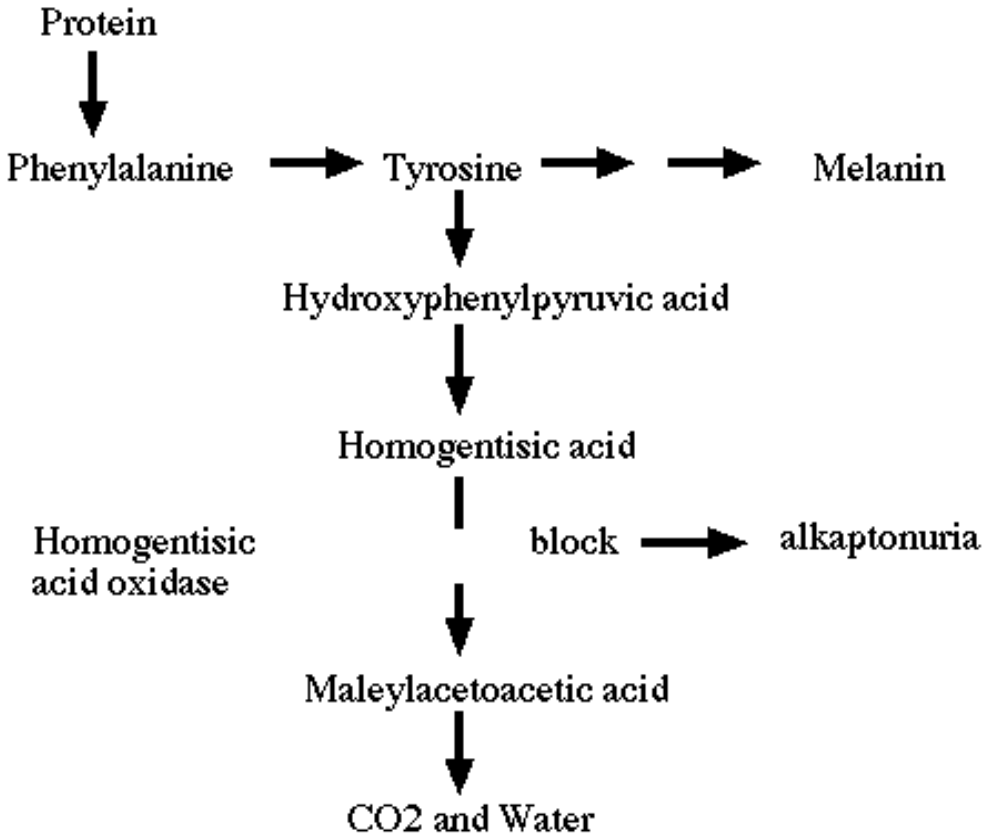
- 2. Effects: Homogentisic acid increases and causes:

- a) Deposition in joints causing arthritis.

- b) Deposition in connective tissue causing generalized pigmentation (ochronosis).

- c) Excreted in large amounts in urine, that is oxidized in the air giving the dark urine (black urine when left to stand).





- **Albinism:**

- 1. It is a hereditary deficiency of tyrosine hydroxylase enzyme in melanocytes. This results in defective synthesis of melanin pigments. Eye, skin and hair are affected.

- 2. Types of albinism: according to the site affected:

- a) Eye: ocular albinism.

- b) Skin: cutaneous albinism.

- c) Eye and skin: oculo-cutaneous albinism.

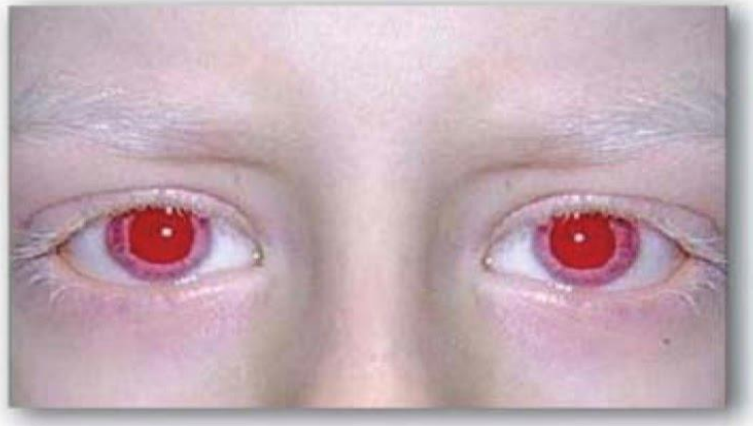


Figure 20.21
Patient with oculocutaneous albinism, showing white eyebrows and lashes and eyes that appear red in color.

tryptophan

- It is glycogenic and ketogenic essential amino acid.
- **Functions:** Tryptophan is the precursor of:
- • Serotonin.
- • Melatonin.
- • Niacin (nicotinic acid)

- **Serotonin**

Functions of serotonin:

- Neurotransmitter: it is stimulatory one.
- stabilizes mood, feelings of well-being, and happiness
- Vasoconstriction.
- Contraction of smooth muscle fibers

- **Melatonin:**
- Melatonin is secreted only at night (dark). This is because the release of melatonin is inhibited by light entering the eye

Functions of melatonin:

- It has sleep inducing effect.
- Regulation of circadian rhythm, being synthesized mostly at night.
- It inhibits synthesis and secretion of other neurotransmitters such as dopamine.

- **Niacin (nicotinic acid):**
- **Functions of niacin:**
- Niacin is a member of vitamin B complex, being synthesized in liver.
- a) It is essential for synthesis of NAD+ and NADP+ coenzymes, which act as hydrogen carriers in varieties of metabolic reactions.
- b)· Niacin lowers plasma cholesterol.
- **Pellagra:** This is a disease resulting from deficiency of niacin formation.
- It is the disease of 3 Ds. These are diarrhea, dermatitis and dementia.

- **Hartnup 's disease:**
- 1-It is a hereditary abnormality in tryptophan metabolism where the intestinal absorption and renal tubular reabsorption of this amino acid are impaired.

- 2-It is characterized by pellagra skin rashes, psychiatric changes

And can lead to mental retardation.

- There is excess excretion of tryptophan in urine (aminoaciduria).

Branched chain amino acids

- The normal metabolism of the branched chain amino acids Leucine, Isoleucine, and valine. Valine is glucogenic; Leucine is ketogenic while Isoleucine is both ketogenic and glucogenic.
- All the three are essential amino acids.
- These amino acids serve as an alternate source of fuel for the brain especially under conditions of starvation.

Maple syrup urine disease

- Maple syrup urine disease is due to inherited defect in the branched chain α -keto acid dehydrogenase. Due to this defect α-keto acids of leucine, isoleucine and valine cannot be further metabolized. As a result, the branched chain amino acids, leucine, isoleucine and valine, and their α-keto acids accumulate in blood, urine and CSF.

- α-keto acids impart a characteristic sweet odor to the urine of the affected individuals which resembles with maple syrup or burnt sugar hence the name.

- The disease presents during the first week of life and, if not treated, severe neurological lesions develop which cause death within a few weeks or months.
- The diagnosis of maple syrup urine disease is made by demonstrating raised concentrations of branched-chain amino acids in plasma and urine.
- If a diet low in branched-chain amino acids is given, normal development is possible.

Cystine

- Cystine (di-cysteine) amino acid.

Function :

- A. Protein structure: The . -s-s- group of·cystine is important for tertiary and quaternary structure of proteins.
- B. Cysteine formation: By cystine reductase

Cystinuria

- Cystinuria is the result of an autosomal recessive inherited abnormality of tubular reabsorption, with excessive urinary excretion, of the amino acids cystine, ornithine, arginine and lysine.
- Cystine may precipitated in renal tubules forming renal stones.
- The diagnosis of cystinuria is made by demonstrating excessive urinary excretion of the characteristic amino acids.

Thank you