Amino Acid Metabolism: Conversion of Amino Acids to Specialized Products

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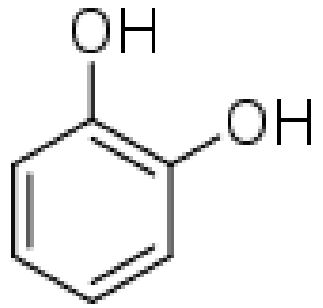
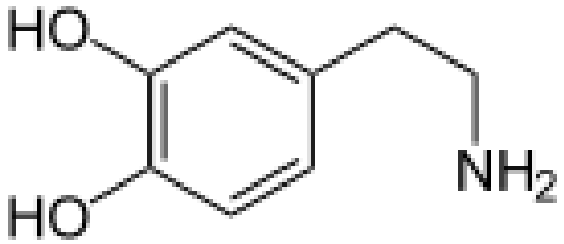
Medical students-First semester

All images are taken from Lippincott's Biochemistry textbook except where noted

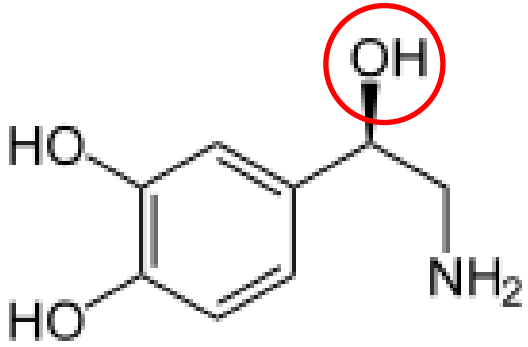
Catecholamines
(Dopamine, norepinephrine, and epinephrine)



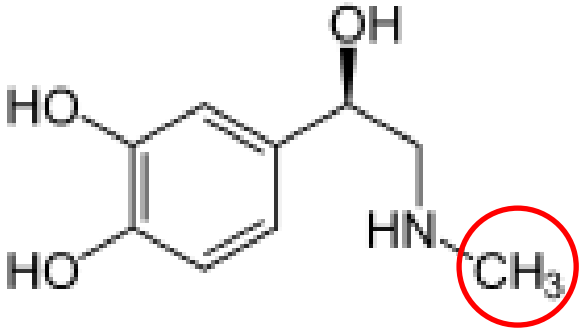
Catechol



Dopamine



Norepinephrine



Epinephrine

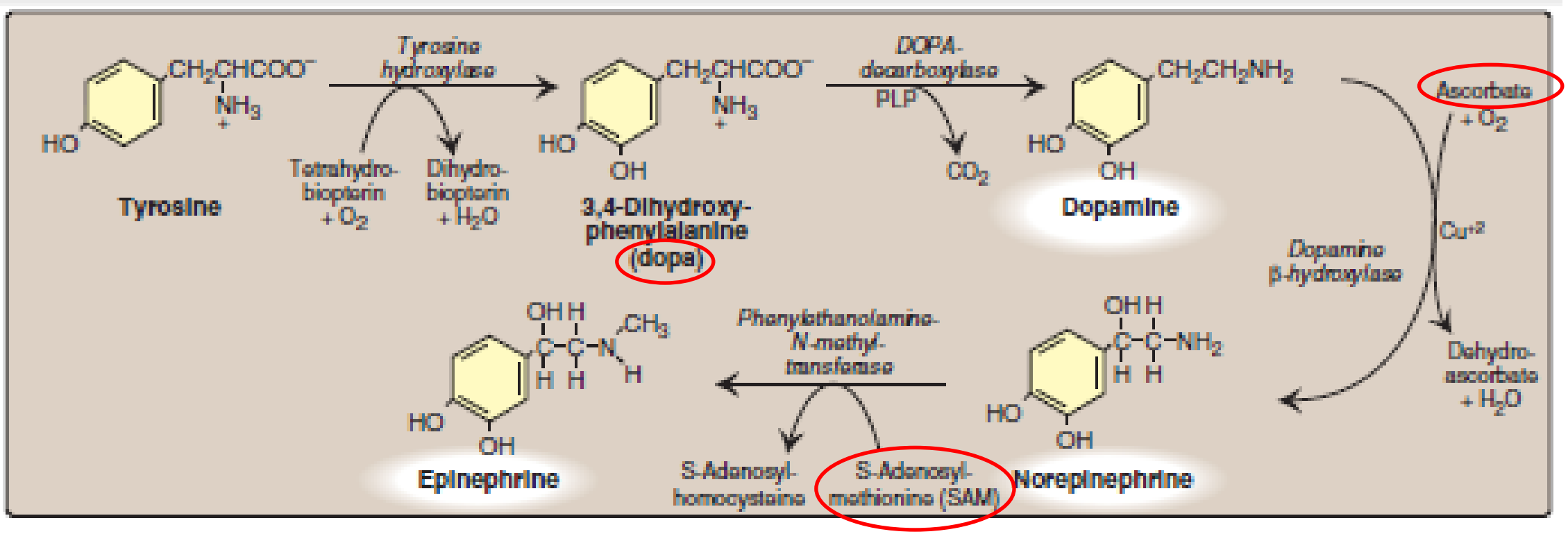
Dopamine and norepinephrine are synthesized in the brain and function as neurotransmitters.

Norepinephrine and epinephrine are synthesized in the adrenal medulla

Outside the nervous system, norepinephrine and epinephrine, are hormone regulators of **carbohydrate and lipid metabolism**.

Norepinephrine and epinephrine are released from storage vesicles in the adrenal medulla in response to fright, exercise, cold, and low levels of blood glucose to increase the degradation of glycogen and TAG, and increase blood pressure and the output of the heart (to prepare for "**fight-or-flight**" reactions).

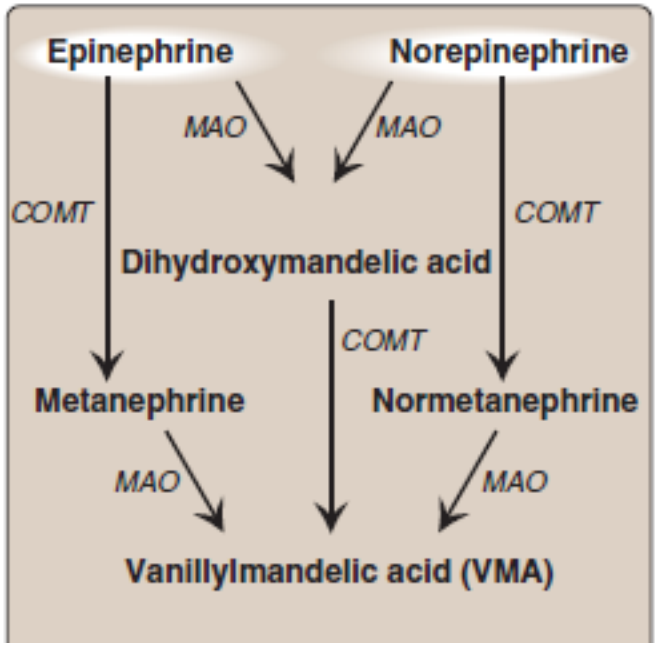
Synthesis of catecholamines

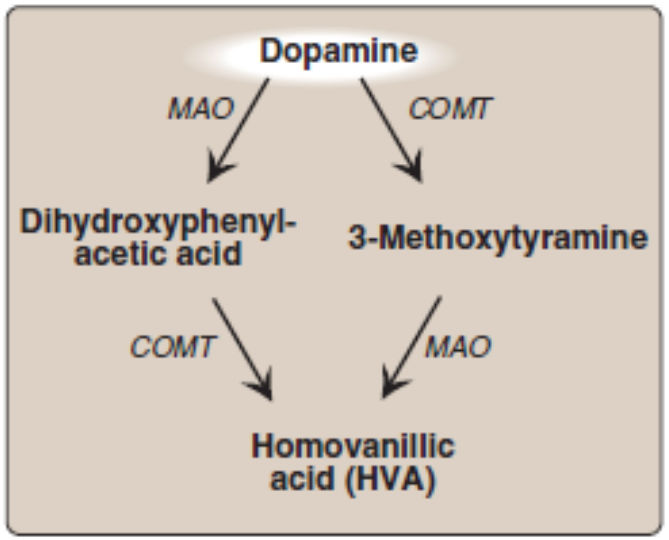


Parkinson disease, a neurodegenerative movement disorder, is due to insufficient dopamine production due to an idiopathic loss of dopamine-producing cells in the brain.

Administration of L-DOPA (levodopa) is the most common treatment.

Degradation of catecholamines





Catecholamine inactivation by:

A. Oxidative deamination catalyzed by monoamine oxidase (MAO)

A. O-methylation by catechol-O-methyltransferase (COMT) using SAM as the methyl donor

The aldehyde products of the MAO reaction are oxidized to the corresponding acids.

The metabolic products of these reactions (VMA, HVA) are excreted in the urine

VMA is increased with pheochromocytomas (adrenal tumor with increased catecholamine production).

MAO inhibitors

MAO is found in neural and other tissues, such as the intestine and liver.

Neuron

MAO oxidatively deaminates and inactivates any excess neurotransmitters (norepinephrine, dopamine, or serotonin) that may leak out of synaptic vesicles when the neuron is at rest.

MAO inhibitors

Irreversible or reversible MAO inactivation
Neurotransmitter molecules escape degradation, accumulate within the presynaptic neuron and leak into the synaptic space.

Activation of norepinephrine and serotonin receptors leads to the antidepressant action of MAO inhibitors

Histamine

Histamine is a chemical messenger that mediates a wide range of cellular responses

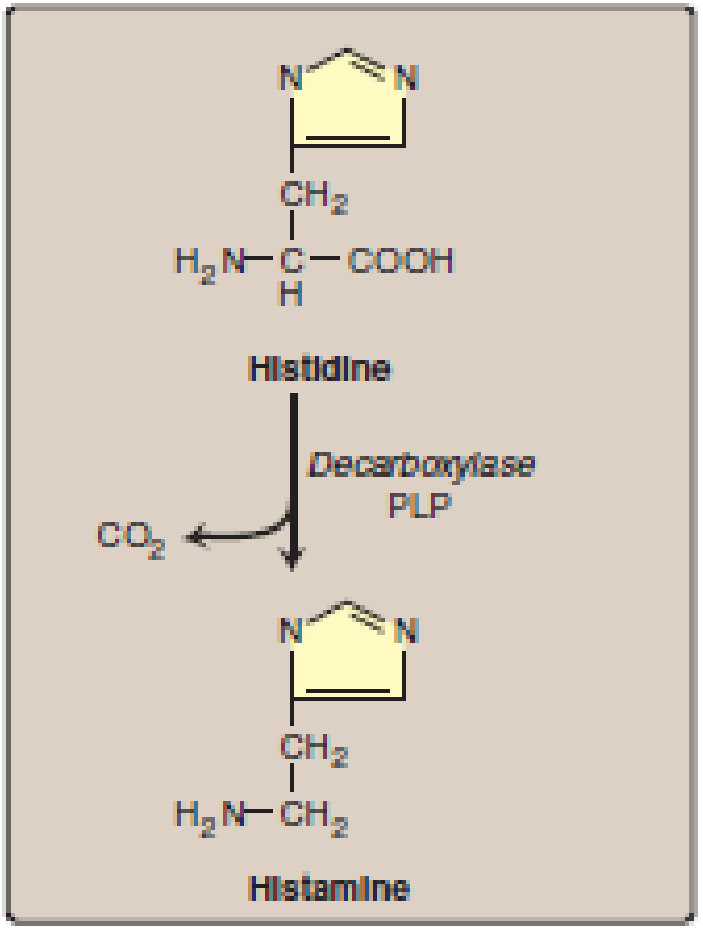
Roles include mediation of:

1. Allergic and inflammatory reactions
2. Gastric acid secretion
3. Neurotransmission in parts of the brain.

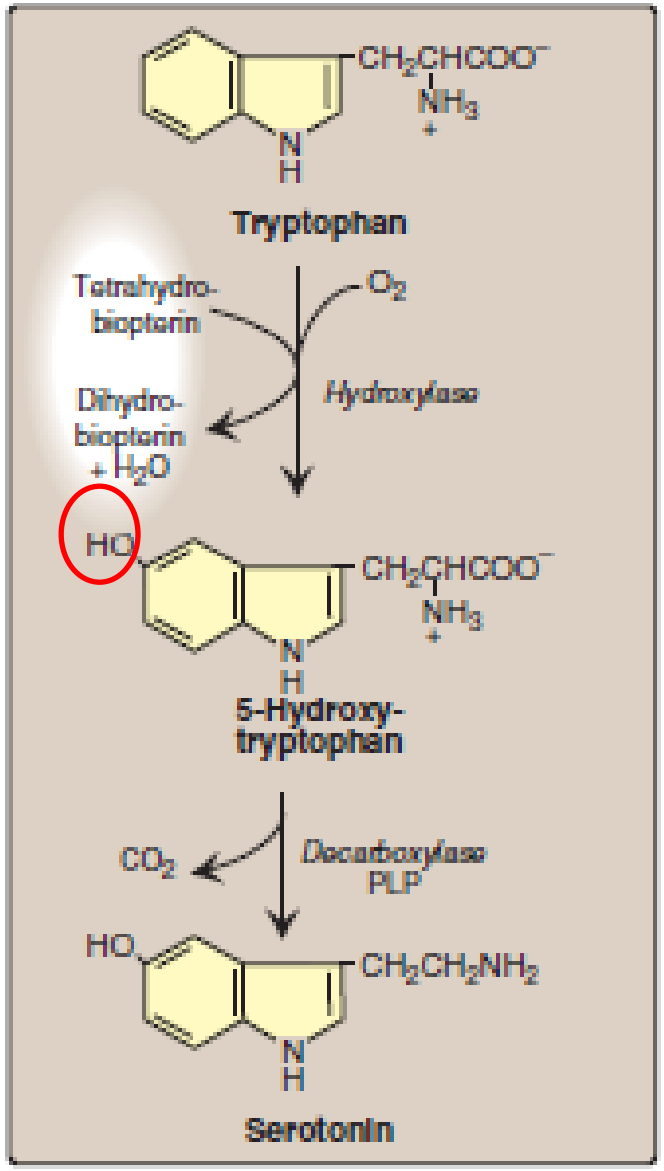
It is secreted by mast cells as a result of allergic reactions or trauma.

Histamine is a **vasodilator**

Histamine is formed by decarboxylation of **histidine** in a reaction requiring PLP



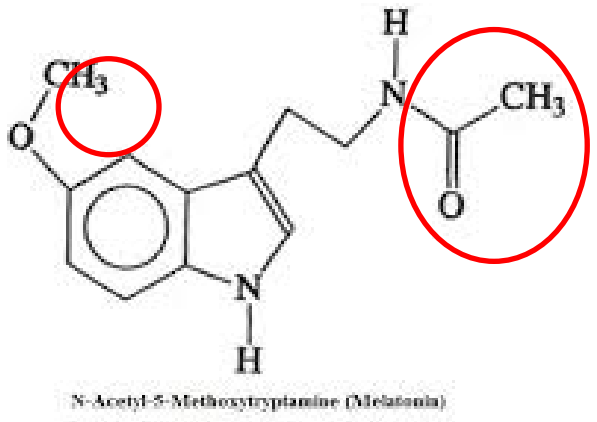
Serotonin, or 5-hydroxytryptamine (5HT)



Is synthesized and stored at several sites in the body, mostly in intestinal mucosal cells

Smaller amounts in the CNS (functions as a neurotransmitter), and in platelets.

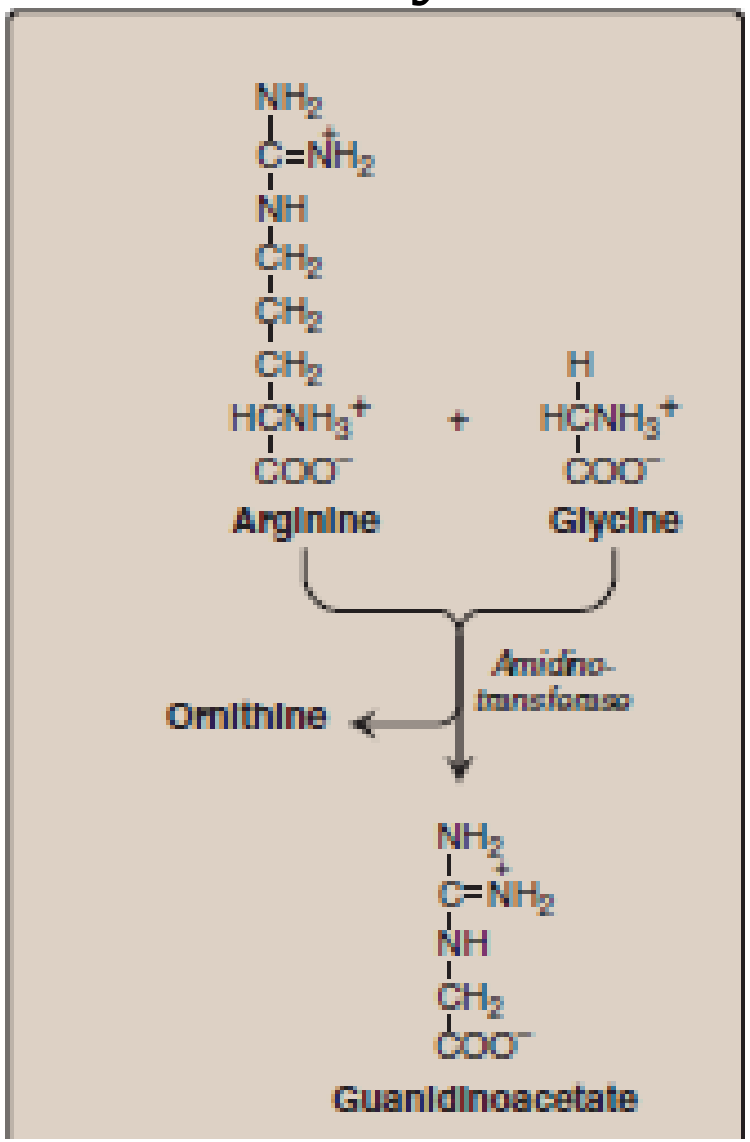
Physiologic roles are pain perception, regulation of sleep, appetite, temperature, blood pressure, cognitive functions, and mood (causes a feeling of well-being)

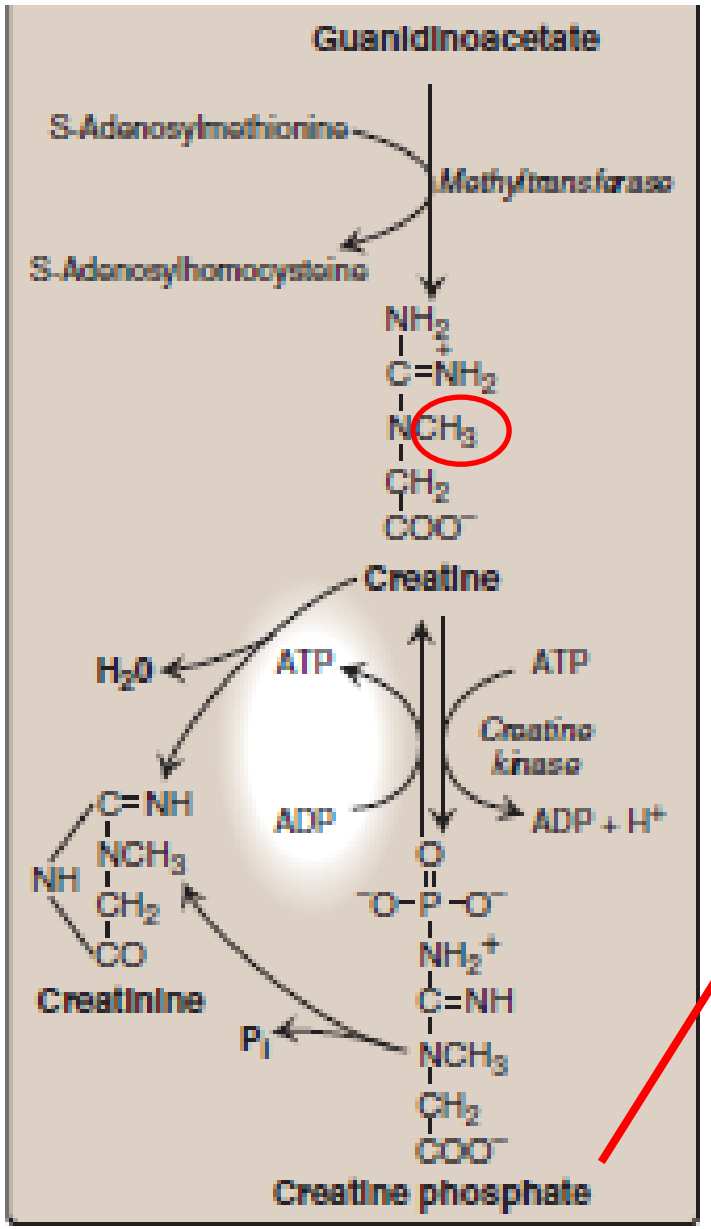


Serotonin is converted to melatonin in the pineal gland via acetylation and methylation.

Creatine

Creatine Synthesis





-The presence of creatine kinase in the plasma indicates heart damage, and is used in the diagnosis of MI

-The amount of creatine phosphate in the body is proportional to the muscle mass.

or phosphocreatine
a high-energy compound found in muscle and provides a small but rapidly mobilized reserve of high-energy phosphates

Creatine Degradation

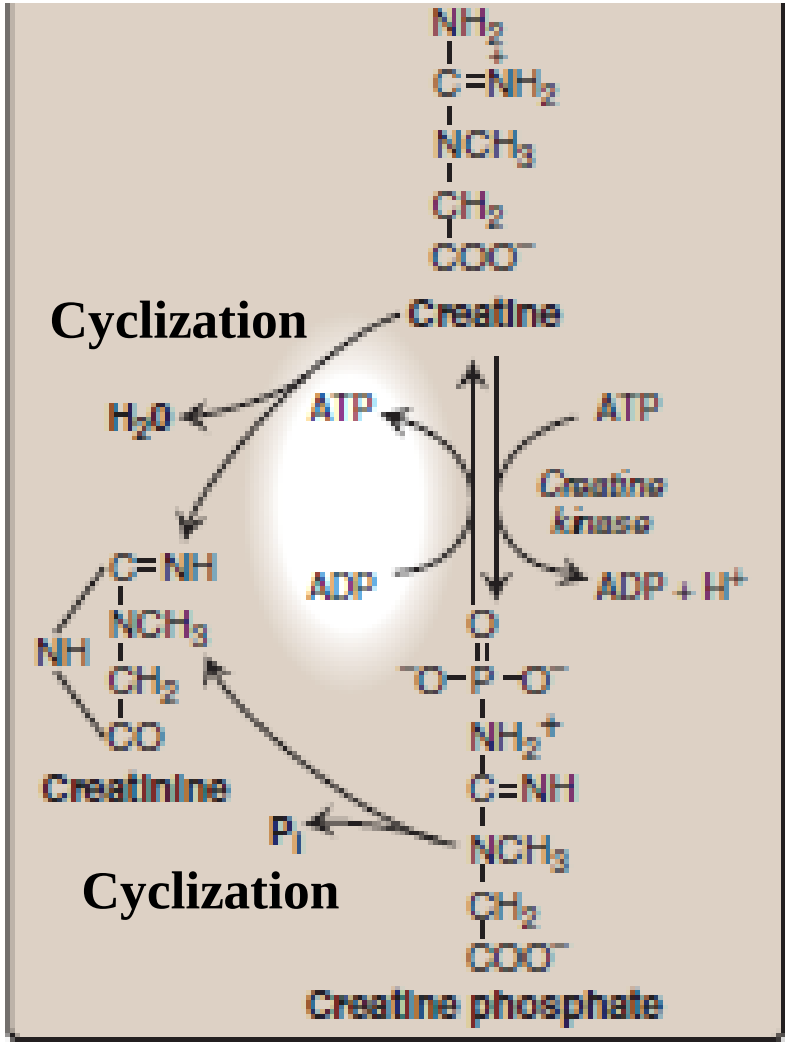
Creatinine is excreted in the urine.

Excreted creatinine amount is proportional to the total creatine phosphate content of the body, and thus can be used to estimate muscle mass.

When muscle mass decreases (paralysis or muscular dystrophy), the creatinine content of the urine falls.

Rise in blood creatinine is a sensitive indicator of kidney malfunction

A typical adult male excretes ~15 mmol of creatinine per day.



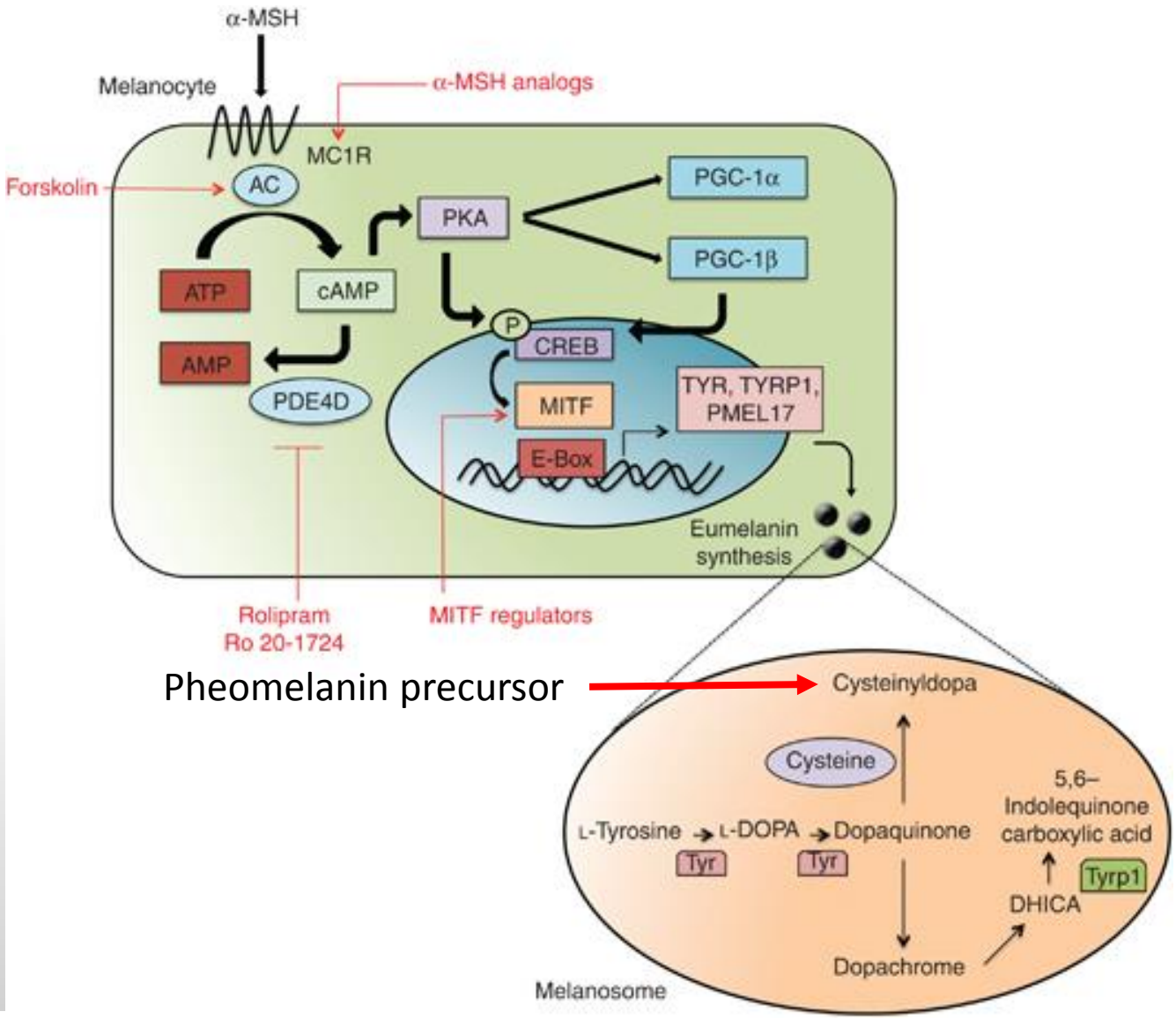
Melanin

A pigment in several tissues, particularly the eye, hair, and skin.

It is synthesized from tyrosine in the epidermis by melanocytes.

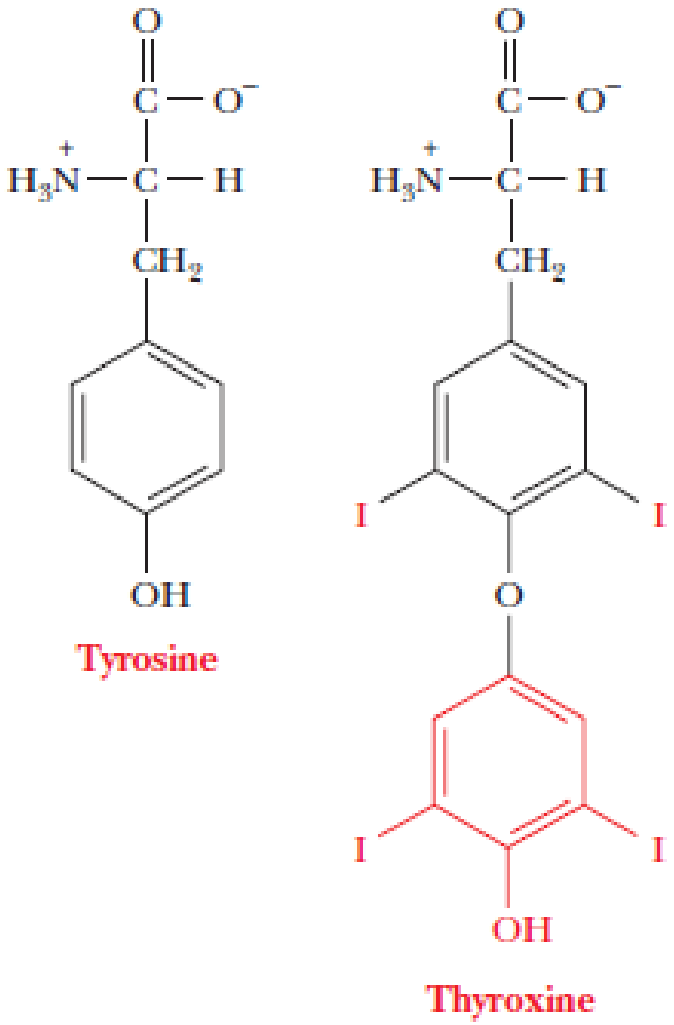
Melanin protects the underlying cells from the harmful effects of sunlight.

A defect in melanin production results in albinism (the most common form is due to defects in copper-containing tyrosinase)



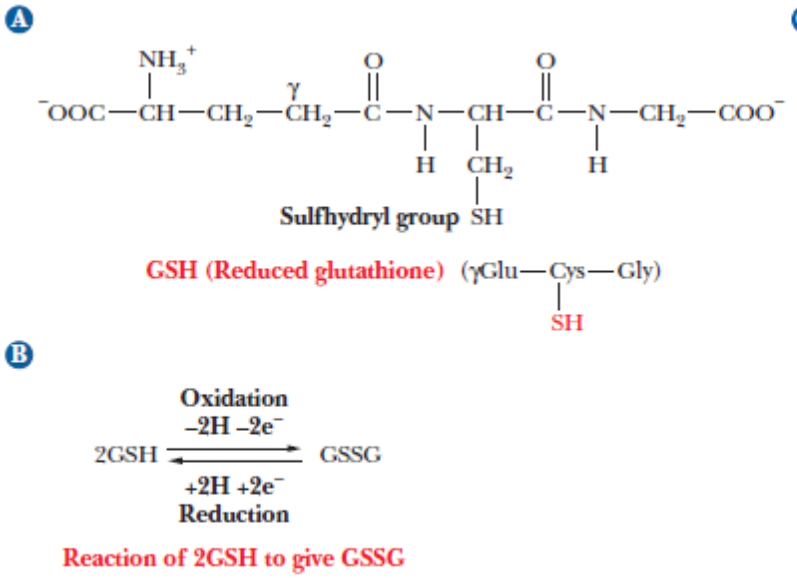
Chen et al (2014)

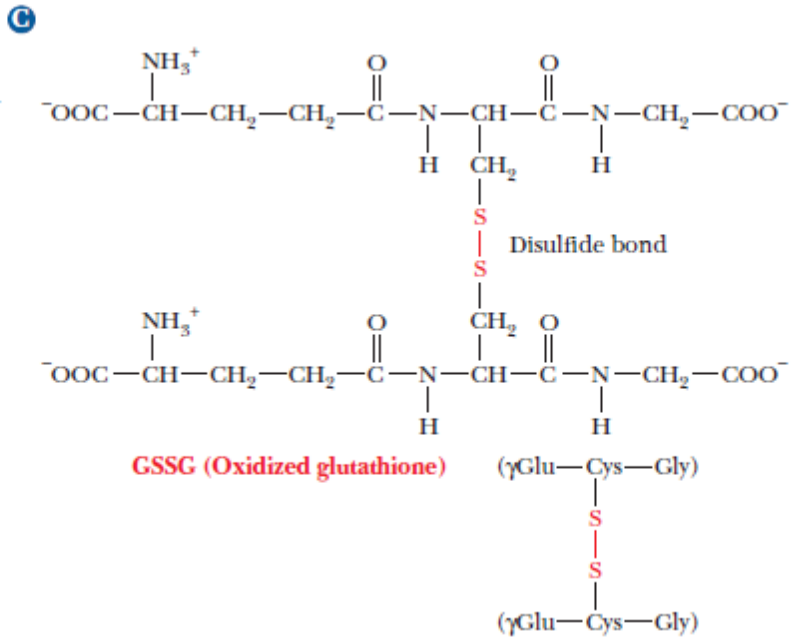
Thyroxine

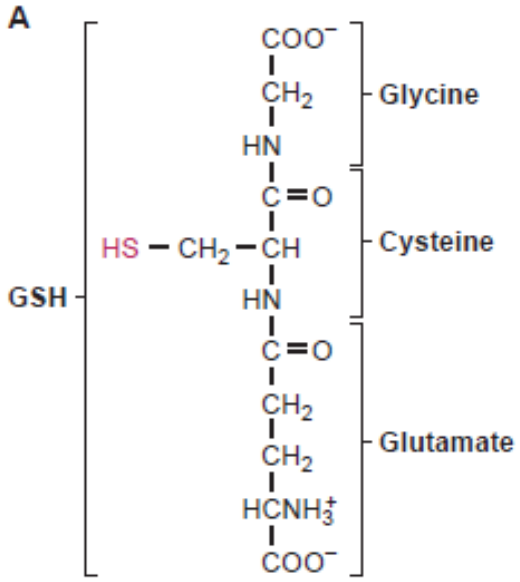


Glutathione

- Glu+Cys+Gly



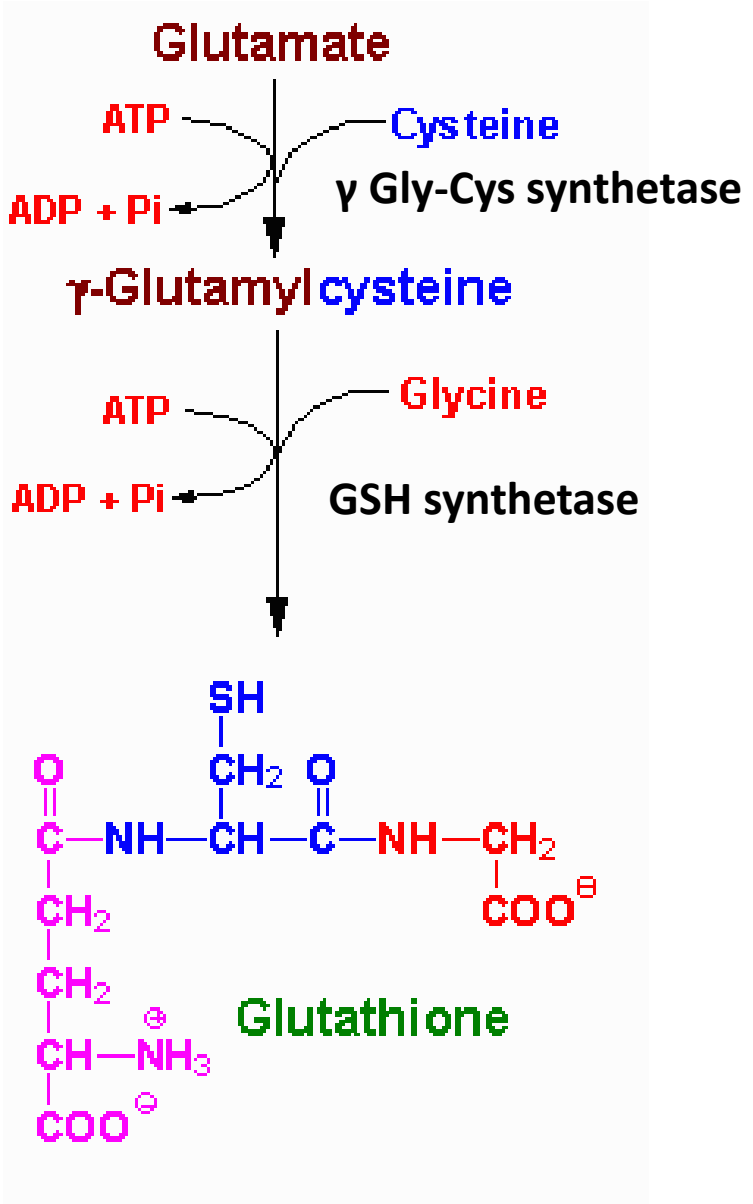




Functions:

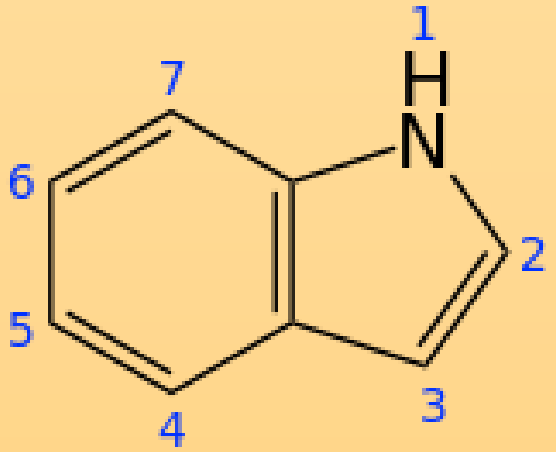
- ✓ Reductant
- ✓ Conjugation of drugs (more polar)
- ✓ Transport of AA across cell membrane
- ✓ Cofactor
- ✓ Facilitate rearrangement of protein S-S bridges

Glutathione



Nitrogen-containing compounds synthesized from AA

- Serine → ethanolamine + choline +Acetyl-CoA → Acetylcholine
- Gly + Succinyl-CoA → Heme
- Trp+ GI bacteria → Indoles
- Trp in the liver → Nicotinamide



- Glu → GABA (inhibitory neurotransmitter)
- Lys methylation → → → → Carnitine
- Ornithine → → → → Spermine (characteristic odor of semen)