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DEPARTMENT: PHYSIOLOGY

COURSE CODE: BCH 308

 SYNTHESIS OF TWO NEUROTRANSMITTERS

(1)DOPAMINE: Dopamine is [synthesized](https://en.wikipedia.org/wiki/Biosynthesis) in a restricted set of cell types, mainly neurons and cells in the [medulla](https://en.wikipedia.org/wiki/Adrenal_medulla) of the [adrenal glands](https://en.wikipedia.org/wiki/Adrenal_gland). The primary and minor [metabolic pathways](https://en.wikipedia.org/wiki/Metabolic_pathway) respectively are:

Primary: L-Phenylalanine → L-Tyrosine → L-DOPA → Dopamine

Minor: L-Phenylalanine → L-Tyrosine → *p*-Tyramine → Dopamine

Minor: L-Phenylalanine → [*m*-Tyrosine](https://en.wikipedia.org/wiki/L-m-tyrosine) → [*m*-Tyramine](https://en.wikipedia.org/wiki/Meta-tyramine) → Dopamine

The direct precursor of dopamine, [L-DOPA](https://en.wikipedia.org/wiki/L-DOPA), can be synthesized indirectly from the [essential amino acid](https://en.wikipedia.org/wiki/Essential_amino_acid) [phenylalanine](https://en.wikipedia.org/wiki/Phenylalanine) or directly from the non-essential amino acid [tyrosine](https://en.wikipedia.org/wiki/Tyrosine). These [amino acids](https://en.wikipedia.org/wiki/Amino_acid) are found in nearly every protein and so are readily available in food, with tyrosine being the most common. Although dopamine is also found in many types of food, it is incapable of crossing the [blood–brain barrier](https://en.wikipedia.org/wiki/Blood%E2%80%93brain_barrier) that surrounds and protects the brain. It must therefore be synthesized inside the brain to perform its [neuronal activity](https://en.wikipedia.org/wiki/Neurotransmission).

L-Phenylalanine is converted into L-tyrosine by the [enzyme](https://en.wikipedia.org/wiki/Enzyme) [phenylalanine hydroxylase](https://en.wikipedia.org/wiki/Phenylalanine_hydroxylase), with [molecular oxygen](https://en.wikipedia.org/wiki/Allotropes_of_oxygen#Dioxygen) (O2) and [tetrahydrobiopterin](https://en.wikipedia.org/wiki/Tetrahydrobiopterin%22%20%5Co%20%22Tetrahydrobiopterin) as [cofactors](https://en.wikipedia.org/wiki/Cofactor_%28biochemistry%29). L-Tyrosine is converted into L-DOPA by the enzyme [tyrosine hydroxylase](https://en.wikipedia.org/wiki/Tyrosine_hydroxylase), with tetrahydrobiopterin, O2, and iron (Fe2+) as cofactors. L-DOPA is converted into dopamine by the enzyme [aromatic L-amino acid decarboxylase](https://en.wikipedia.org/wiki/Aromatic_L-amino_acid_decarboxylase) (also known as DOPA decarboxylase), with [pyridoxal phosphate](https://en.wikipedia.org/wiki/Pyridoxal_phosphate%22%20%5Co%20%22Pyridoxal%20phosphate) as the cofactor.

Dopamine itself is used as precursor in the synthesis of the neurotransmitters norepinephrine and epinephrine. Dopamine is converted into norepinephrine by the enzyme [dopamine β-hydroxylase](https://en.wikipedia.org/wiki/Dopamine_beta_hydroxylase), with O2 and [L-ascorbic acid](https://en.wikipedia.org/wiki/Ascorbic_acid) as cofactors. Norepinephrine is converted into epinephrine by the enzyme [phenylethanolamine *N*-methyltransferase](https://en.wikipedia.org/wiki/Phenylethanolamine_N-methyltransferase) with [*S*-adenosyl-L-methionine](https://en.wikipedia.org/wiki/S-Adenosyl_methionine) as the cofactor.

Some of the cofactors also require their own synthesis. Deficiency in any required amino acid or cofactor can impair the synthesis of dopamine, norepinephrine, and epinephrine.

(2)SEROTONIN: serotonin is [synthesized](https://en.wikipedia.org/wiki/Biosynthesis) from the [amino acid](https://en.wikipedia.org/wiki/Amino_acid) L-[tryptophan](https://en.wikipedia.org/wiki/Tryptophan) by a short [metabolic pathway](https://en.wikipedia.org/wiki/Metabolic_pathway) consisting of two [enzymes](https://en.wikipedia.org/wiki/Enzyme), [tryptophan hydroxylase](https://en.wikipedia.org/wiki/Tryptophan_hydroxylase) (TPH) and [aromatic amino acid decarboxylase](https://en.wikipedia.org/wiki/Aromatic_L-amino_acid_decarboxylase) (DDC), and the coenzyme [pyridoxal phosphate](https://en.wikipedia.org/wiki/Pyridoxal_phosphate%22%20%5Co%20%22Pyridoxal%20phosphate). The TPH-mediated reaction is the rate-limiting step in the pathway. TPH has been shown to exist in two forms: [TPH1](https://en.wikipedia.org/wiki/TPH1), found in several [tissues](https://en.wikipedia.org/wiki/Biological_tissue), and [TPH2](https://en.wikipedia.org/wiki/TPH2), which is a neuron-specific [isoform](https://en.wikipedia.org/wiki/Protein_isoform%22%20%5Co%20%22Protein%20isoform).

Serotonin can be synthesized from tryptophan in the lab using *[Aspergillus niger](https://en.wikipedia.org/wiki/Aspergillus_niger%22%20%5Co%20%22Aspergillus%20niger)* and *[Psilocybe coprophila](https://en.wikipedia.org/wiki/Psilocybe_coprophila%22%20%5Co%20%22Psilocybe%20coprophila)* as catalysts. The first phase to 5-hydroxytryptophan would require letting tryptophan sit in ethanol and water for 7 days, then mixing in enough HCl (or other acid) to bring the pH to 3, and then adding NaOH to make a pH of 13 for 1 hour. *Asperigillus niger* would be the catalyst for this first phase. The second phase to synthesizing tryptophan itself from the 5-hydroxytryptophan intermediate would require adding ethanol and water, and letting sit for 30 days this time. The next two steps would be the same as the first phase: adding HCl to make the pH = 3, and then adding NaOH to make the pH very basic at 13 for 1 hour. This phase uses the *Psilocybe coprophila* as the catalyst for the reaction.

Serotonin taken orally does not pass into the serotonergic pathways of the central nervous system, because it does not cross the [blood–brain barrier](https://en.wikipedia.org/wiki/Blood%E2%80%93brain_barrier). However, [tryptophan](https://en.wikipedia.org/wiki/Tryptophan) and its [metabolite](https://en.wikipedia.org/wiki/Metabolite) [5-hydroxytryptophan](https://en.wikipedia.org/wiki/5-hydroxytryptophan) (5-HTP), from which serotonin is synthesized, does cross the blood–brain barrier. These agents are available as [dietary supplements](https://en.wikipedia.org/wiki/Dietary_supplement), and may be effective serotonergic agents. One product of serotonin breakdown is [5-hydroxyindoleacetic acid](https://en.wikipedia.org/wiki/5-hydroxyindoleacetic_acid) (5-HIAA), which is excreted in the [urine](https://en.wikipedia.org/wiki/Urine). Serotonin and 5-HIAA are sometimes produced in excess amounts by certain [tumors](https://en.wikipedia.org/wiki/Tumor) or [cancers](https://en.wikipedia.org/wiki/Cancer), and levels of these substances may be measured in the urine to test for these tumors.