

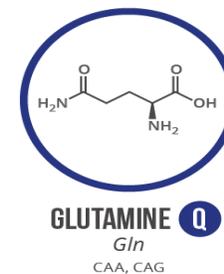
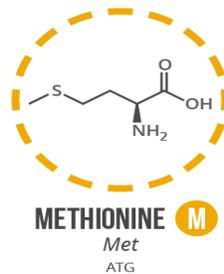
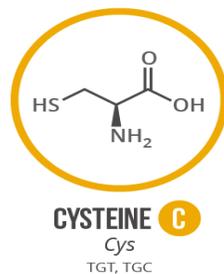
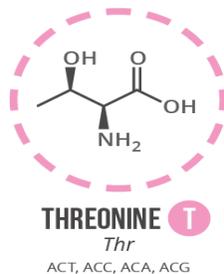
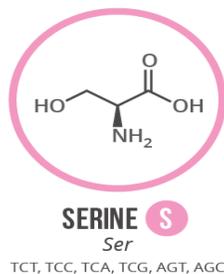
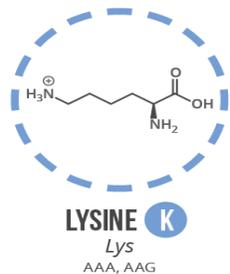
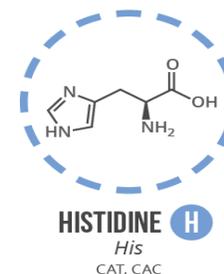
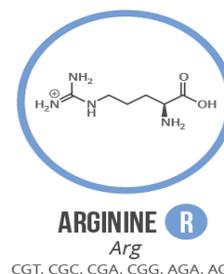
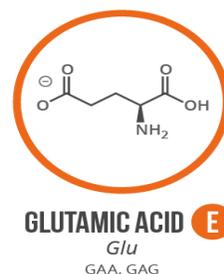
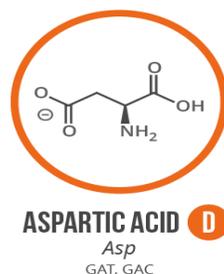
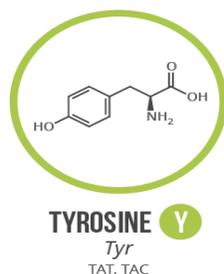
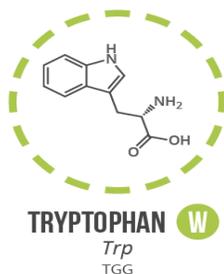
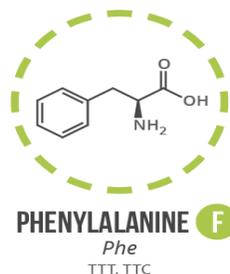
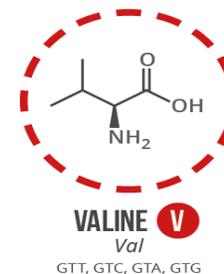
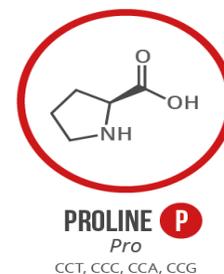
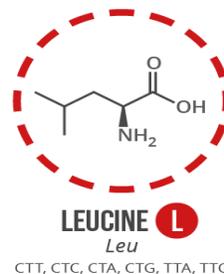
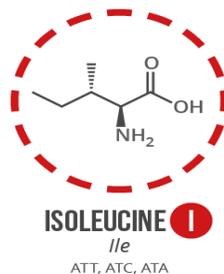
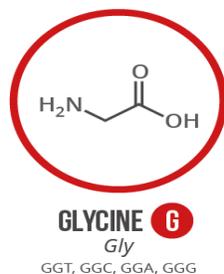
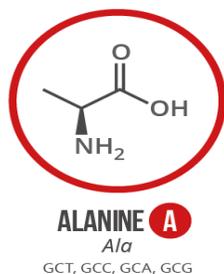
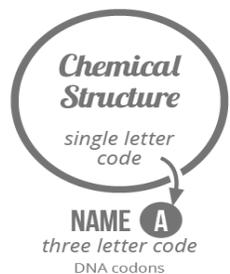
Let's talk!

- Amino Acid structures
- Urea cycle
- Amino acid degradation
- Fancy things amino acids make

A GUIDE TO THE TWENTY COMMON AMINO ACIDS

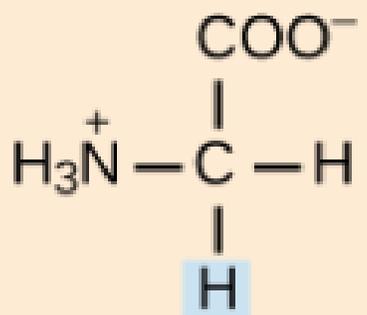
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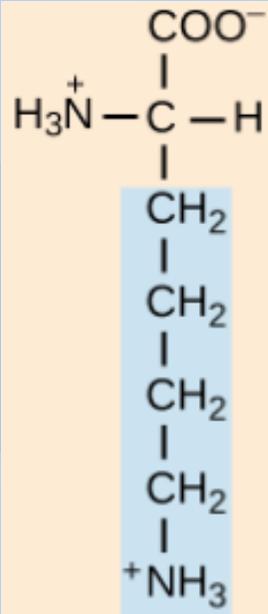


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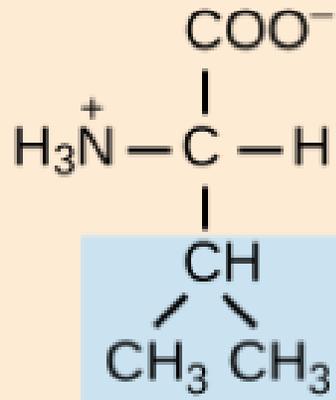




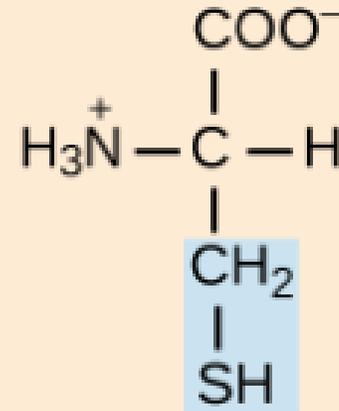
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Glycine



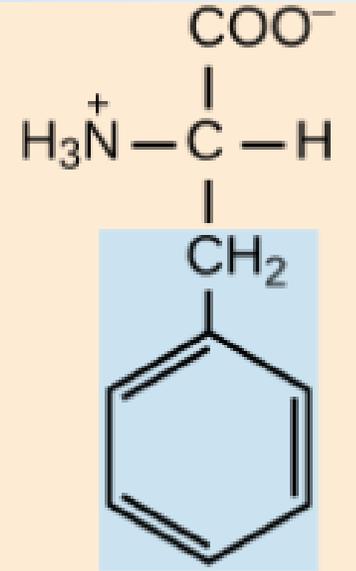
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Lysine



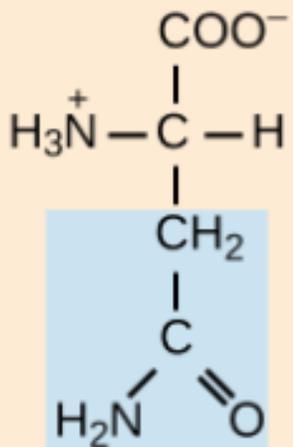
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Valine



4
Cysteine

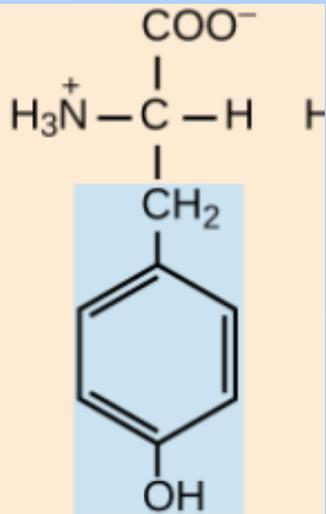


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Phenylalanine



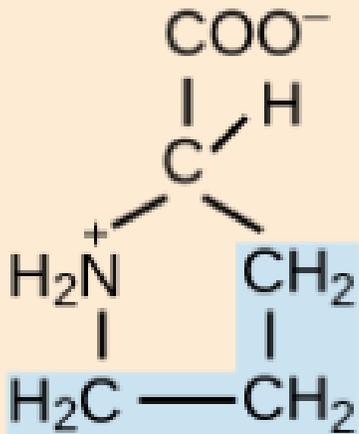
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Asparagine



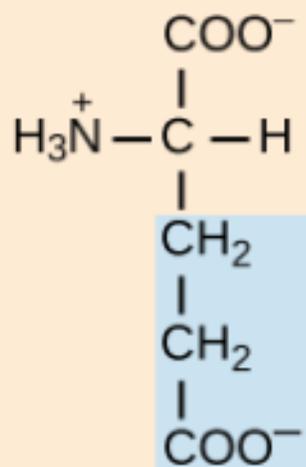
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Tyrosine



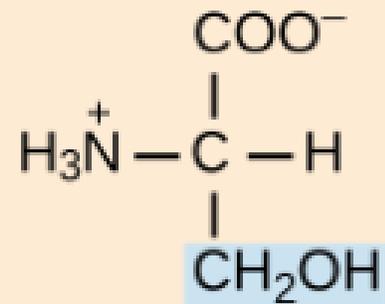
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Proline



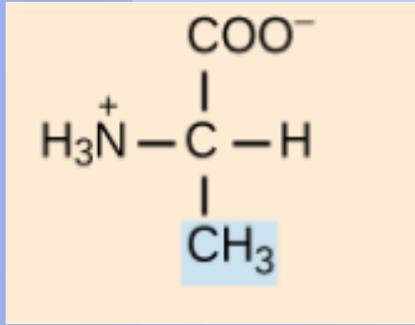
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Glutamate

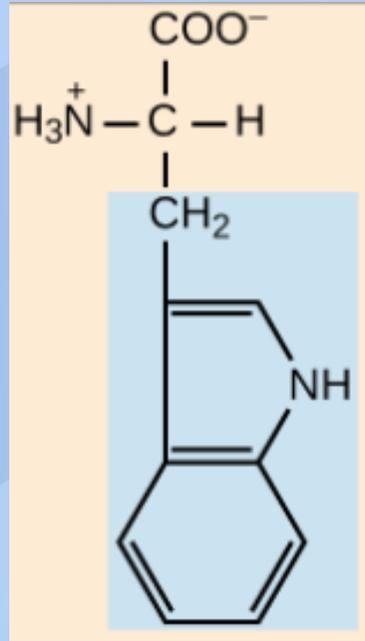


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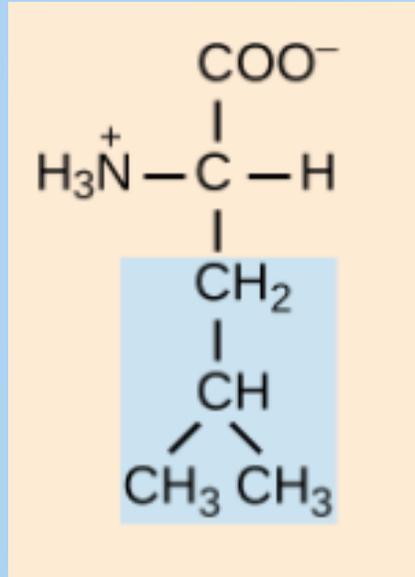
Serine



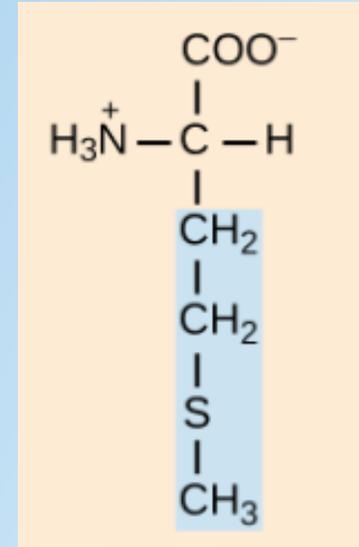
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Alanine



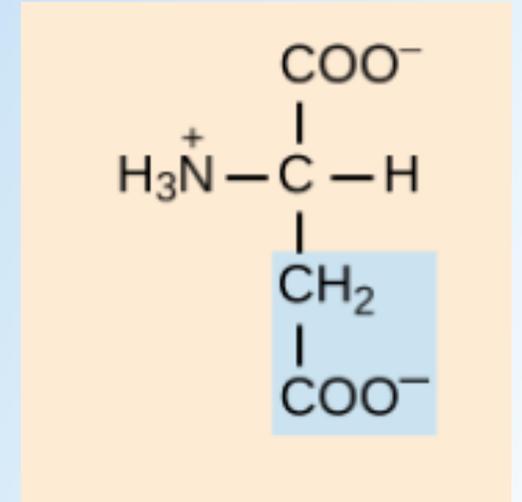
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Tryptophan



3
Leucine



4
Methionine

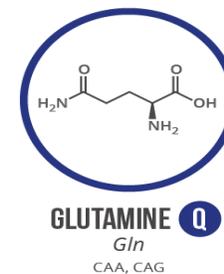
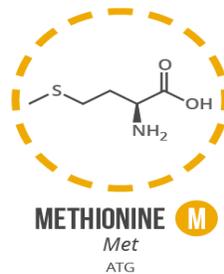
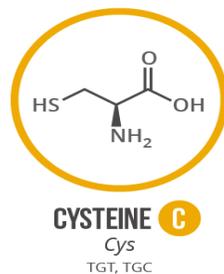
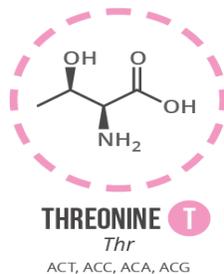
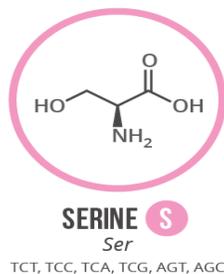
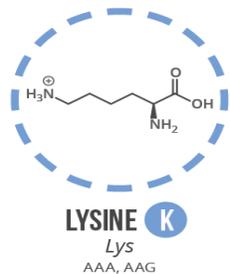
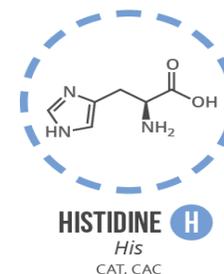
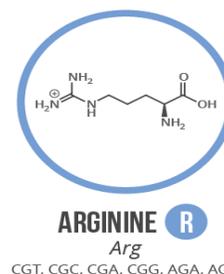
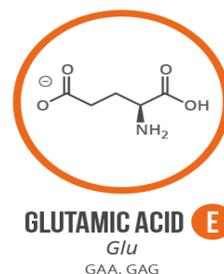
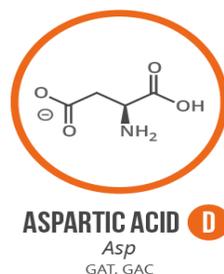
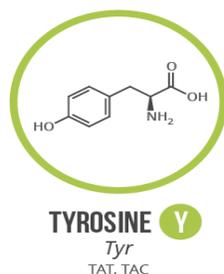
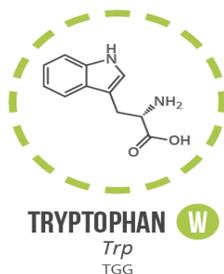
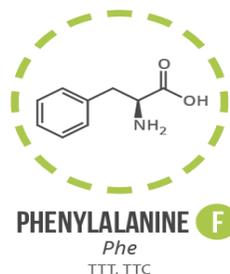
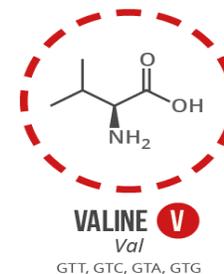
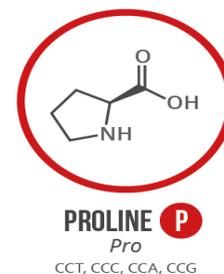
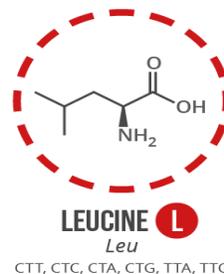
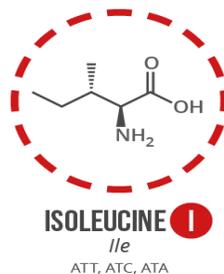
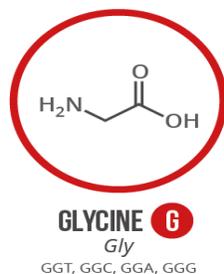
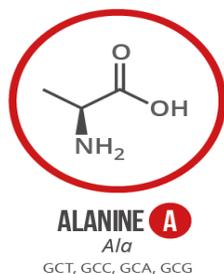
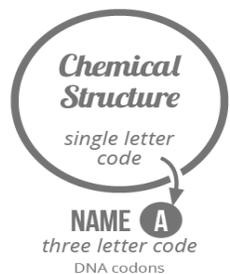


5
Aspartate

A GUIDE TO THE TWENTY COMMON AMINO ACIDS

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10 Essential Amino Acids

PVT

P - Phenylalanine

V - Valine

T - Threonine

TIM

T - Tryptophan

I - Isoleucine

M - Methionine

HALL

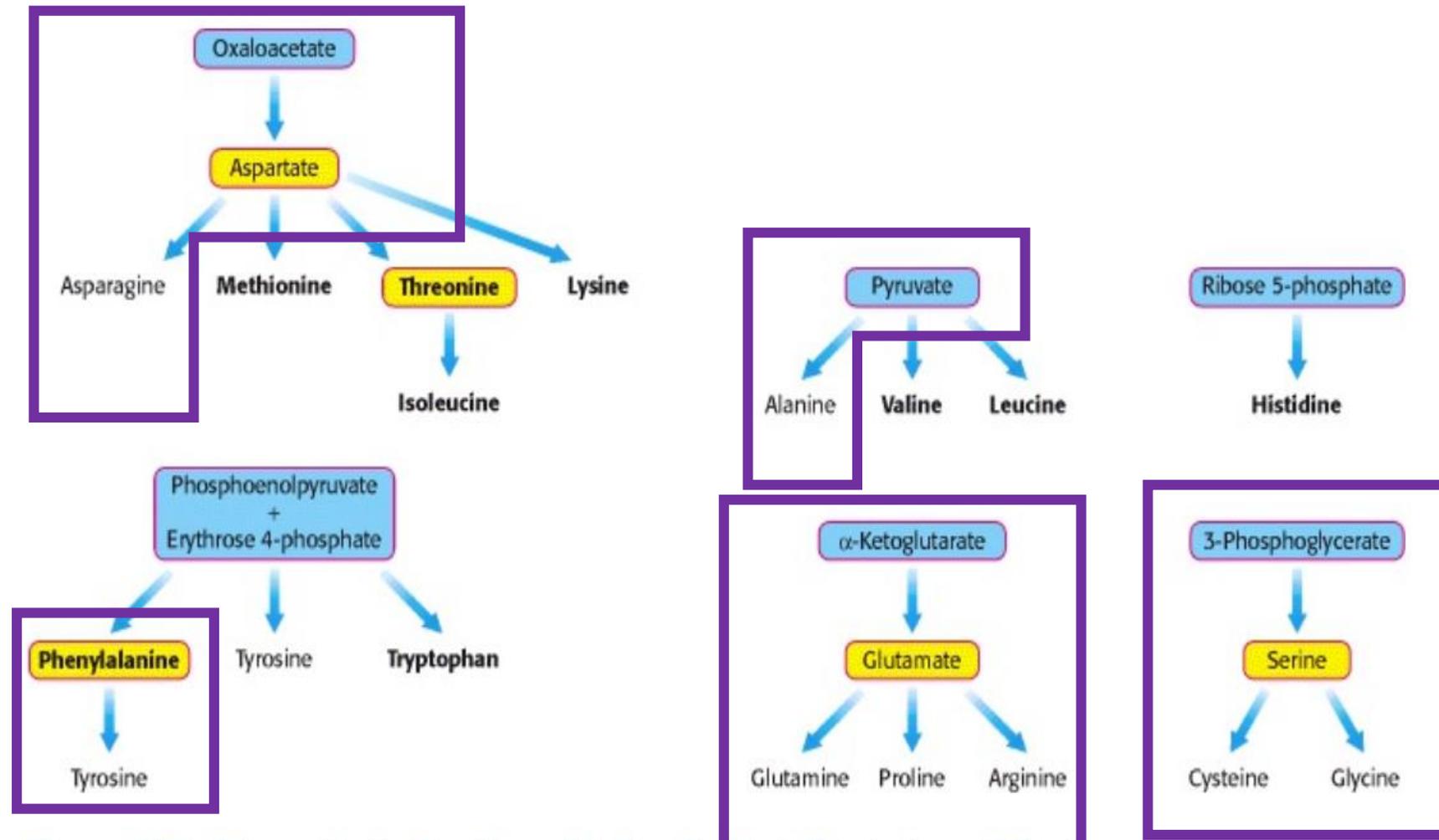
H - Histidine

A - Arginine

L - Leucine

L - Lysine

Amino Acid Biosynthesis



OAA → **Aspartate** → **Asparagine**

Pyruvate → **Alanine**

α-Ketoglutarate → **Glutamate** → **Glutamine, Proline, Arginine**

3-Phosphoglycerate → **Serine** → **Cysteine, Glycine**

Phenylalanine → **Tyrosine**

Figure 24.7 Biosynthetic Families of Amino Acids in Bacteria and Plants

Major metabolic precursors are shaded blue. Amino acids that give rise to other amino acids are shaded yellow. Essential amino acids are in boldface type.

Overview of Nitrogen transport

Note

- Most cells use Glutamine to transport NH_3
- Muscle cells use Alanine to transport NH_3
- Intestinal bacteria can create significant amounts of NH_3

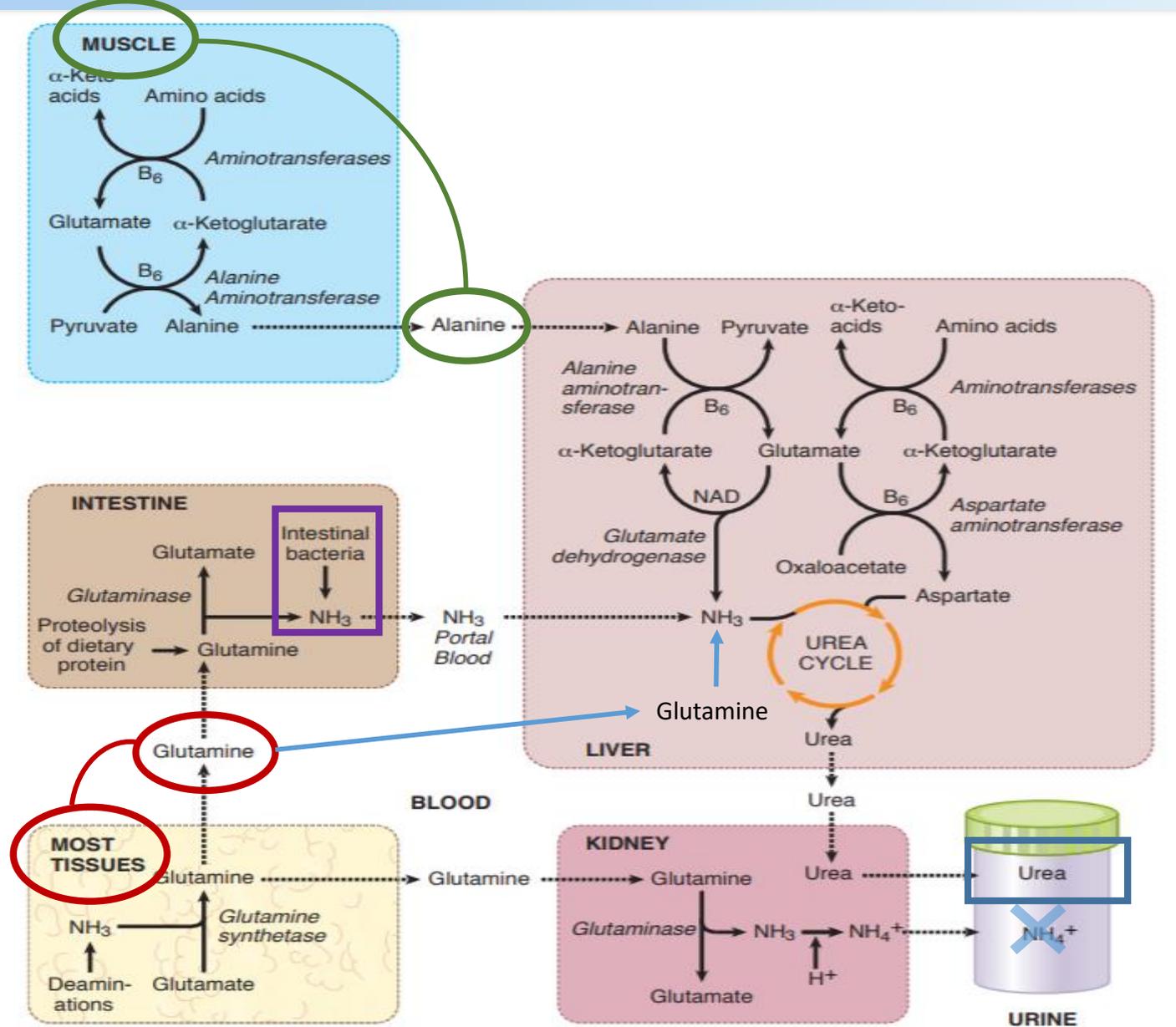
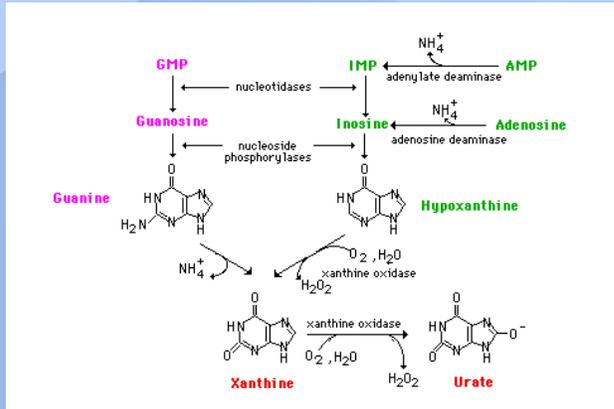
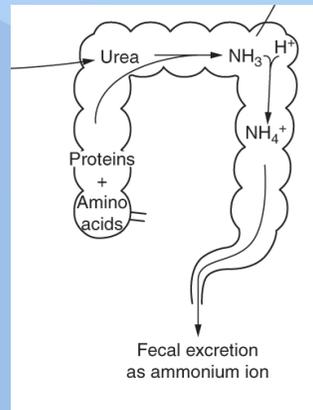


Figure I-17-1. Amino Group Removal for Elimination as Urea

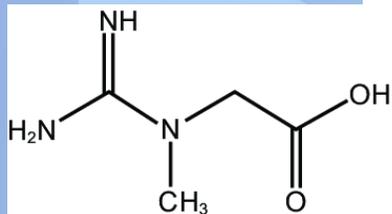
Other ways to excrete nitrogen?



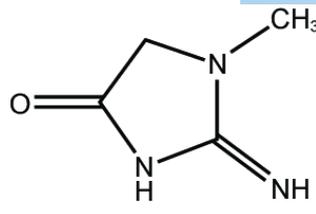
Nucleotides (nitrogenous bases) are excreted in the urine



Ammonia produced by gut bacteria is excreted in the feces



Creatine

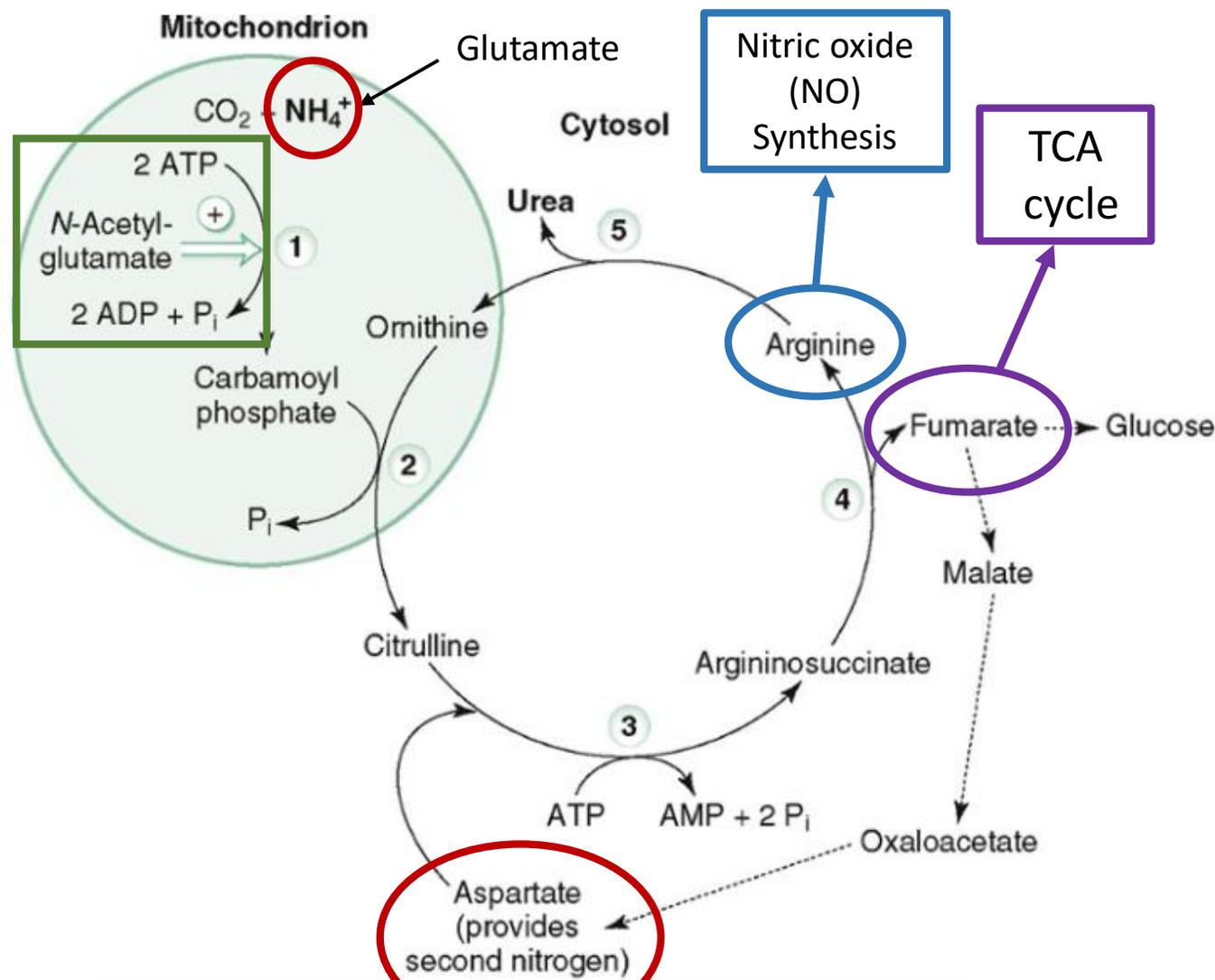


Creatinine

Creatinine is a nitrogenous end product that comes from Creatine phosphate in muscle cells

Note The level of Creatinine in the blood is proportional to the person's muscle mass

Urea Cycle

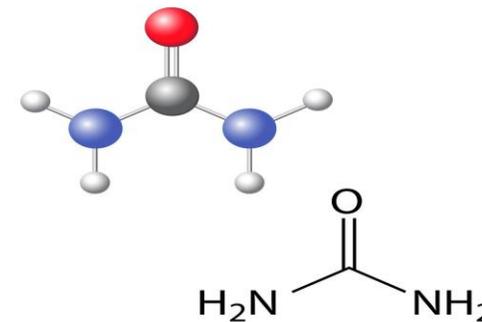


Note

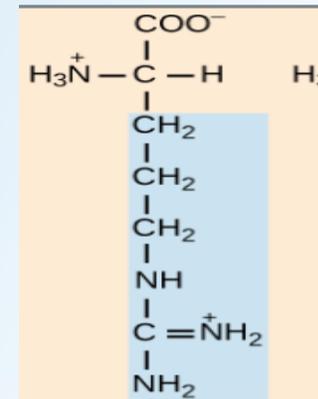
- 2 Nitrogens come from Glutamate and Aspartate
- The first step (Carbamoyl phosphetase) requires 2 ATP and N-acetyl-glutamate
- Fumarate is directly produced which can participate in The Citric Acid cycle
- Arginine is produced which can be used for NO synthesis

- | | |
|---|--------------------------------|
| 1 Carbamoyl phosphate synthetase, CPS I (rate-limiting) | 3 Argininosuccinate synthetase |
| 2 Omithine transcarbamoylase | 4 Argininosuccinate lyase |
| | 5 Arginase |

Urea



Arginine



Genetic deficiencies of Urea cycle enzymes

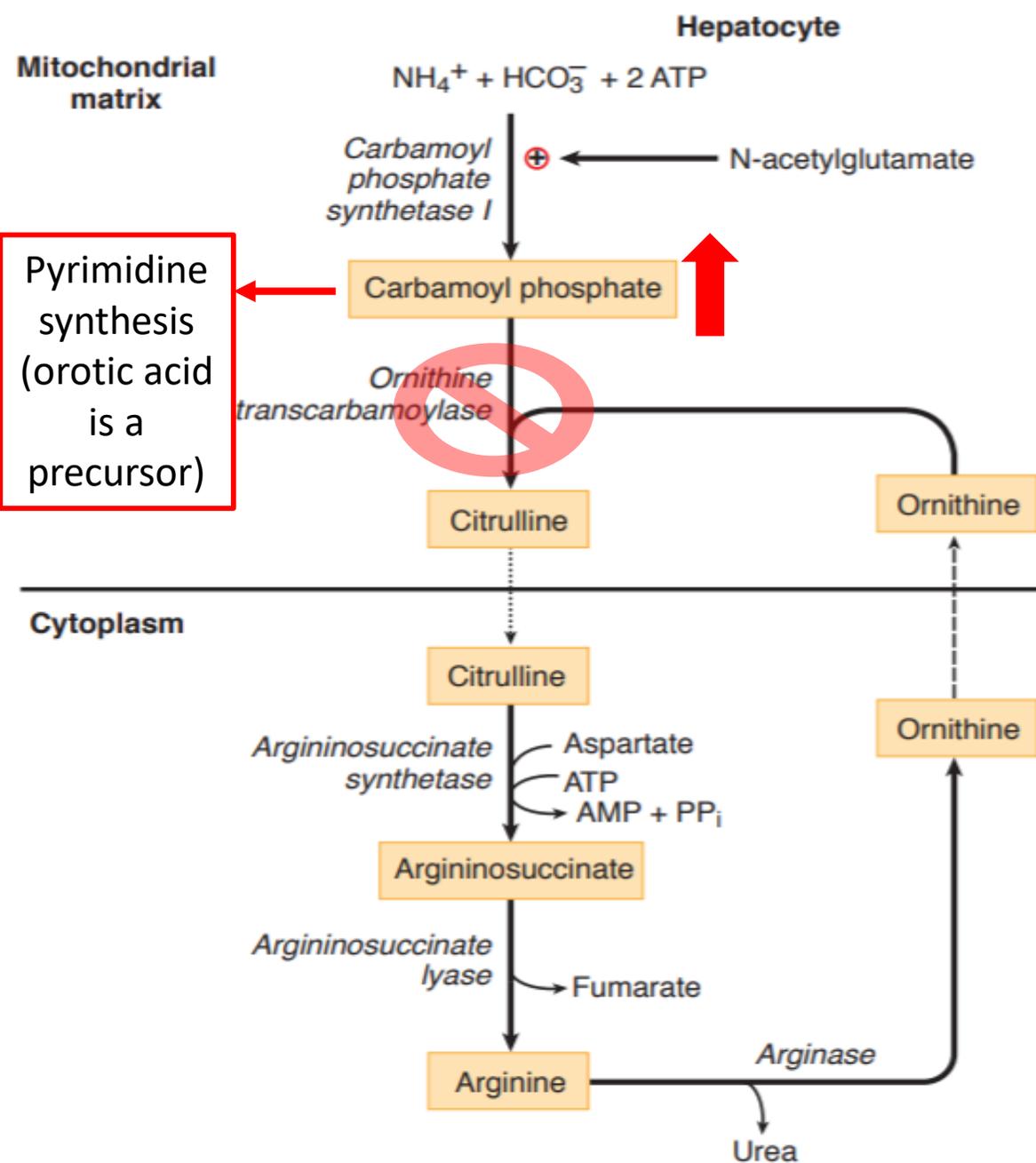


Figure I-17-2. The Urea Cycle in the Liver

Table I-17-1. Genetic Deficiencies of Urea Synthesis

Carbamoyl Phosphate Synthetase	Ornithine Transcarbamoylase
↑ [NH ₄ ⁺]; hyperammonemia	↑ [NH ₄ ⁺]; hyperammonemia
Blood glutamine is increased	Blood glutamine is increased
BUN is decreased	BUN is decreased
No orotic aciduria	Orotic aciduria
Autosomal recessive	X-linked recessive
Cerebral edema	Cerebral edema
Lethargy, convulsions, coma, death	Lethargy, convulsions, coma, death

Let's break 'em down

Recall: How do we get nitrogens to the liver for the Urea cycle?

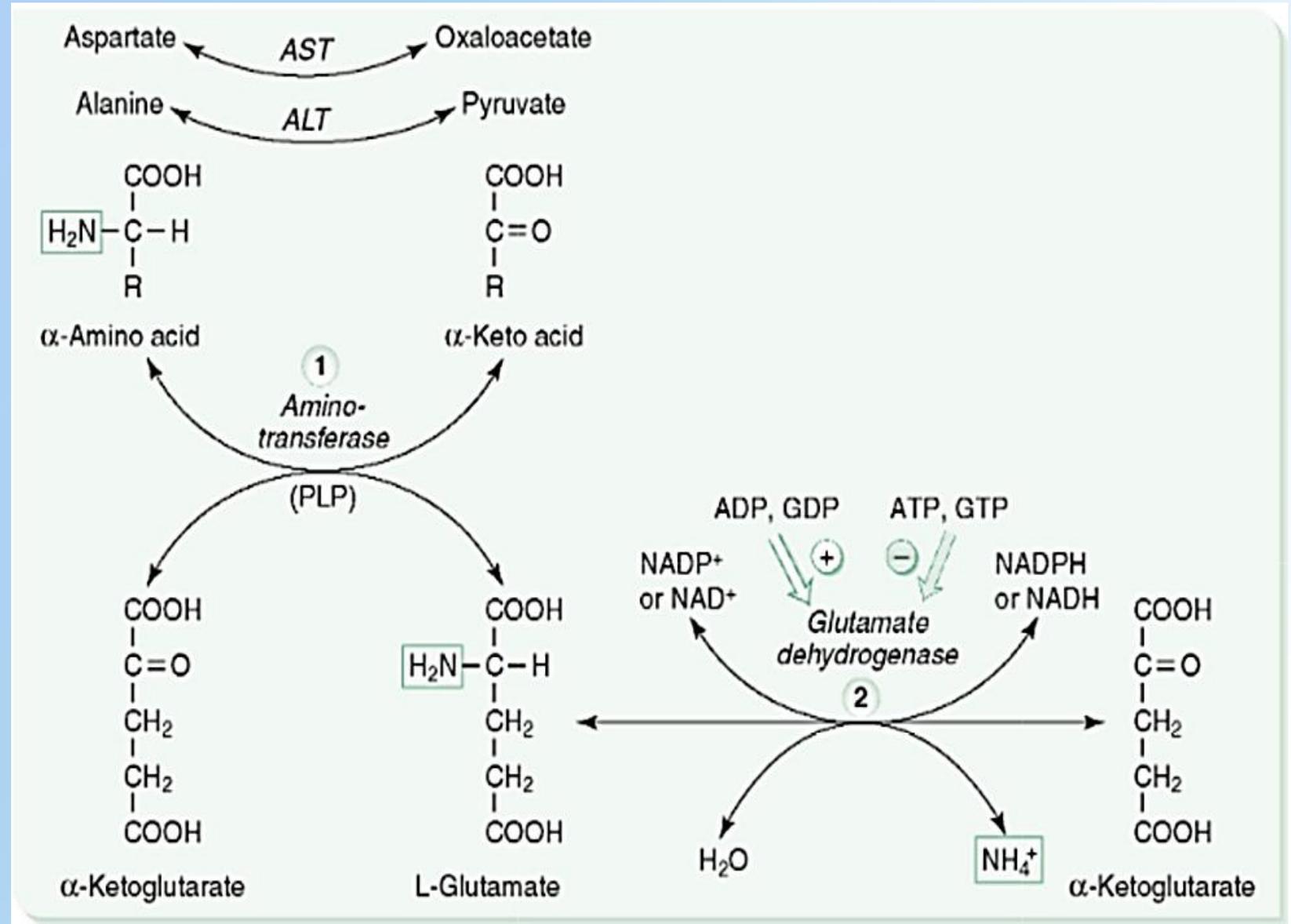
Glutamate

Glutamate

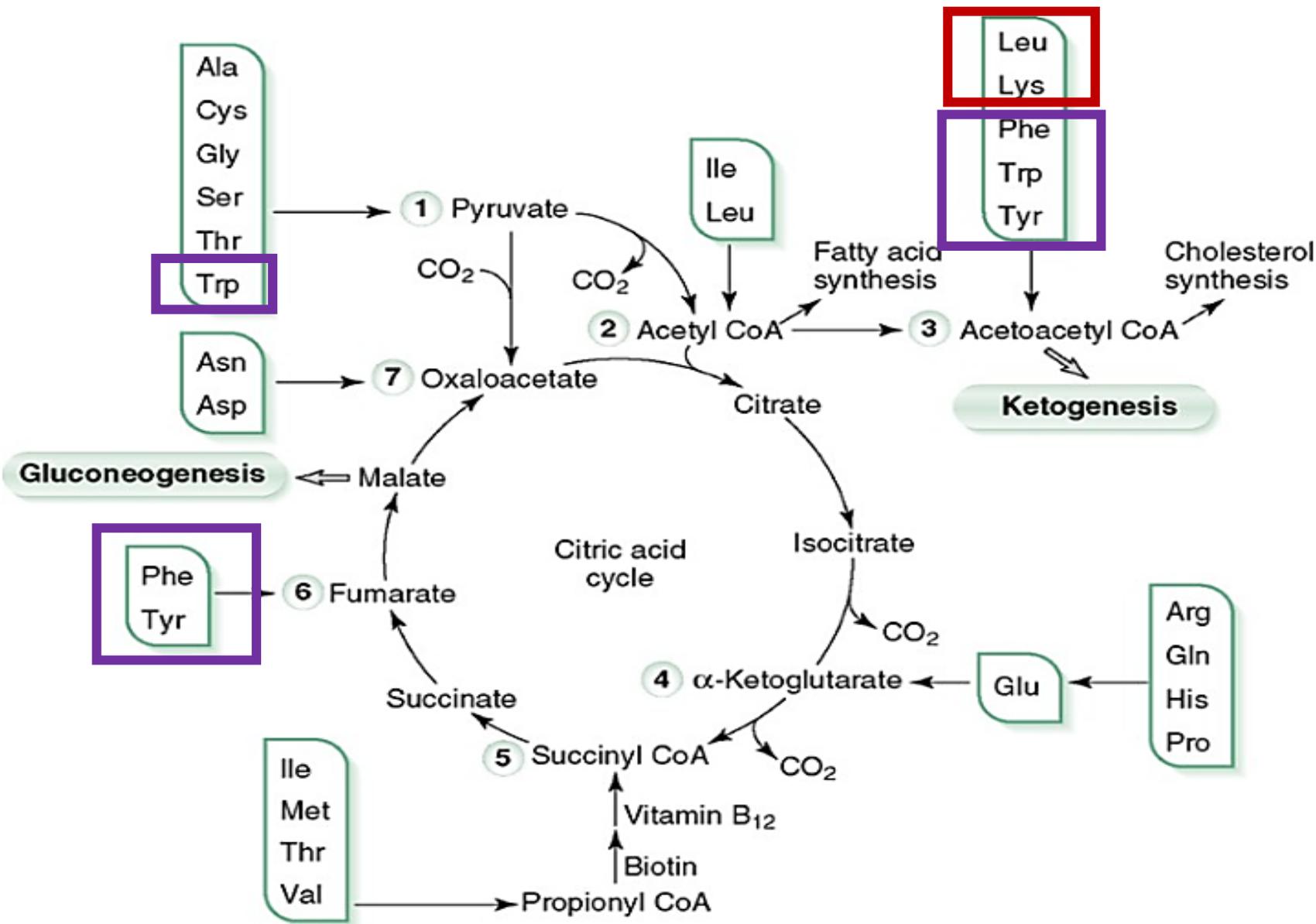
GLUTAMATE

***ALL amino-transferases transfer amino group (NH₂) to α-ketoglutarate

After NH₂ is gotten rid of, we just have to get rid of those pesky Carbons!



Amino Acid Carbon skeleton breakdown



Ketogenic – Next letter after K is L so – Lysine and Leucine

Ketogenic + Glucogenic – Aromatics + Isoleucine (Phenylalanine, Tyrosine, Tryptophan)

Glucogenic – The rest

Congenital deficiencies in Amino Acid metabolism

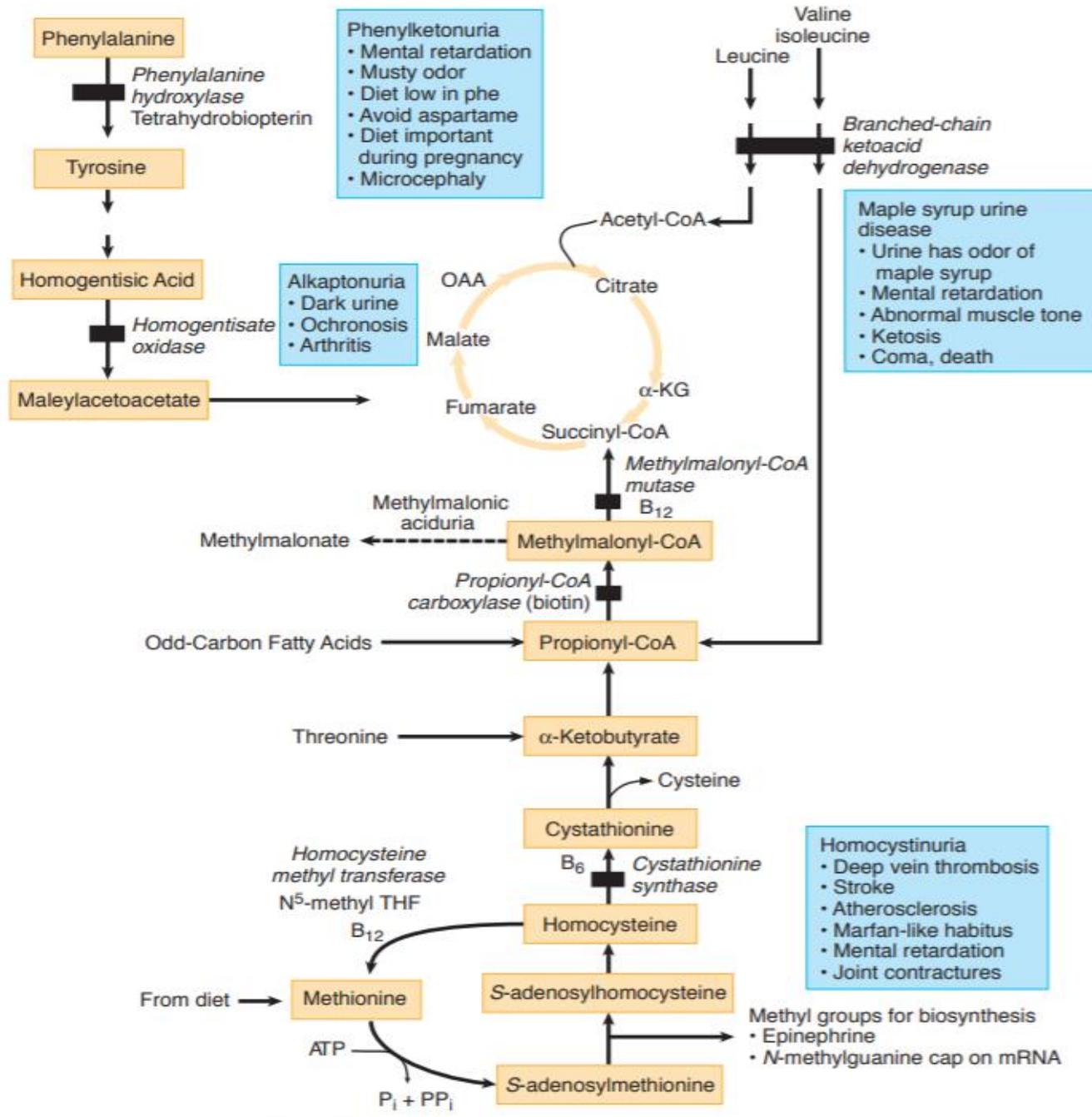
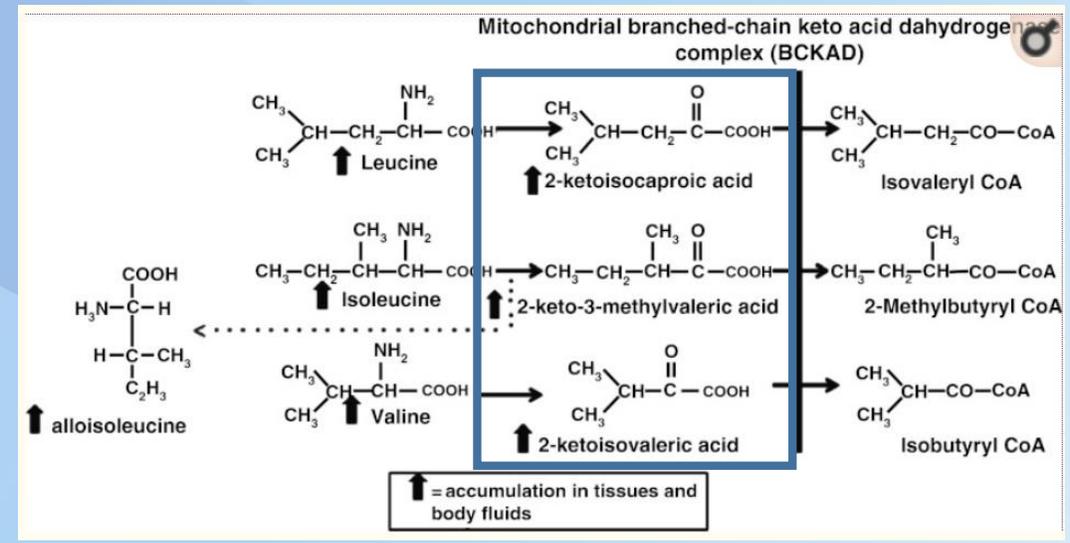
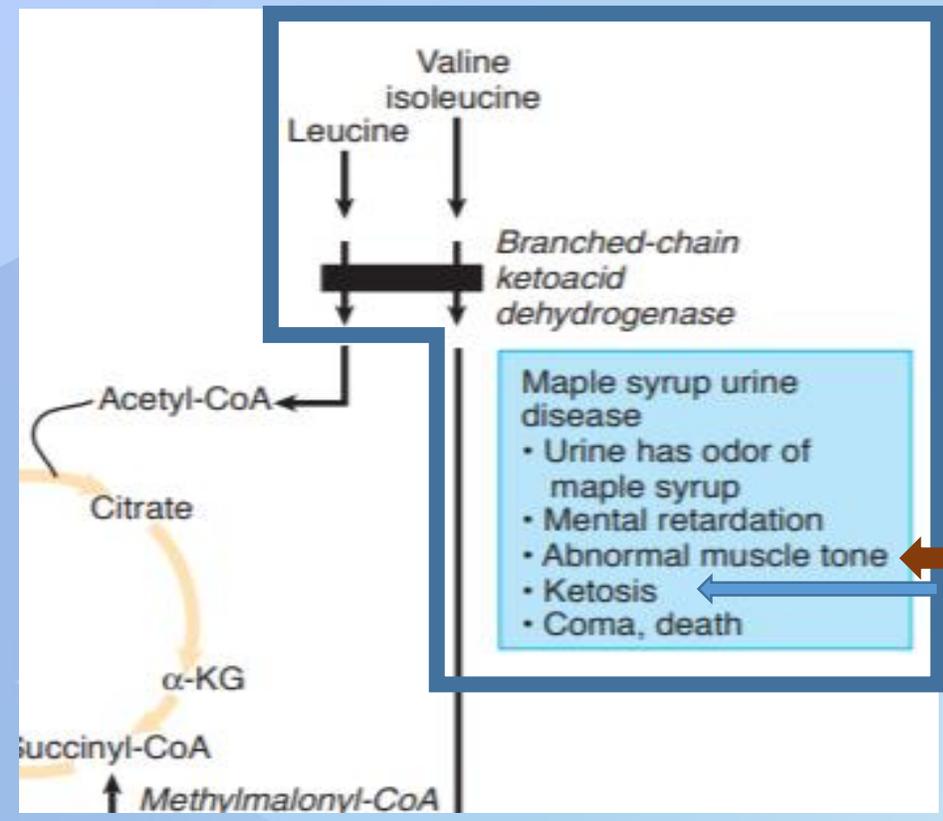
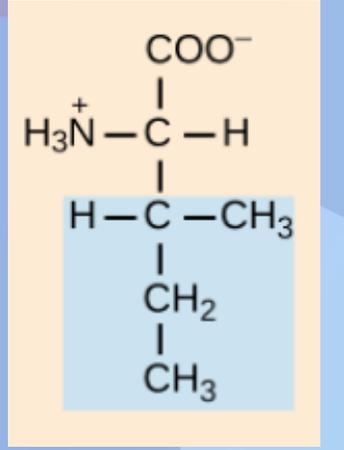
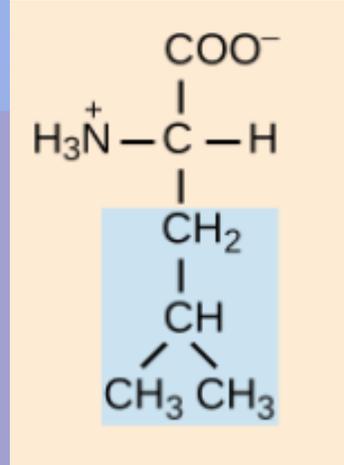
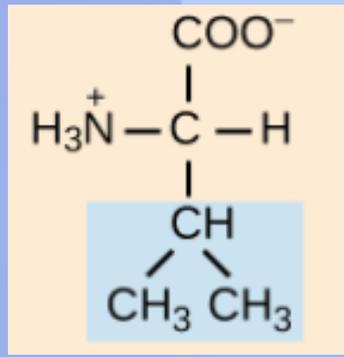


Figure I-17-3. Genetic Deficiencies of Amino Acid Metabolism



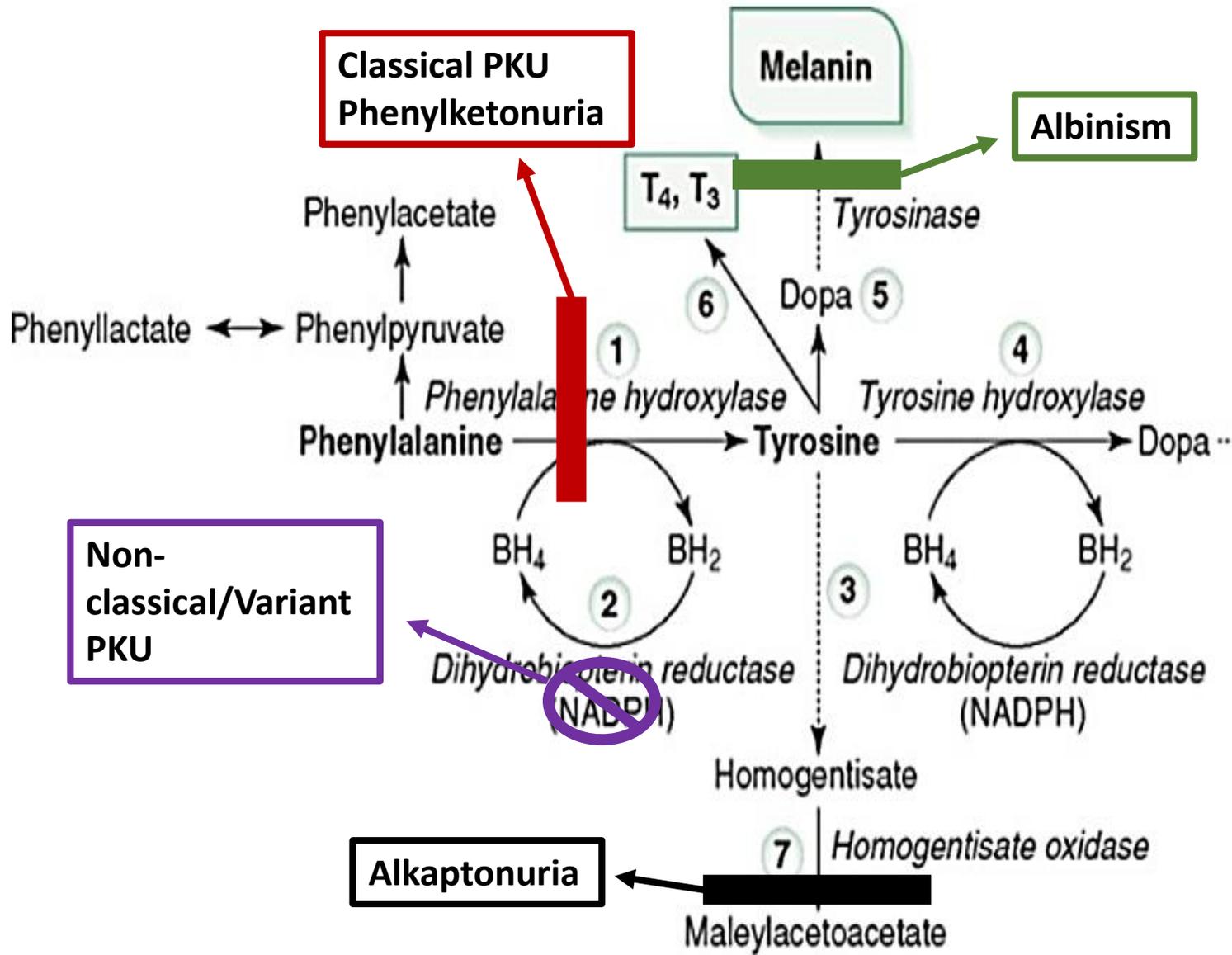
Maple Syrup Urine disease
BCAA – Branched Chain ketoacid
dehydrogenase deficiency
Valine, leucine, Isoleucine



Note

- Muscle preferentially used BCAAs that's why the low muscle tone
- The ketosis is not with the "traditional" ketones found after fatty acid breakdown, it is with the α-ketoacids of each deaminated BCAA respectively.

Deficiencies in Tyrosine metabolism



Classical PKU – Phenylalanine hydroxylase

Symptoms – Mental retardation → seizures, Musty body odor, light skin, eczema

Note the phenylalanine accumulation and then the liver conjugates it to make it water soluble (excretable in the urine)

Treatment is to limit Phenylalanine intake and supplement tyrosine

Non-classical/Variant PKU – BH₂ reductase

Presents as mild PKU – low phenylalanine diet

Albinism – any enzyme in the melanin pathway.

Complete albinism is a deficiency of Tyrosinase

Symptoms – white skin, white eyes, white hair.

Go in the sun uncovered → get cancer

Alkaptonuria – Homogentisate oxidase

Symptoms – Black spots (ochronosis), Black joints/Arthritis, Urine turns black if left to stand for a while. The arthritis is bad but it's a relatively harmless disease



PKU



Albinism



ocronosis

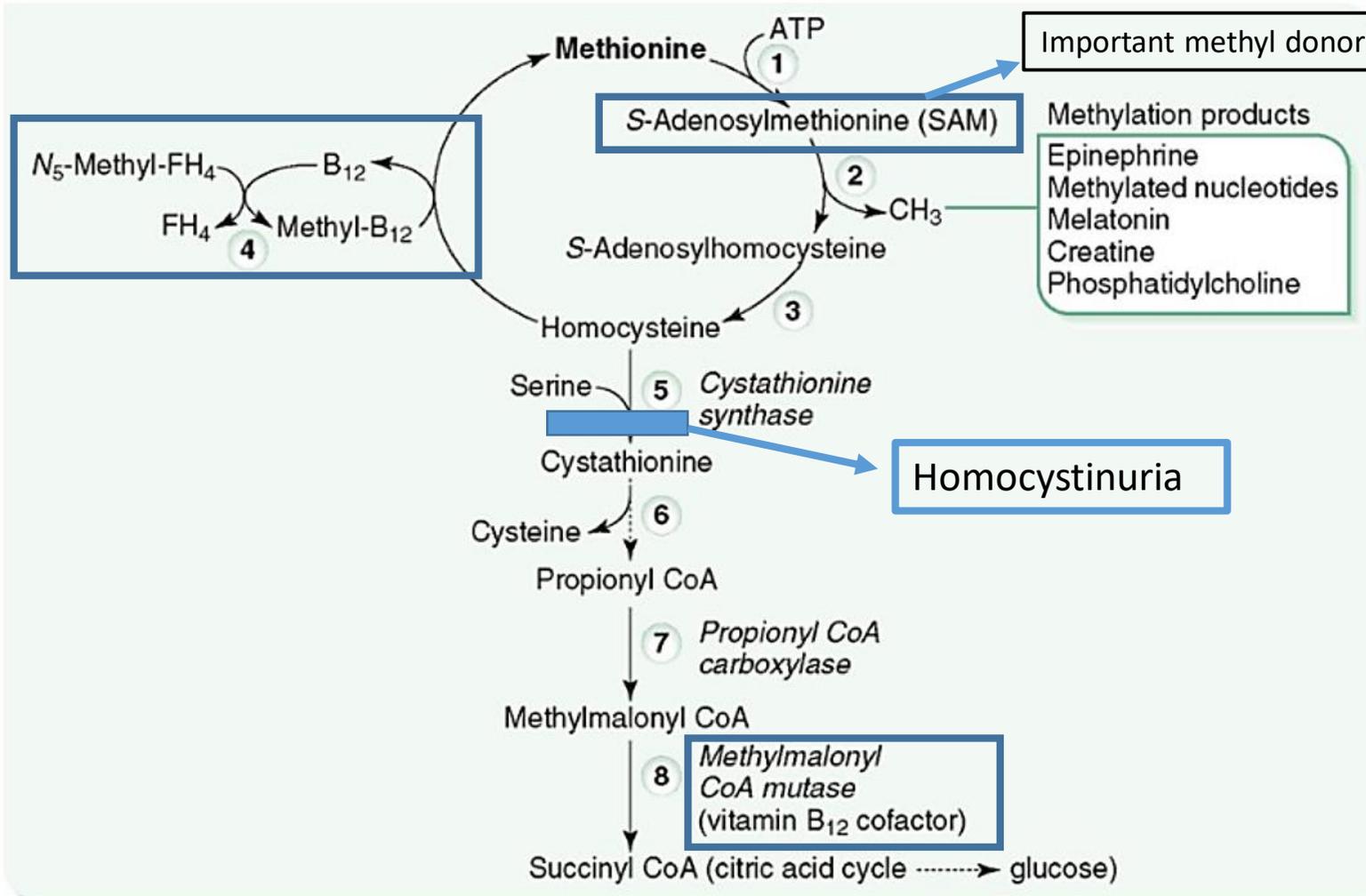


Depósito tisular de pigmento



Alcaptonuria

Deficiencies of Methionine Metabolism



Homocystinuria – Cystathionine synthase

You get an accumulation of Homocysteine which is extremely toxic to vessels. think Atherosclerosis+MI in your 20s!!

It also attacks connective tissue so you get a Marfanoid Habitus – Tall and lanky

Mild forms of Homocystinuria can come from Folate/B12 deficiencies

Homocystinuria



Elevated homocysteine levels affect collagen, result in a Marfanoid habitus, ectopia lentis but lens dislocation in homocystinemia is downward unlike in marfan its upward, mental retardation and strokes, its harmful to the bones and body. Arachnodycty.

Note the importance of SAM as a methyl donor. It is the MOST IMPORTANT methyl donor in the body

B12 is only used in two enzymes in the body!! But think how devastating is B12 deficiency

Let's make things!

YAY!

Table I-17-3. Products of Amino Acids

Amino Acid	Products
Tyrosine	Thyroid hormones T ₃ and T ₄ Melanin Catecholamines
Tryptophan	Serotonin NAD, NADP
Arginine	Nitric oxide (NO)
Glutamate	γ-Aminobutyric acid (GABA)
Histidine	Histamine

Tyrosine Metabolites

Cofactors necessary for Epinephrine synthesis

- Tetrahydrobiopterin
- B6 – Pyridoxine (PLP)
- Vitamin C + Copper
- SAM (S-adenosylmethionine)

Breakdown products of NorEpi/Epi are Metanephrines and VMA (vannilylmandelic Acid)
Finding these in the urine is the diagnostic test for a Pheochromocytoma

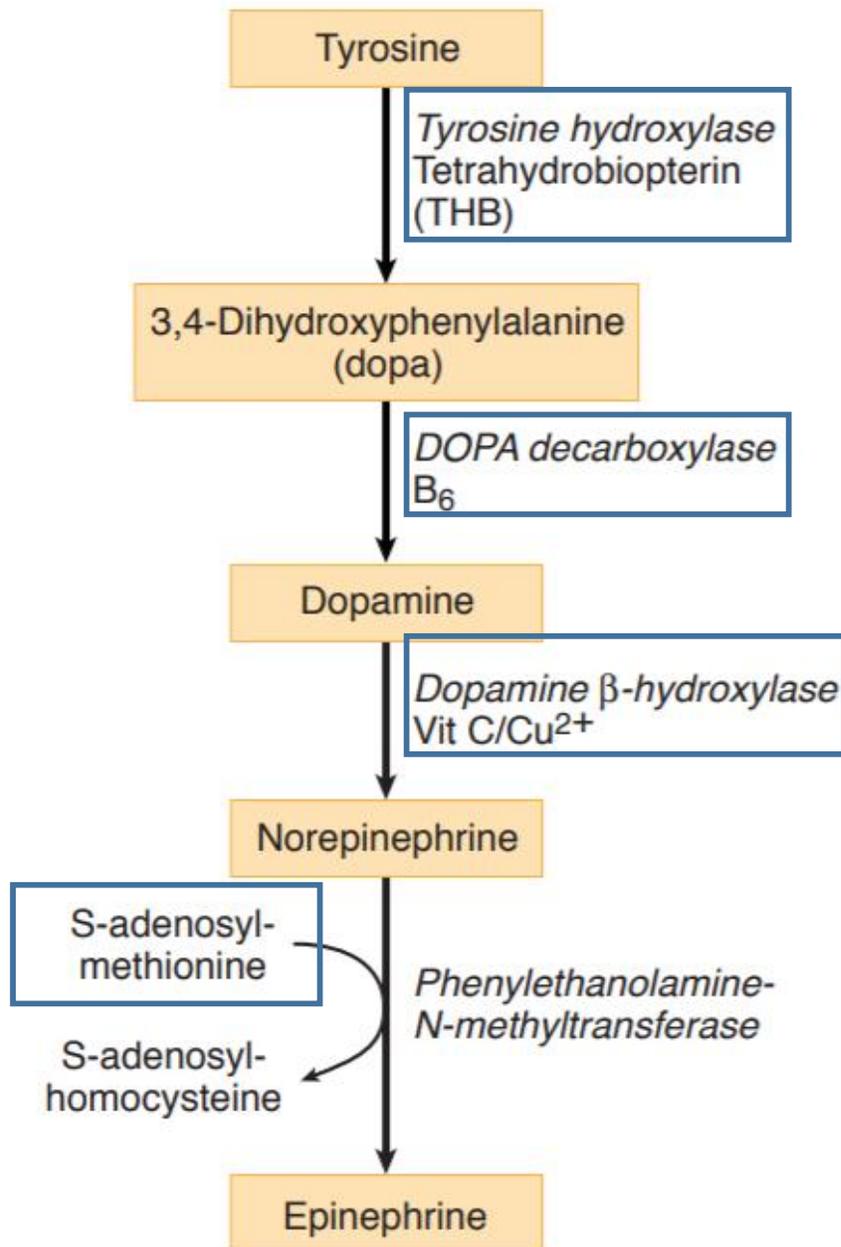
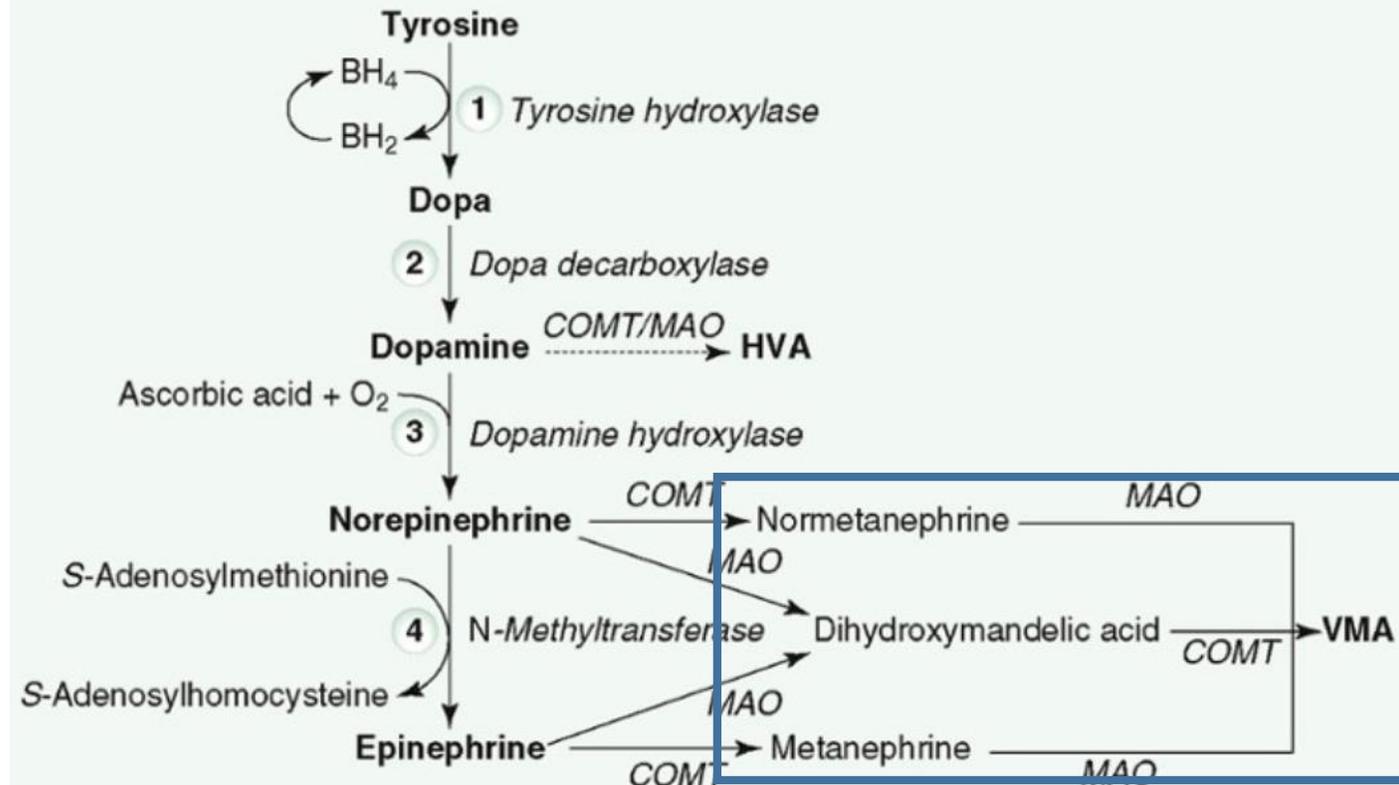
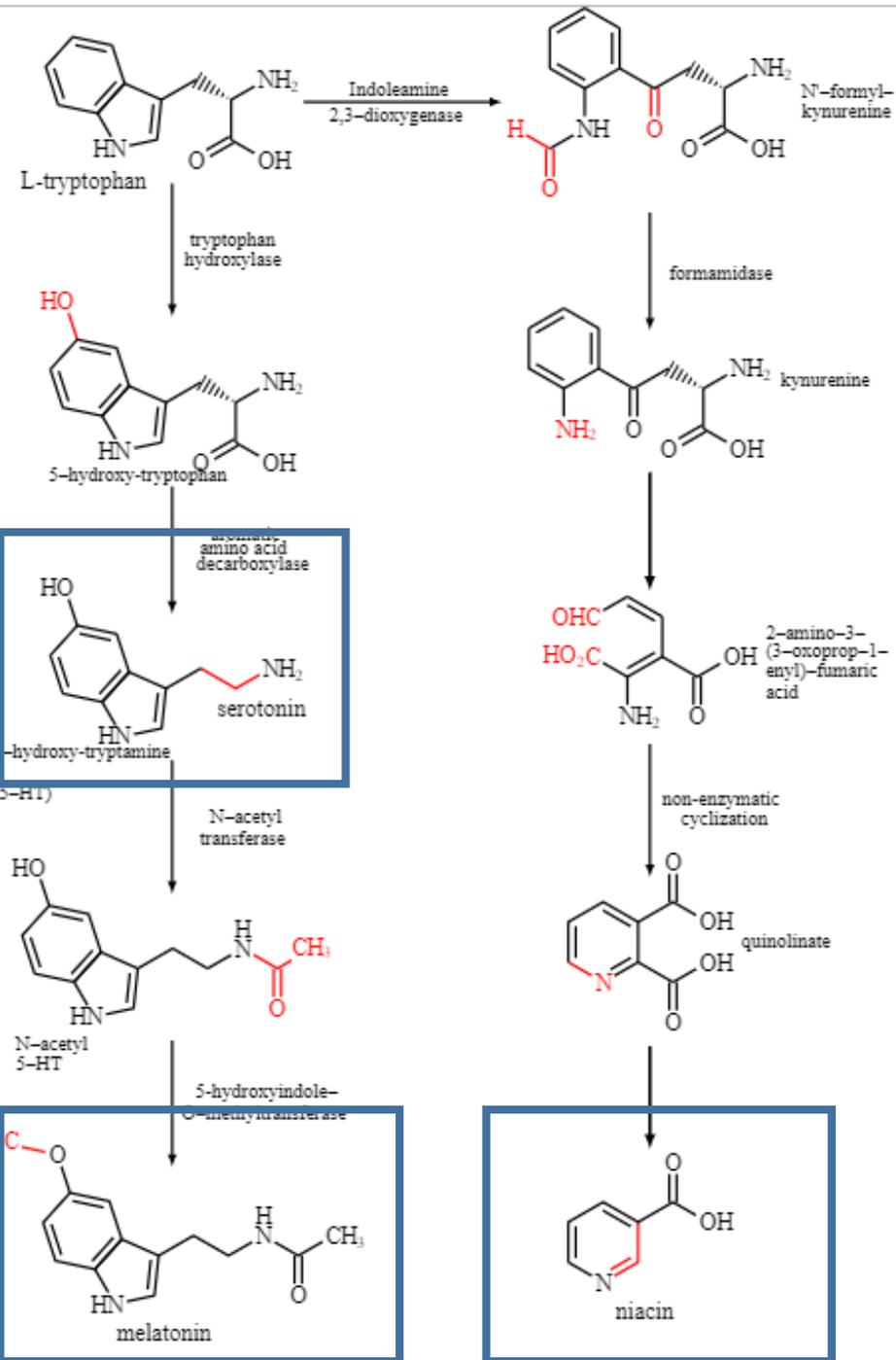
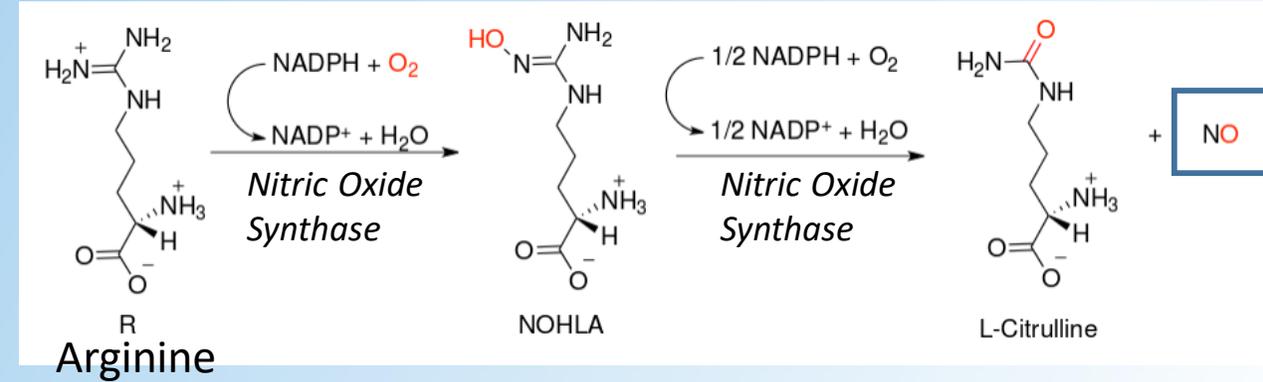


Figure I-17-4. Catecholamine Synthesis



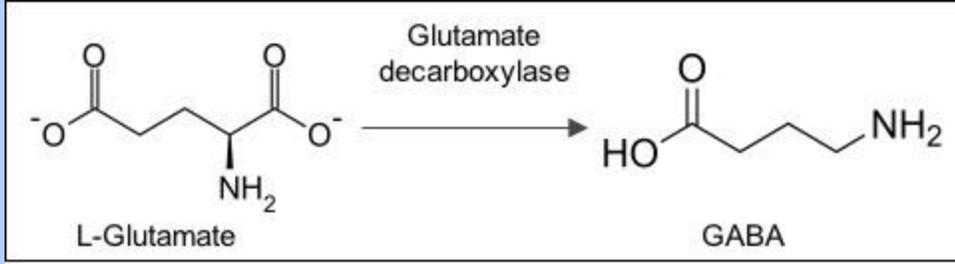


Things Tryptophan and Arginine make



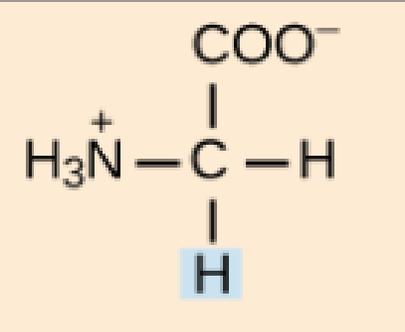
Nitric Oxide is extremely important for Vasodilation as well as cell to cell signaling

Tryptophan can make Serotonin and Melatonin
 Niacin can actually be made by the liver from Tryptophan



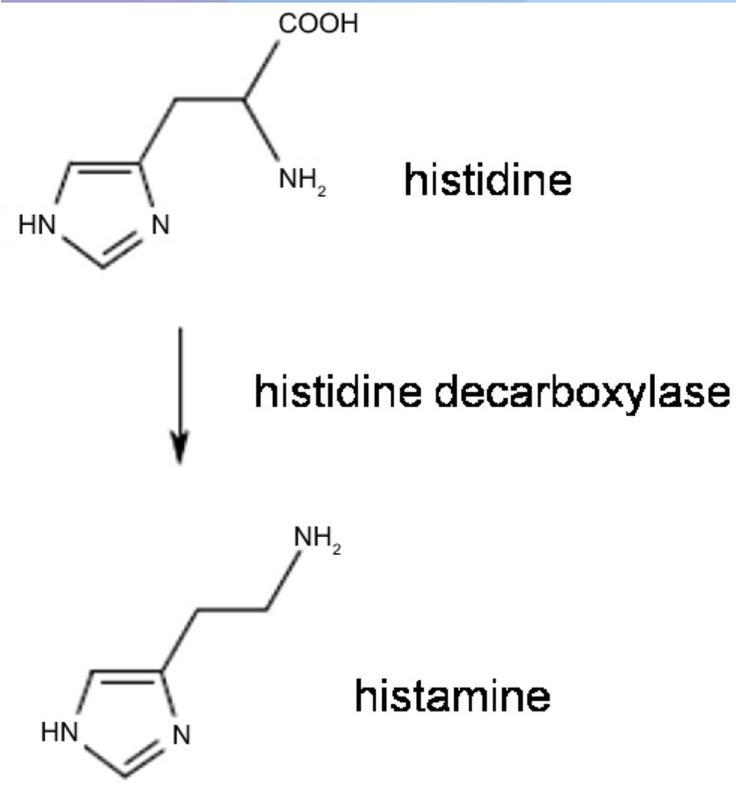
Note that
Glutamate is the
major Excitatory
neurotransmitter

GABA is an
inhibitory
neurotransmitter



The Amino Acid
Glycine is also an
inhibitory
neurotransmitter

Things Glutamate and Histidine make



Histamine is a Potent
vasodilator and is the cause of
edema in the allergic response

Note Glutamate directly
makes GABA but the NH_3
group from Glutamate is used
for a ton of stuff!!!
Recall that it is the major
transporter of Nitrogen in the
body

Questions!

1. What are the essential amino acids?
2. How do most cells transport NH_3 to the liver?
3. How do muscle cells transport NH_3 to the liver?
4. How does the body get rid of/excrete nitrogen?
5. Where does Urea get its 2 NH_3 ?
6. What are the 2 requirements for the first step of Urea synthesis?
7. What TCA intermediate is directly produced from the Urea cycle?
8. What are the two major congenital urea cycle enzyme deficiencies and how can you tell them apart?
9. Which amino acids are only ketogenic, which are both glucogenic+ketogenic, which are only glucogenic?
10. What is Maple syrup urine disease, what enzyme is deficient and what amino acids are involved?
11. Why do babies with Maple syrup urine disease present with hypotonia?
12. What is Classical PKU, what enzyme is deficient, what are the main symptoms and what is the treatment?
13. In classical PKU, what are the Phenyl-ketones and why are they in the urine?
14. What is Non-classical/variant PKU?
15. What is Albinism and what should these patients avoid?
16. What is Alkaptonuria, what enzyme is deficient and what are the symptoms of this disease? Is it a dangerous disease?
17. What is Homocystinuria, what do these patients look like and what do they die from?
18. The deficiency of what two vitamins can cause a mild form of Homocystinuria?
19. Name all the compounds in order of the metabolic pathway from Tyrosine to Epinephrine
20. What are the necessary cofactors of the pathway from Tyrosine to Epinephrine

Questions!

21. What are the breakdown products of Epi/NorEpi and what disease is present if they are found in the urine?
22. What is a neurotransmitter made from Tryptophan? How about Glutamate?
23. What is a hormone made by Tryptophan?
24. What Vasodilator can be made by Histidine? How about Arginine?
25. Which two amino acids directly act as neurotransmitters? Which is stimulatory and which is inhibitory?