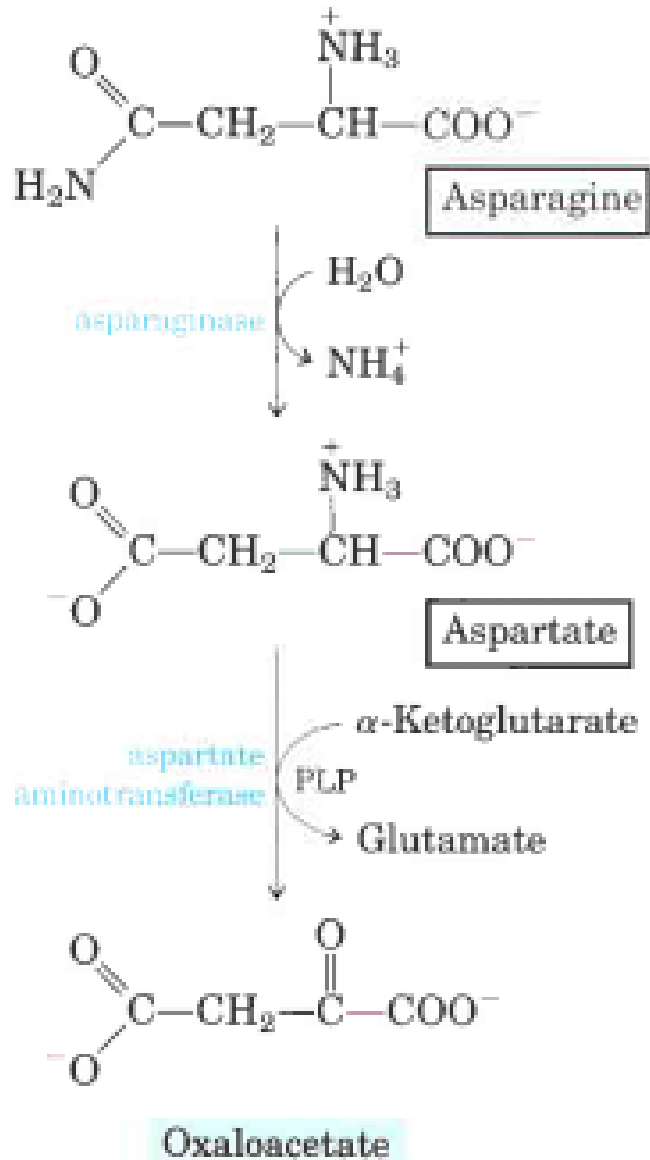


BIOCHEMISTRY: AMINO ACID METABOLISM

Lecture 3

Lecturer: Dr Victor Mobegi

Catabolism of 4 Carbon amino acids



- The carbon skeletons of asparagine and aspartate enter the TCA cycle as oxaloacetate (OAA)
- The enzyme asparaginase catalyzes the hydrolysis of asparagine to aspartate, which undergoes transamination with α -ketoglutarate to yield glutamate and oxaloacetate

Biosynthesis of nonessential amino acids

- The 20 amino acids that occur in proteins can be classified as essential or nonessential amino acids.
- Humans are incapable of synthesizing half of the 20 common amino acids, and these must be provided in the diet. These amino acids are called essential amino acids.
- Nonessential amino acids are those that human body is capable of synthesizing.

Classification of amino acids for humans

Nonessential	Conditionally Essential*	Essential
Alanine	Arginine	Histidine
Asparagine	Cysteine	Isoleucine
Aspartate	Glutamine	Leucine
Glutamate	Glycine	Lysine
Serine	Proline	Methionine
	Tyrosine	Phenylalanine
		Threonine
		Tryptophan
		valine

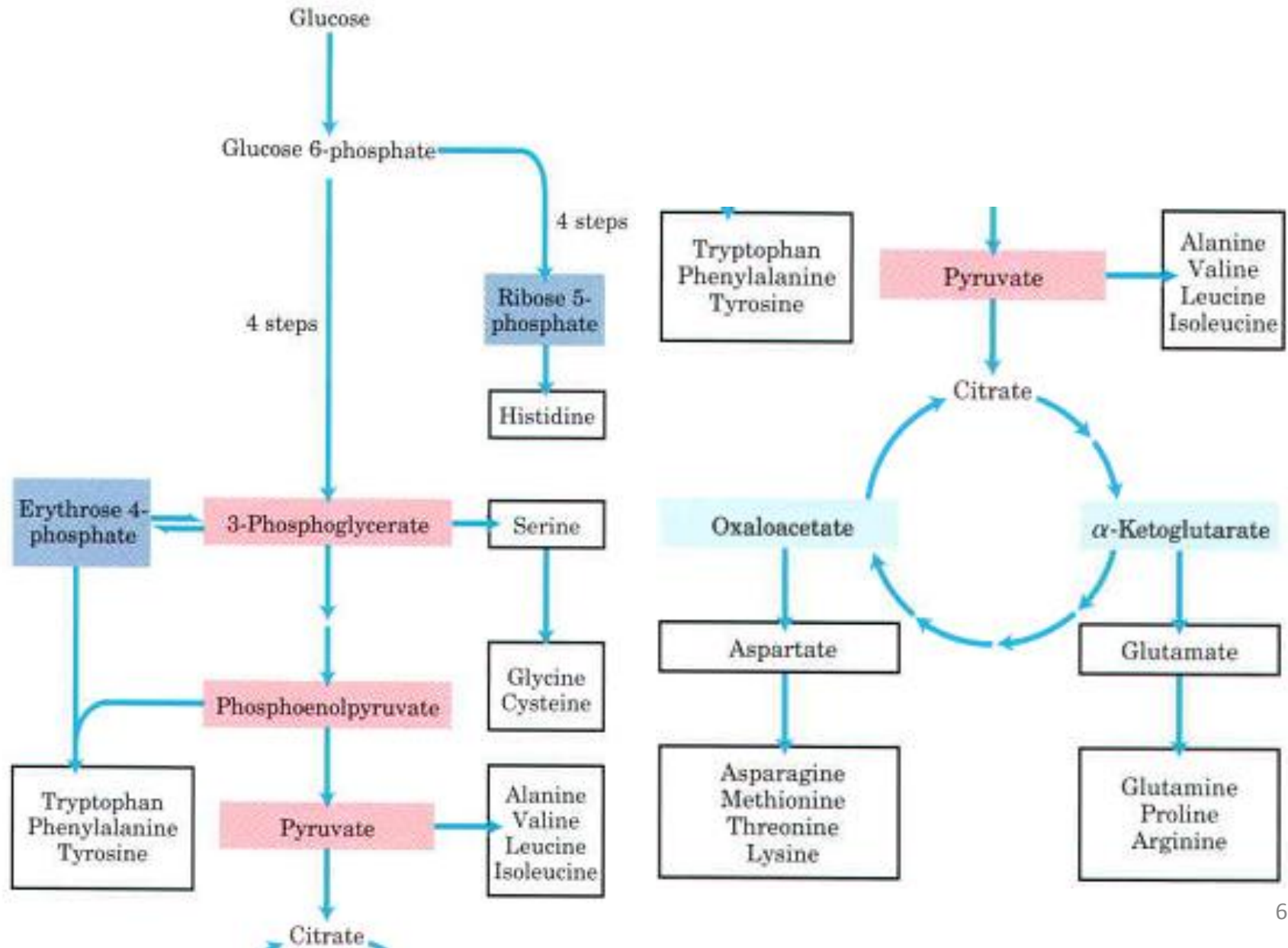
*Required to some extent in young, growing individuals and/or sometimes during illness

Metabolic precursors of nonessential amino acids

Amino acid(s)	Precursor
Glutamate Glutamine Proline Arginine	α -Ketoglutarate
Alanine	Pyruvate
Serine Glycine Cysteine	3-phosphoglycerate
Aspartate Asparagine	Oxaloacetate
Tyrosine*	Phosphoenolpyruvate and Erythrose-4-phosphate

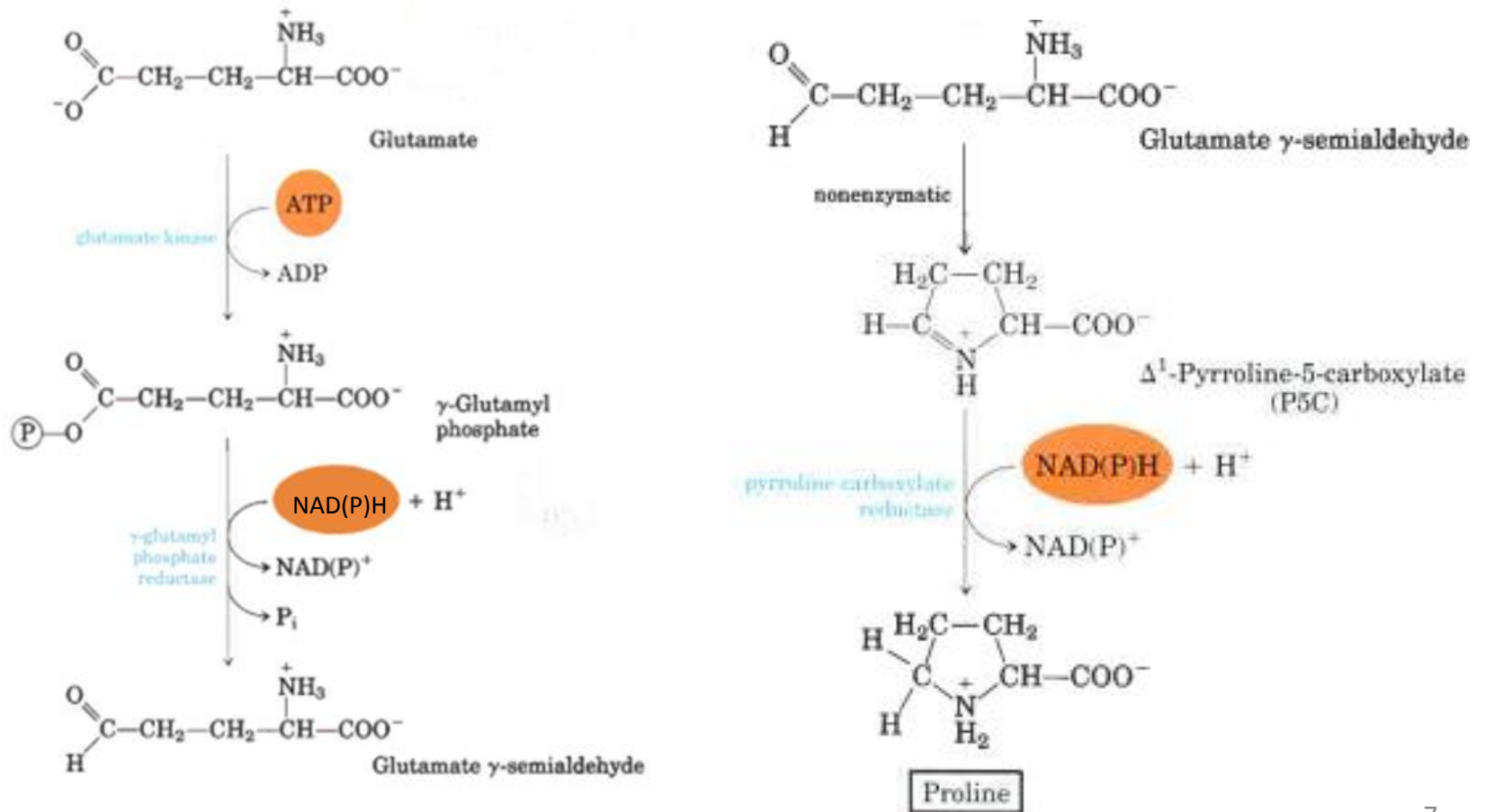
*Derived from phenylalanine in mammals

Overview of amino acid biosynthesis



Biosynthesis of amino acids from α -Ketoglutarate

- Proline is a cyclized derivative of glutamate



Steps in proline synthesis

- In the first step of proline synthesis, ATP reacts with the γ -carboxyl group of glutamate to form an γ -glutamyl phosphate, which is reduced by NADPH or NADH to glutamate γ -semialdehyde.
- glutamate γ -semialdehyde undergoes rapid spontaneous (nonenzymatic) cyclization and is then reduced further to yield proline.

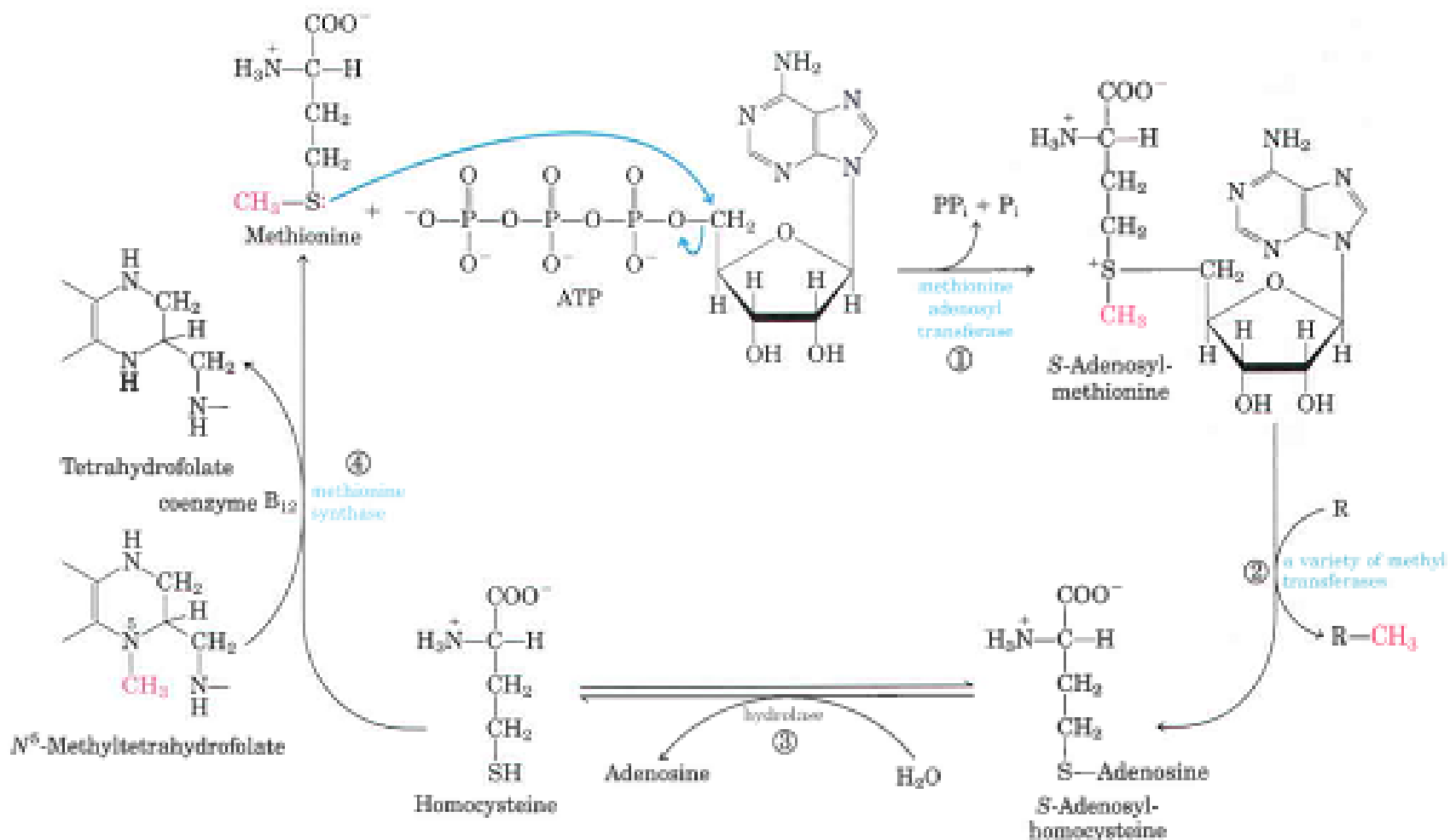
Arginine synthesis

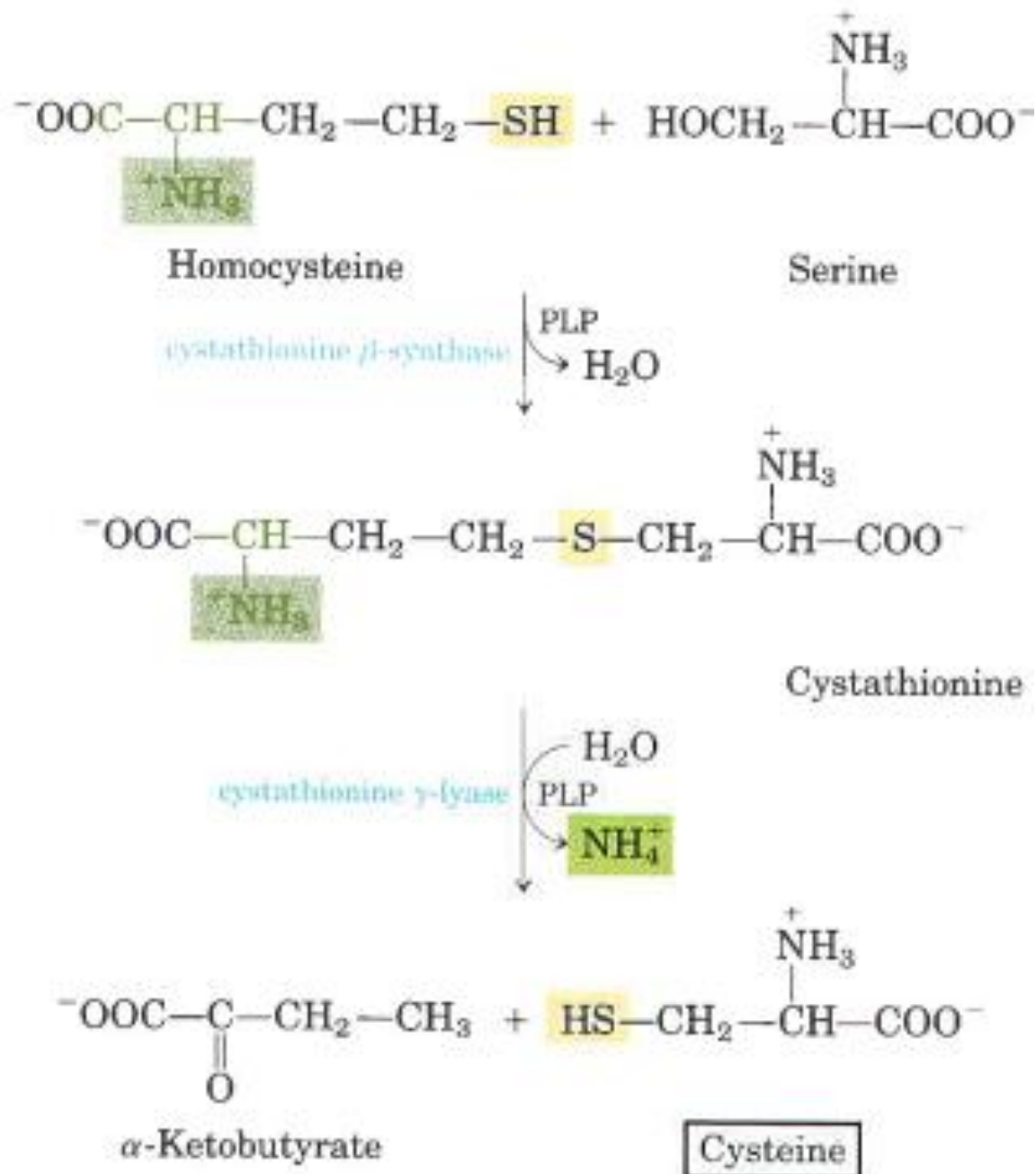
- Arginine is synthesized from glutamate via ornithine and the urea cycle in animals(Refer to Lecture 2).

Biosynthesis of cysteine from methionine

- Mammals synthesize cysteine from two amino acids: methionine and serine. Methionine provides the sulfur atom and serine furnishes the carbon skeleton.
- Methionine is first converted to S-adenosylmethionine, which loses its methyl group to any of a number of acceptors to form S-adenosylhomocysteine (adoHcy).
- S-adenosylhomocysteine is hydrolyzed to free homocysteine, which undergoes a reaction with serine, catalyzed by cystathionine β -synthase, to yield cystathionine.
- Finally, cystathionine γ -lyase which requires PLP, catalyzes removal of ammonia and cleavage of cystathionine to yield free cysteine.

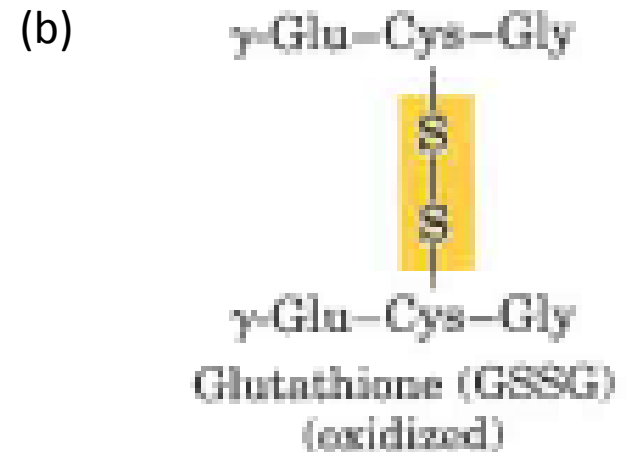
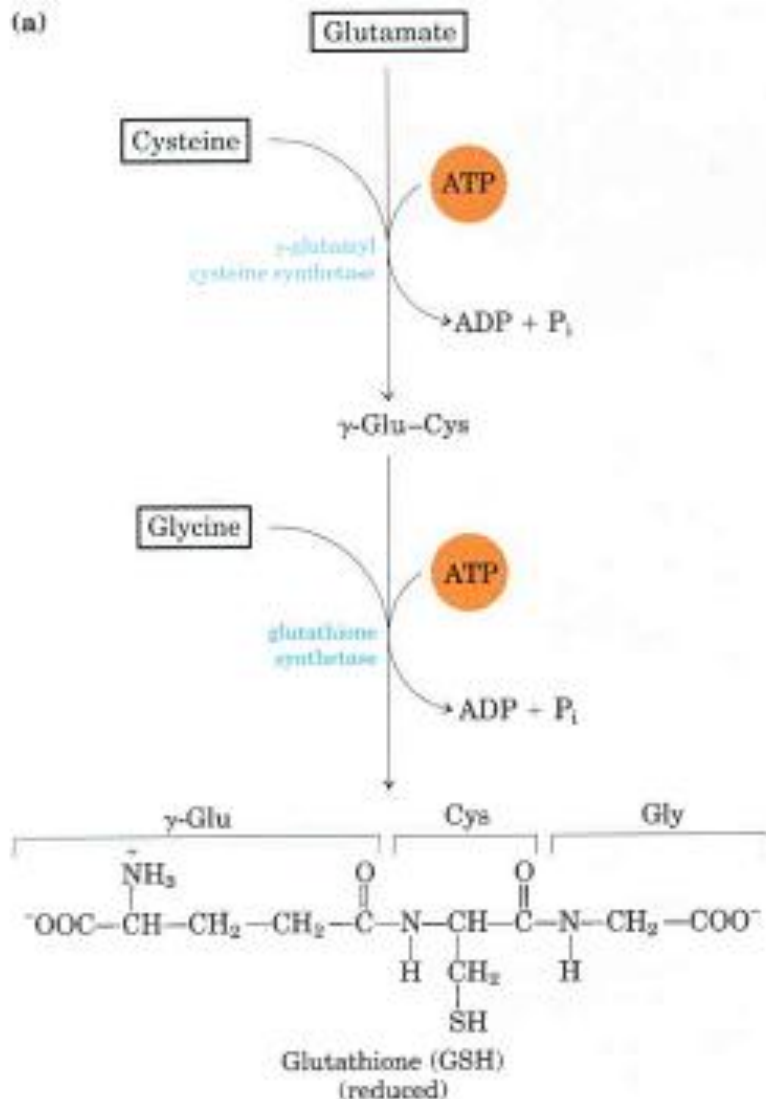
Synthesis of homocysteine from methionine





Glutathione metabolism

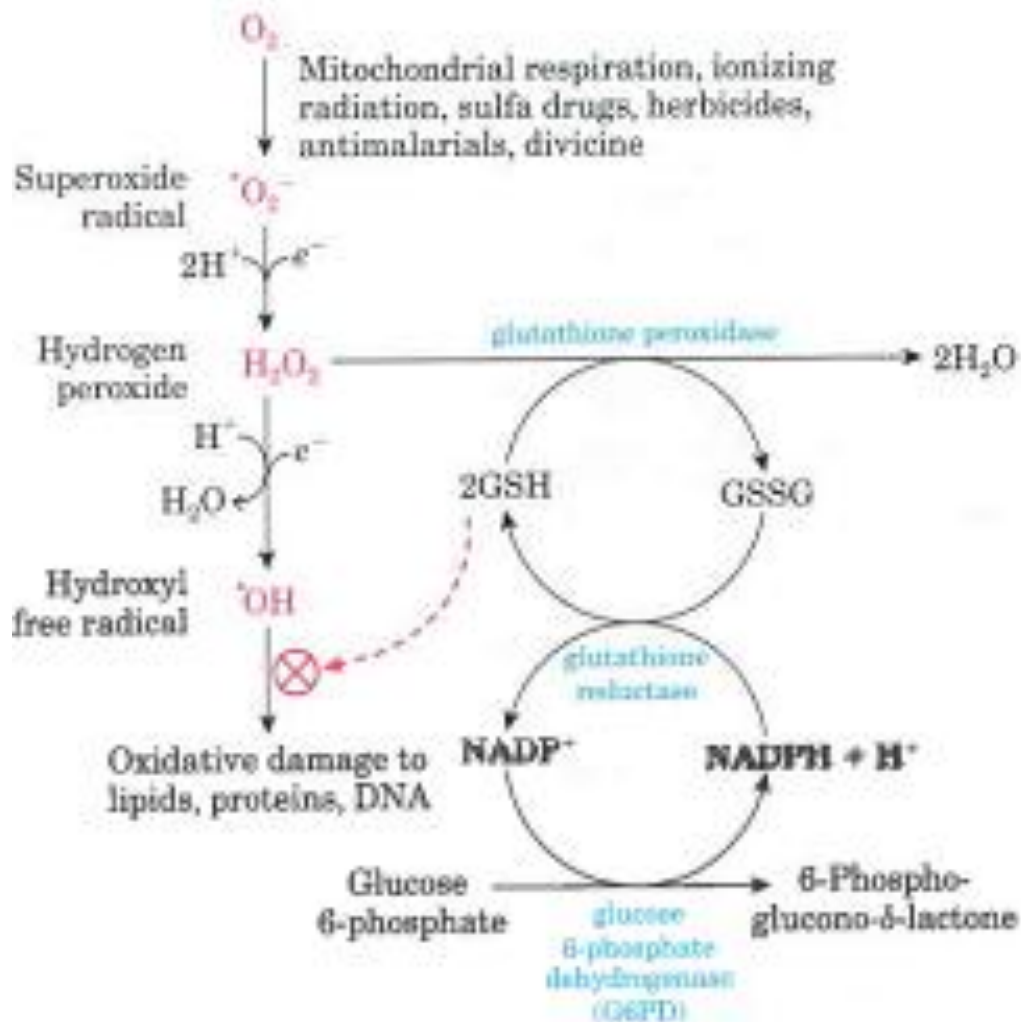
- Glutathione is derived from glutamate, cysteine, and glycine



a=Biosynthesis of glutathione
b=Oxidized form of glutathione

- The oxidized form of glutathione (GSSG), produced in the course of its redox activities, contains two glutathione molecules linked by a disulfide bond.
- Glutathione helps maintain the sulfhydryl groups of proteins in the reduced state and the iron of heme in the ferrous (Fe^{2+}) or Iron II state. This prevents conversion of hemoglobin to methemoglobin (iron III state) .
- It serves as a reducing agent for glutaredoxin in deoxyribonucleotide synthesis (Reduction of ribonucleotides to deoxyribonucleotides by ribonucleotide reductase)
- Glutathione is used to remove toxic peroxides formed in the normal course of growth and metabolism under aerobic conditions





- Glutathione protects cells against highly reactive oxygen derivatives.
- Reduced glutathione (GSH) protects the cell by destroying hydrogen peroxide and hydroxyl free radicals.
- Regeneration of GSH from its oxidized form (GSSG) requires the NADPH produced in the glucose 6-phosphate dehydrogenase reaction

- Sulfur conjugates of drugs by glutathione renders them more polar for excretion
- Glutathione is involved in transport of amino acids across cell membranes
- Glutathione acts as a cofactor for some enzymatic reactions