BIOCHEMISTRY LECTURES

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INTERMEDIARY METABOLISM

- Principal metabolic pathways of intermediary metabolism
- Key junctions of metabolic pathways
- Compartmentation of metabolic pathways
- Interrelationship of carbohydrate, lipid and protein metabolism

THE PRINCIPAL METABOLIC PATHWAYS OF INTERMEDIARY METABOLISM

- CITRIC ACID CYCLE

The citric acid cycle is the hub of intermediary metabolism. The citric acid cycle and electron transport chain are final common oxidative pathways for fatty acids, glucose and amino acids.

- GLYCOLYSIS
- GLUCONEOGENESIS

- GLYCOGEN SYNTHESIS
- GLYCOGEN DEGRADATION
- FATTY ACID SYNTHESIS
- FATTY ACID DEGRADATION
- AMINO ACID DEGRADATION

KEY JUNCTIONS OF METABOLIC PATHWAYS

- The factors governing the flow of molecules in metabolism can be further explained by examining three important molecules:
- Acetyl CoA
- Glucose-6-phosphate
- Pyruvate

ACETYL COA

- The major sources of this activated two carbon unit are : the oxidative decarboxylation of pyruvate and the beta oxidation of fatty acids. It is also derived from ketogenic amino acids.

The fate of Acetyl CoA includes:

- Complete oxidation to CO_2 by TCA cycle
- For Biosynthesis of fatty acids, cholesterol and ketone bodies

GLUCOSE 6-PHOSPHATE

- Glucose on entering a cell is rapidly phosphorylated to glucose 6-phosphate and is subsequently :
- Stored as glycogen (glycogenesis)
- Degraded to pyruvate

Or

- Converted into ribose -5-phosphate via Pentose phosphate pathway

PYRUVATE

- This major metabolic junction is derived primarily from glucose, Alanine and lactate.

- Pyruvate can be reduced to lactate by LDH to regenerate NAD^+

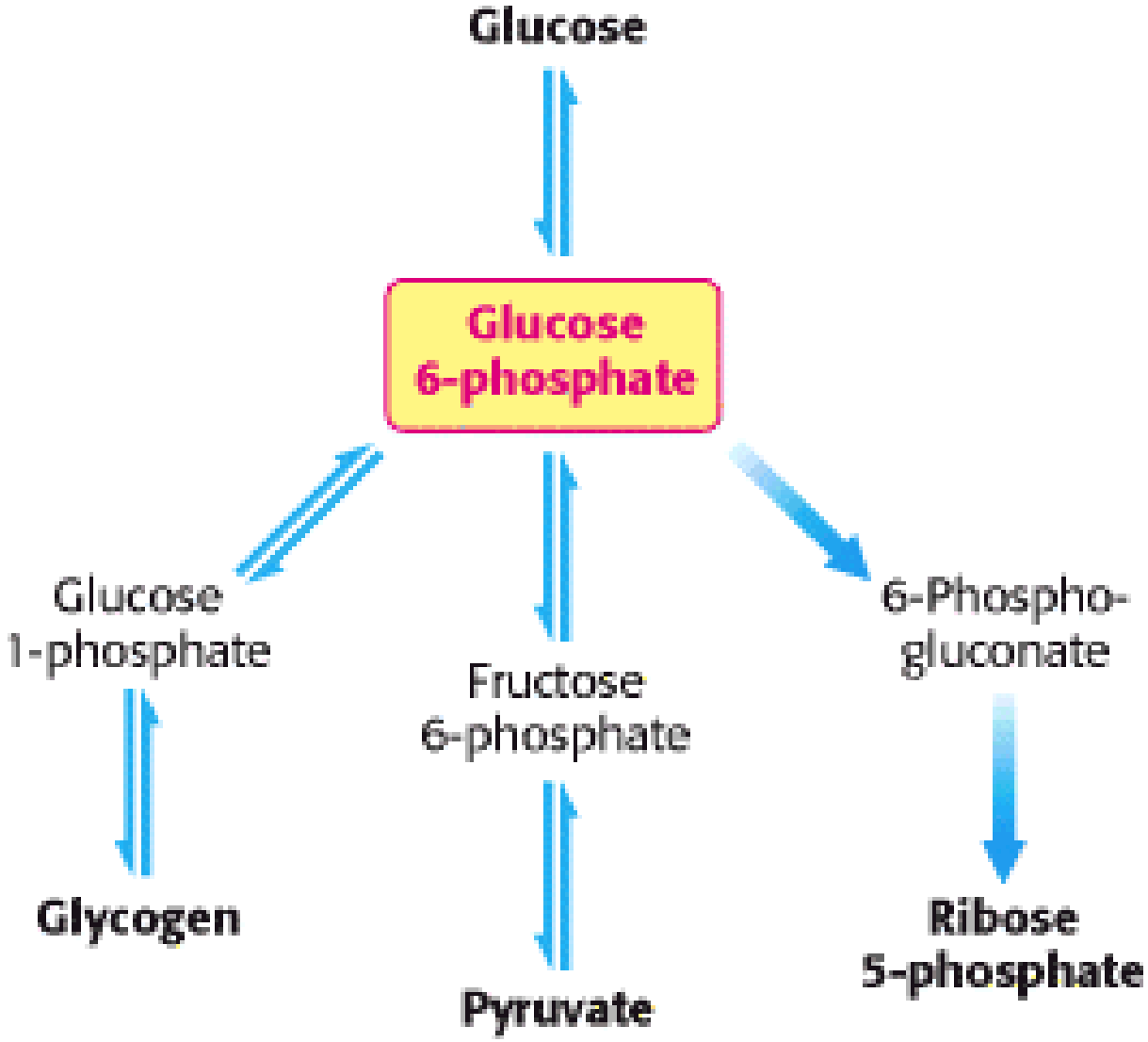
- Another reversible reaction in the cytosol is the transamination of pyruvate to Alanine, the corresponding amino acid

PYRUVATE

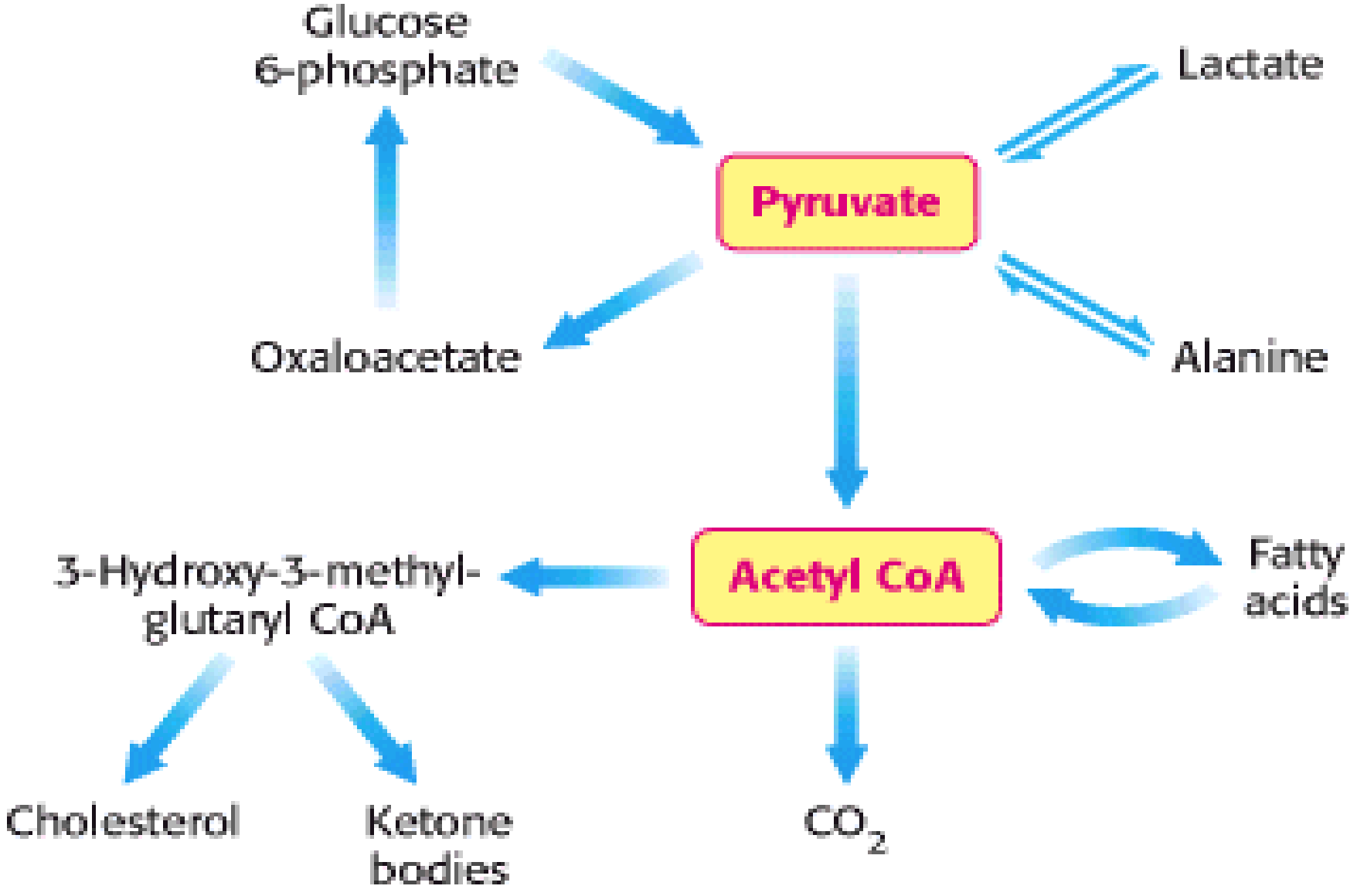
- A third metabolic fate of pyruvate is its carboxylation to oxaloacetate inside the mitochondria, the first step in gluconeogenesis

- A fourth fate of pyruvate is its oxidative decarboxylation to acetyl CoA.

Metabolic Fates of Glucose 6-Phosphate



Major Metabolic Fates of Pyruvate and Acetyl CoA in Mammals

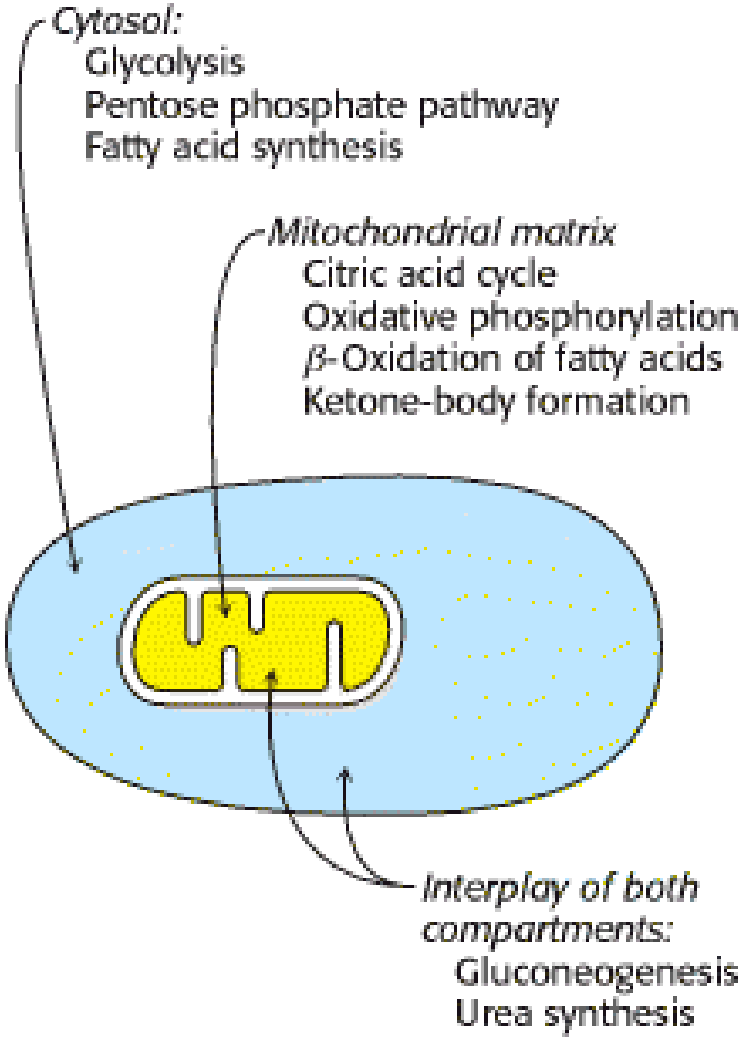


COMPARTMENTATION OF METABOLIC PATHWAYS

- In compartmentation, there is physical separation of the biosynthesis and catabolism of a metabolite in different organelles.

- The aim of this concept is to avoid furtile cycles. For example, fatty acid biosynthesis takes place in the cytosol, while its degradation takes place in the mitochondria

Compartmentation of the Major Pathways of Metabolism.



INTERRELATIONSHIP OF CARBOHYRATE, LIPID AND PROTEIN METABOLISM

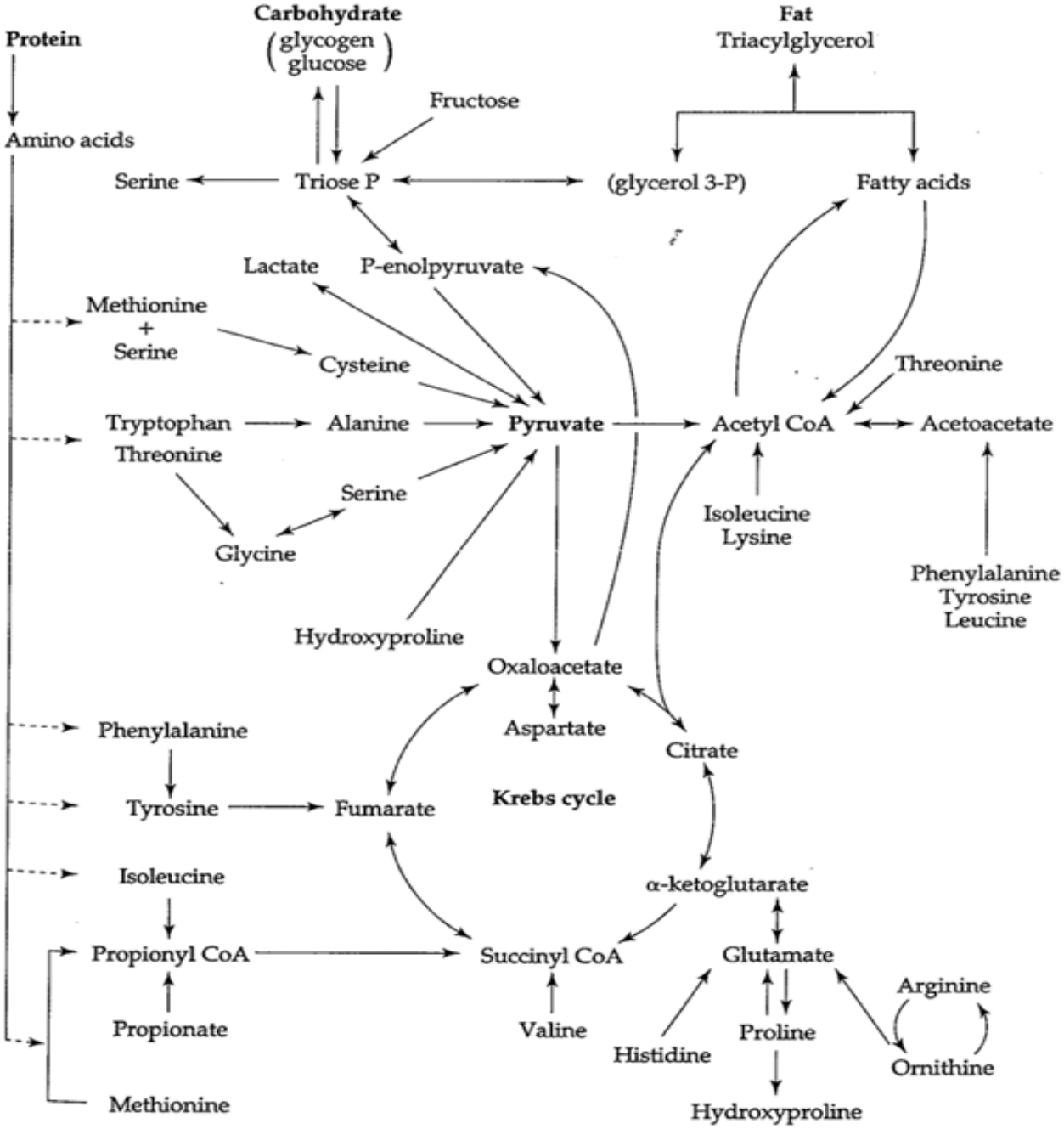
- (A) Certain amino acids can be synthesized in the body from carbohydrates. Conversely, most amino acids can serve as precursors for carbohydrate (glucogenic amino acids)

- Some amino acids can serve as precursors for fat synthesis (ketogenic amino acids)
- (B) Carbohydrate (glucose) can be converted to fat

- Glucose is the precursor for both the glycerol and the fatty acid components of triacylglycerols. The glycerol portion can be formed from dihydroxyacetone phosphate

- A very significant reaction linking glucose metabolism to fatty acid synthesis is the reaction of pyruvate dehydrogenase complex.

- It should be noted that although carbohydrate can be converted into both the glycerol and the fatty acids components of fat, only the glycerol portion of fat can be converted to carbohydrate, this is because the pyruvate dehydrogenase reaction is not reversible.


Protein
Amino acids
Carbohydrate
(glycogen
glucose)
Fructose
Fat
Triacylglycerol
Serine
Triose P
(glycerol 3-P)
Fatty acids
Lactate
P-enolpyruvate
Methionine
+
Serine
Cysteine
Threonine
Tryptophan
Threonine
Alanine
Pyruvate
Acetyl CoA
Acetoacetate
Serine
Glycine
Isoleucine
Lysine
Phenylalanine
Tyrosine
Leucine
Hydroxyproline
Oxaloacetate
Aspartate
Citrate
Phenylalanine
Tyrosine
Fumarate
Krebs cycle
Isoleucine
α-ketoglutarate
Propionyl CoA
Succinyl CoA
Glutamate
Arginine
Propionate
Valine
Histidine
Proline
Ornithine
Methionine
Hydroxyproline