Integration of Metabolism of Carbohydrates, Lipids and Proteins

Though metabolism of each of major food nutrients, carbohydrates, lipids and proteins have been considered separately, it actually takes place simultaneously and are closely interrelated to one another. The metabolic processes involving these three major food nutrients and their inter relationship can be broadly divided into three stages

1st stage: Stage of hydrolysis to simpler units

2nd stage: Preparatory stage

3rd stage: Oxidative stage–Aerobic final (TCA Cycle).

1st Stage

Stage of Hydrolysis to Simpler Units

• The complex polysaccharides, starch/glycogen are broken down to glucose; and disaccharides are hydrolysed to monosaccharides in GI tract by various carbohydrate-splitting enzymes present in digestive juices.

• Similarly, principal lipids, triacylglycerol (TG) is hydrolysed to form FFA and glycerol.

• Proteins are hydrolysed by proteolytic enzymes to amino acids.

The above is the prelude to either further synthesis of new substances or for their oxidation. Very little of energy is produced in this hydrolytic phase and it is dissipated away as heat. There is no storage of energy at this stage.

2nd Stage

Preparatory Stage

• The monosaccharide glucose runs through the glycolytic reactions to produce the 3-C keto acid pyruvic acid (PA) in the cytosol, which in turn is transported to mitochondrion where it undergoes oxidative decarboxylation to produce 2-C compound "acetyl-CoA" ("active" acetate).

• The glycerol of fat, either goes into formation of glucose (gluconeogenesis) or by entering the same glycolytic pathway through the triose-P, forms PA and then finally 2-C compound "acetyl-CoA"

• The fatty acids undergo principally β-oxidation and form several molecules of "acetyl-CoA".

• The amino acids are deaminated/and/or transaminated first and the C-skeleton is metabolised differently from amino acid to amino acid

• In the case of amino acids, eg. Glycine, Alanine, Serine, Cysteine/Cystine and threonine when catabolised form pyruvic acid (PA) similar to carbohydrates and is finally converted to 'Acetyl CoA'

• In the case of amino acids, eg. Glutamic acid, Histidine, Proline and OH-proline, Arginine and Ornithine produces α-ketoglutaric acid when catabolised and thus they enter the TCA cycle.

• Yet a few others like Leucine, Phenyl alanine, Tyrosine and Isoleucine yield acetate or acetoacetate, the latter can be converted to "acetyl- CoA".

During the second stage (glycolysis, β-oxidation, etc.) relatively small amount of energy is produced and this is stored as ATP.

3rd Stage

Oxidative Stage: Aerobic Final (TCA Cycle) In presence of oxygen, acetyl-CoA is oxidized to CO2 and H2O by common final pathway TCA cycle. The carbohydrates, lipids and proteins all form acetate or some other intermediates like oxaloacetate (OAA), α-ketoglutarate, succinyl-CoA, or fumarate, which are all intermediates of TCA cycle. Having gained entry into the TCA cycle at any site, two of carbons of "citrate" constituting an acetate moiety are oxidized finally to CO2 and H2O and the energy of oxidation by the electron transport chain is captured as energy-rich $PO4^{-}$ ATP mostly. This stage yields the largest amount of energy of all three stages. Thus, the pathways are similar to a large extent and identical in the final stage of oxidation of the metabolites, whether derived from carbohydrates, lipids or proteins. This is schematically represented in Figure 2 along with the entry of various amino acids

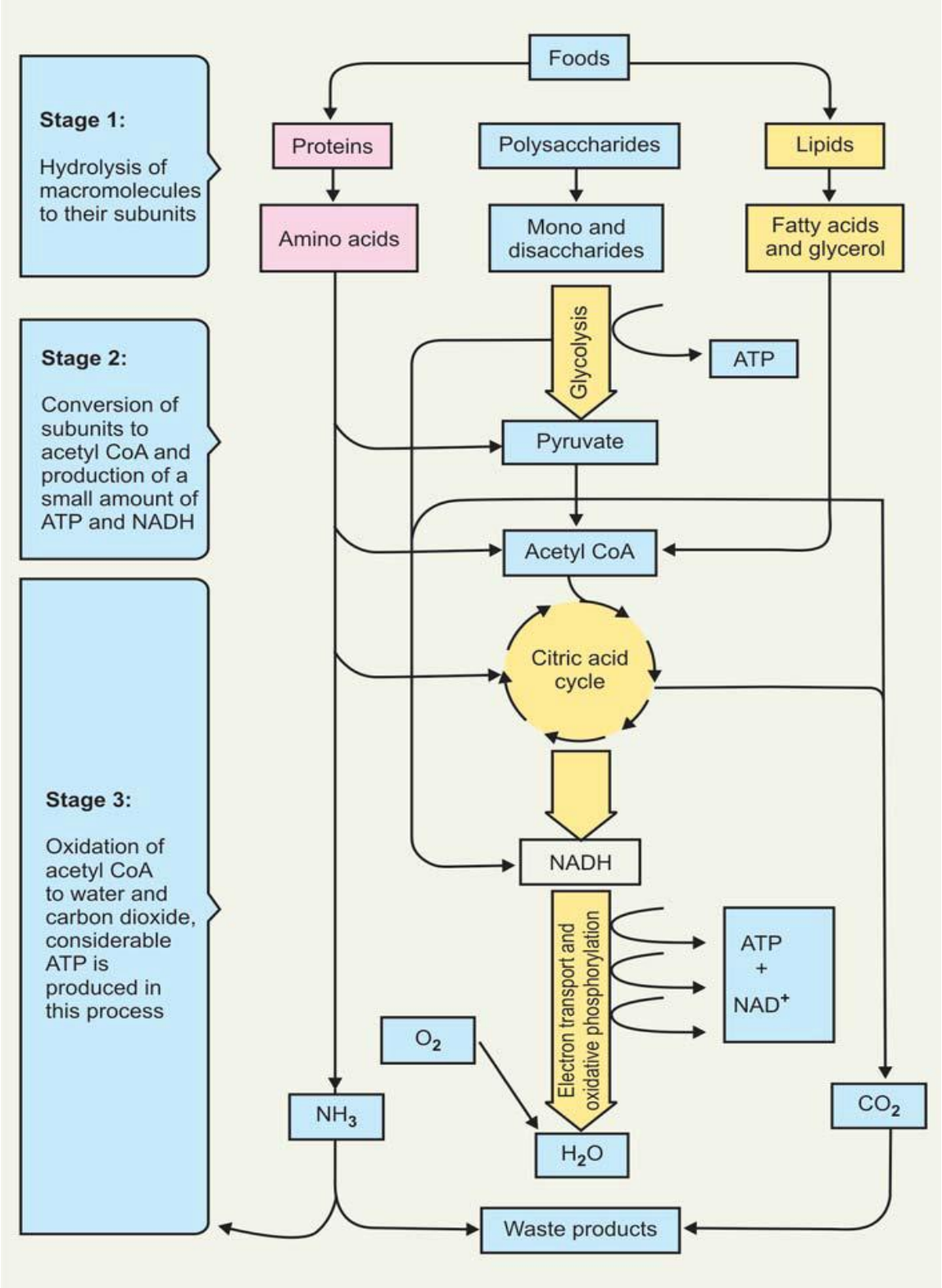

Figure1: Three stages of metabolism

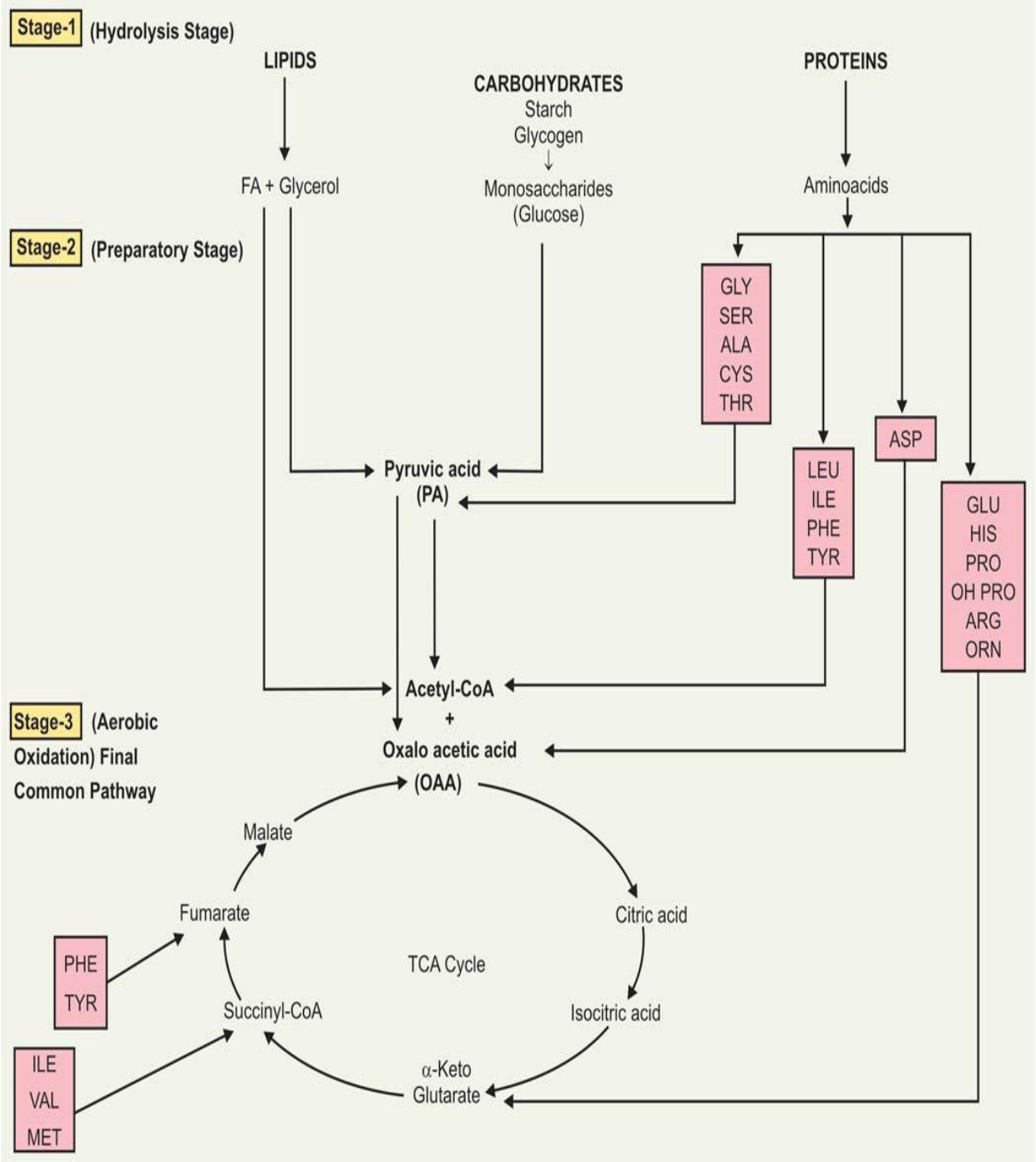

Figure 2: Three stages and their relationship with various amino acids

Interconversion Between The Three Principal Components

I. Carbohydrates

1. Carbohydrates can form lipids: Through formation of: (a) α-glycero-P from glycerol or di-hydroxy acetone- P (from glycolysis) which is necessary for Triacyl glycerol (TG) and (b) FA from acetyl-CoA-extra mitochondrial de novo synthesis.

2. Carbohydrates can form non-essential amino acids: Through amination of α-ketoacids, viz. pyruvic acid (PA), oxaloacetic acid (OAA) and α-ketoglutarate to form amino acids alanine, aspartate and glutamate respectively.

II. Fats

1. Fatty acids can be converted to some amino acids by forming the dicarboxylic acids like malic acid, oxaloacetic acids and α-ketoglutarate.

2. Fatty acid carbon may theoretically be incorporated into carbohydrates by the acetate running through TCA cycle. But there is no net gain in carbohydrates, since two carbons, equivalent of acetate are oxidised in the cycle.

3. However acetate can form glucose by running through the glyoxylate cycle.

4. Acetone, one of the ketone bodies may be glucogenic. Acetone can be converted to acetol-P which in turn can produce propanediol-P. Propanediol-(P) is glucogenic.

III. Proteins

Proteins can form both carbohydrates and lipids through the glucogenic and ketogenic amino acids.