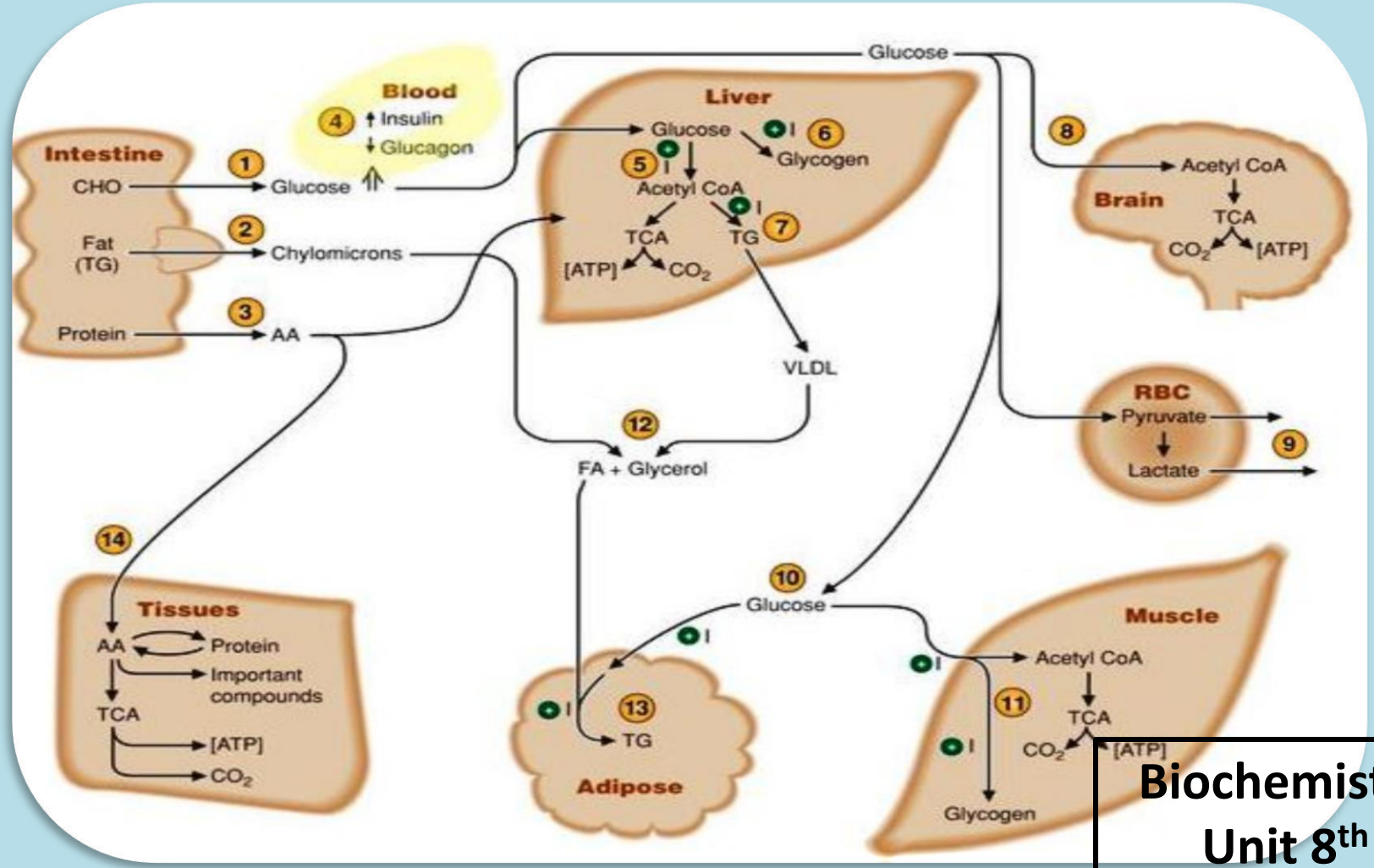
Metabolism



Biochemistry
Unit 8th

Introduction

- Metabolism is the term used to describe
  - The interconversion of chemical compounds in the body
  - The pathways taken by individual molecules,
  - Their interrelationships, and the mechanisms that regulate the flow of metabolites through the pathways
- It falls mainly in 3 categories: catabolism, anabolism and amphibolic pathways

Metabolism

- **Anabolic pathways**
  - Involved in the synthesis of larger and more complex compounds from smaller precursors
  - Ex: Synthesis of protein from amino acids and the synthesis of reserves of tri-acylglycerol and glycogen.
  - Anabolic pathways are **endothermic.**
- **Catabolic pathways**
  - Involved in the breakdown of larger molecules, commonly involving oxidative reactions;
  - They are **exothermic**, producing reducing equivalents, and, mainly via the respiratory chain
- **Amphibolic pathways**
  - Occur at the "**crossroads**" of metabolism, acting as links between the anabolic and catabolic pathways
  - Ex: Citric acid cycle

Metabolism

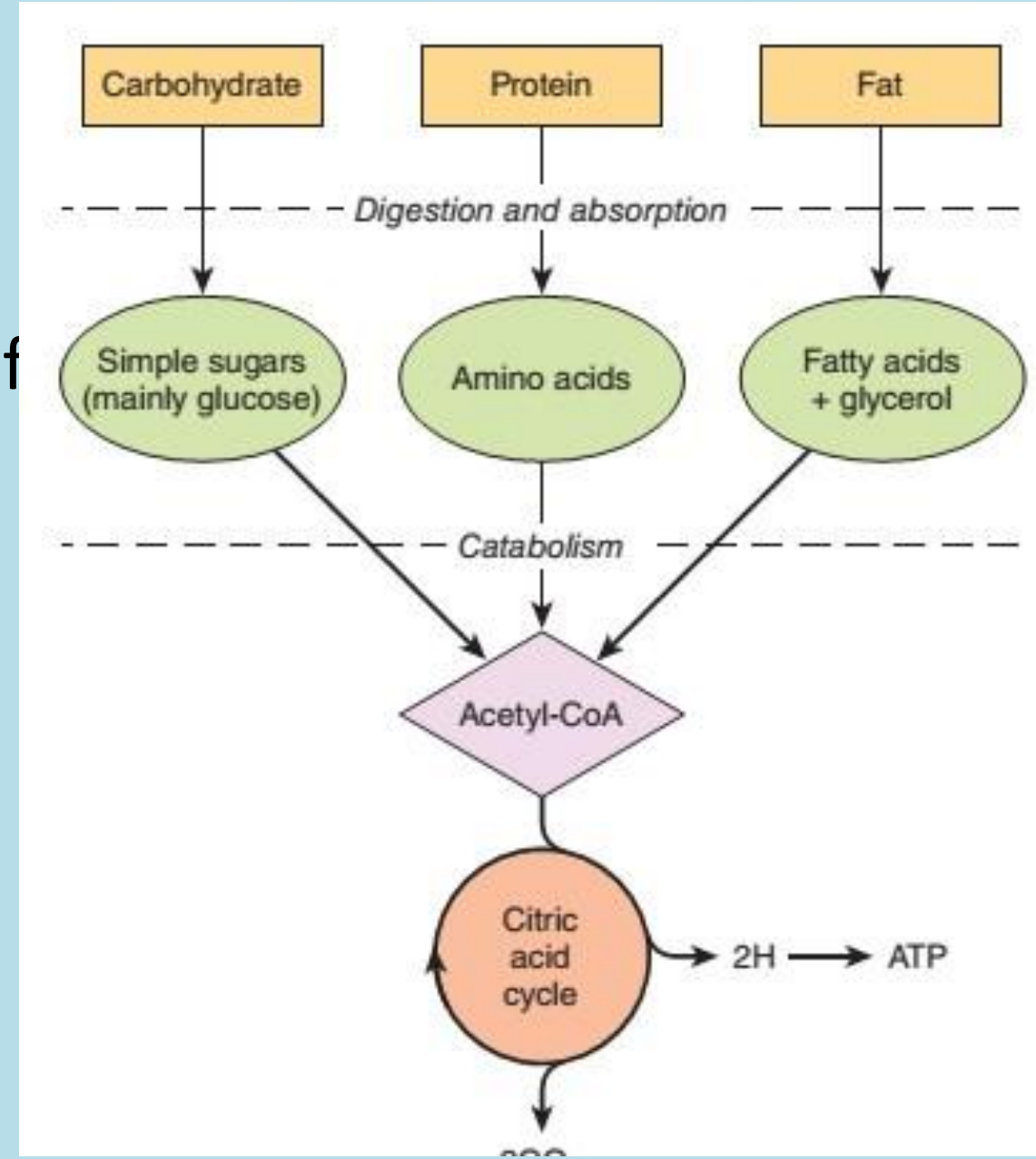
- A 70-kg adult human being requires about 1920-2900 kcal from metabolic fuels each day, depending on physical activity.
- This energy requirement is met from
  - Carbohydrates (40%-60%)
  - Lipids (mainly triacylglycerol, 30%-40%)
  - Protein (10%-15%), as well as alcohol.
- There is a constant requirement for metabolic fuels throughout the day
- Most people consume their daily intake of metabolic fuels in two or three meals, so there is a need to form reserves

Metabolism

- Reserves of
  - **Carbohydrate**: glycogen in liver and muscle
  - **Lipid**: triacylglycerol in adipose tissue
  - **Labile protein**
- If the intake of metabolic fuels is consistently greater than energy expenditure.
  - Surplus is stored, largely as triacylglycerol in adipose tissue,
  - Leading to the development of **obesity**
- If the intake of metabolic fuels is consistently lower than energy expenditure
  - Reserves of fat and carbohydrate, and amino acids are used for energy-yielding metabolism
  - This leads to **emaciation,** wasting, and, eventually, death

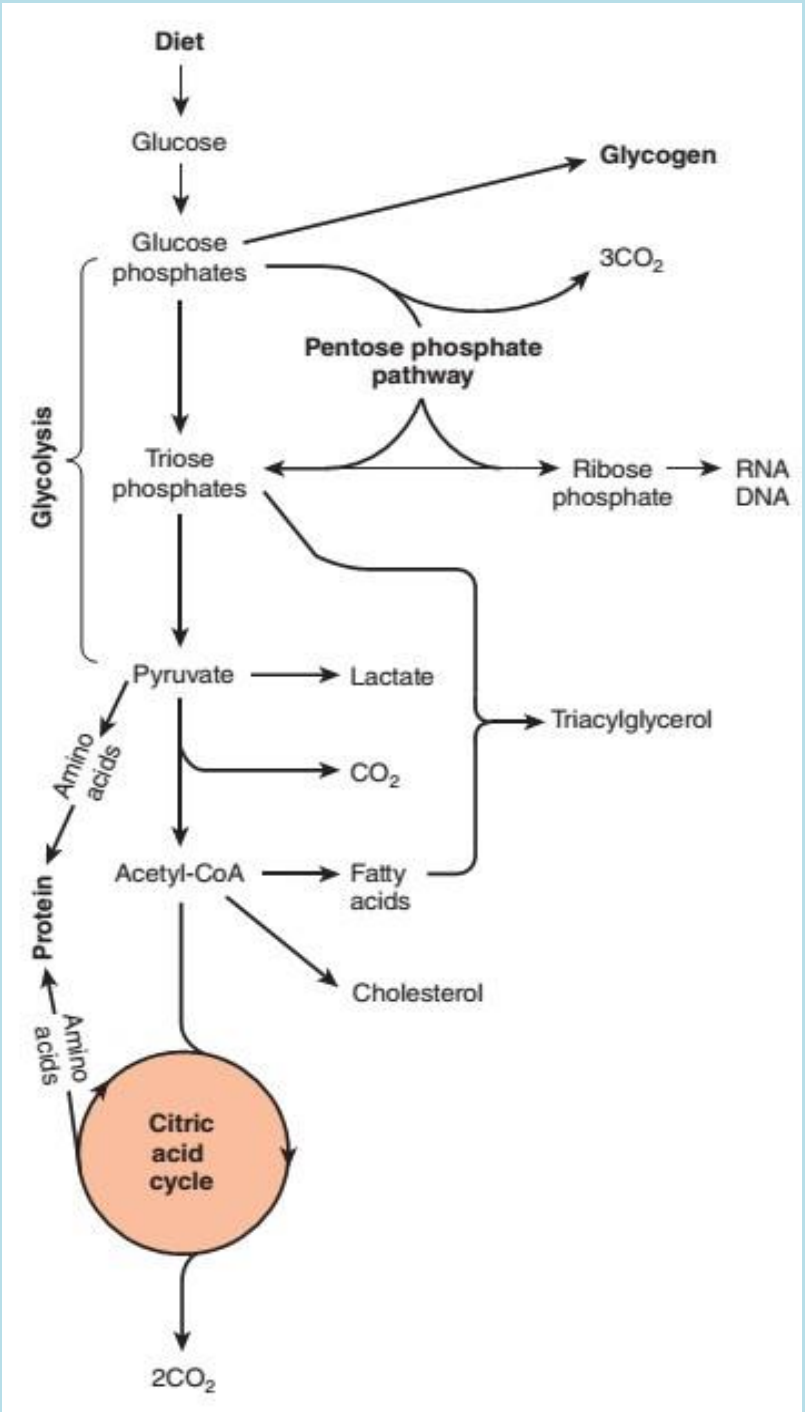
Metabolism

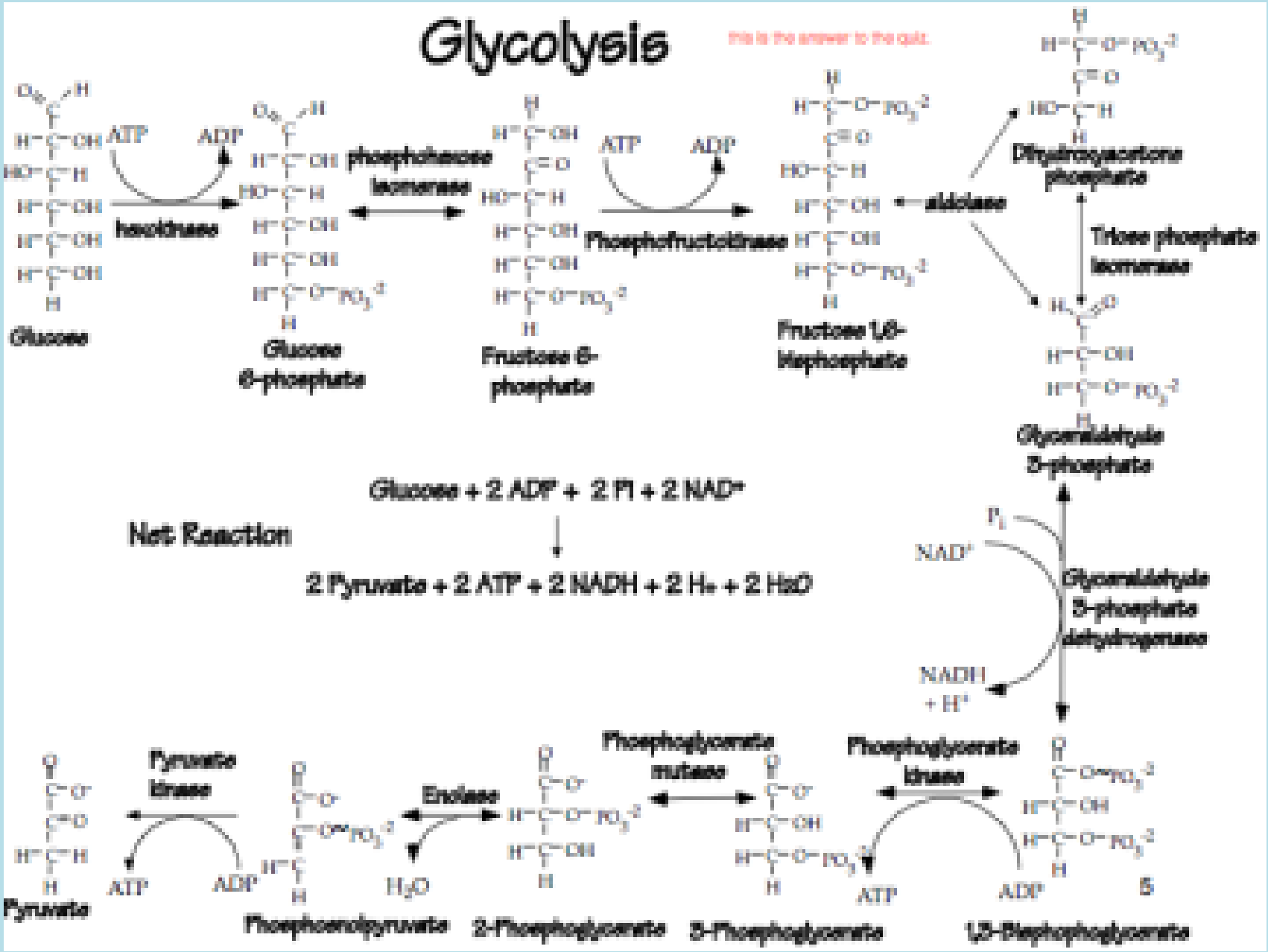
- All the products of digestion are metabolized to **acetyl-CoA -** oxidized by the **citric acid cycle**



Carbohydrate Metabolism

- Glucose - major fuel of most tissues
- Metabolized to **pyruvate** aerobically and **lactate** anaerobically by the pathway of **glycolysis** which further gets reduced to **acetyl-CoA**
- Enter the **Citric acid cycle** - formation of ATP in the process of **oxidative phosphorylation**




Glycolysis
this is the answer to the quiz
Glucose
ATP
ADP
hexokinase
Glucose 6-phosphate
phosphohexose isomerase
Fructose 6-phosphate
ATP
ADP
Phosphofructokinase
Fructose 1,6-bisphosphate
aldolase
Dihydroxyacetone phosphate
Triose phosphate isomerase
Glyceraldehyde 3-phosphate
Glucose + 2 ADP + 2 Pi + 2 NAD+
Net Reaction
2 Pyruvate + 2 ATP + 2 NADH + 2 H+ + 2 H2O
Pi
NAD+
Glyceraldehyde 3-phosphate dehydrogenase
NADH + H+
Phosphoglycerate kinase
ATP
ADP
1,3-Bisphosphoglycerate
Phosphoglycerate mutase
3-Phosphoglycerate
Enolase
H2O
2-Phosphoglycerate
Phosphoenolpyruvate
Pyruvate kinase
ATP
ADP
Pyruvate

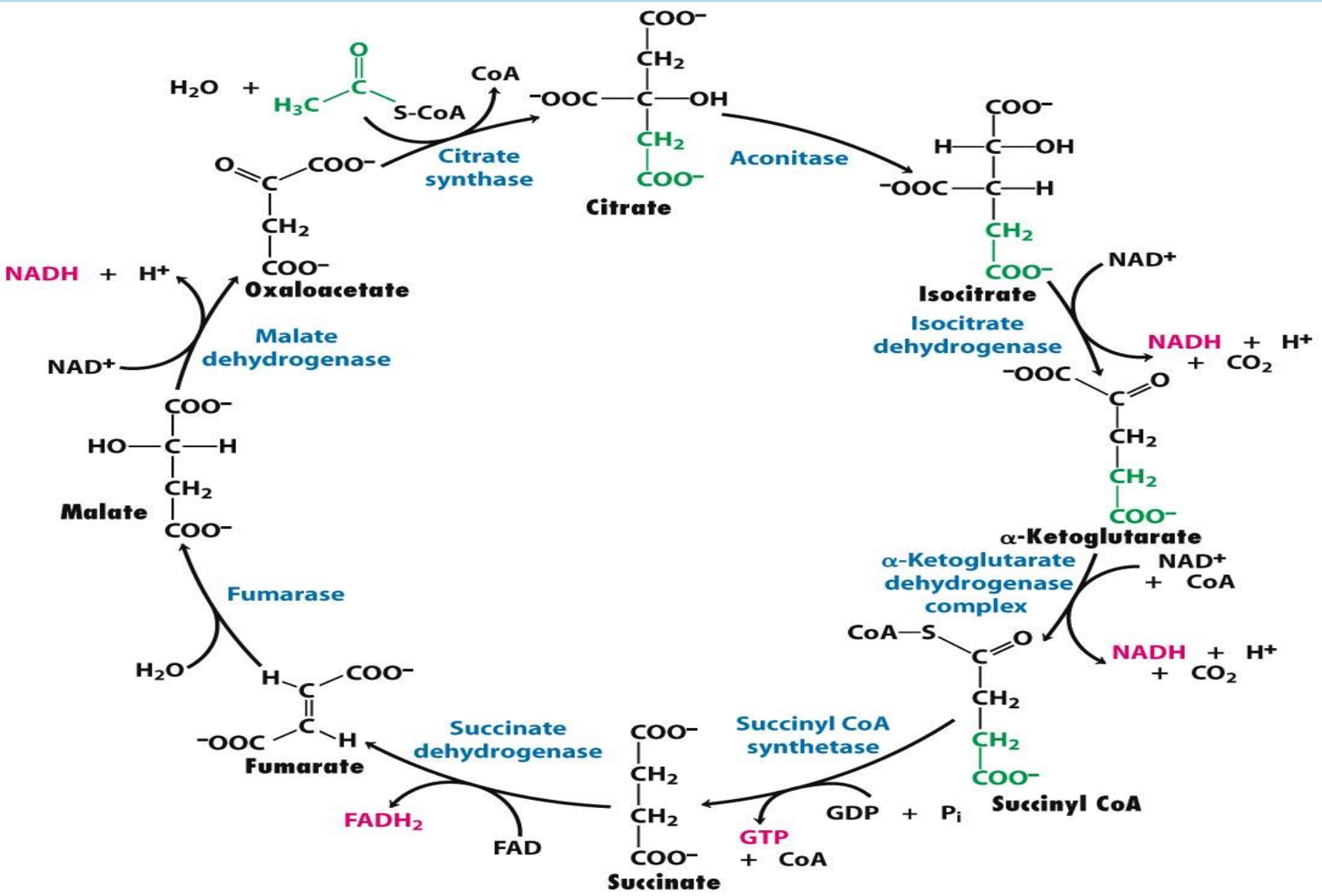


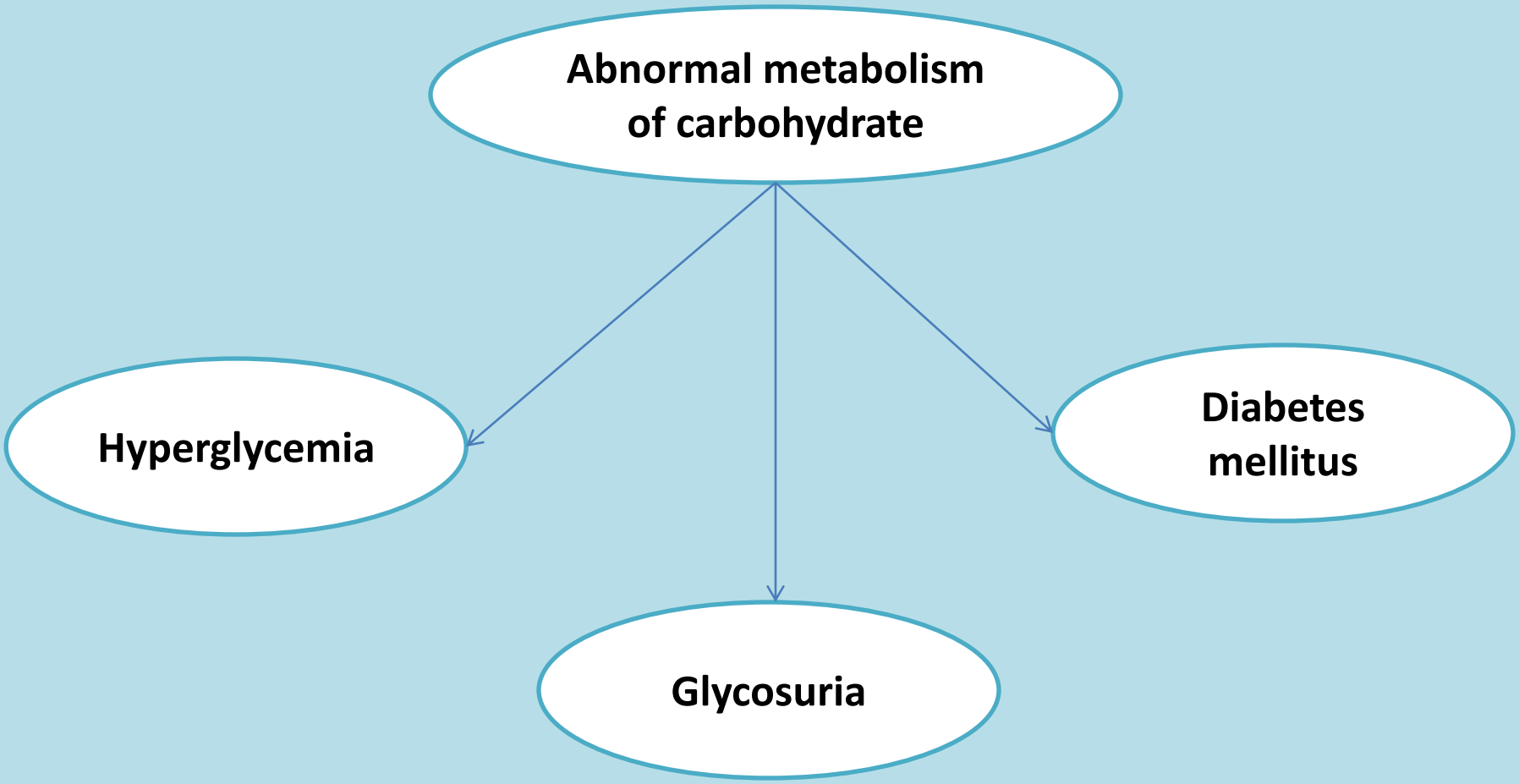
Figure 17.15
***Biochemistry*, Seventh Edition**

Carbohydrate Metabolism

- Glucose may also undergo **Glycogenesis** - synthesis of the storage polymer **glycogen** in skeletal muscle and liver
- It may also enter **Pentose Phosphate Pathway (PPP)**
  - source of reducing equivalents (NADPH) for fatty acid synthesis
  - **ribose** for nucleotide and nucleic acid synthesis
- **Pyruvate and intermediates** of the Citric Acid Cycle - carbon skeletons for the synthesis of nonessential **amino acids**
- Acetyl-CoA is the precursor of **fatty acids** and **cholesterol** (steroid hormones synthesized in the body)
- **Gluconeogenesis -** process of synthesizing glucose from noncarbohydrate precursors such as, lactate, amino acids, and glycerol

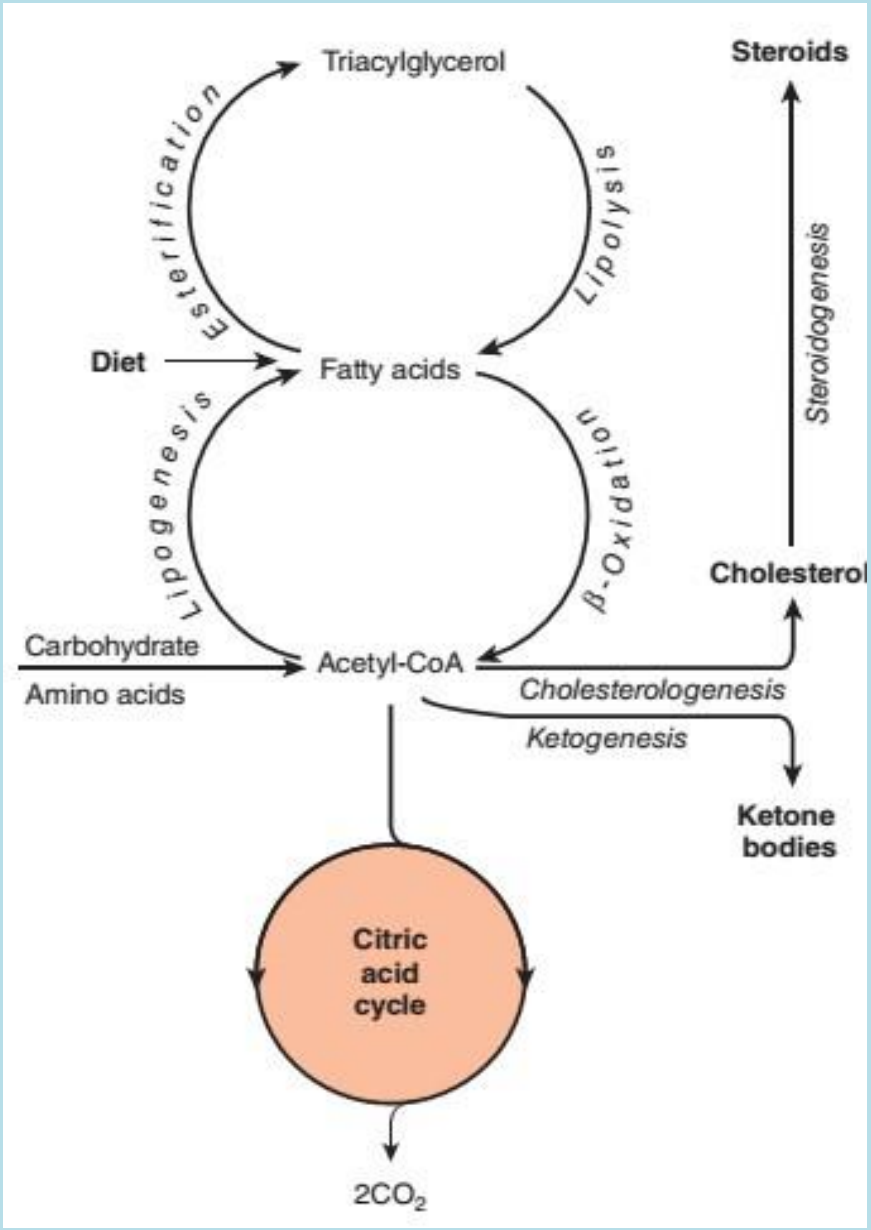
FUNCTIONS OF CARBOHYDRATES

- Main source of energy in the body. Energy production from carbohydrates will be 4 k calories/g (16 k Joules/g).
- Storage form of energy (starch and glycogen).
- Excess carbohydrate is converted to fat.
- Glycoproteins and glycolipids are components of cell membranes and receptors.
- Structural basis of many organisms. For example, cellulose of plants,exoskeleton of insects etc.


Abnormal metabolism of carbohydrate
Hyperglycemia
Glycosuria
Diabetes mellitus

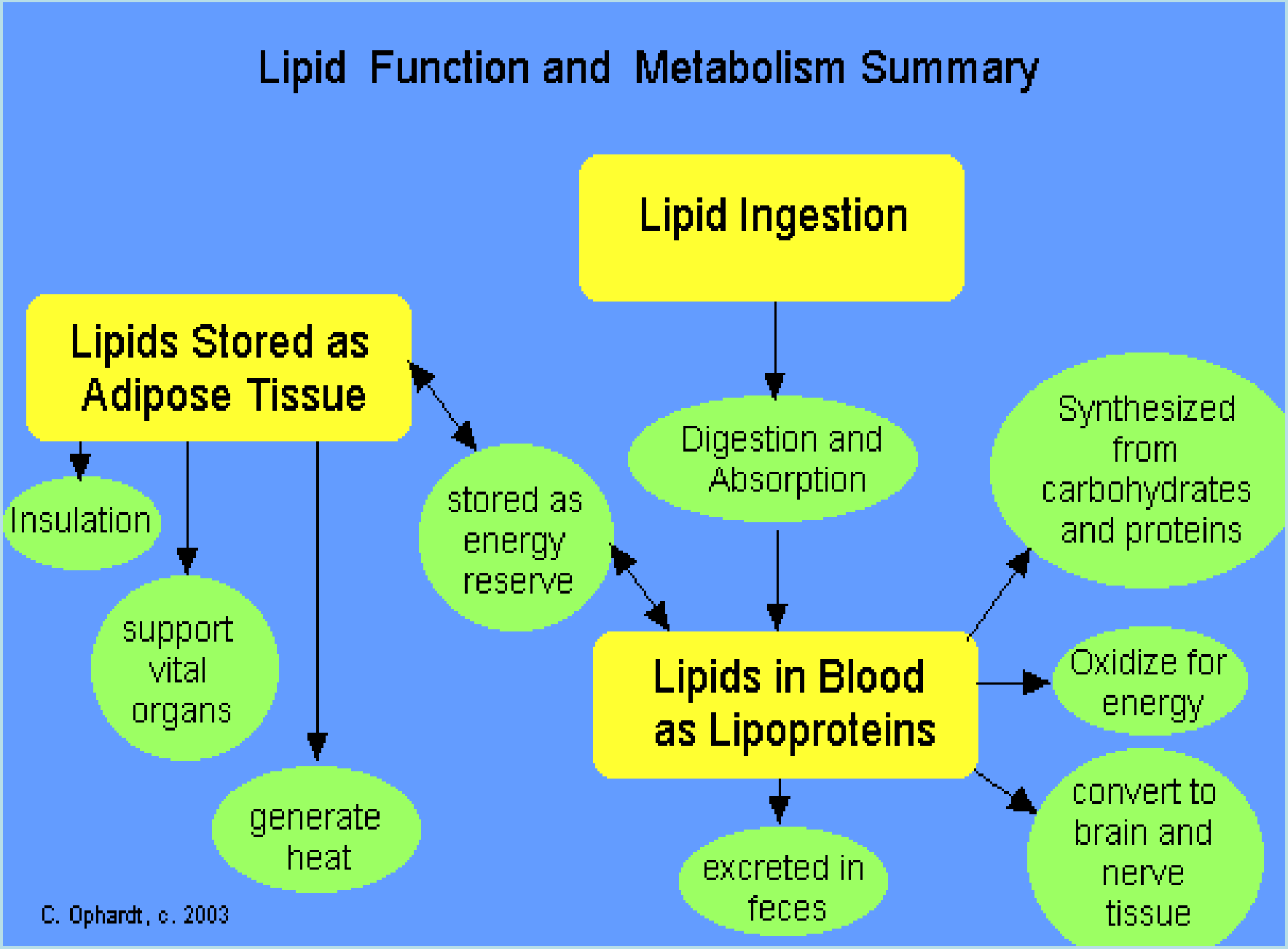
Lipid Metabolism

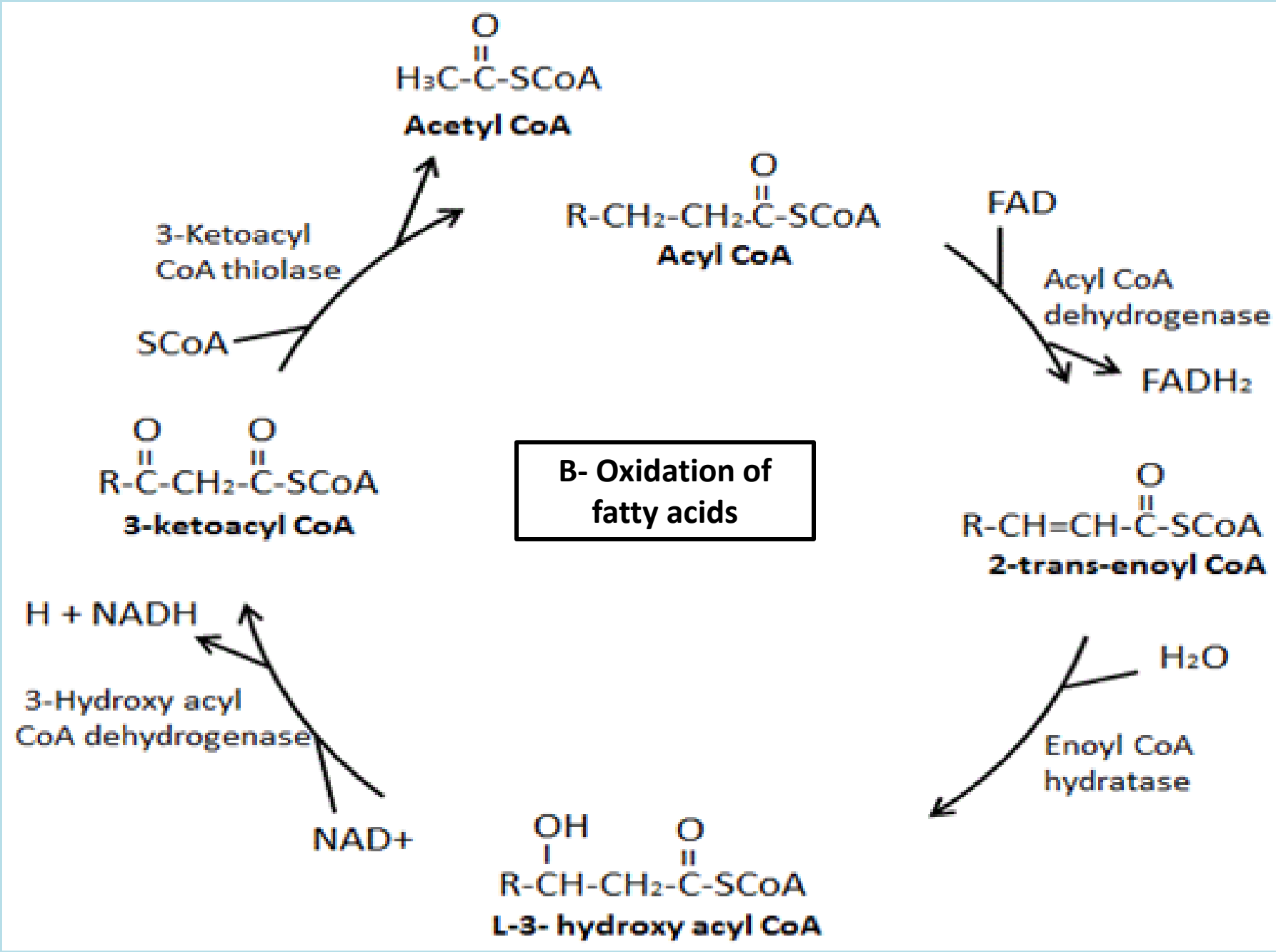
- Source of long-chain fatty acids
  - either dietary lipid
  - Or de novo synthesis from acetyl-CoA
- Fatty acids may either
  - gets oxidized to **acetyl-CoA (β-oxidation)**
  - esterified with glycerol forming **triacylglycerol -** body's main fuel reserve



Lipid Metabolism

- **Acetyl-CoA** formed by **β-oxidation** of fatty acids may undergo three fates
  - **oxidized** via the citric acid cycle
  - precursor for synthesis of **cholesterol** and other **steroids.**
  - In the liver, it is used to form the **ketone bodies,** acetoacetate and 3-hydroxybutyrate - important fuels in prolonged fasting and starvation.

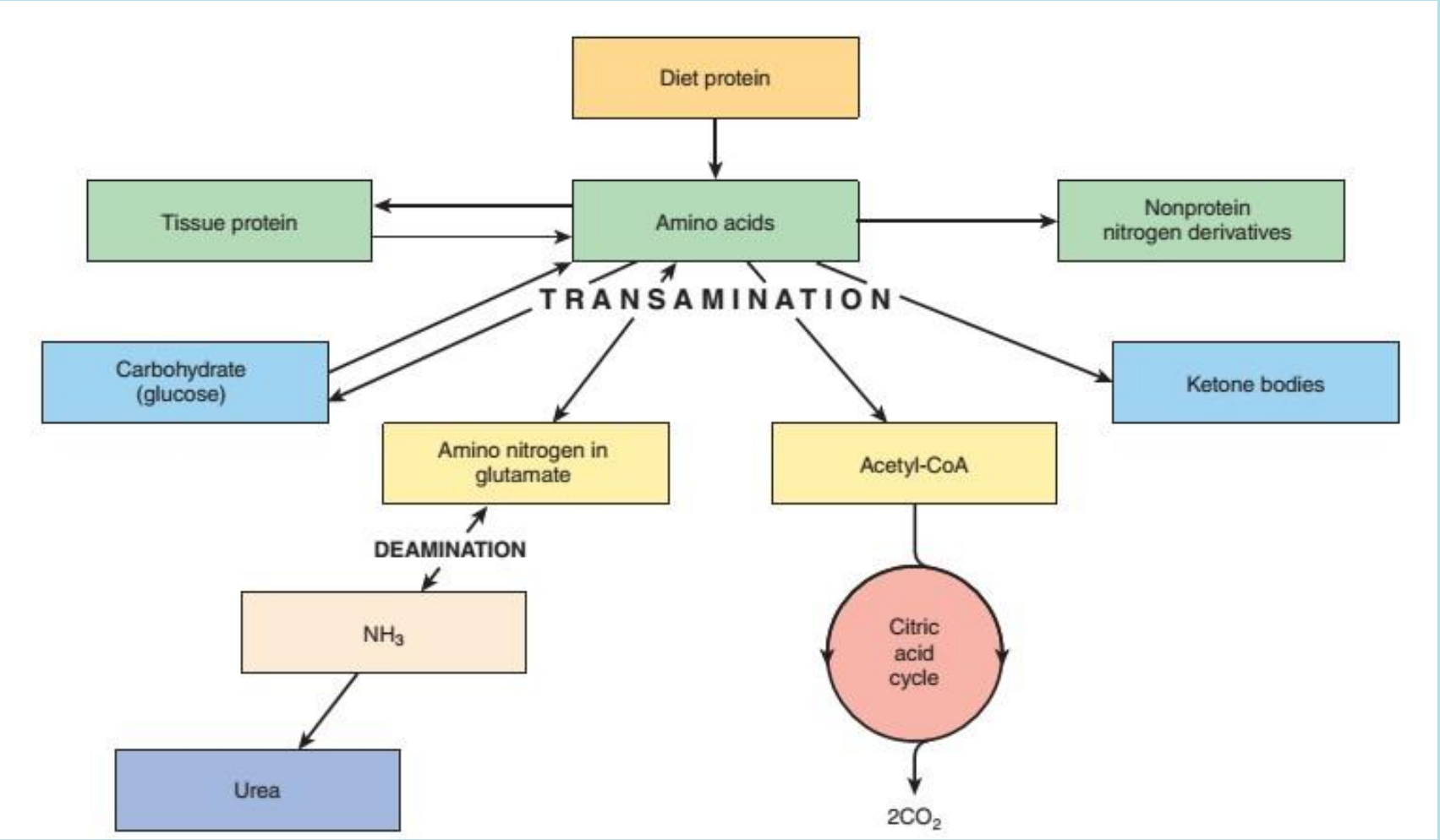

Lipid Function and Metabolism Summary
Lipid Ingestion
Lipids Stored as Adipose Tissue
Digestion and Absorption
Synthesized from carbohydrates and proteins
Insulation
stored as energy reserve
support vital organs
Lipids in Blood as Lipoproteins
Oxidize for energy
generate heat
excreted in feces
convert to brain and nerve tissue
C. Ophardt, c. 2003

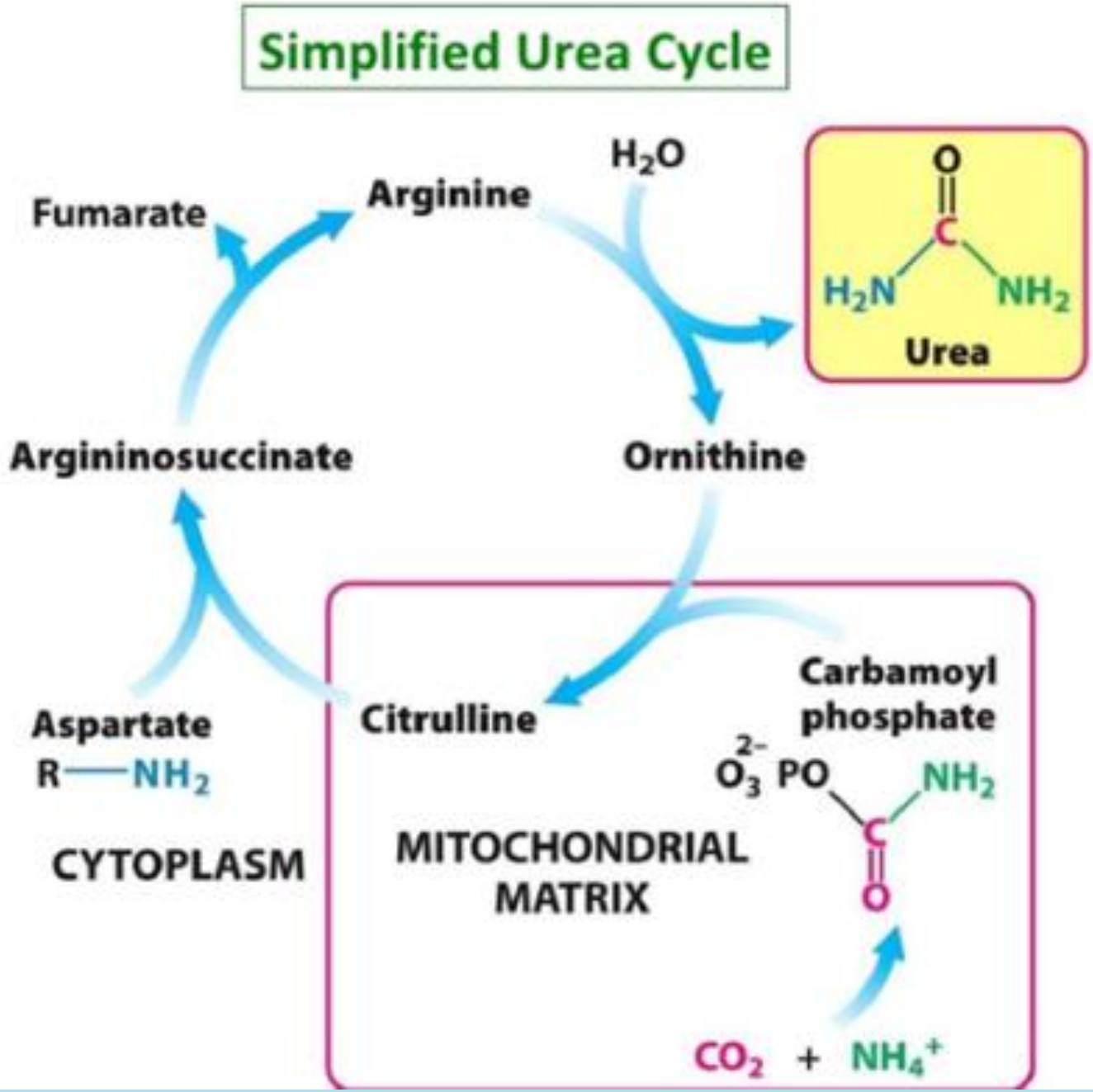

H₃C-C-SCoA
Acetyl CoA
3-Ketoacyl
CoA thiolase
SCoA
R-CH₂-CH₂-C-SCoA
Acyl CoA
FAD
Acyl CoA
dehydrogenase
FADH₂
R-C-CH₂-C-SCoA
3-ketoacyl CoA
B- Oxidation of
fatty acids
R-CH=CH-C-SCoA
2-trans-enoyl CoA
H + NADH
3-Hydroxy acyl
CoA dehydrogenase
NAD+
H₂O
Enoyl CoA
hydratase
R-CH-CH₂-C-SCoA
L-3- hydroxy acyl CoA

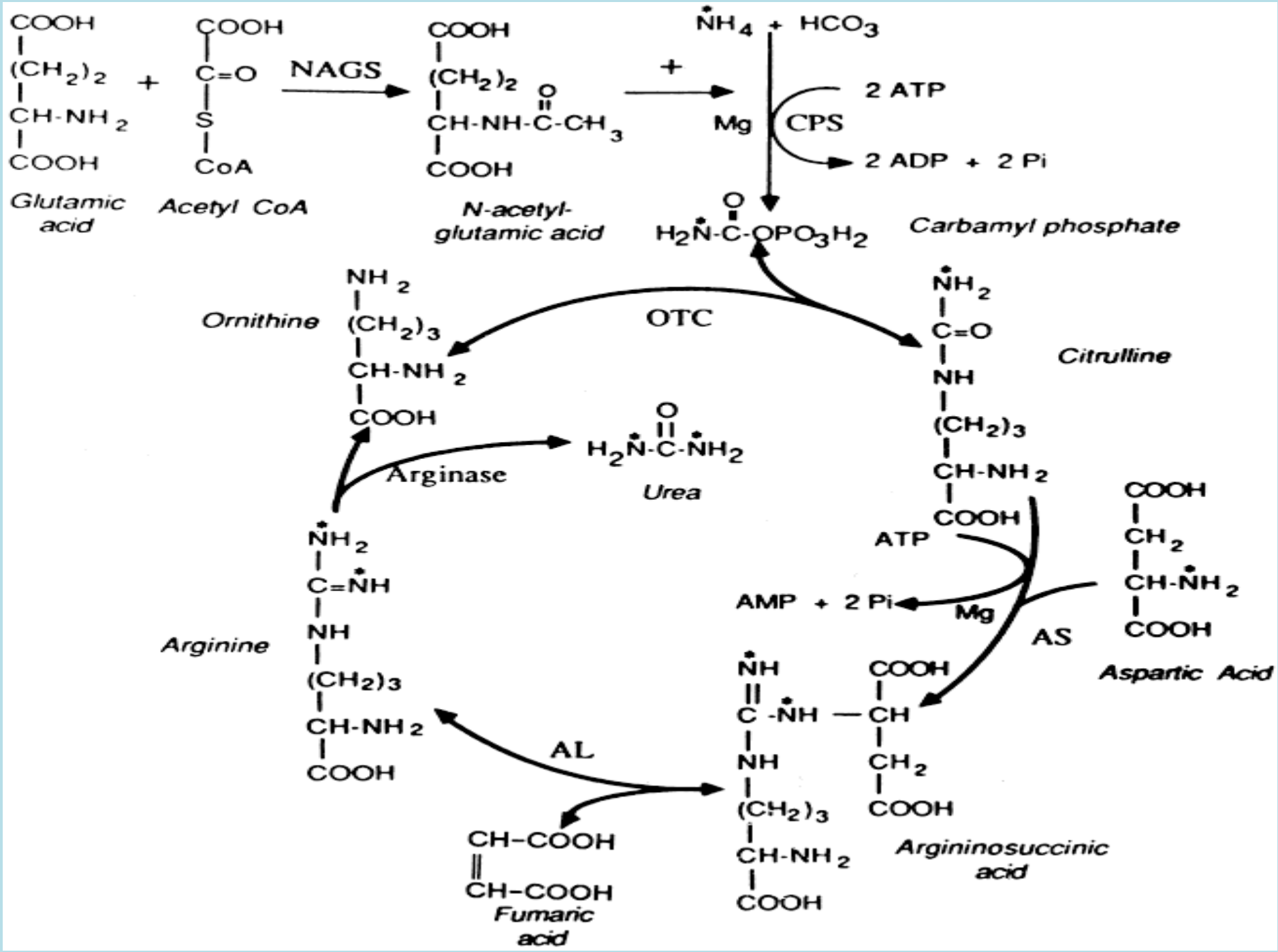
Amino Acid Metabolism

- AA forms metabolic intermediates by **transamination** using the amino group from other amino acids
- **Deamination –** removal of amino nitrogen as **urea** via Urea cycle**,**
- The carbon skeletons that remain after **transamination**
  - oxidized via the **citric acid cycle**,
  - used to synthesize glucose (**gluconeogenesis**)
  - form **ketone bodies** or acetyl CoA, which may be oxidized or used for synthesis of fatty acids
- AA may also be precursors of other compounds
  - Purines and pyrimidines,
  - Hormones such as epinephrine and thyroxine,
  - Neurotransmitters.

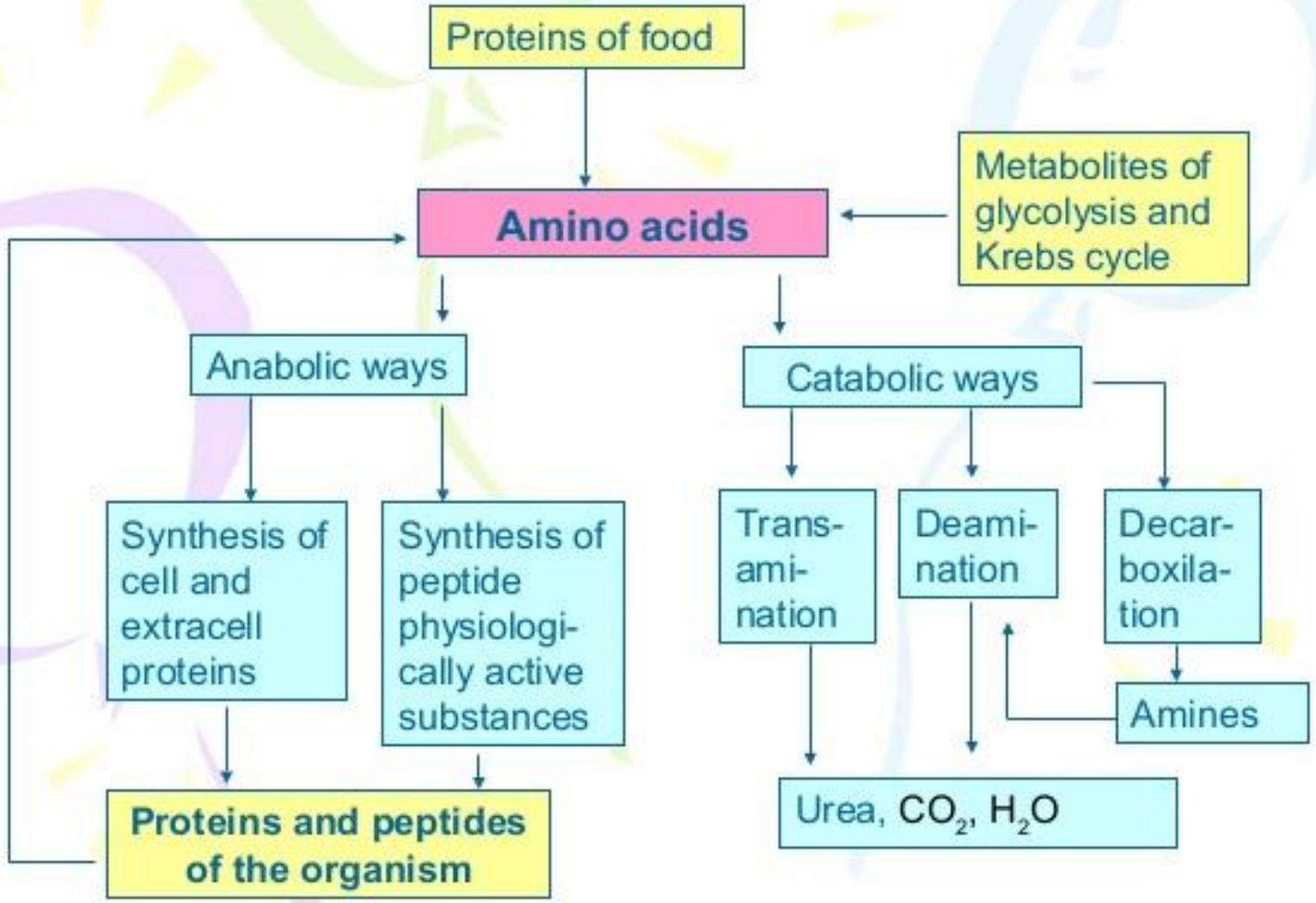
Amino Acid Metabolism




Simplified Urea Cycle
Fumarate
Arginine
H_2O
O
C
H_2N
NH_2
Urea
Argininosuccinate
Ornithine
Aspartate
R—NH_2
Citrulline
Carbamoyl phosphate
O_3PO^{2-}
NH_2
C
O
CYTOPLASM
MITOCHONDRIAL MATRIX
CO_2 + NH_4^+


Glutamic acid
Acetyl CoA
NAGS
N-acetyl-glutamic acid
NH_4 + HCO_3
Mg
CPS
2 ATP
2 ADP + 2 Pi
Carbamyl phosphate
OTC
Ornithine
Citrulline
Arginase
Urea
ATP
AMP + 2 Pi
Mg
AS
Aspartic Acid
Arginine
AL
Fumaric acid
Argininosuccinic acid

GENERAL PATHWAYS OF AMINO ACIDS METABOLISM



Summary

Organ	Major Pathways	Main Substrates	Major Products Exported	Specialist Enzymes
Liver	Glycolysis, gluconeogenesis, lipogenesis, β-oxidation, citric acid cycle, ketogenesis, lipoprotein metabolism, drug metabolism, synthesis of bile salts, urea, uric acid, cholesterol, plasma proteins	Nonesterified fatty acids, glucose (in fed state), lactate, glycerol, fructose, amino acids, alcohol	Glucose, triacylglycerol in VLDL,[a] ketone bodies, urea, uric acid, bile salts, cholesterol, plasma proteins	Glucokinase, glucose-6-phosphatase, glycerol kinase, phosphoenolpyruvate carboxykinase, fructokinase, arginase, HMG CoA synthase, HMG CoA lyase, alcohol dehydrogenase
Brain	Glycolysis, citric acid cycle, amino acid metabolism, neurotransmitter synthesis	Glucose, amino acids, ketone bodies in prolonged starvation	Lactate, end products of neurotransmitter metabolism	Those for synthesis and catabolism of neurotransmitters

Summary

Heart	β-Oxidation and citric acid cycle	Ketone bodies, nonesterified fatty acids, lactate, chylomicron and VLDL triacylglycerol, some glucose	—	Lipoprotein lipase, very active electron transport chain
Adipose tissue	Lipogenesis, esterification of fatty acids, lipolysis (in fasting)	Glucose, chylomicron and VLDL triacylglycerol	Nonesterified fatty acids, glycerol	Lipoprotein lipase, hormone-sensitive lipase enzymes of the pentose phosphate pathway
Fast twitch muscle	Glycolysis	Glucose, glycogen	Lactate, (alanine and ketoacids in fasting)	—
Slow twitch muscle	β-Oxidation and citric acid cycle	Ketone bodies, chylomicron and VLDL triacylglycerol	—	Lipoprotein lipase, very active electron transport chain
Kidney	Gluconeogenesis	Nonesterified fatty acids, lactate, glycerol, glucose	Glucose	Glycerol kinase, phosphoenolpyruvate carboxykinase
Erythrocytes	Anerobic glycolysis, pentose phosphate pathway	Glucose	Lactate	Hemoglobin, enzymes of pentose phosphate pathway


Thank you