METABOLISM OF CARBOHYDREATES

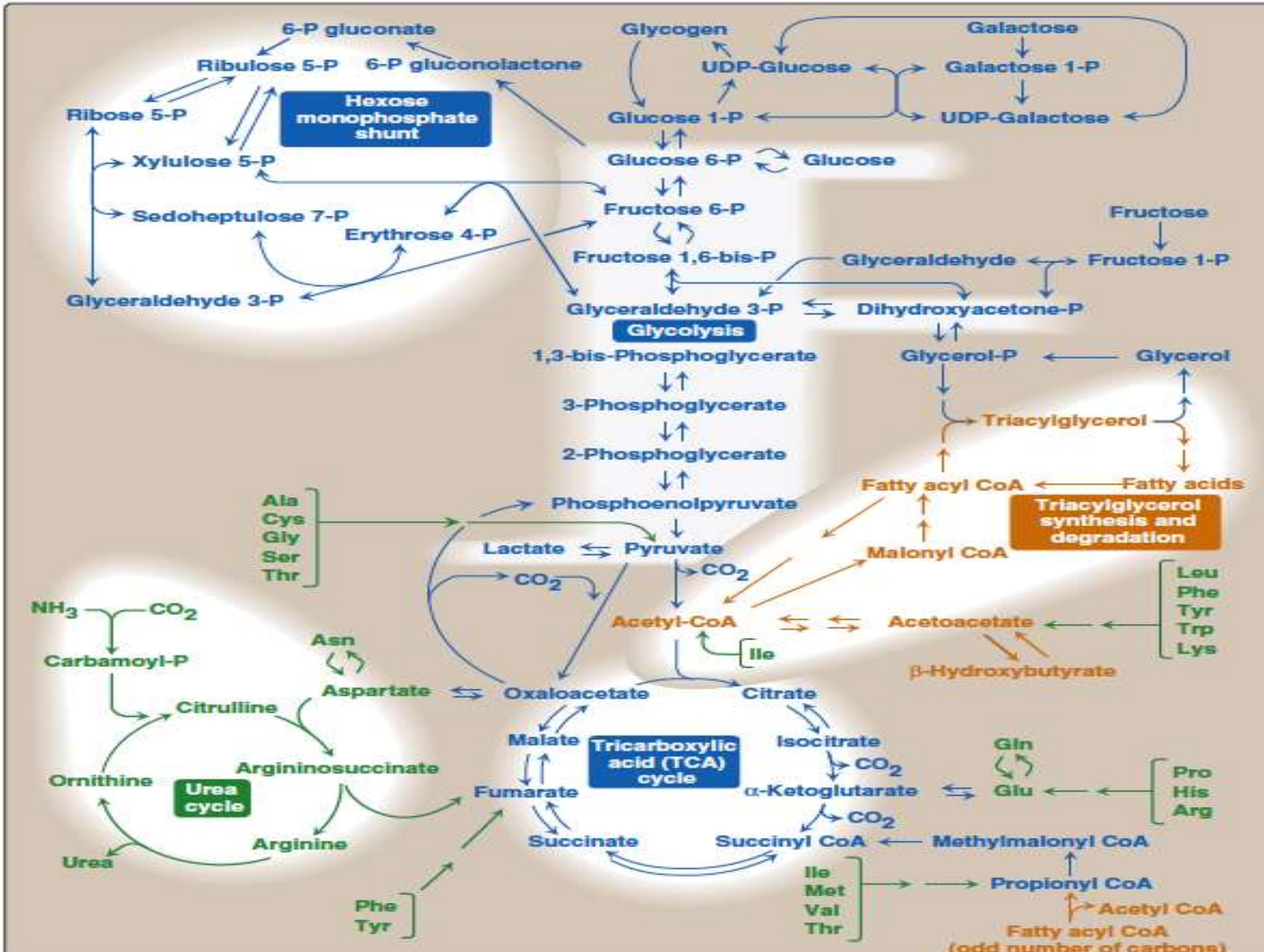
UNIVERSITY OF SARGODHA

2006

SARGODHA MEDICAL COLLEGE

METABOLISM

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.



6-P gluconate
Ribulose 5-P
6-P gluconolactone
Hexose monophosphate shunt
Ribose 5-P
Xylulose 5-P
Sedoheptulose 7-P
Erythrose 4-P
Glyceraldehyde 3-P
Glycogen
UDP-Glucose
Galactose
Galactose 1-P
UDP-Galactose
Glucose 1-P
Glucose 6-P
Glucose
Fructose 6-P
Fructose 1,6-bis-P
Fructose
Glyceraldehyde
Fructose 1-P
Glyceraldehyde 3-P
Dihydroxyacetone-P
Glycolysis
1,3-bis-Phosphoglycerate
Glycerol-P
Glycerol
3-Phosphoglycerate
Triacylglycerol
2-Phosphoglycerate
Fatty acyl CoA
Fatty acids
Phosphoenolpyruvate
Triacylglycerol synthesis and degradation
Ala
Cys
Gly
Ser
Thr
Lactate
Pyruvate
Malonyl CoA
CO_2
CO_2
Leu
Phe
Tyr
Trp
Lys
NH_3
CO_2
Acetyl-CoA
Acetoacetate
Carbamoyl-P
Asn
Ile
β-Hydroxybutyrate
Aspartate
Oxaloacetate
Citrate
Citrulline
Malate
Tricarboxylic acid (TCA) cycle
Isocitrate
Gln
CO_2
Argininosuccinate
Pro
Ornithine
Urea cycle
Fumarate
α-Ketoglutarate
Glu
His
Arg
CO_2
Arginine
Succinate
Succinyl CoA
Methylmalonyl CoA
Urea
Ile
Met
Val
Thr
Propionyl CoA
Phe
Tyr
Acetyl CoA
Fatty acyl CoA (odd number of carbons)

Categories of Metabolism

Metabolic pathways fall into three categories:

- Anabolic pathways
- Catabolic pathways
- Amphibolic pathways

Anabolic pathways

- The pathways which are involved in the synthesis of larger and more complex compounds from smaller precursors— for example, the synthesis of protein from amino acids and the synthesis of reserves of triacylglycerol and glycogen (glycogenesis)
- Anabolic pathways are endothermic.

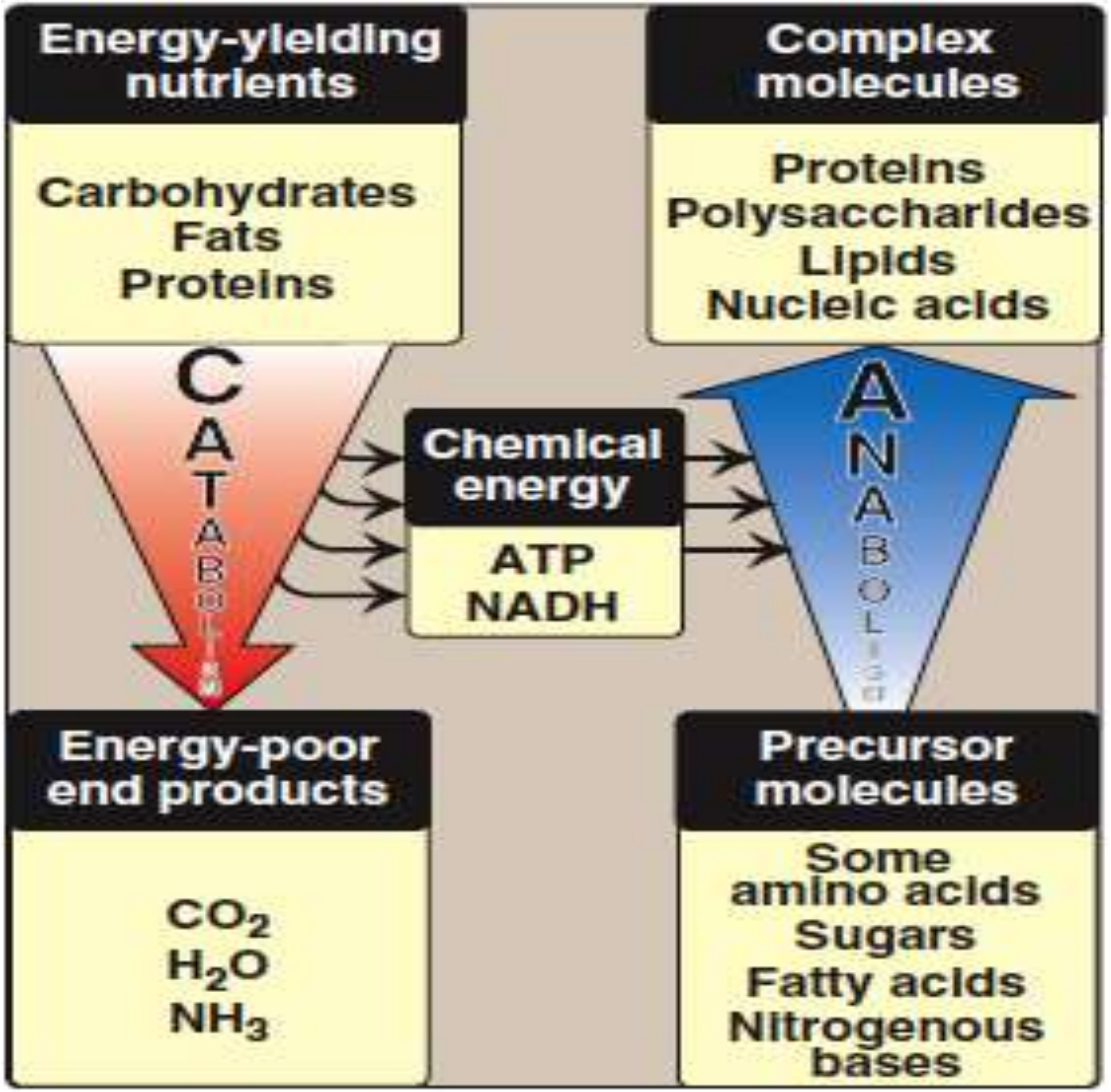
Catabolic pathways

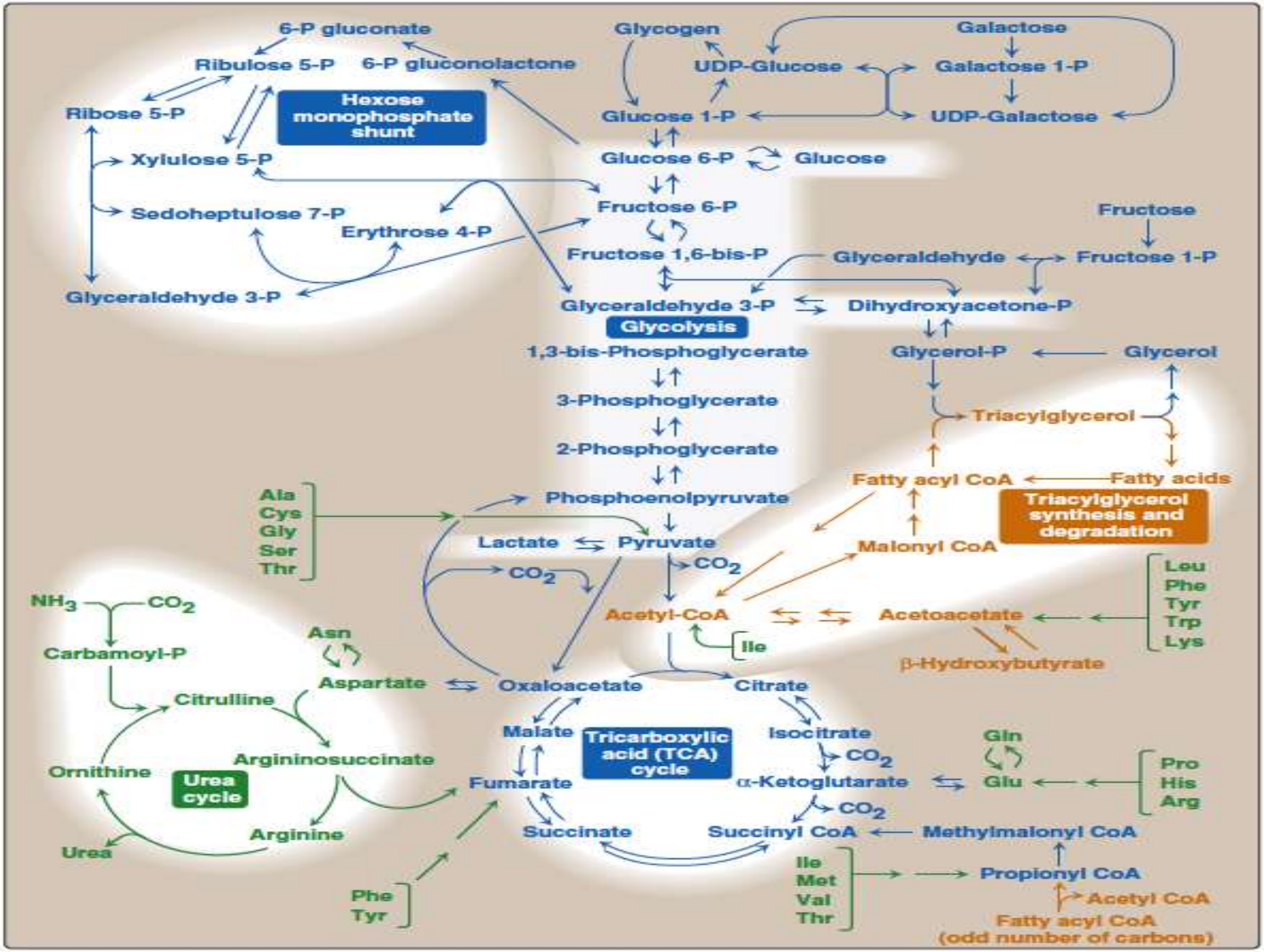
- The pathways which are involved in the breakdown of larger molecules eg., HMP-shunt and uronic acid pathway
- Commonly involve oxidative reactions
- They are exothermic, producing reducing equivalents and ATP

Amphibolic pathways

The pathways which occur at the “crossroads” of metabolism, acting as links between the anabolic and catabolic pathways, for example, the citric acid cycle

Anabolic vs Catabolic pathways





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Fructose
Glyceraldehyde
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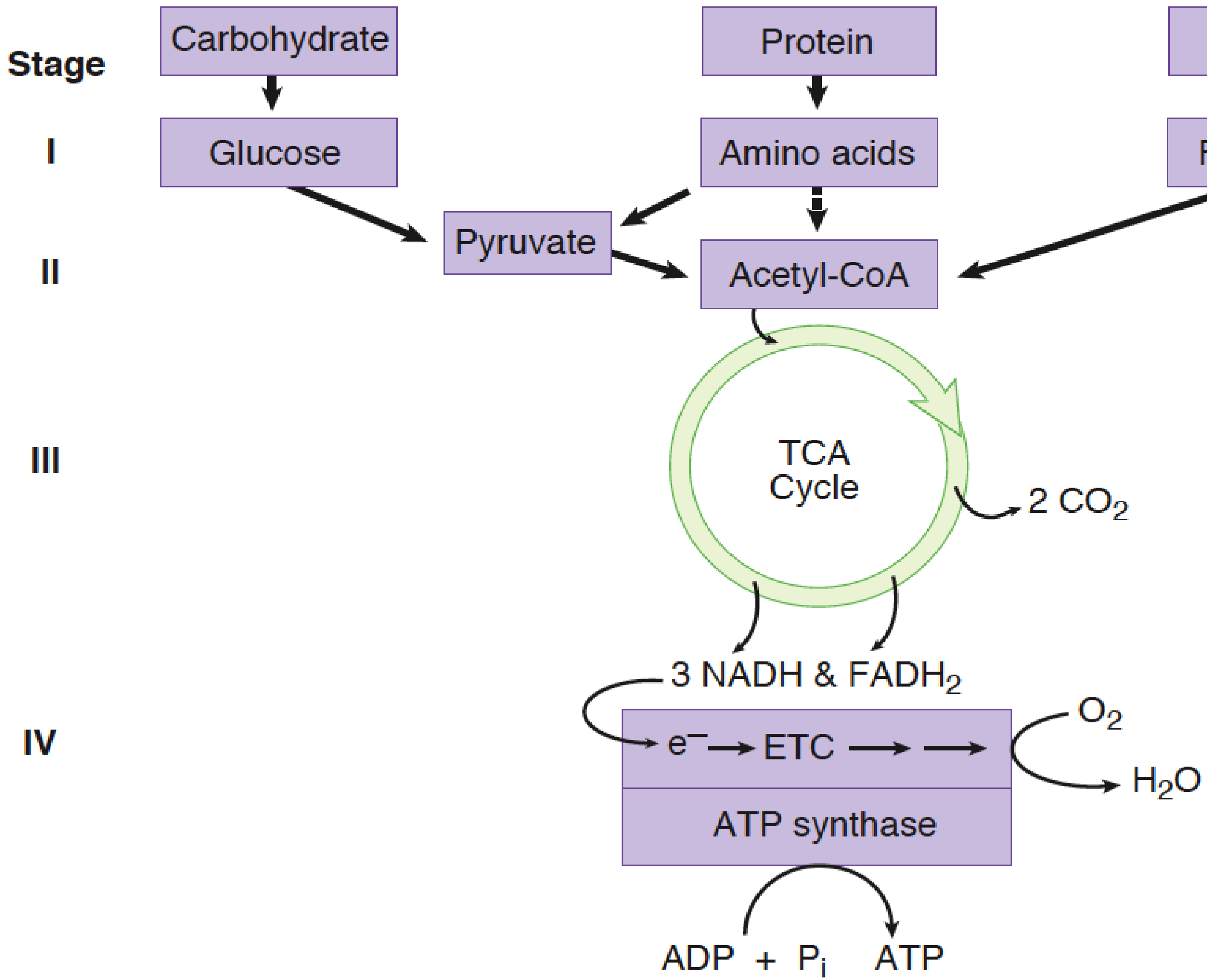
Glyceraldehyde 3-P
Dihydroxyacetone-P
Glycolysis
1,3-bis-Phosphoglycerate
Glycerol-P
Glycerol
3-Phosphoglycerate
Triacylglycerol
2-Phosphoglycerate
Fatty acyl CoA
Fatty acids
Triacylglycerol synthesis and degradation
Ala
Cys
Gly
Ser
Thr
Phosphoenolpyruvate
Lactate
Pyruvate
CO_2
Malonyl CoA
CO_2
Leu
Phe
Tyr
Trp
Lys
NH_3
CO_2
Carbamoyl-P
Acetyl-CoA
Acetoacetate
Ile
β-Hydroxybutyrate
Asn
Aspartate
Oxaloacetate
Citrate
Citrulline
Malate
Tricarboxylic acid (TCA) cycle
Isocitrate
CO_2
Gln
Argininosuccinate
Ornithine
Urea cycle
Fumarate
α-Ketoglutarate
Glu
Pro
His
Arg
CO_2
Arginine
Succinate
Succinyl CoA
Methylmalonyl CoA
Urea
Ile
Met
Val
Thr
Propionyl CoA
Phe
Tyr
Acetyl CoA
Fatty acyl CoA (odd number of carbons)

- These pathways must be coordinated

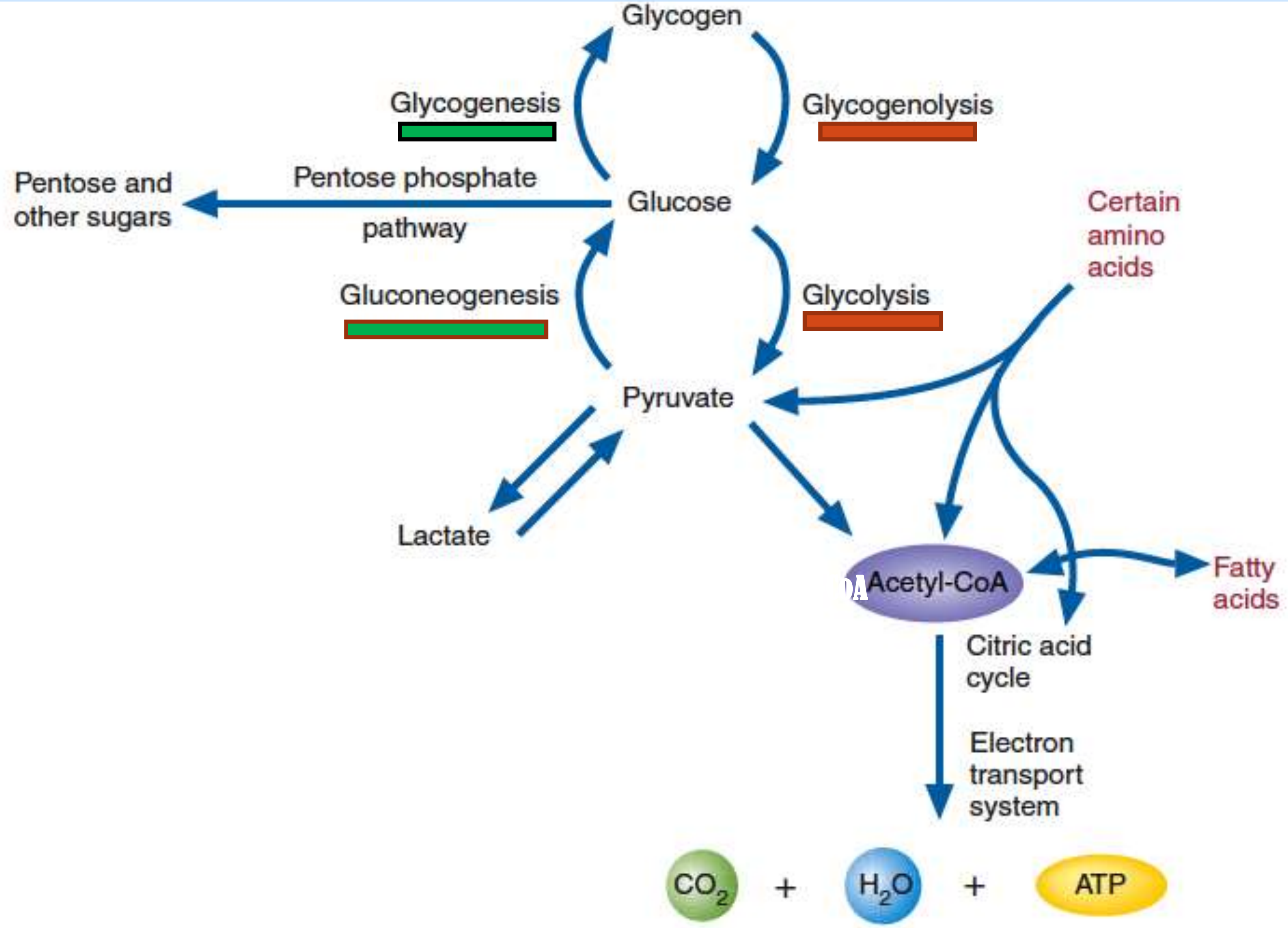
- There is sophisticated communication system

- Regulatory signals
    - Hormones
    - Neurotransmitter
    - Product of the reaction

Stages of Metabolism – 4 stages



Carbohydrate Metabolism



Carbohydrate Metabolism

Digestible carbohydrates:

starch, glycogen, maltose, sucrose, and lactose (oligosaccharides and polysaccharides).

Ready-to-absorb carbohydrates:

Which do not need digestion and are absorbed as such, e.g., monosaccharides: glucose, galactose, fructose, etc.

Non-digestible carbohydrates:

Which are called dietary fibers.

These include cellulose, gums and pectins.

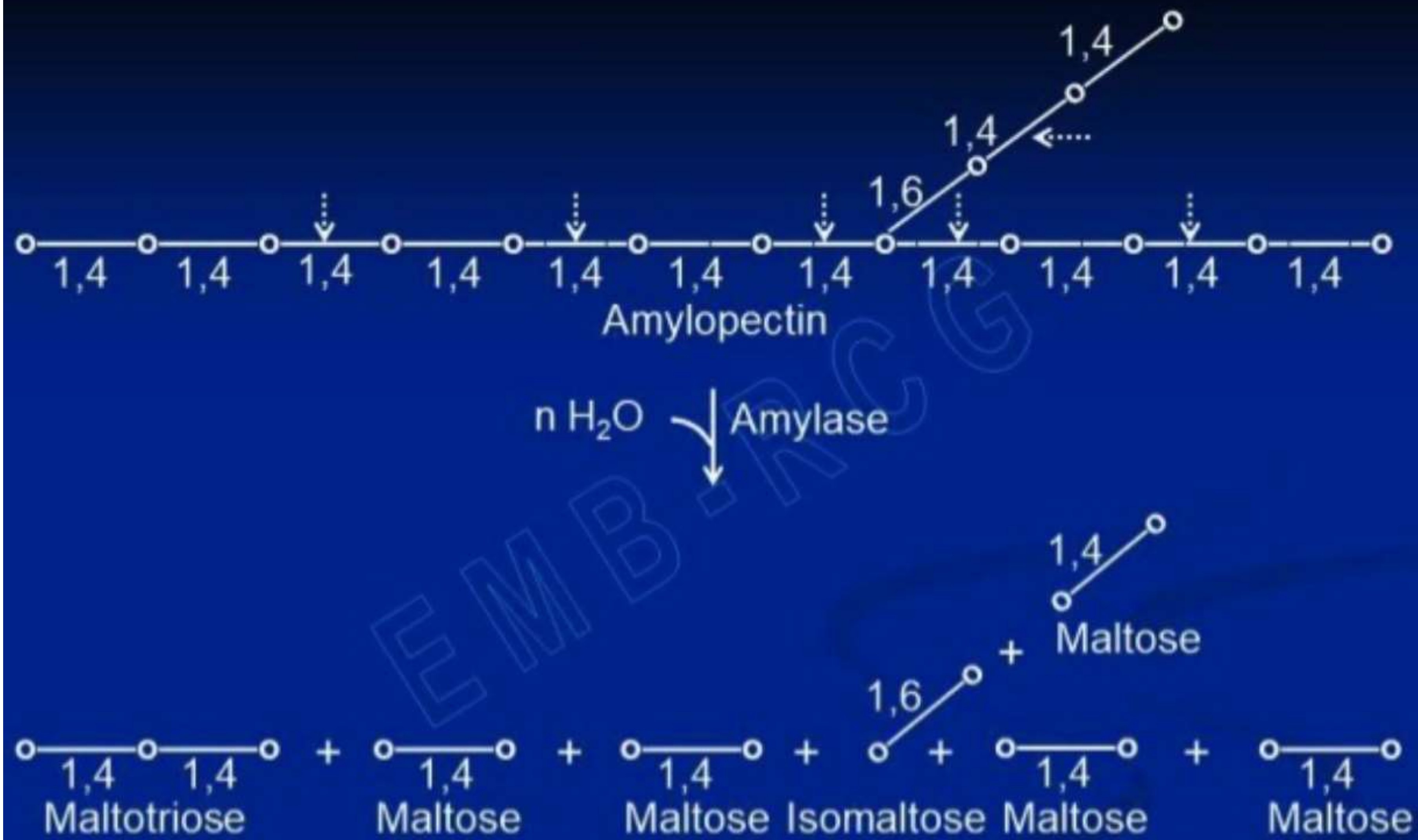
They are very important for stools excretion and are anticancer and intestinal bacteria feed on it to release certain vitamins.

Carbohydrate Metabolism

- Human beings get energy requirement from carbohydrates (40%-60%), lipids (mainly triacylglycerol, 30%- 40%), and protein (10%-15%).
- Starch, glycogen, sucrose, lactose and cellulose are the chief carbohydrates in our food. Before intestinal absorption, they are hydrolysed to hexose sugars (glucose, galactose and fructose).
- A family of a glycosidases that degrade carbohydrate into their monohexose components.

Carbohydrate Metabolism

- Starch and glycogen also contain 1-6 bonds, the resulting digest contains isomaltose [a disaccharide in which two glucose molecules are attached by 1-6 linkage].
- Digestion of starch and glycogen in the mouth and small intestine gives maltose, isomaltose and starch dextrins



Action of amylase
(broken arrows are the sites of action)

Carbohydrate Metabolism

The disaccharidases include:

1. Lactase (β-galactosidase) hydrolyses lactose :

Lactase

Lactose → Glucose + Galactose

2. Maltase (α-glucosidase) hydrolyses maltose :

Maltase

Maltose → Glucose + Glucose

3. Sucrase (α-fructofuranosidase) hydrolyses sucrose :

Sucrase

Sucrose → Glucose + Fructose

4. α - dextrinase (oligo-1,6 glucosidase) which hydrolyze (1 ,6) linkage of isomaltose.

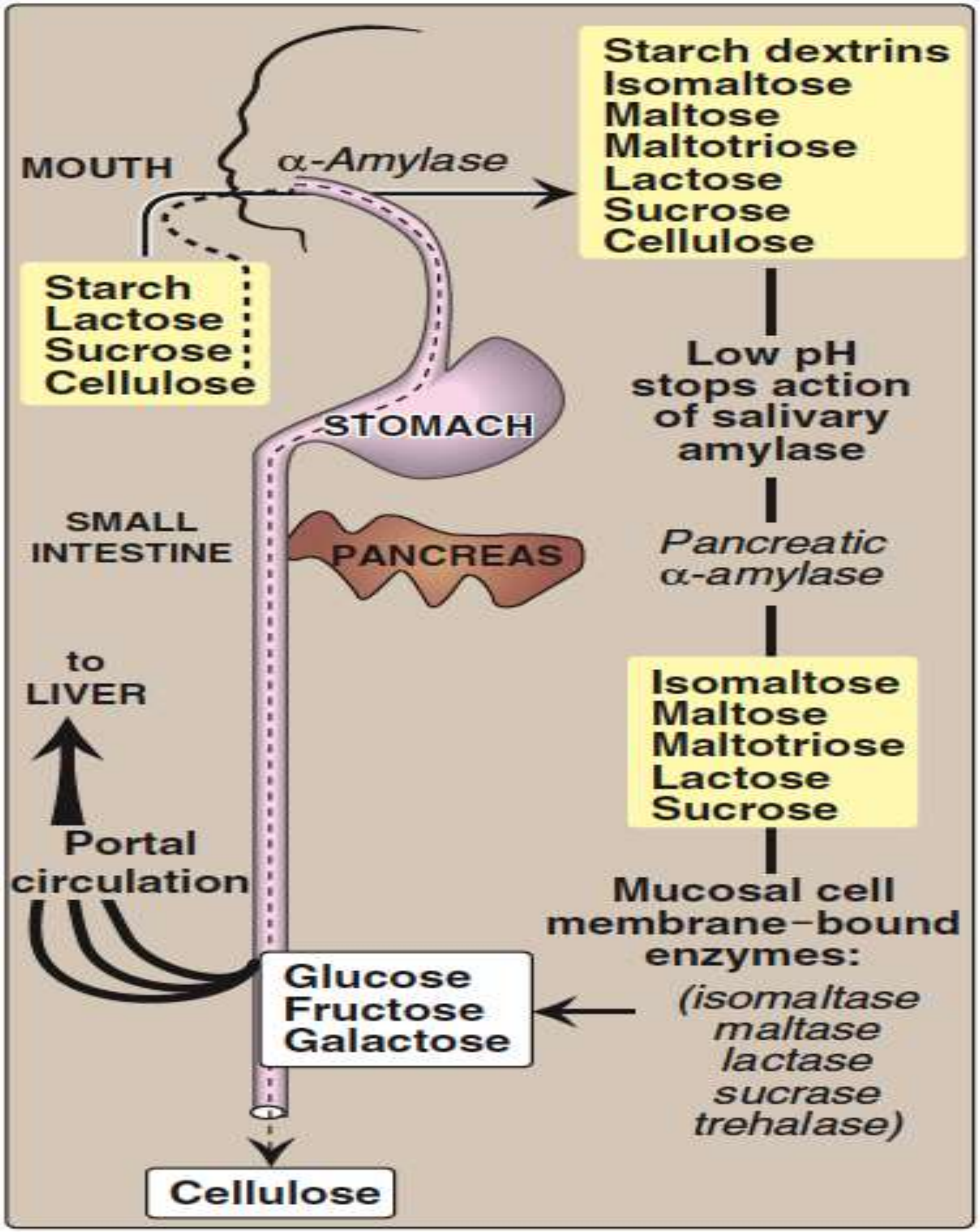
Dextrinase

Isomaltose → Glucose + Glucose

Carbohydrate Metabolism

Digestion of cellulose:

- **Cellulose contains β(1-4) bonds between glucose molecules.**
- **In humans, there is no β (1-4) glucosidase that can digest such bonds. So cellulose passes as such in stool.**
- **Cellulose helps water retention during the passage of food along the intestine → producing larger and softer feces → preventing constipation.**


MOUTH
α-Amylase
Starch dextrins
Isomaltose
Maltose
Maltotriose
Lactose
Sucrose
Cellulose
Starch
Lactose
Sucrose
Cellulose
STOMACH
Low pH
stops action
of salivary
amylase
SMALL
INTESTINE
PANCREAS
Pancreatic
α-amylase
to
LIVER
Isomaltose
Maltose
Maltotriose
Lactose
Sucrose
Portal
circulation
Mucosal cell
membrane–bound
enzymes:
(isomaltase
maltase
lactase
sucrase
trehalase)
Glucose
Fructose
Galactose
Cellulose

Transport of glucose

Glucose cannot diffuse directly into cells, but enters by one of two transport mechanisms:

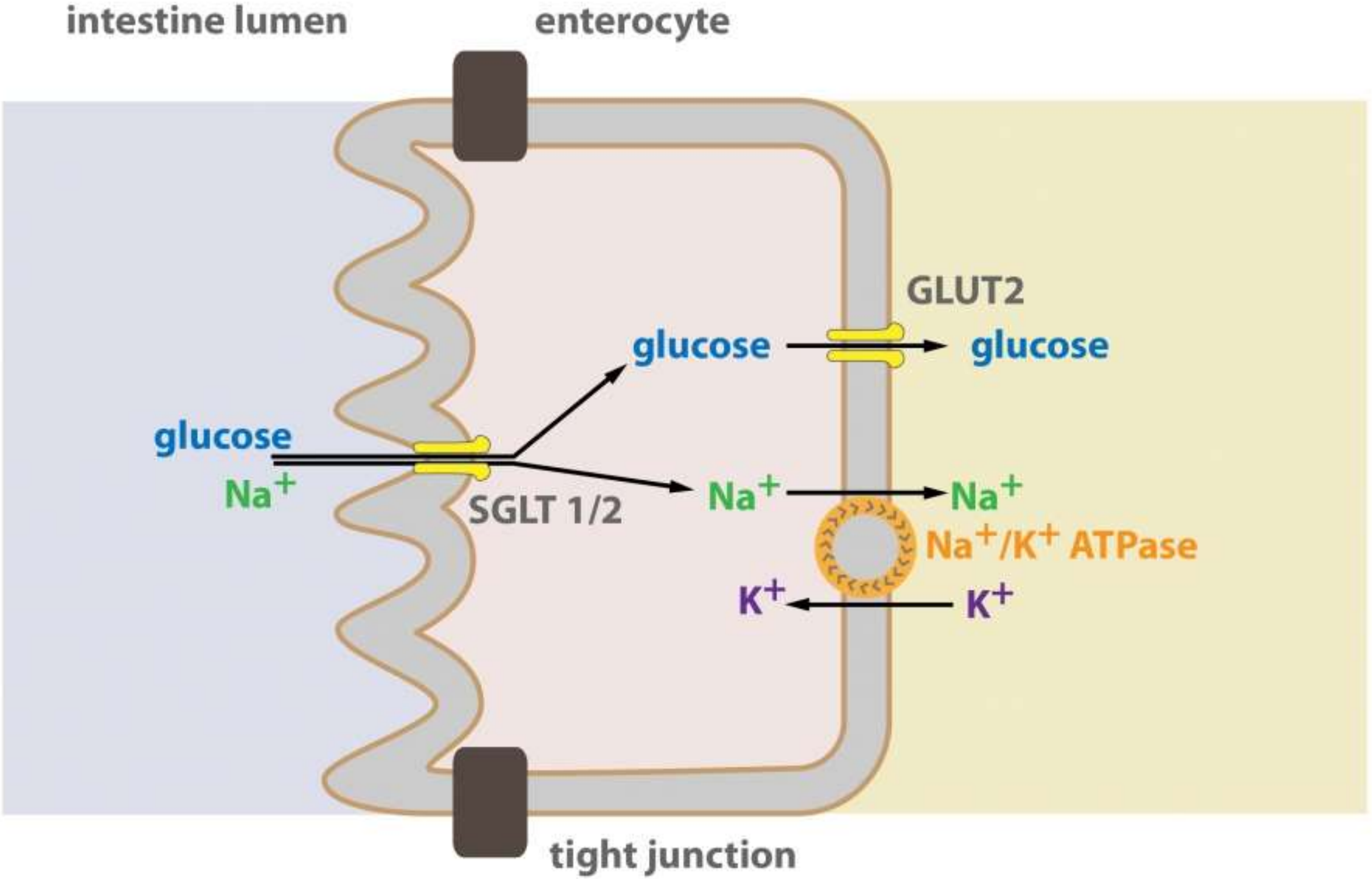
- **Na^+-independent, facilitated diffusion transport system**

a family of 14 glucose transporters in cell membranes. They are designated GLUT-1 to GLUT-14 (glucose transporter isoforms 1–14).

- **Na^+-monosaccharide cotransporter system**

an energy-requiring process that transports glucose “against” a concentration gradient. The carrier is a sodium-dependent–glucose transporter or SGLT.

Na-dependent transporter or SGLT



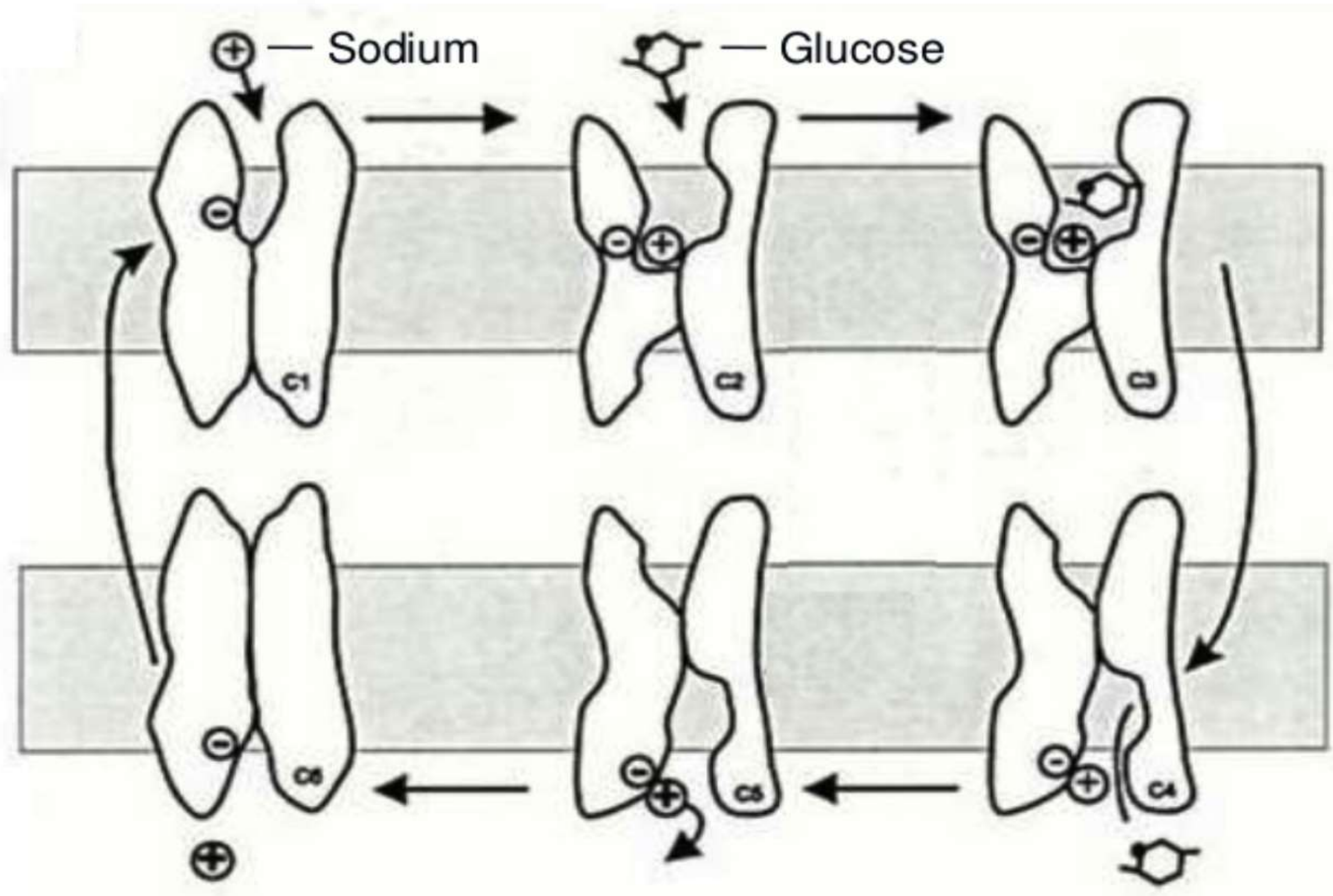
Na-dependent transporter or SGLT

Glucose is absorbed actively from the intestinal lumen into the mucosal cells by Sodium Glucose Transporter (SGLT 1)

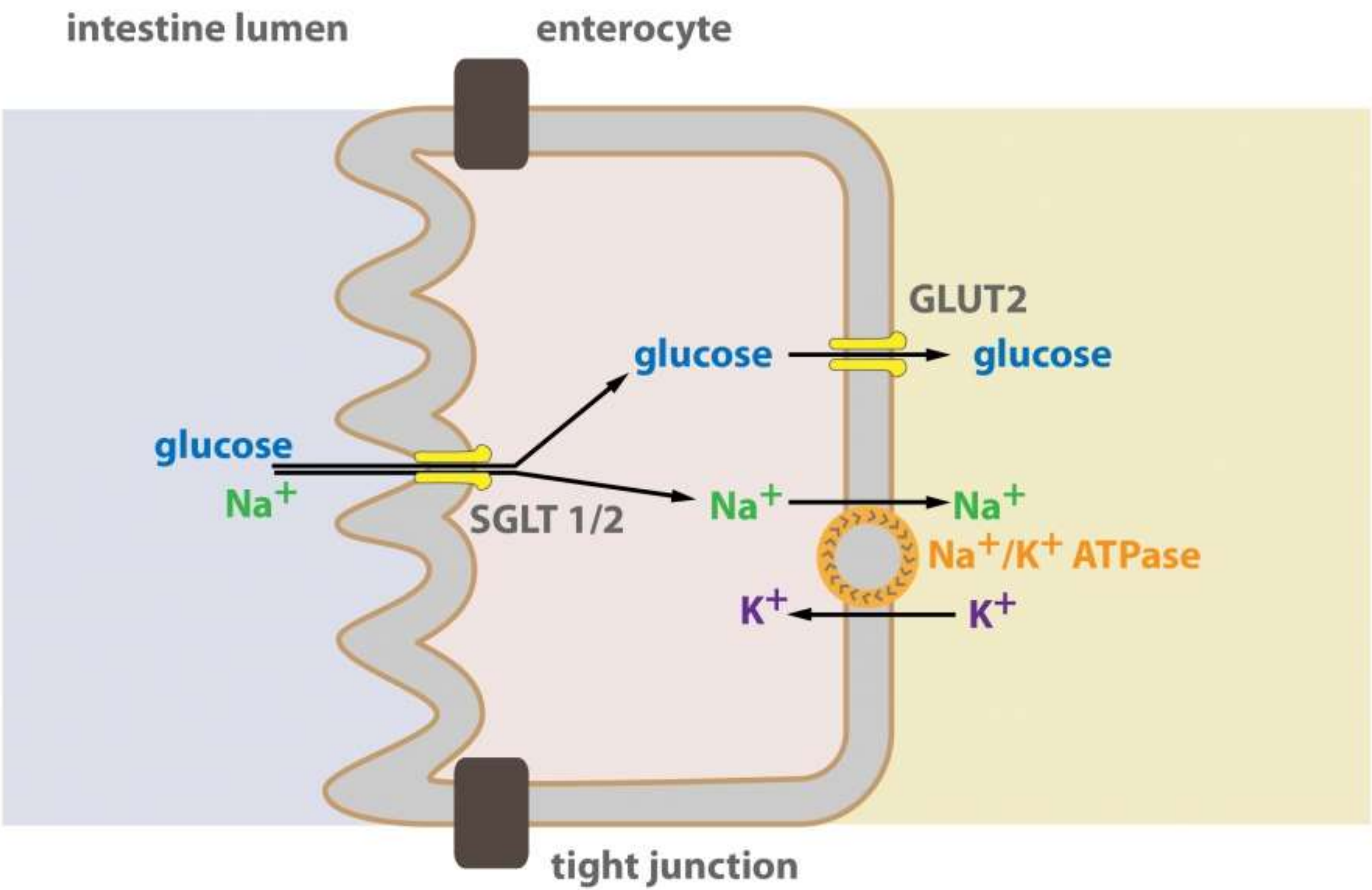
SGLT 1, present in the cell membrane, has two binding sites – one for sodium and the other for glucose

Sodium and glucose, present in the lumen, bind to SGLT 1

Na-dependent transporter or SGLT



Na-dependent transporter or SGLT



Fate of glucose

A-Oxidative fate:

Major pathways:

- Glycolysis.
- Krebs' cycle.

Minor pathways:

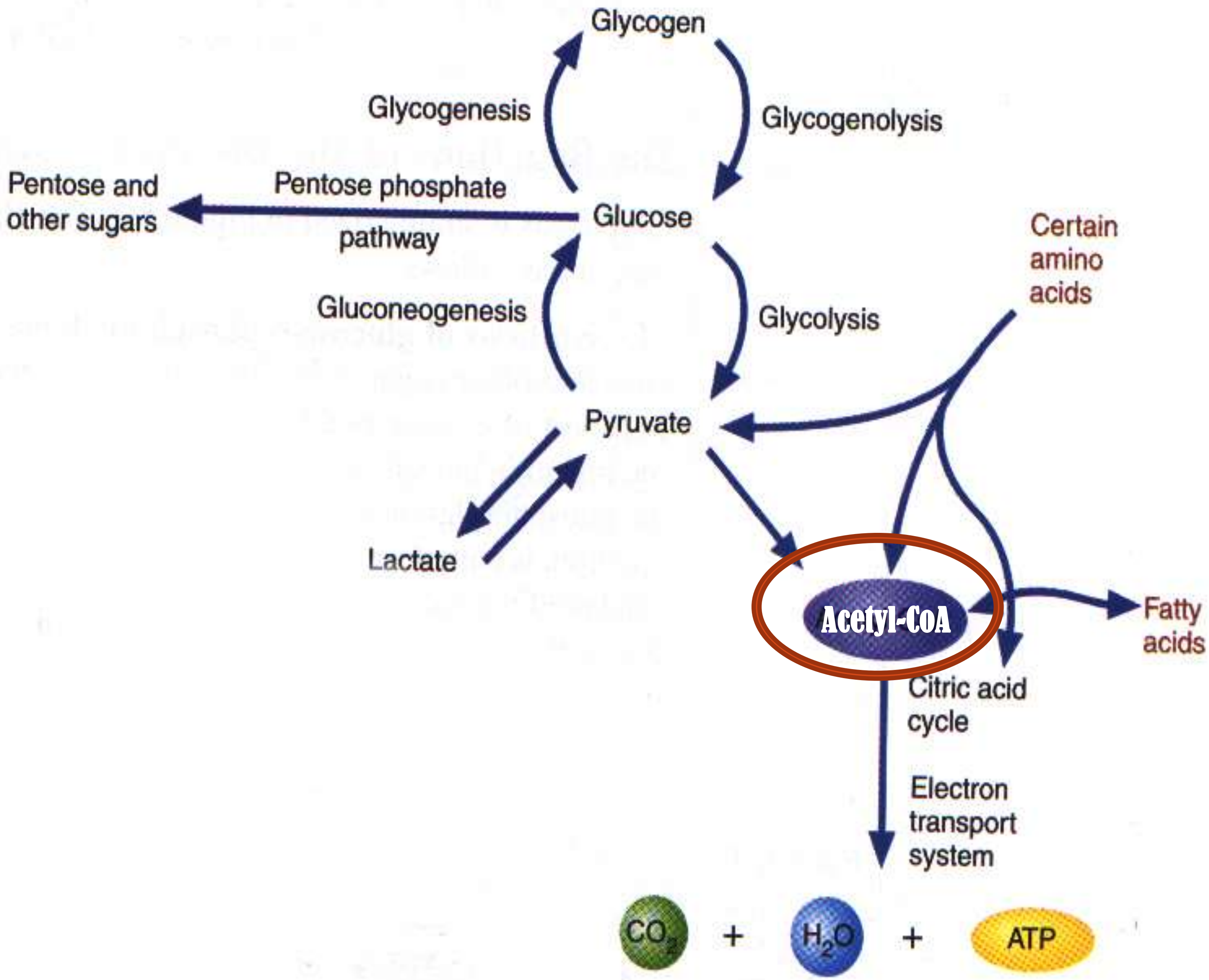
- Pentose shunt.
- Uronic acid pathway.

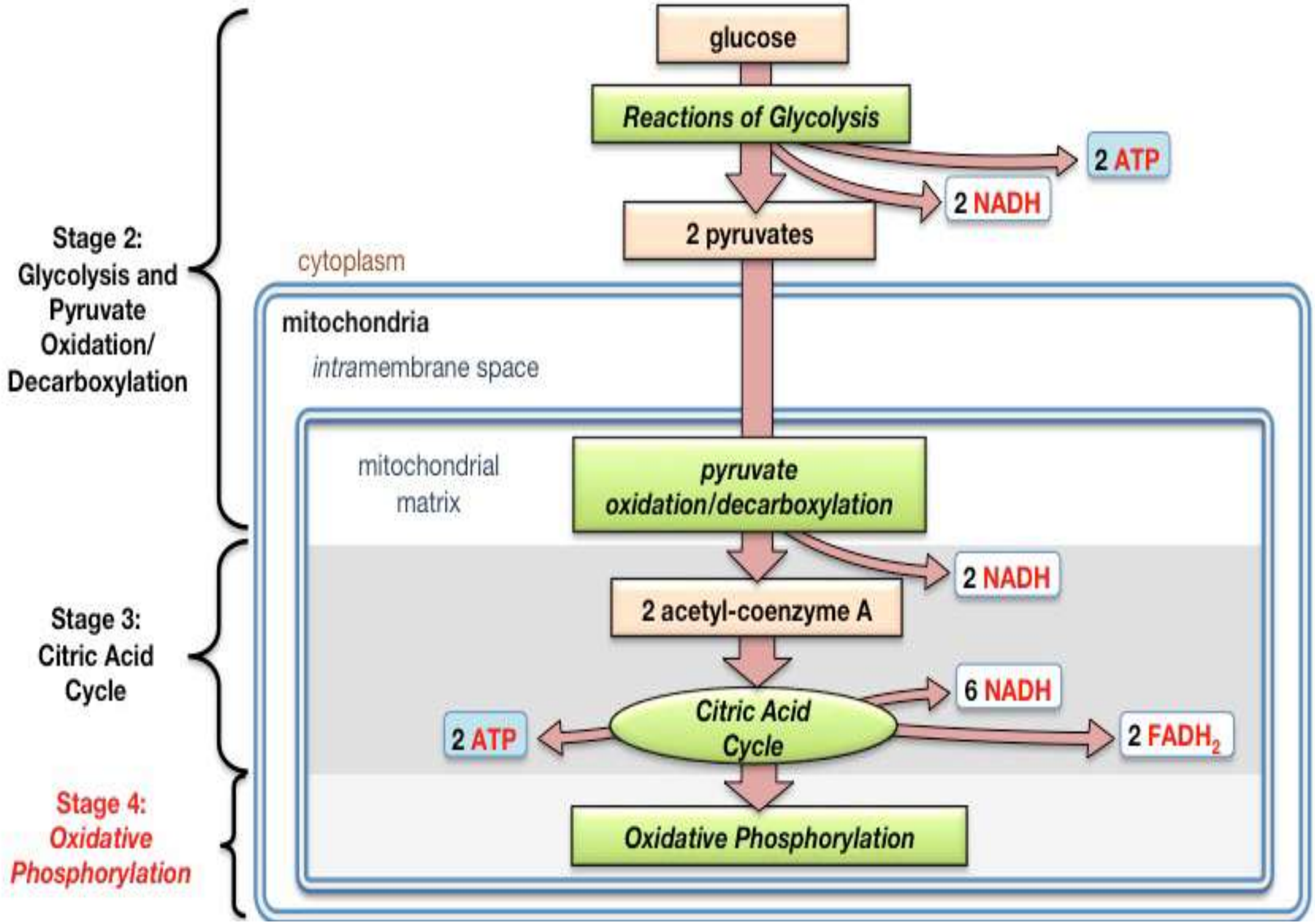
B- **Anabolic fates:**

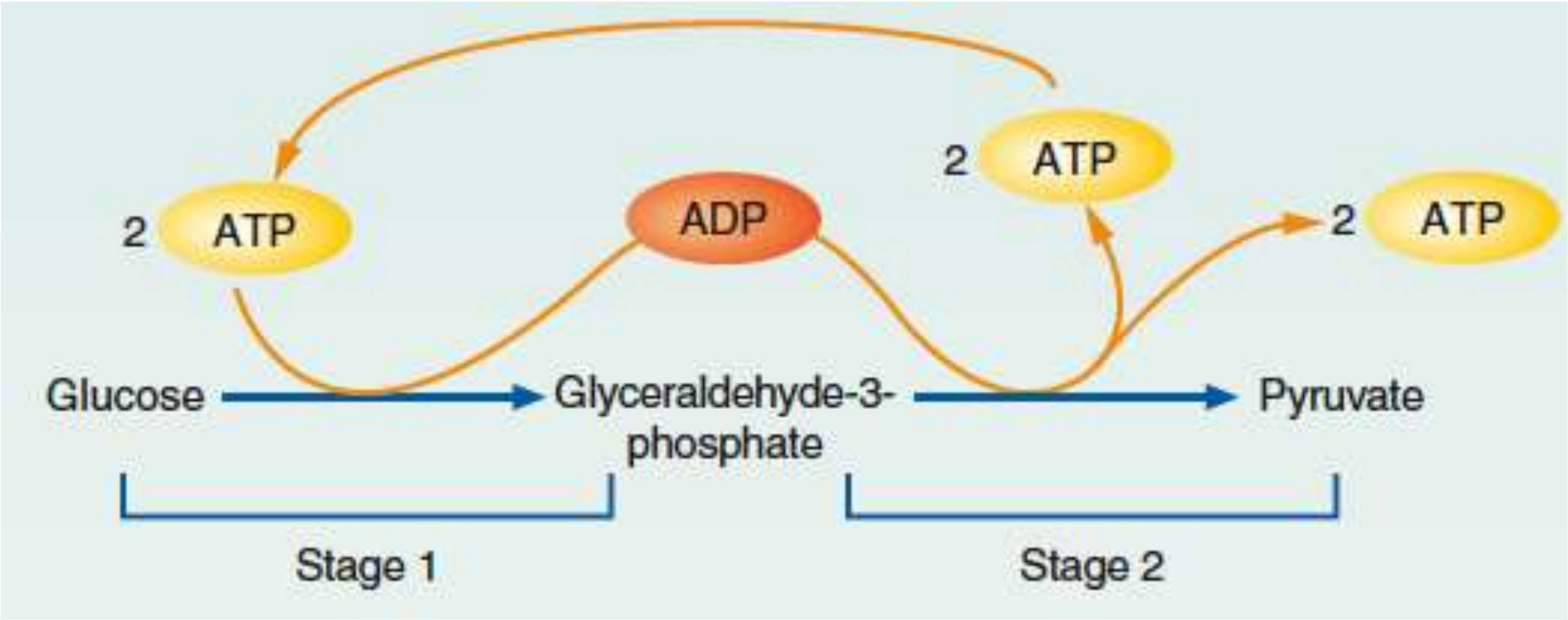
- Glycogenesis/glycogenolysis.
- Gluconeogenesis.
- Monosaccharides synthesis.
- Lactose synthesis.
- Glycolipids, glycoproteins and Proteoglycans synthesis.

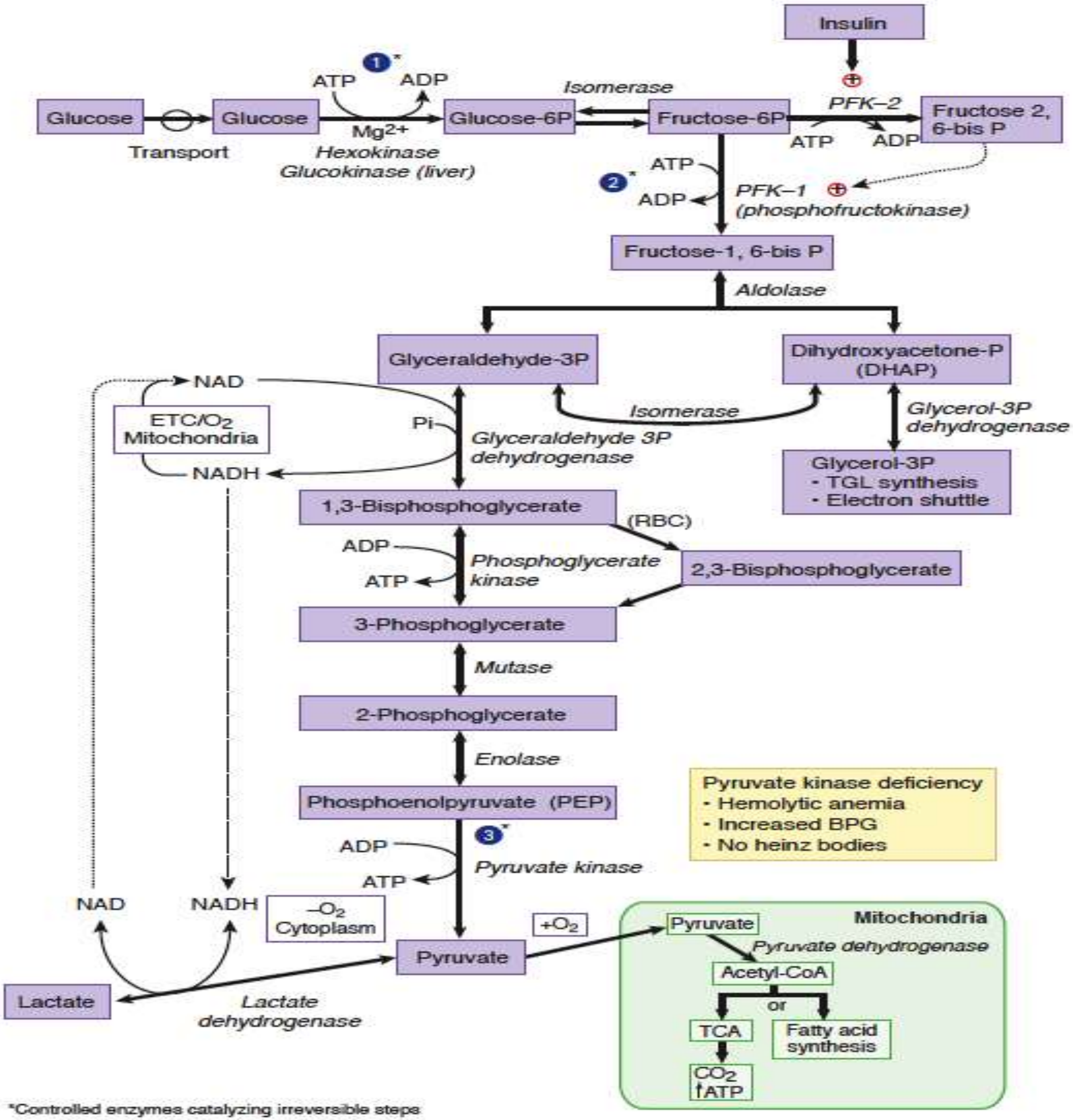
CHO metabolism in mammalian cells are:

1. **Glycolysis**: Oxidation of glucose to pyruvate (aerobic state) or lactate (anaerobic state)
2. **Krebs cycle:** After oxidation of pyruvate to acetyl CoA, acetyl CoA enters the Krebs cycle for the aim of production of ATP.
3. **Hexose monophosphate shunt:** Enables cells to produce ribose-5-phosphate and NADPH.
4. **Glycogenesis:** Synthesis of glycogen from glucose, when glucose levels are high
5. **Glycogenolysis**: Degradation of glycogen to glucose when glucose in short supply.
6. **Gluconeogenesis:** Formation of glucose from noncarbohydrate sources.

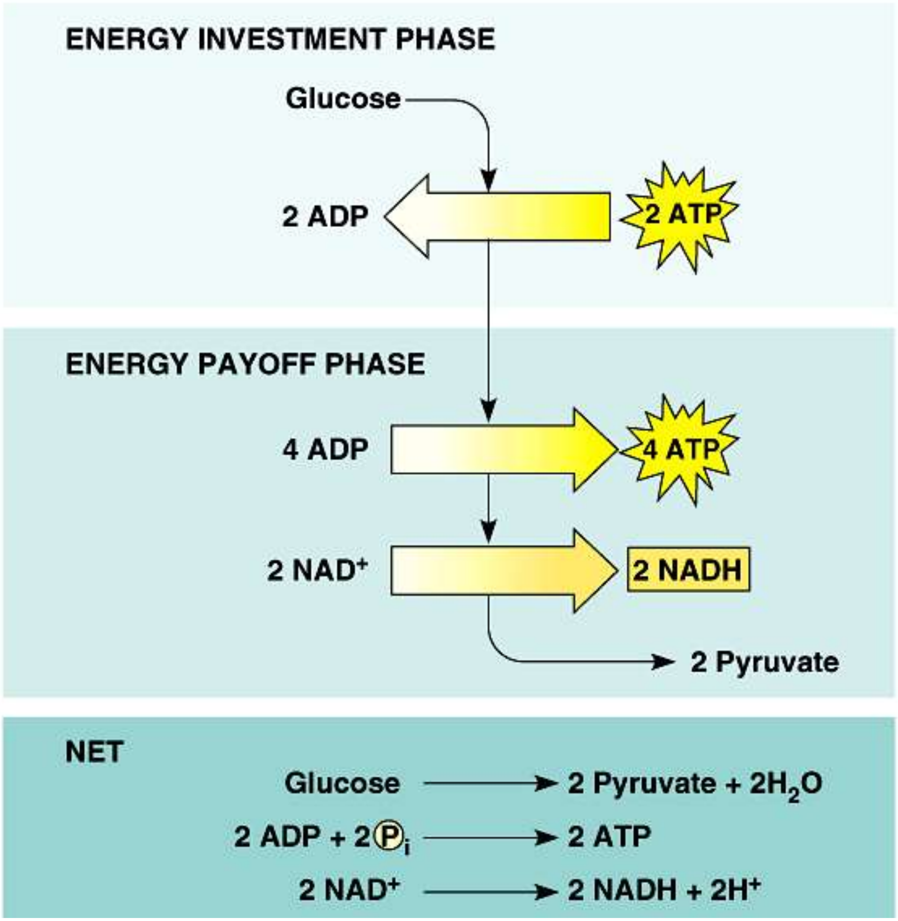

Glycogen
Glycogenesis
Glycogenolysis
Pentose and
other sugars
Pentose phosphate
pathway
Glucose
Certain
amino
acids
Gluconeogenesis
Glycolysis
Pyruvate
Lactate
Acetyl-CoA
Fatty
acids
Citric acid
cycle
Electron
transport
system
CO2
+
H2O
+
ATP


Stage 2:
Glycolysis and
Pyruvate
Oxidation/
Decarboxylation
Stage 3:
Citric Acid
Cycle
Stage 4:
Oxidative
Phosphorylation
glucose
Reactions of Glycolysis
2 ATP
2 NADH
2 pyruvates
cytoplasm
mitochondria
intramembrane space
mitochondrial
matrix
pyruvate
oxidation/decarboxylation
2 NADH
2 acetyl-coenzyme A
6 NADH
Citric Acid
Cycle
2 ATP
2 FADH2
Oxidative Phosphorylation


2 ATP
ADP
2 ATP
2 ATP
Glucose
Glyceraldehyde-3-phosphate
Pyruvate
Stage 1
Stage 2


Insulin
Glucose
Glucose
Transport
ATP
ADP
Mg2+
Hexokinase
Glucokinase (liver)
Glucose-6P
Isomerase
Fructose-6P
PFK–2
ATP
ADP
Fructose 2, 6-bis P
ATP
ADP
PFK–1 (phosphofructokinase)
Fructose-1, 6-bis P
Aldolase
Glyceraldehyde-3P
Dihydroxyacetone-P (DHAP)
NAD
ETC/O2 Mitochondria
NADH
Pi
Isomerase
Glyceraldehyde 3P dehydrogenase
Glycerol-3P dehydrogenase
Glycerol-3P
- TGL synthesis
- Electron shuttle
1,3-Bisphosphoglycerate
(RBC)
2,3-Bisphosphoglycerate
ADP
ATP
Phosphoglycerate kinase
3-Phosphoglycerate
Mutase
2-Phosphoglycerate
Enolase
Phosphoenolpyruvate (PEP)
Pyruvate kinase deficiency
- Hemolytic anemia
- Increased BPG
- No heinz bodies
ADP
ATP
Pyruvate kinase
NAD
NADH
–O2 Cytoplasm
+O2
Pyruvate
Lactate
Lactate dehydrogenase
Mitochondria
Pyruvate
Pyruvate dehydrogenase
Acetyl-CoA
or
TCA
Fatty acid synthesis
CO2
↑ATP
*Controlled enzymes catalyzing irreversible steps

- In the energy investment phase, ATP provides activation energy by phosphorylating glucose.
  - This requires 2 ATP per glucose.
- In the energy payoff phase, ATP is produced by substrate-level phosphorylation and NAD^+ is reduced to NADH.
- 2 ATP (net) and 2 NADH are produced per glucose.



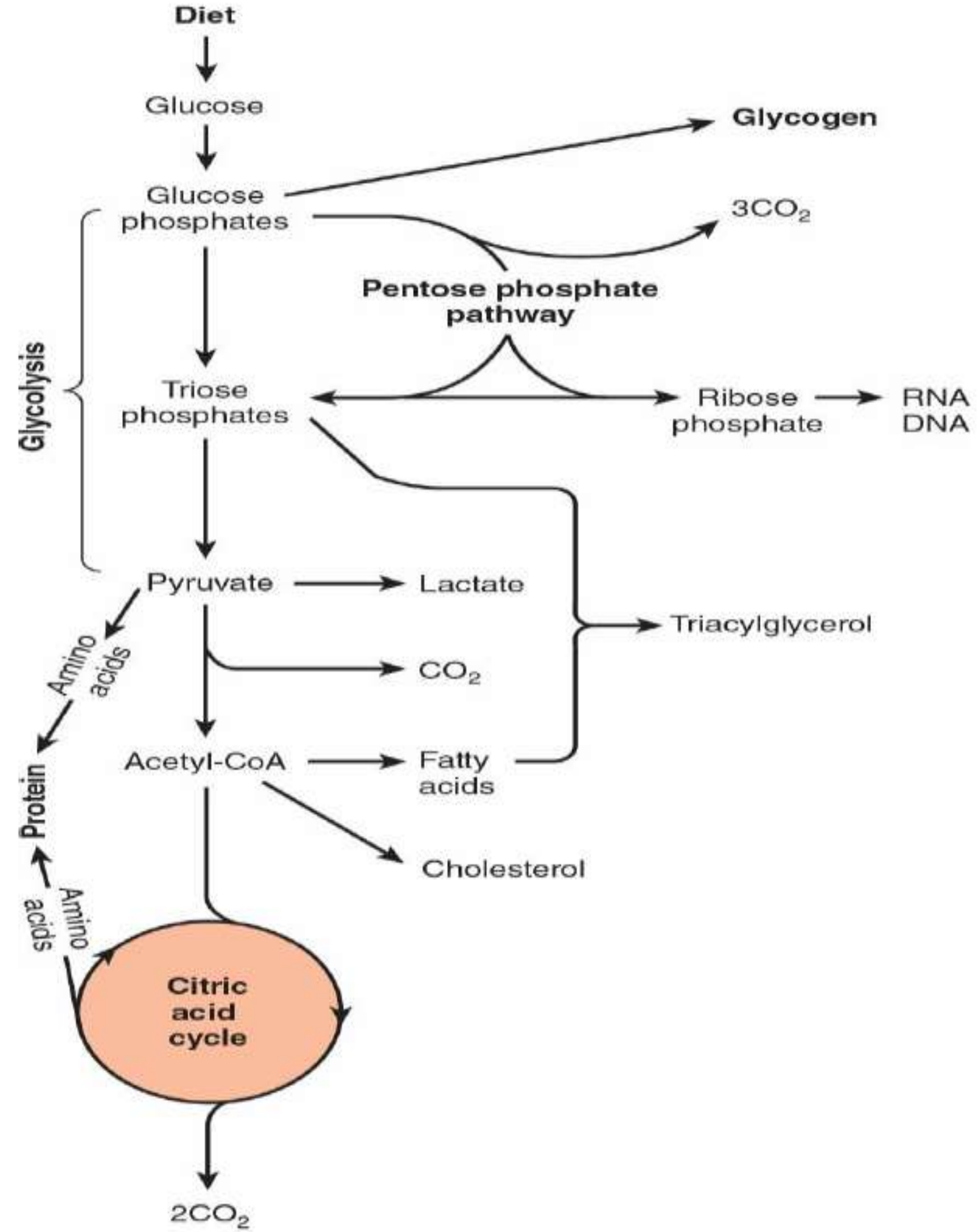
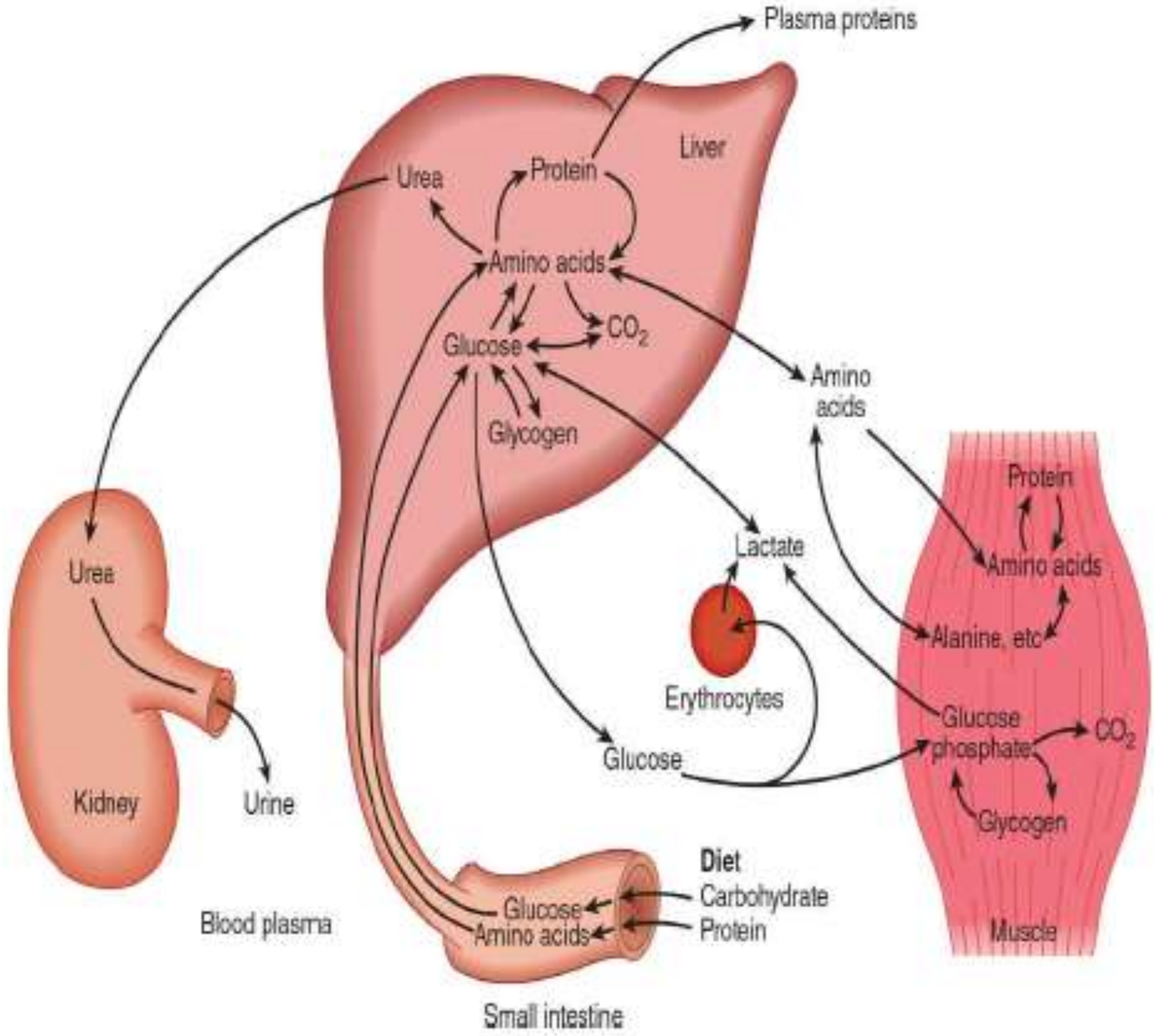
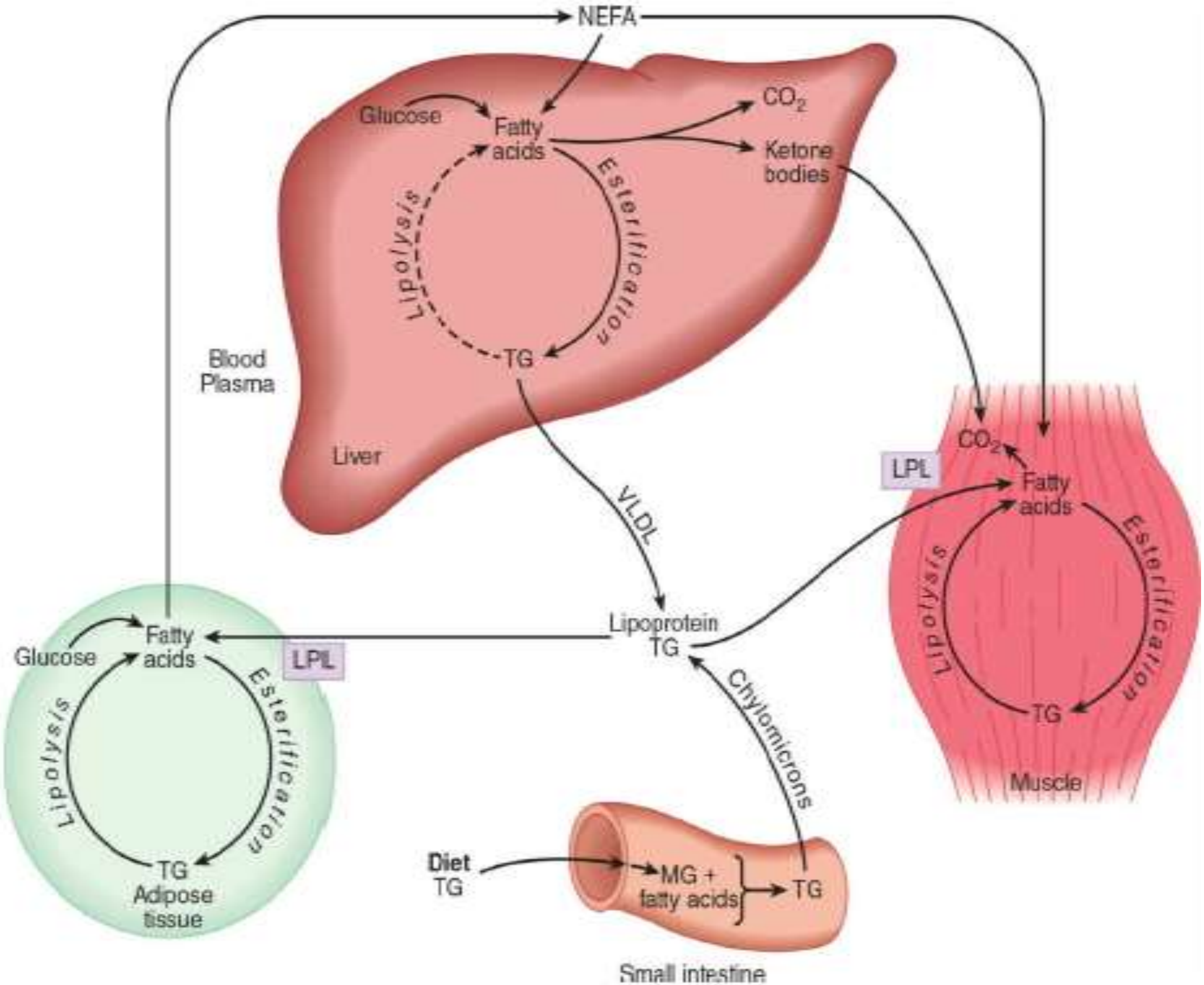


FIGURE 14–2 Overview of carbohydrate metabolism showing the major pathways and end products. Gluconeogenesis is not shown.



Plasma proteins
Liver
Urea
Protein
Amino acids
CO_2
Glucose
Glycogen
Amino
acids
Protein
Amino acids
Lactate
Alanine, etc
Erythrocytes
Glucose
phosphate
CO_2
Glucose
Glycogen
Urea
Kidney
Urine
Diet
Carbohydrate
Protein
Glucose
Amino acids
Blood plasma
Muscle
Small intestine


NEFA
Glucose
Fatty acids
CO2
Ketone bodies
Lipolysis
Esterification
TG
Blood Plasma
Liver
VLDL
LPL
CO2
Fatty acids
Lipolysis
Esterification
TG
Muscle
Glucose
Fatty acids
LPL
Lipoprotein TG
Chylomicrons
Lipolysis
Esterification
TG
Adipose tissue
Diet TG
MG + fatty acids
TG
Small intestine

☺

Thanks for your attention!

☺