

CHY2026: General Biochemistry



UNIT 7& 8: CARBOHYDRATE METABOLISM

Metabolism



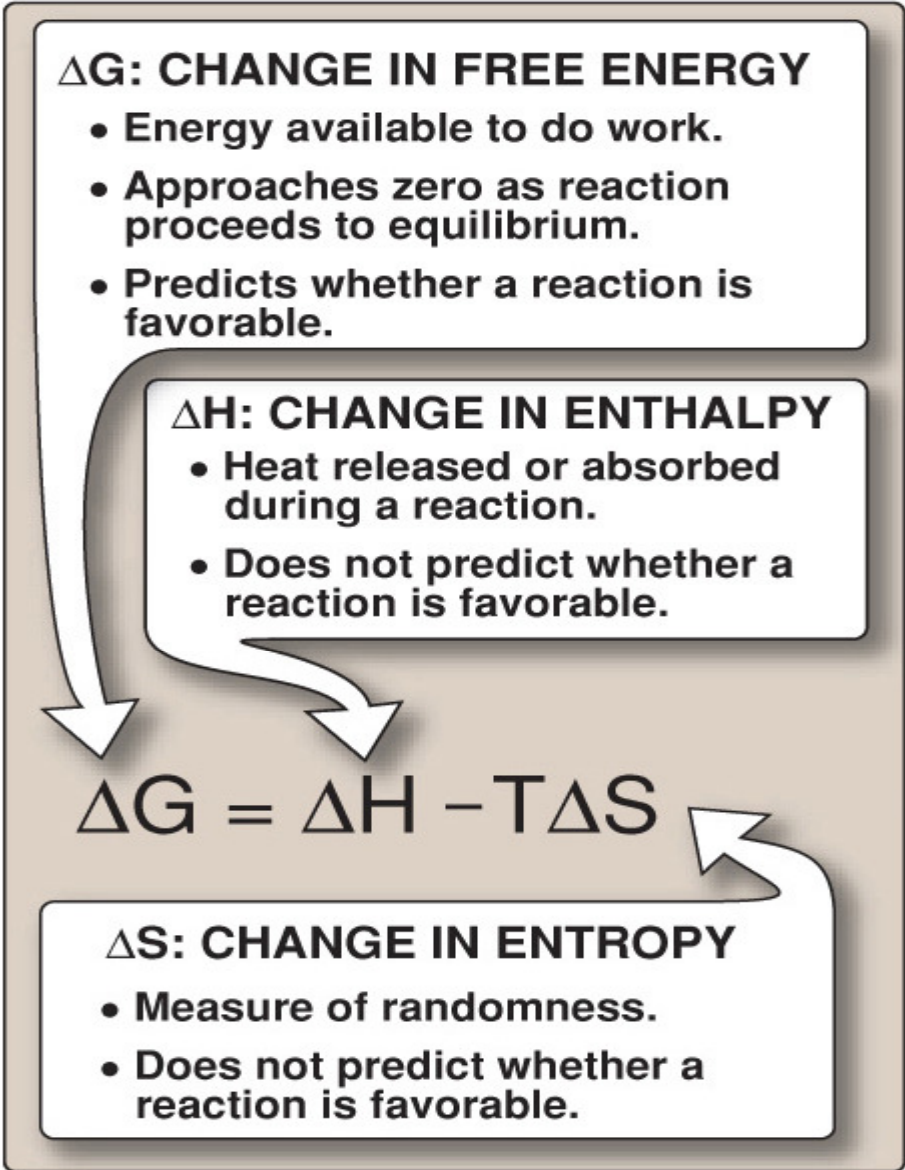
- ❖ **Bioenergetics** is the transfer and utilization of energy in biological systems
- ❖ The direction and extent to which a chemical reaction proceeds is determined by the degree to which two factors (enthalpy and entropy) change during the reaction
- ❖ Enthalpy (ΔH) a measure of the change in the heat content of reactants and products
- ❖ Entropy (ΔS) a measure in the change of randomness or disorder of reactants and products
- ❖ Changes in free energy (ΔG) provides a measure of energetic feasibility of a chemical reaction

ΔG : CHANGE IN FREE ENERGY

- Energy available to do work.
- Approaches zero as reaction proceeds to equilibrium.
- Predicts whether a reaction is favorable.

ΔH : CHANGE IN ENTHALPY

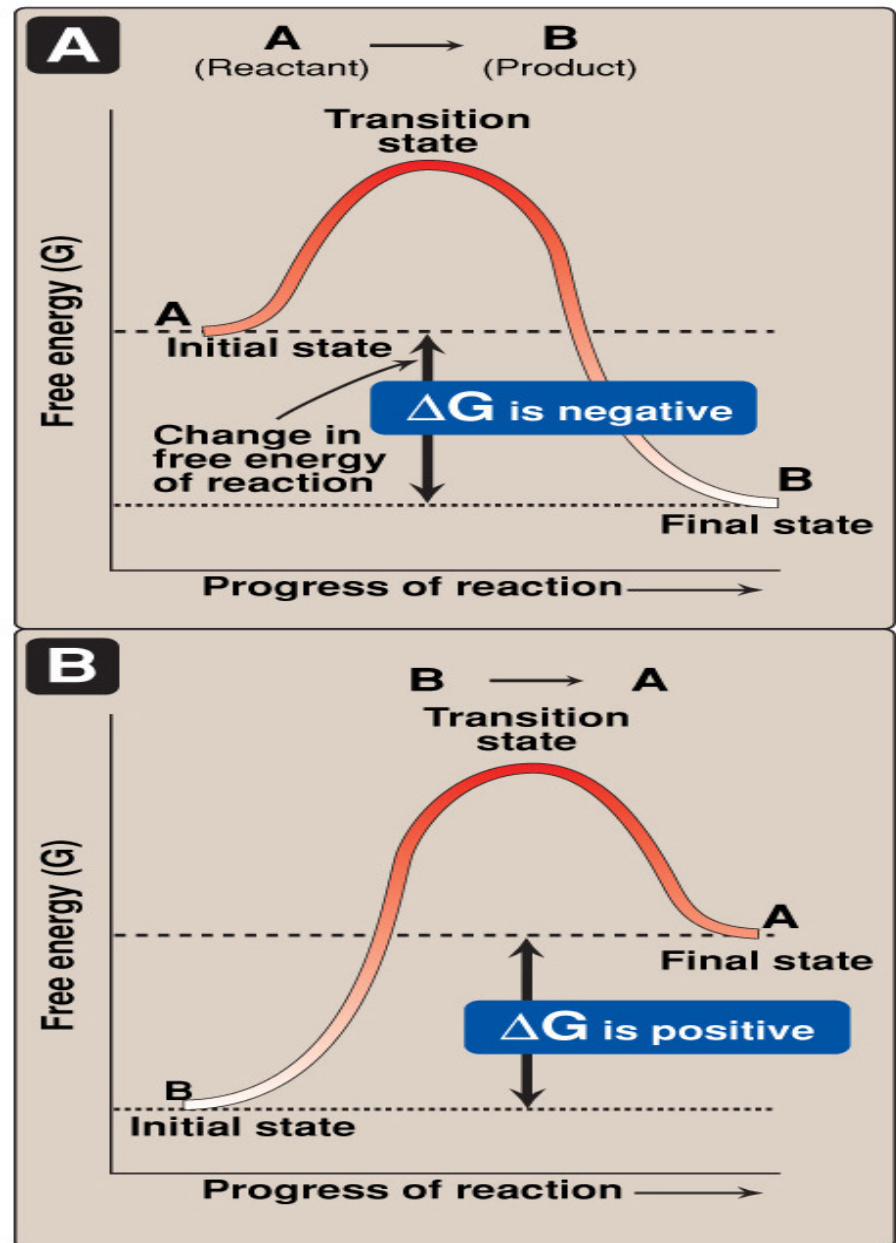
- Heat released or absorbed during a reaction.
- Does not predict whether a reaction is favorable.


$$\Delta G = \Delta H - T\Delta S$$

ΔS : CHANGE IN ENTROPY

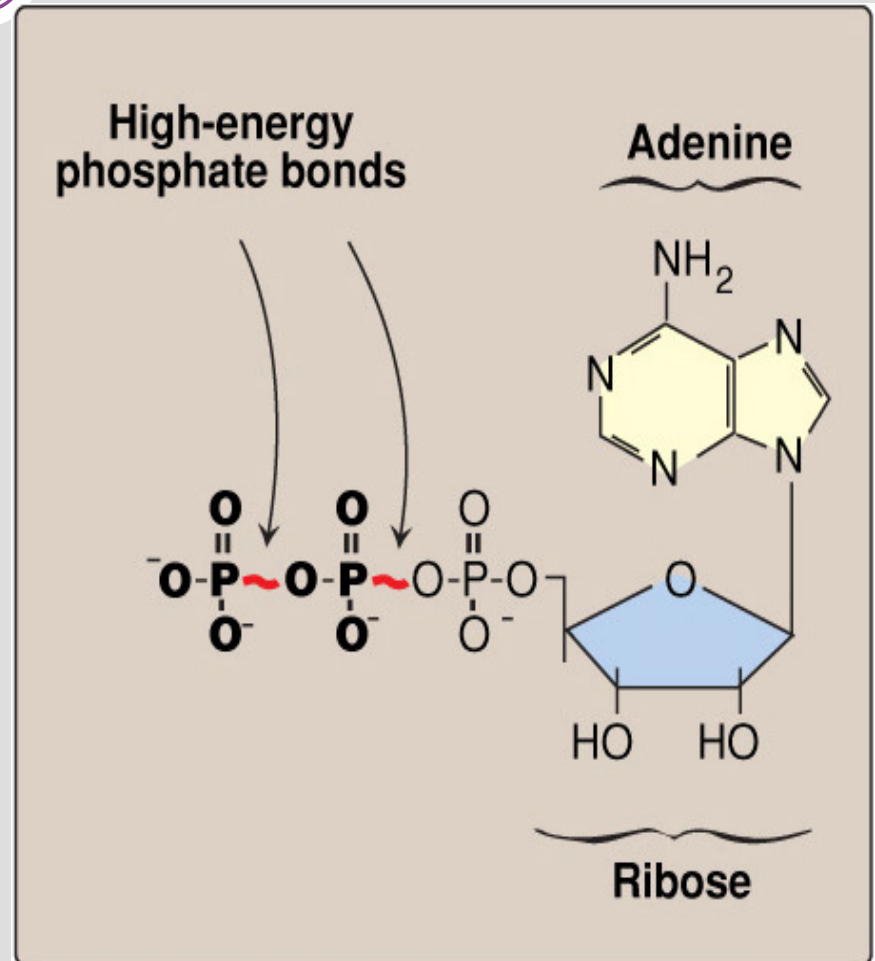
- Measure of randomness.
- Does not predict whether a reaction is favorable.

- ❖ $-\Delta G$ = there is a net loss of energy and reaction goes spontaneously
- ❖ $+\Delta G$ = there is a net gain of energy and the reaction does not go spontaneously
- ❖ $\Delta G = 0$ the reactants are in equilibrium



Copyright © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins

- ❖ ATP is a high energy phosphate compound
- ❖ The ΔG° is approximately -7.3 kcalmol⁻¹ for each of the two terminal phosphate groups



Copyright © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins



- ❖ **Metabolism** is the assembly of biochemical reactions used by an organism for the synthesis of cell materials and the utilization of energy from the environment
- ❖ Metabolism → Anabolic (assimilation) or Catabolic (dissimilation)

Metabolism



- ❖ **Anabolic reactions** are the synthesis of large molecules from simple or smaller molecules

- ❖ Energy is used in the process → **Endergonic**



- ❖ Example, Photosynthesis

sunlight; chlorophyll

carbon dioxide + water → carbohydrate + oxygen

- ❖ Anabolic reactions are involved in chemical reduction

Metabolism



❖ **Catabolic reactions** are the breakdown of large molecules to smaller or simpler molecules

❖ Energy is released in this process → **Exergonic**



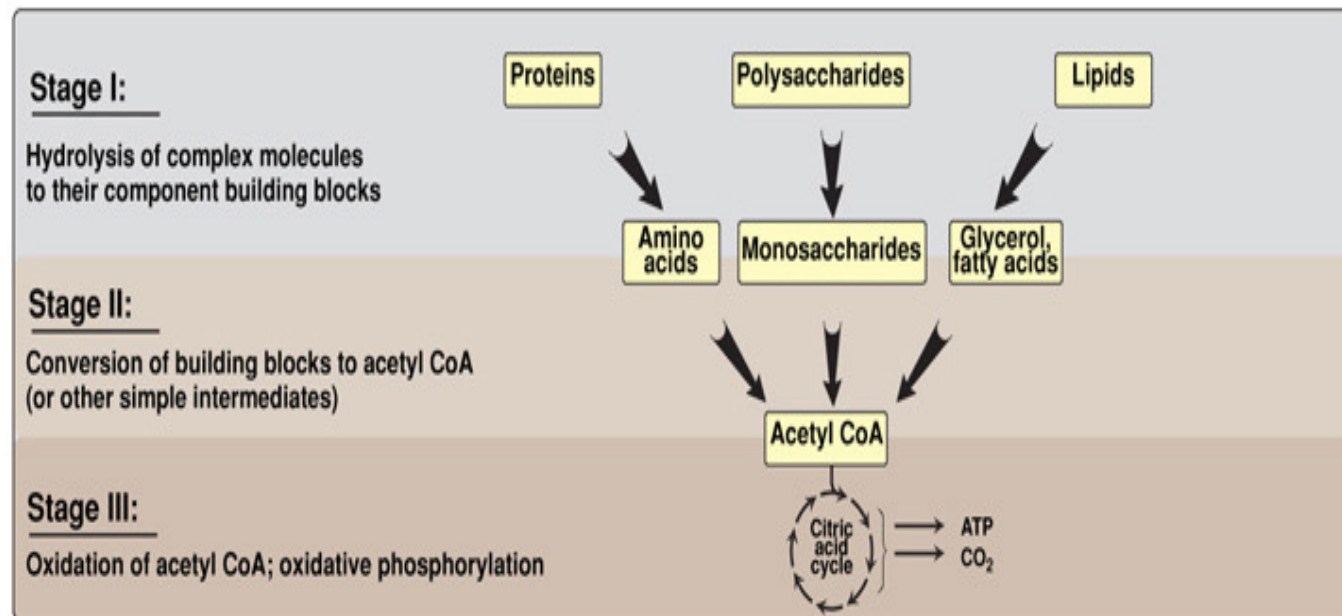
❖ E.g. Digestion

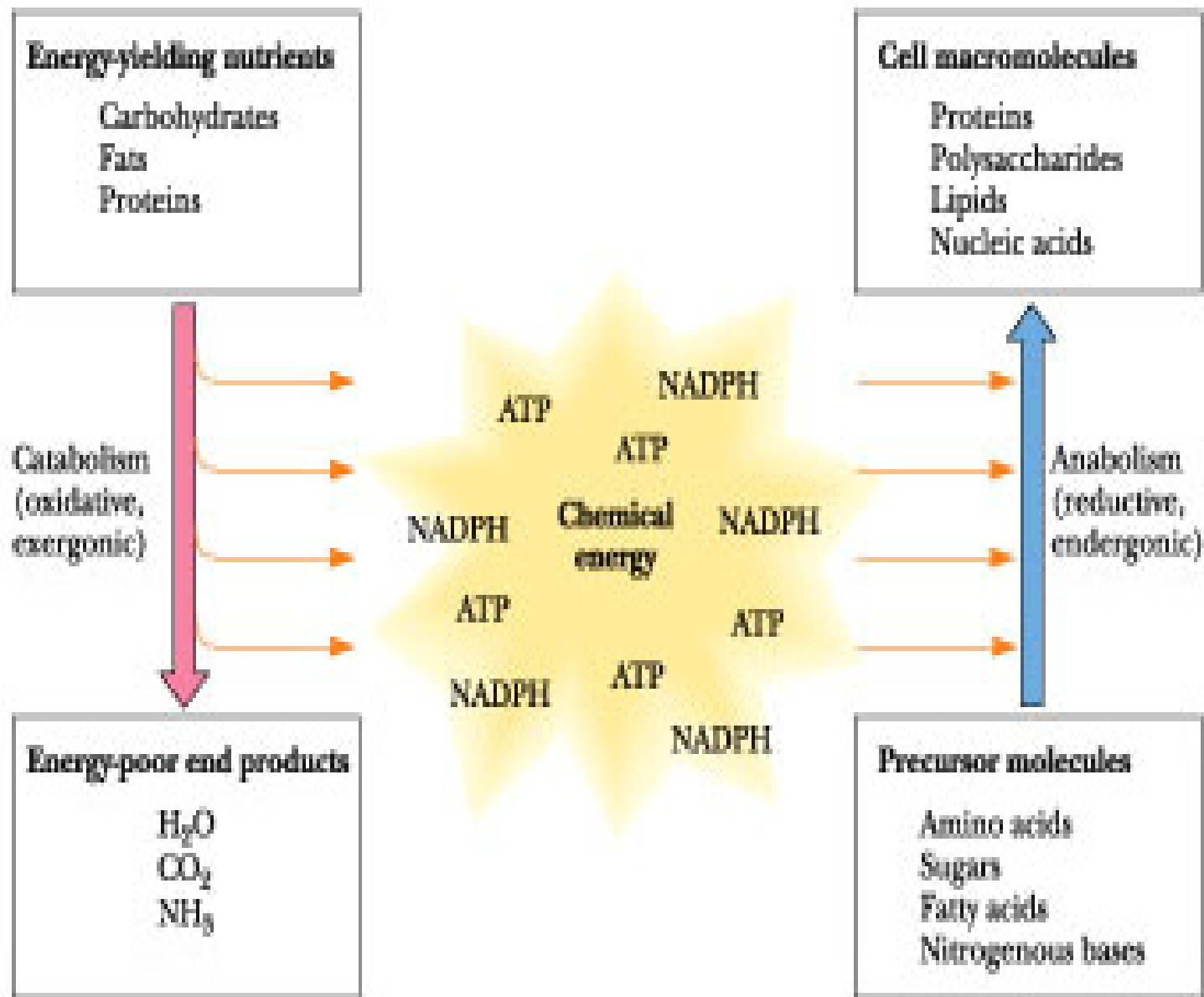
❖ Catabolic reactions are typically oxidative and require the coenzymes NAD^+

Metabolism

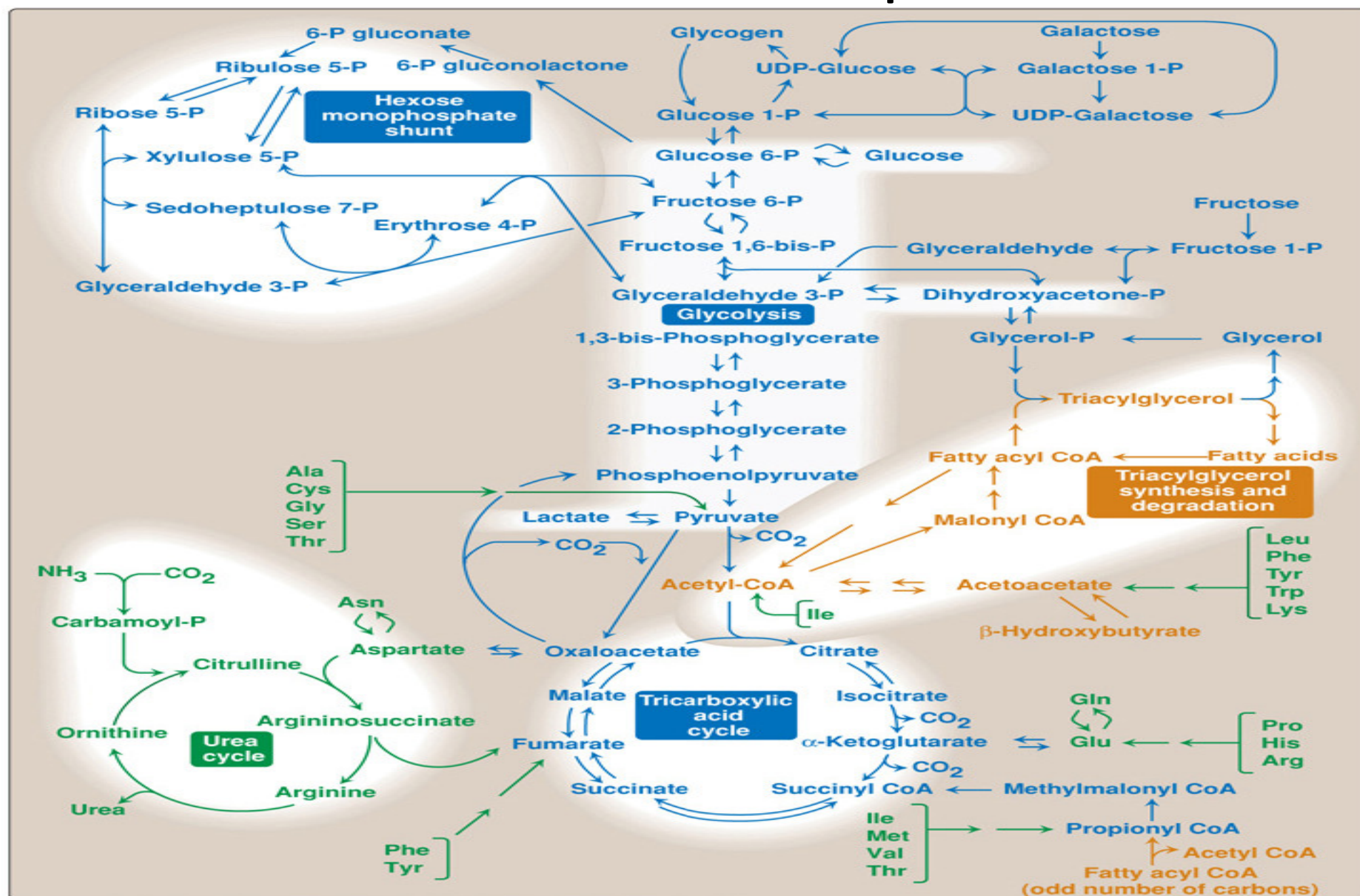
❖ Three stages of catabolism –

- (a) Hydrolysis of complex molecules e.g. Proteins → amino acids
- (b) Conversion of building blocks into simple intermediates i.e. the building blocks → acetyl coenzyme A (CoA) + smaller molecules
- (c) Oxidation of acetyl CoA [Tricarboxylic acid (TCA) cycle]





Metabolic Map





Carbohydrate Metabolism

Carbohydrate Metabolism



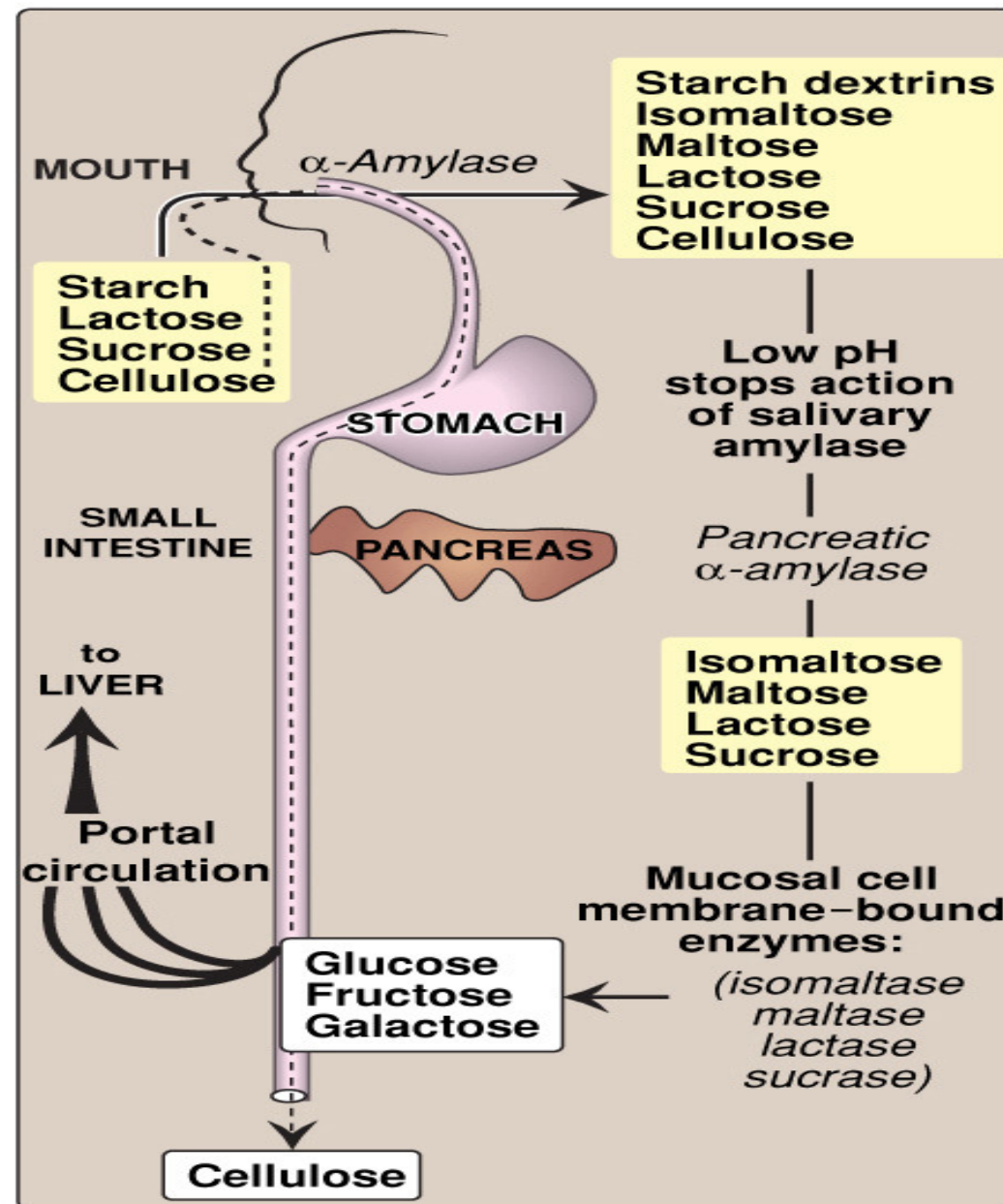
Catabolic Reactions	Anabolic Reactions
Glycolysis	Gluconeogenesis
Glycogenolysis	

❖ Other reactions include TCA Cycle, Oxidative phosphorylation and electron transport

Carbohydrate Metabolism

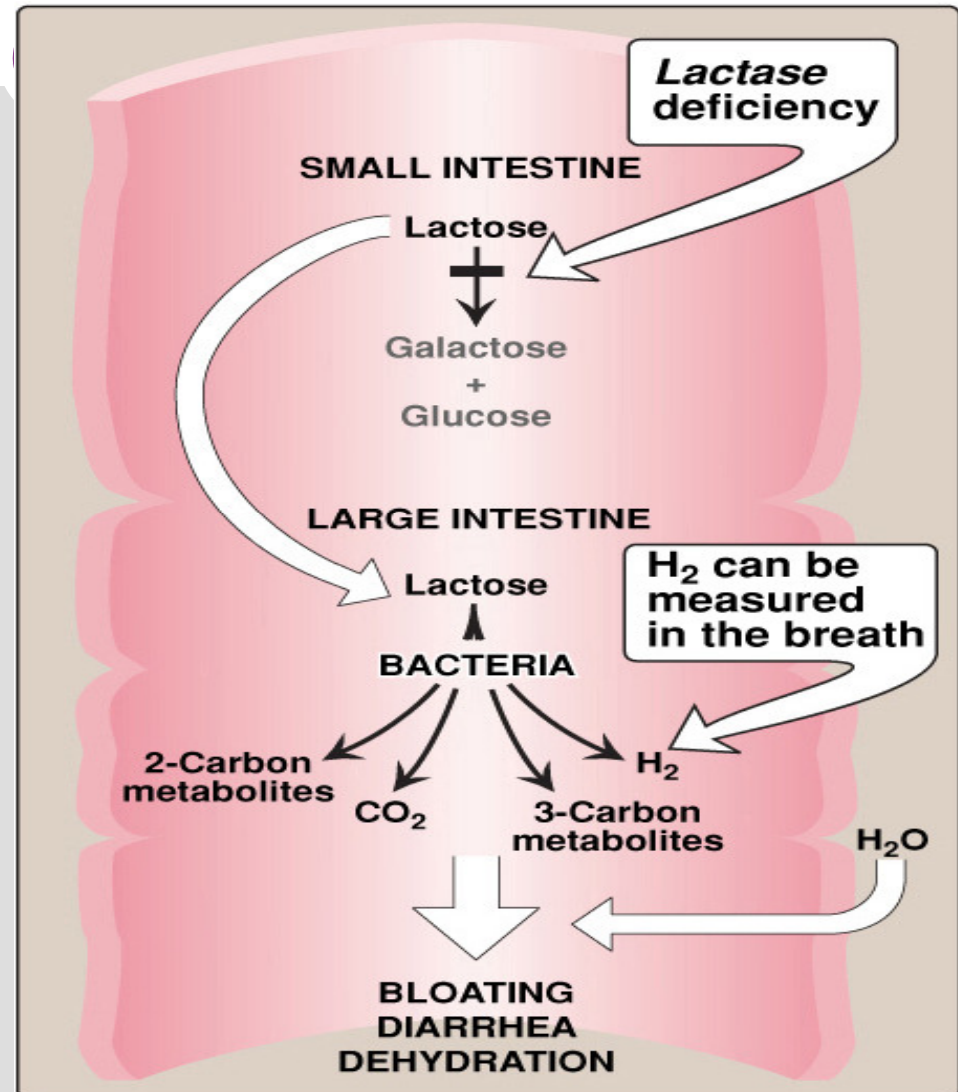


- ❖ Carbohydrates are metabolized to yield a vast array of other organic compounds
- ❖ Animals ingest large quantities of carb. that can either be stored, oxidized to obtain energy, converted to lipid for more efficient energy storage or use for the synthesis of many cellular constituents
- ❖ Major function is to be oxidized and provide energy for metabolic processes
- ❖ Carbohydrate is utilized by the cells mainly as glucose
- ❖ Fructose and galactose are easily converted to glucose in the liver



Abnormal Lactose Metabolism

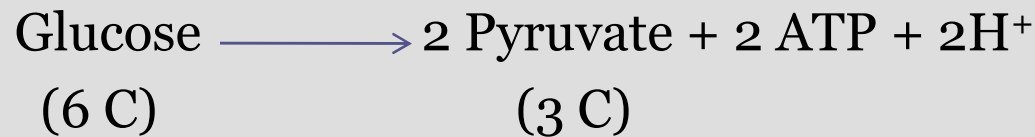
- ❖ More than $\frac{3}{4}$ of the world's adult are lactose intolerant
- ❖ Up to 90 % of adults of African and Asian decent are lactase deficient



Glycolysis



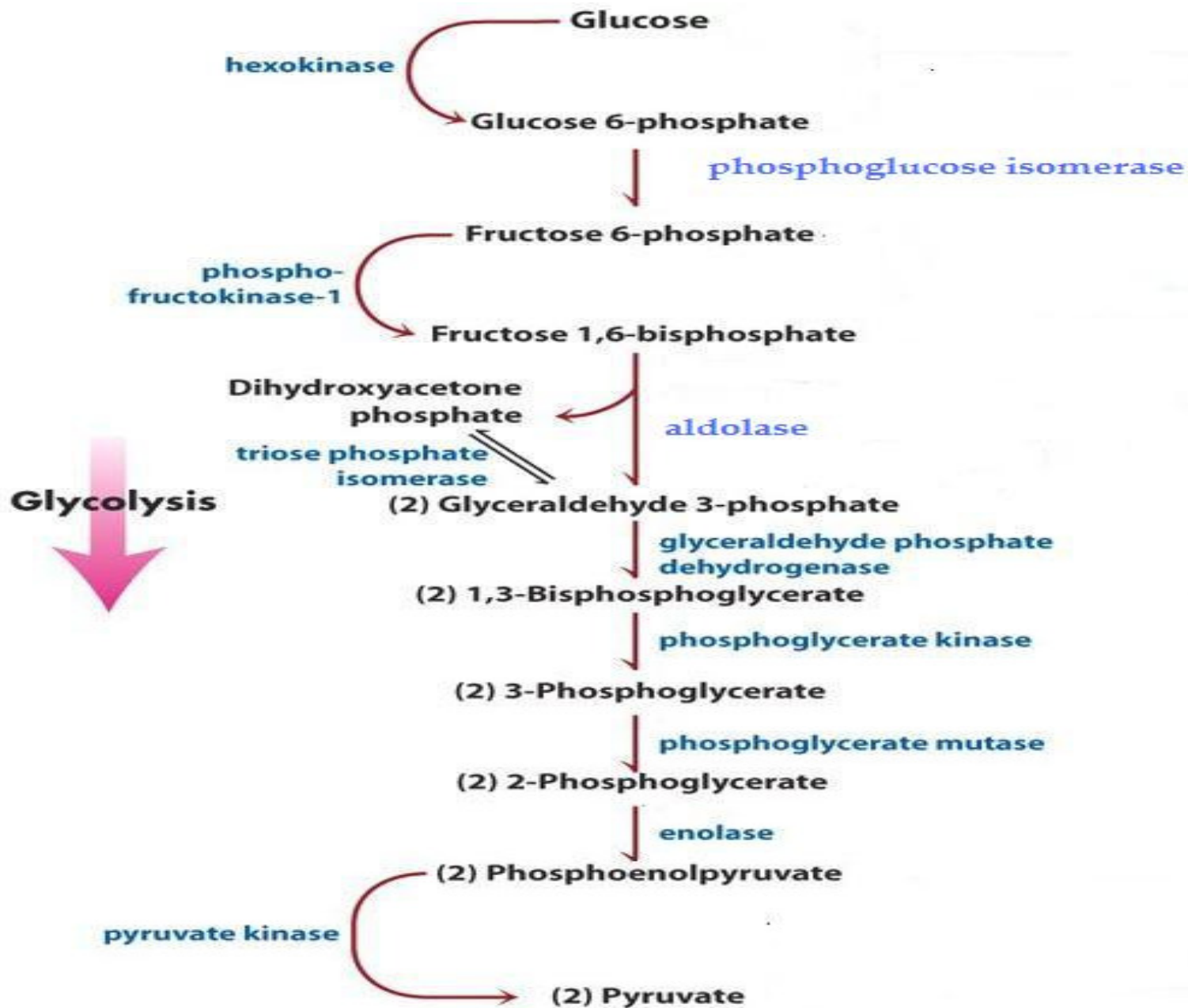
- ❖ *It is the central pathway of glucose catabolism*
- ❖ This is a process by which glucose is broken down to produce energy to all cells



- ❖ It occurs in the cytoplasm of the cell ...*transporters carry glucose molecules to the cells*
- ❖ It is a hub of carbohydrate metabolism because all sugars (whether from diet or via catabolic reactions) can be converted to glucose



- <http://www.bioinfo.org.cn/book/biochemistry/chapt14/sim1.htm> -





Glycolysis



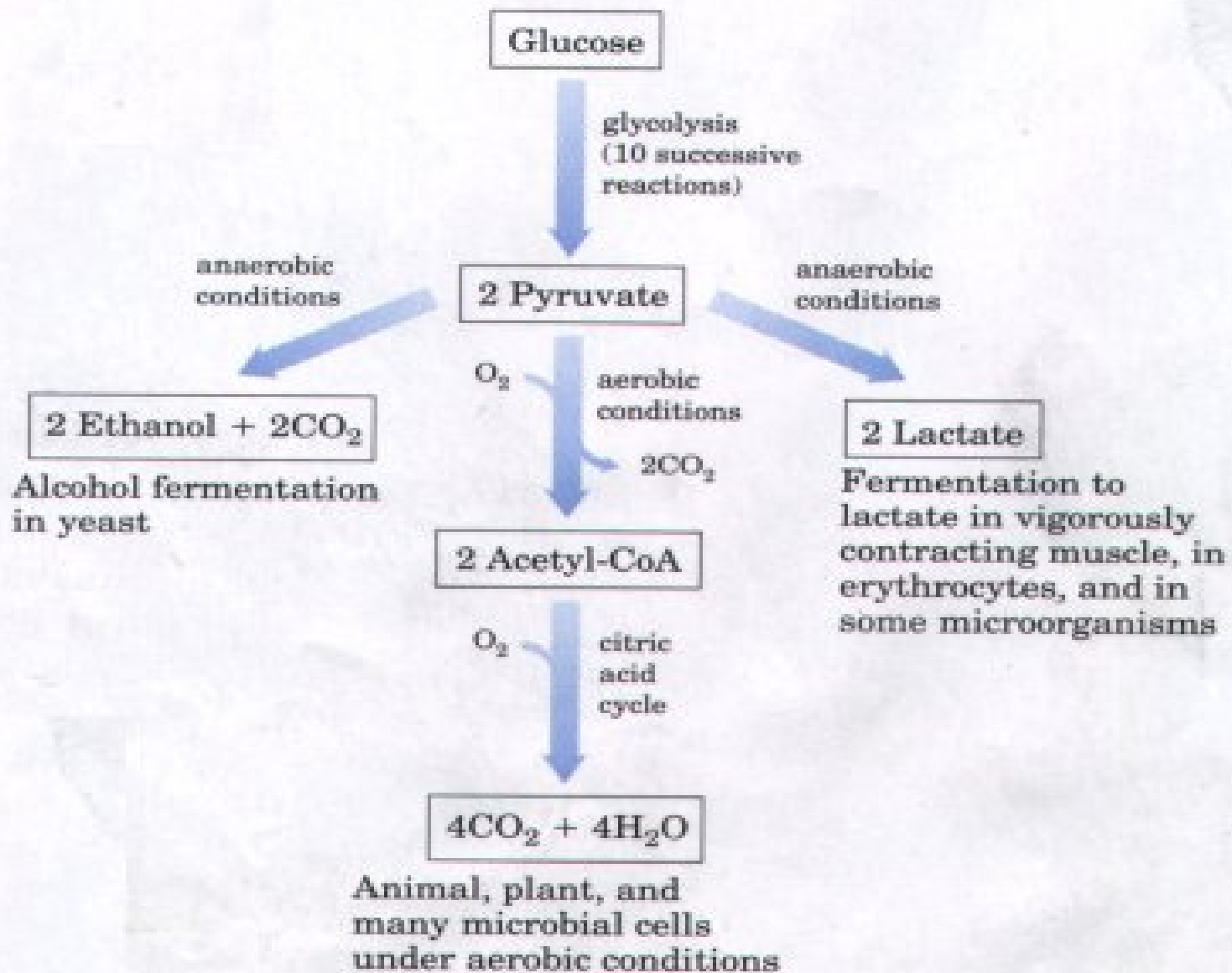
Total Input	Total Output
1 molecule of glucose (6 C)	2 molecules pyruvate (3 C)
2 ATP	4 ATP
4 ADP	2 ADP
2 NAD	2 NADH ₂
2 P _i	2 H ₂ O

Net gain = 2 ATP

Glycolysis



- ❖ The fate of pyruvate depends on the availability of oxygen
- ❖ If oxygen is present, pyruvate enters the mitochondria and will be oxidized to carbon dioxide and water (aerobic respiration)
- ❖ If oxygen is absent then pyruvate is converted into alcohol or lactate (anaerobic respiration)



Aerobic Respiration





❖ This involves two phases

1. Oxidative decarboxylation of pyruvate – removal of CO_2 and oxidation (removal of hydrogen)
2. Carboxylation of pyruvate to oxaloacetate – the addition of CO_2

Oxidative Decarboxylation of Pyruvate



- ❖ Occurs in the mitochondria (matrix)
- ❖ Pyruvate + coenzyme A (CoASH) + NAD^+

\downarrow pyruvate dehydrogenase
acetyl CoA + CO_2 + $\text{NADH} + \text{H}^+$
- ❖ Acetyl CoA  TCA cycle
- ❖ $\text{NADH} + \text{H}^+$  respiratory chain in the mitochondria

Oxidative Decarboxylation of Pyruvate

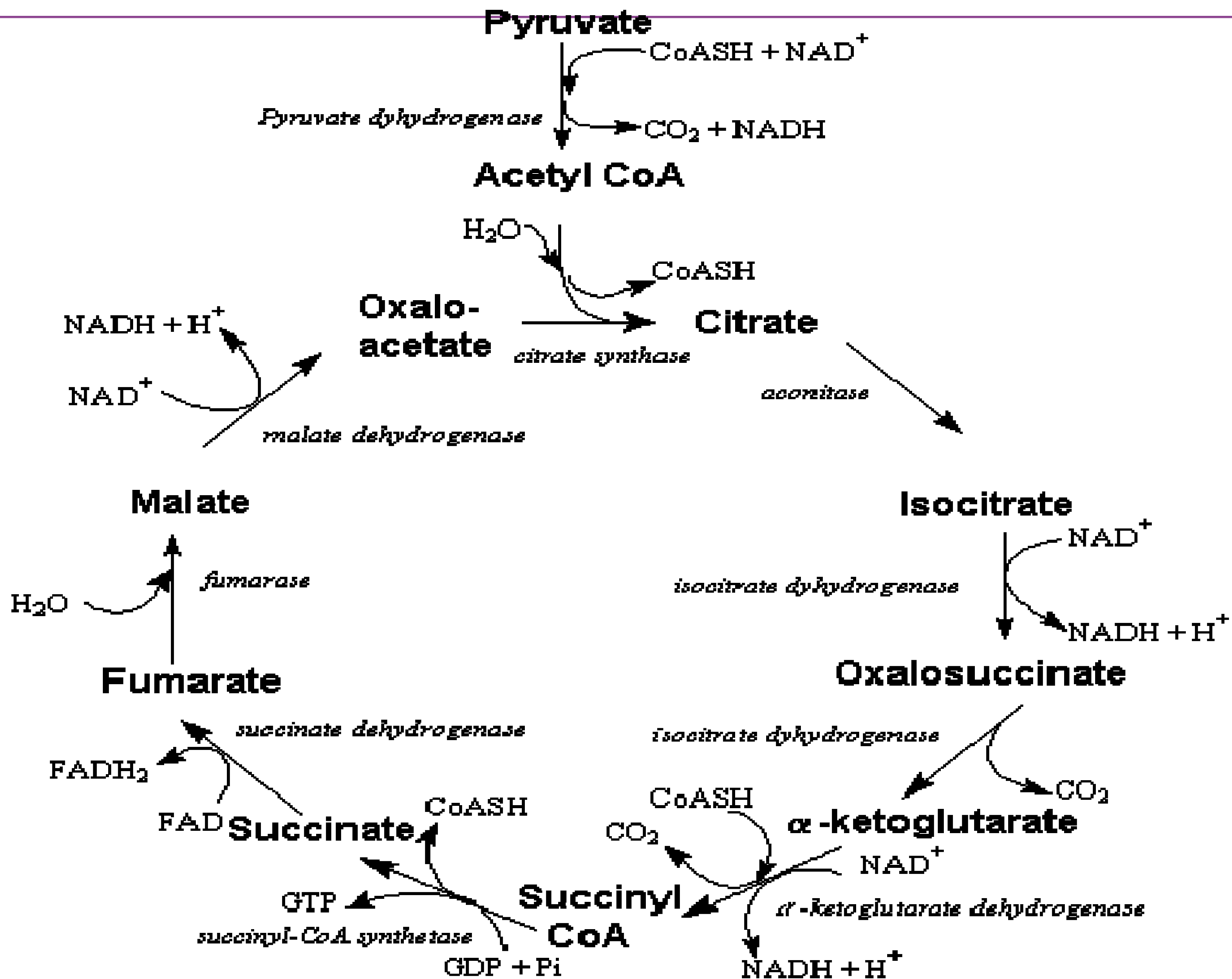


- ❖ A deficiency in pyruvate dehydrogenase leads to lactic acidosis
- ❖ Due to the prevention of acetyl CoA formation from pyruvate
- ❖ The pyruvate therefore forms lactic acid
- ❖ TCA cycle provides most of the energy needed for the brain
- ❖ Since the TCA process is hindered
- ❖ This results in the developmental defects of the brain and nervous system

Carboxylation of Pyruvate



- ❖ This is called **tricarboxylic acid (TCA) cycle/ Krebs cycle/ citric acid cycle**
- ❖ Acetyl CoA is hydrolyzed to form acetyl
- ❖ Acetyl + oxaloacetate \longrightarrow citrate
(2 C) (4 C) (6 C)
- ❖ A series of reaction then follows which results in the formation of 2 molecules of CO_2 and 1 molecule of ATP



Energy from Acetyl CoA



Energy producing reaction	Number of ATP produced
$3 \text{ NADH} \longrightarrow 3 \text{ NAD}^+$	9
$\text{FADH}_2 \longrightarrow \text{FAD}$	2
$\text{GDP} + \text{P}_i \longrightarrow \text{GTP}$	1
	<hr/>
	12 ATP/acetyl CoA oxidized

Carboxylation of Pyruvate



- ❖ Since the oxidation of 1 molecule glucose



2 molecules of acetyl CoA

- ❖ The TCA cycle occurs twice for every molecule of glucose oxidized
- ❖ The net result is 2 ATP and 4 CO₂
- ❖ The overall reaction for glycolysis, acetyl CoA formation and TCA cycle is



Anaerobic Respiration



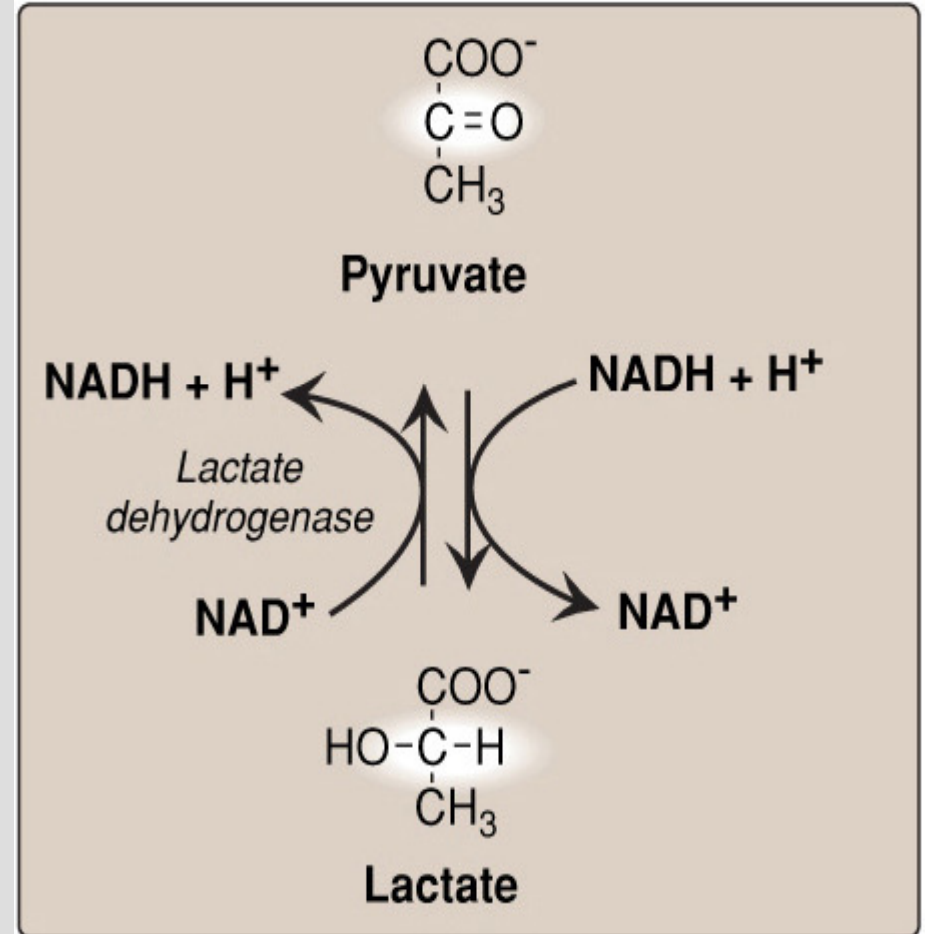
In Plants



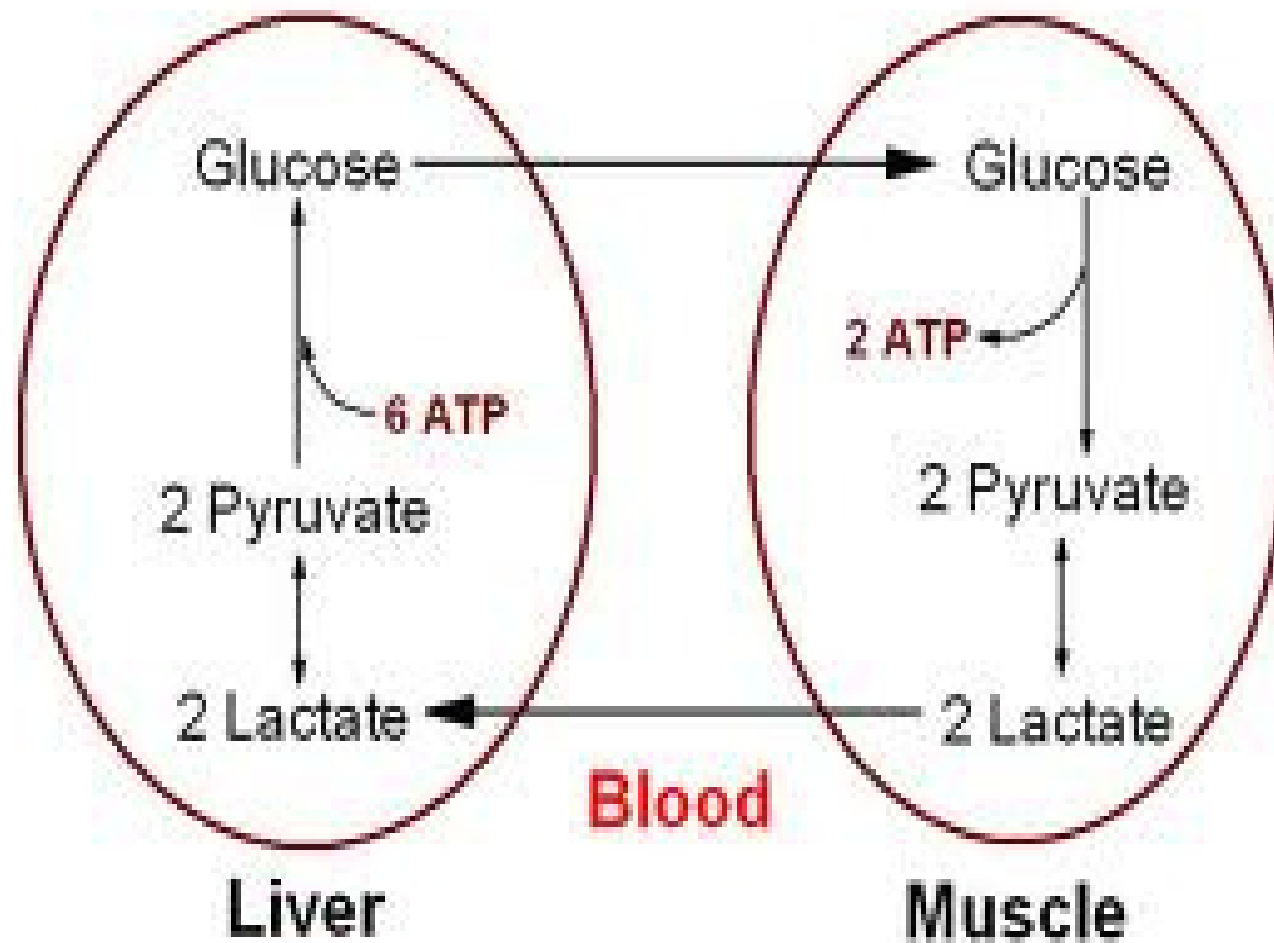
- ❖ This occurs in yeast cells and other microorganisms

Anaerobic Respiration

- ❖ **In Animals ...** Pyruvate is converted to lactate
- ❖ The reaction is catalysed by lactate dehydrogenase
- ❖ This occurs in the red blood cells, exercising muscles and anoxic tissues



The Cori Cycle



Electron Transport Chain

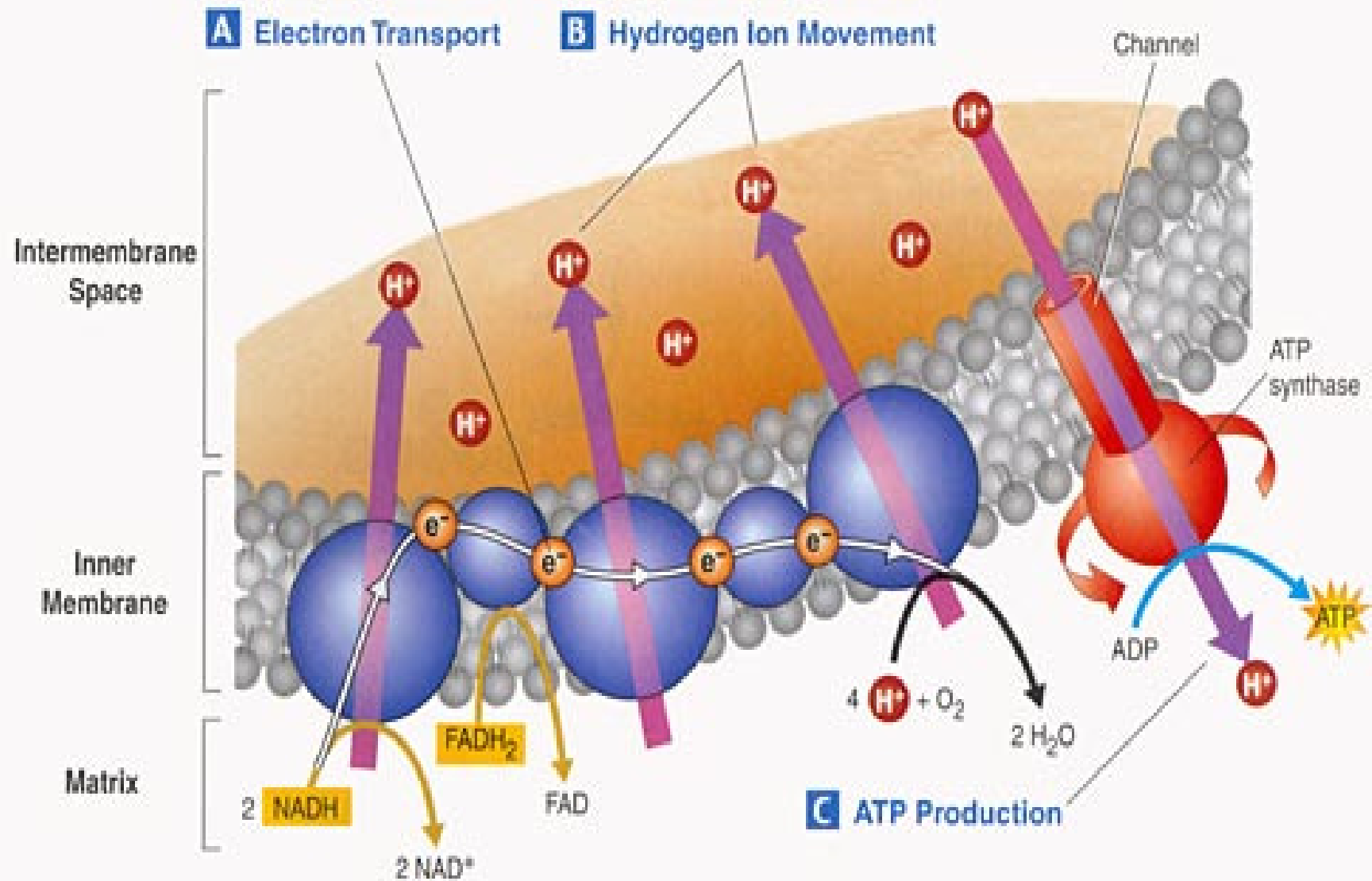


- ❖ The reaction occurs in the inner mitochondrial membrane
- ❖ Electrons from intermediates in Glycolysis and the TCA cycle are donated to specific coenzymes (NAD^+ and FAD) to form energy rich reduced co-enzymes (NADH and FADH_2)
- ❖ Each reduced co-enzyme donate a pair of electrons to electron carriers (flavoprotein, coenzyme Q, cytochromes a, b, and c)
- ❖ As electrons are passed down the chain they lose some of their free energy
- ❖ At the end of the chain, hydrogen combines with oxygen to form water

Oxidative Phosphorylation



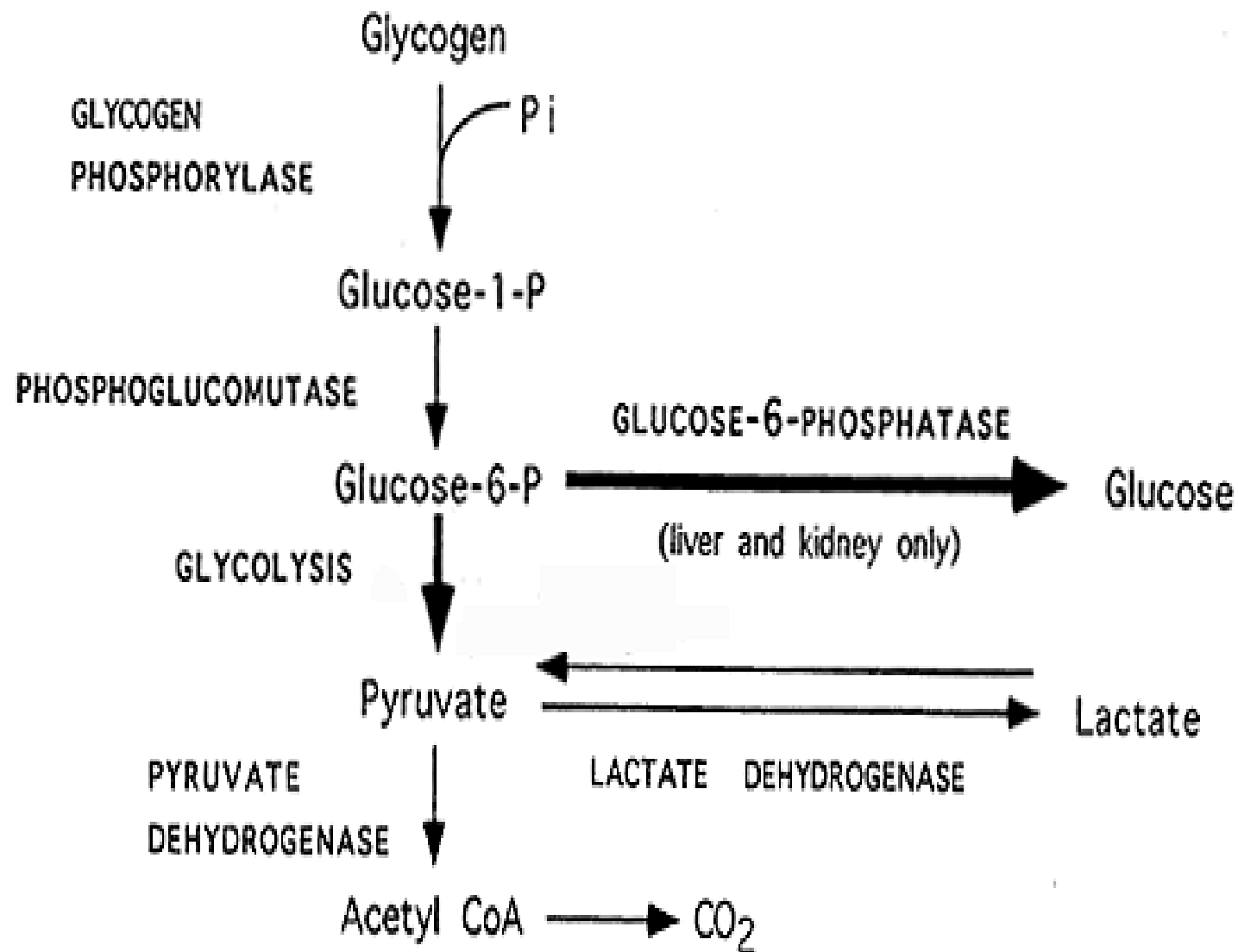
- ❖ Oxidative phosphorylation is the process by which ATP is formed as a result of the transfer of electrons from NADH and FADH₂
- ❖ The reaction occurs in the inner mitochondrial membrane



Glycogenolysis



- ❖ This is the breakdown of glycogen in the liver and skeletal muscle to produce glucose
- ❖ It is not the reversal of glycogen synthesis (glycogenesis)



In-borne Errors of Metabolism



- ❖ Skeletal muscle - glycogen phosphorylase deficiency results in **McArdle syndrome** (Cori Type V)
- ❖ Symptoms include –
 - (a) temporary weakness and cramping of skeletal muscle after exercise
 - (b) no rise in blood lactate after strenuous exercise
 - (c) High levels of glycogen

In-borne Errors of Metabolism



- ❖ Glucose-6-phosphatase deficiency results in **Von Gierke disease**
(Cori Type 1a)
- ❖ Symptoms include –
 - (a) severe fasting hypoglycaemia
 - (b) progressive renal disease
 - (c) increased stored glycogen

Glycogen Metabolism



- ❖ Glycogen metabolism is regulated by the hormones insulin, glucagon and epinephrine
- ❖ Insulin (β -cells pancreas) induces the synthesis of glycogen when the blood glucose concentration is high
- ❖ Glucagon and epinephrine induces the breakdown of glycogen when the blood glucose concentration is low
- ❖ Epinephrine (adrenal medulla) stimulates glycogen breakdown in the muscle
- ❖ Glucagon (α -cells pancreas) stimulates glycogen breakdown in the liver

Pentose Phosphate Pathway



- ❖ Also called the **hexose monophosphate shunt** or **6-phosphogluconate pathway**
- ❖ The reaction occurs in the cytosol of the cell
- ❖ The reaction produces **NADPH** and 5-C sugars
- ❖ The pathway is divided into two portions
 - (a) Irreversible oxidative reactions
 - (b) Reversible non oxidative reactions

Irreversible Oxidative Reactions



- ❖ This portion results in the formation of ribulose-5-phosphate, CO₂ and NADPH per molecule of glucose-6-phosphate oxidized
- ❖ **NADPH** needed for the synthesis of steroids, fatty acid synthesis, drug metabolism and to keep **glutathione** in the reduced form in the erythrocytes

Reversible Non oxidative Reactions

- ❖ This set of reaction occurs in all cell types

Ribose-5-phosphate

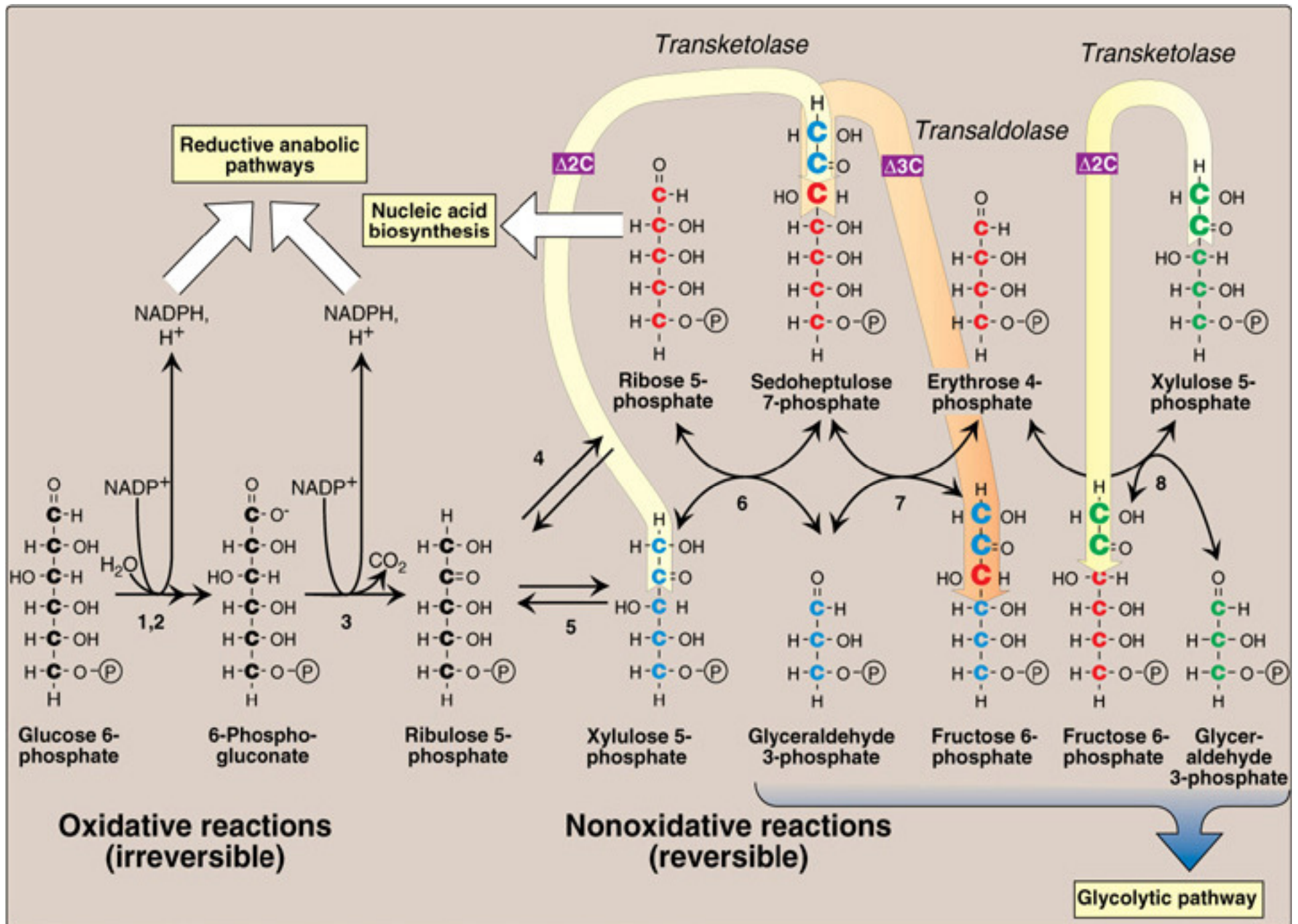


nucleotide synthesis

Glyceraldehyde-3-phosphate and fructose-6-phosphate



intermediate for glycolysis



G6PD Deficiency



- ❖ Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a hereditary disease characterized by haemolytic anaemia
- ❖ This occurs due to the reduction of NADPH formation and thus a decrease in [reduced glutathione]
- ❖ Reduction in the detoxification of free radicals
- ❖ Reduced glutathione helps to prevent the formation of denatured proteins that will attach to the red blood cells and damage to the cell wall resulting in haemolysis

Gluconeogenesis



- ❖ This is the synthesis of glucose from non carbohydrate precursors
- ❖ The major non carbohydrate precursors are
 - (1) Lactate – formed from pyruvate under anaerobic conditions
 - (2) Amino acid – digestion of proteins and breakdown of proteins from skeletal muscles during starvation
 - (3) Glycerol – hydrolysis of triglycerides
- ❖ This process provides a continuous supply of glucose as metabolic fuel
- ❖ Areas that need this continuous supply includes the brain, red blood cells, kidney medulla, lens and cornea of the eye, testes and exercising muscles

Gluconeogenesis



- ❖ Stored glycogen can only provide 10 – 18 h of glucose
(Glycogenolysis) in the absence of carbohydrate intake from the diet
- ❖ During an overnight fast
 - 90% of gluconeogenesis occurs in liver
 - 10% of gluconeogenesis occurs in kidneys
- ❖ In longer period of starvation glucose must be formed from non carbohydrate sources
- ❖ Gluconeogenesis requires both mitochondrial and cytosolic enzymes
 - Pyruvate carboxylase is a mitochondrial enzyme*

