

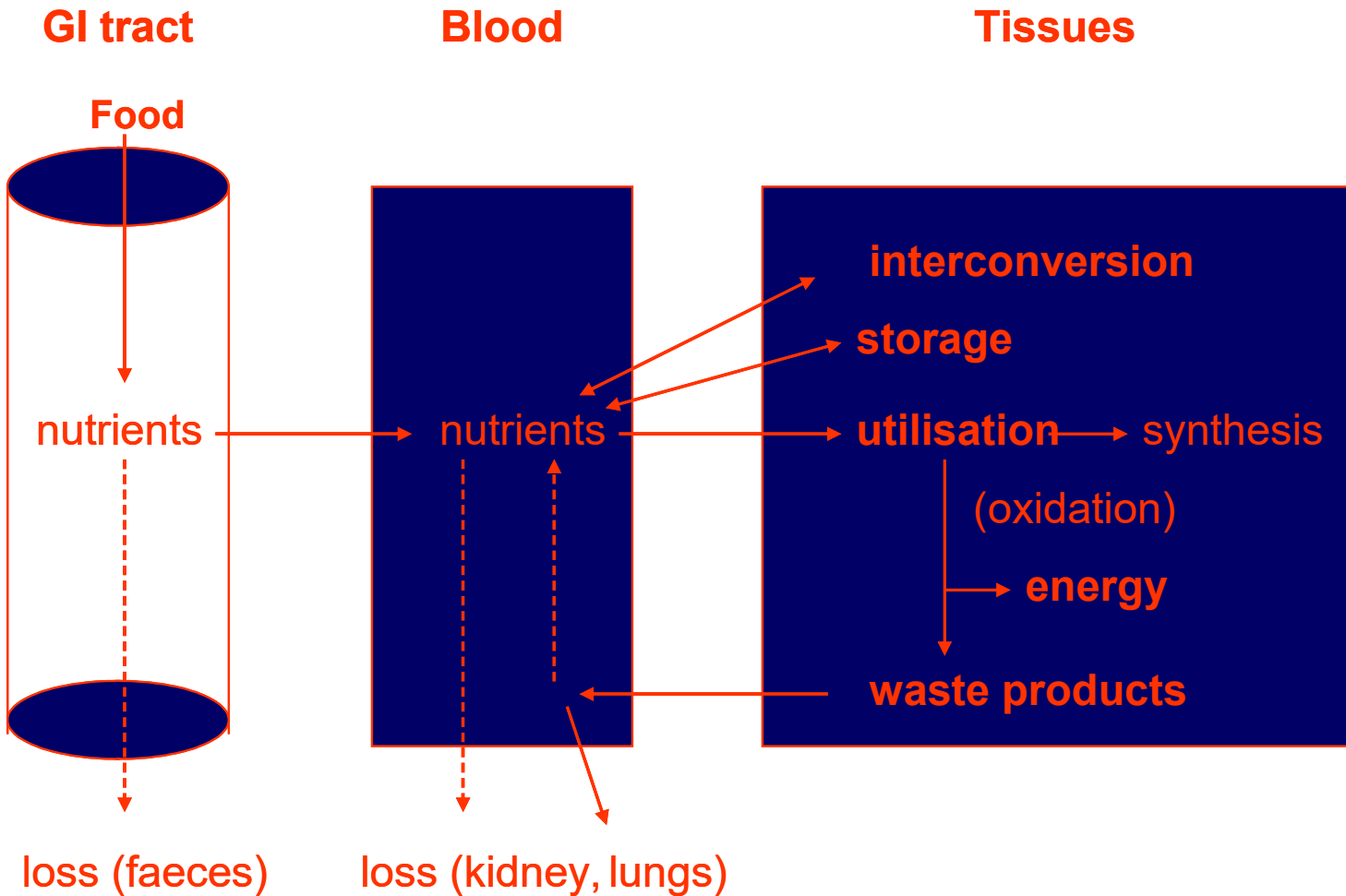
Session 2  
Lecture 1  
Introduction of Metabolism

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# Metabolism

- Is the processes which derive energy and raw materials from food stuffs and use them to support repair, growth and activity of the tissues of the body

# Overview



# Cell metabolism

- A great deal of metabolic activity goes on
- Some things happen in virtually all cells
- Other things in only some cells
- Reactions organised into distinct, but integrated **metabolic pathways**

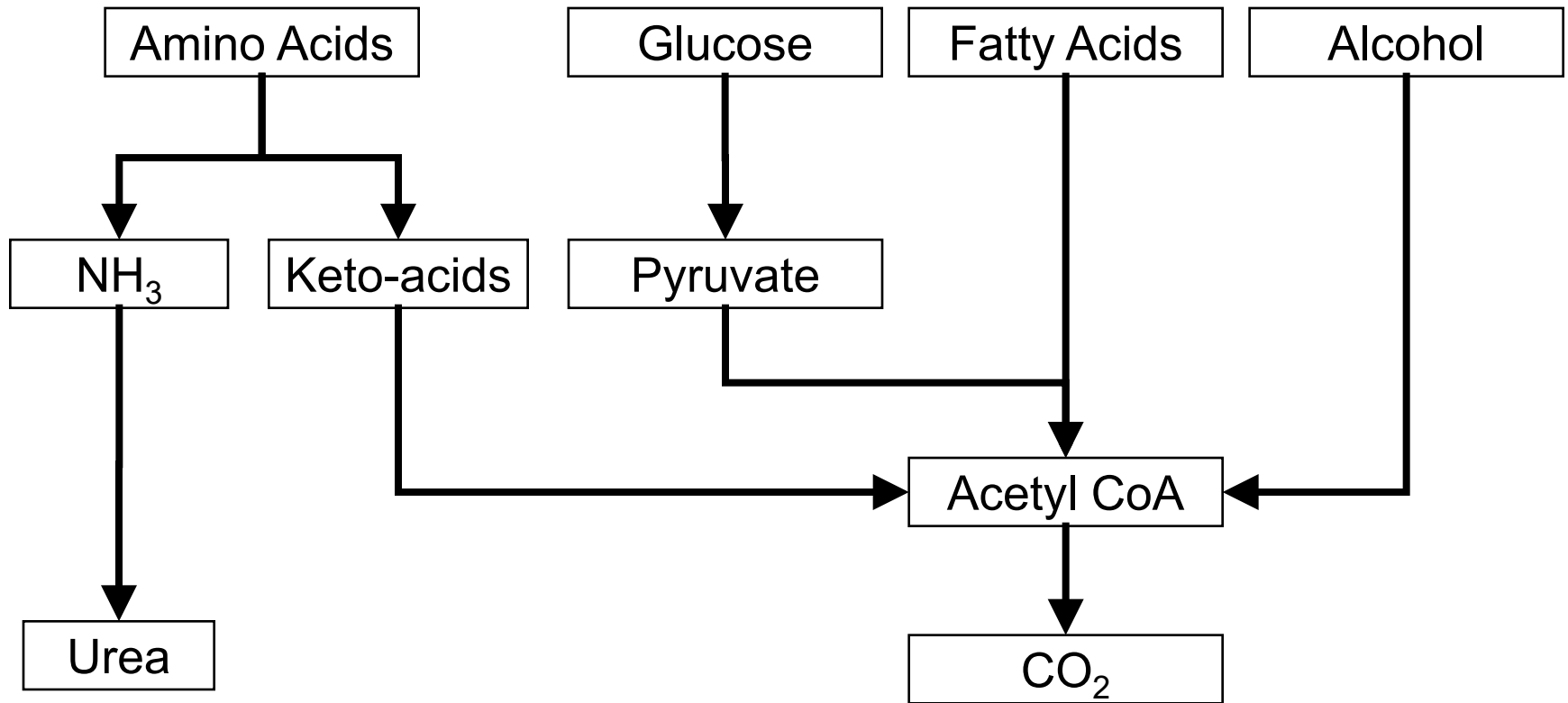
# Metabolic pathways

- Chemicals involved in pathways
  - Metabolites
- Lots of different reactions
  - Few reaction types
  - Small number of molecules in central role
  - Pathways often localised to particular cell compartments
- Pathways are described using metabolic maps
  - Starting points & end points
  - Intermediates
  - Connections

# Breaking things and making things

- Catabolic pathways
  - Break down larger molecules into smaller
  - Oxidative (release H - “reducing power”)
  - Release energy
- Anabolic pathways
  - Build up large molecules from small ones
  - Reductive (use H)
  - Use energy released from catabolism

# Simple Metabolic Map



# Catabolic reactions

- Are oxidative
- Release energy



# Biological oxidation

- Oxidative reactions
  - Oxidation is removal of electrons
  - In biological reactions removal of hydrogen atoms ( $\text{H}^+ + \text{e}^-$ )
  - Often remove two hydrogen atoms
- Redox
  - Hydrogen atom reacts immediately with something else
- Carriers
  - When fuel molecules are oxidised hydrogen atoms are transferred to **carrier molecules**
  - Which carry **reducing power** to other reactions

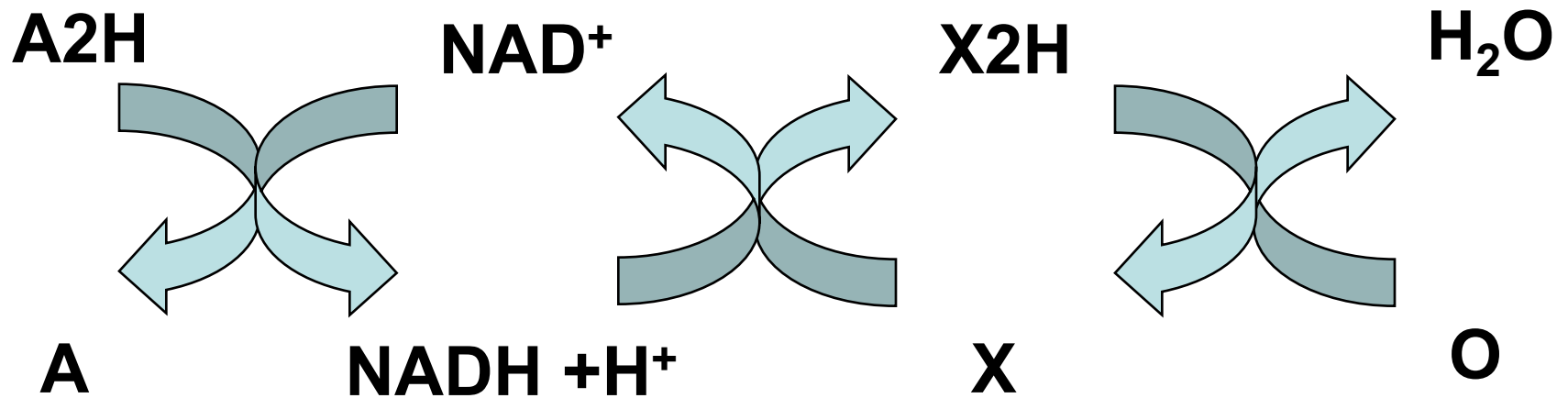
# Major H-carrier molecules

	Oxidised form	Reduced form
• Nicotinamide adenine dinucleotide	• $\text{NAD}^+$	$\text{NADH}$
• Nicotinamide adenine dinucleotide phosphate	• $\text{NADP}^+$	$\text{NADPH}$
• Flavin adenine dinucleotide	• $\text{FAD}^+$	$\text{FADH}$

# H-carrier molecules

- Total of oxidised and reduced form in cells constant
- Pathways which convert oxidised to reduced form must be matched by other pathways converting reduced to oxidised form
- Otherwise reactions will stop

# H-carriers



# Catabolic reactions

- Are oxidative
- Release energy

# Energy

- Exergonic reactions release energy
- Cannot all be used by the cell
  - Some lost by decrease in entropy
- Rest available to do work
  - Free energy or Gibbs Free Energy ( $\Delta G$ )
- When energy is released  $\Delta G$  is negative

# Coupling

- Metabolism is all about coupling the energy released by exergonic reactions to that needed for endergonic reactions
- Needs an intermediate process
  - The ADP/ATP cycle

# Adenosine triphosphate

- Adenine-ribose-phosphate-phosphate-phosphate
- Phosphate-phosphate bond high energy of hydrolysis
- Can give up lots of energy to drive other reactions
- $\text{ATP}^{4-} + \text{H}_2\text{O} \rightleftharpoons \text{ADP}^{3-} + \text{HPO}_4^{2-} + \text{H}^+$



# Standard free energy change

- Under standard conditions
  - Temperature 25 deg C
  - Pressure 101 kPa
  - pH 7.0
  - Concentrations of reactants and products  $1\text{mol.l}^{-1}$
- Standard free energy change ( $\Delta G^{\circ'}$ )
- Conditions in cells not standard

# $\Delta G^{\circ'}$ for ATP ADP hydrolysis

- $\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i$ 
  - $\Delta G = -31 \text{ kJ.mol}^{-1}$
- $\text{ADP} + \text{H}_2\text{O} \rightarrow \text{AMP} + \text{P}_i$ 
  - $\Delta G = -31 \text{ kJ.mol}^{-1}$
- This energy can drive endergonic reactions

# Phosphorylated compounds

- Many phosphorylated compounds have high energies of hydrolysis (large negative  $\Delta G$ )
- Can form a hierarchy
  - Phosphoenolpyruvate –  $\Delta G$  -62 kJ.mol<sup>-1</sup>
  - Creatine phosphate –  $\Delta G$  -43 kJ.mol<sup>-1</sup>
  - ATP  $\Delta G$  -31 kJ.mol<sup>-1</sup>

# Balancing catabolism and anabolism

- Catabolic pathways increase intra-cellular concentrations of
  - Reduced H carriers (eg NADH)
  - Phosphorylated high energy carriers (ATP)
- Anabolic pathways increase intra-cellular concentrations of
  - Oxidised H carriers (eg NAD<sup>+</sup>)
  - Hydrolysed high energy carriers (ADP)

# Energy signals

- Cell must respond to 'low energy signals'
  - Increased oxidised H carriers
  - Increased hydrolysed energy carriers
- By increasing catabolism
- And vice versa for 'high energy signals'
  - Increased reduced H carriers
  - Increased phosphorylated energy carriers

# Energy stores in cells

- Some cell types need to increase metabolic activity very quickly (eg muscle)
- Need a reserve of high energy stores
  - Can be called on immediately
- Use Creatine phosphate

# Creatine Phosphate

- Creatine + ATP  $\leftrightarrow$  Creatine Phosphate + ADP
- Catalysed by **creatine kinase**
- When ATP plentiful reaction goes forward
- If ATP concentration falls suddenly, reaction reverses providing short term boost to [ATP]

# Creatine Kinase

- In different forms in different muscles
  - Different sub-units in molecule
- One specific to heart muscle
- Released from cells if they are damaged, in myocardial infarction (heart attack)
- Appears in blood after a few hours
- Diagnostic of MI



# Creatinine

- Breakdown product of creatine
- Produced at very constant rate
  - Unless muscle is wasting
- Excreted via kidneys
- Urine concentration a marker of urine dilution
- Can be used to estimate true urinary loss of many substances
  - Eg hormones in pregnancy

# Clinical importance of creatine phosphate

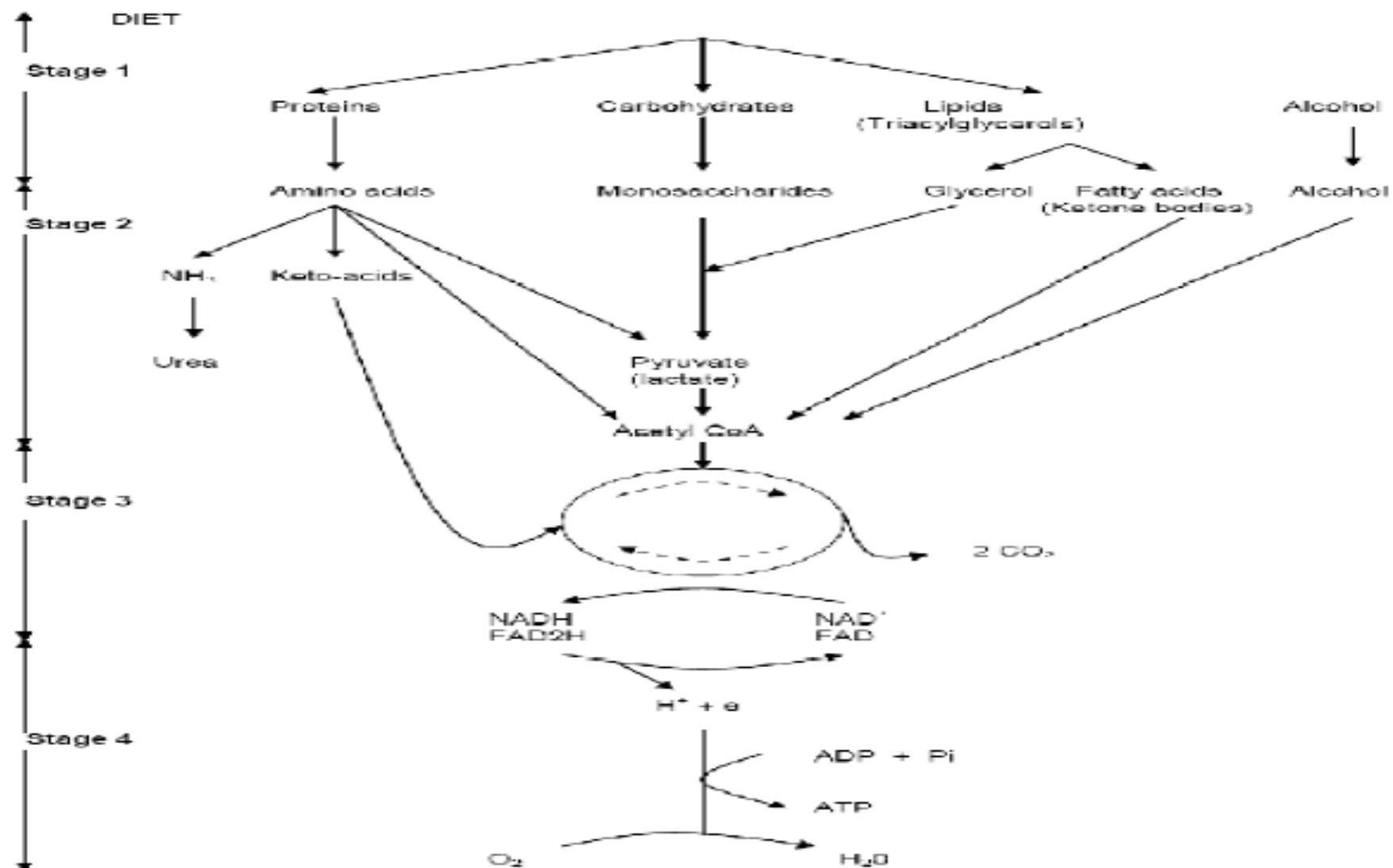
- Amount in body determined by to muscle mass

# Session 2

## Lecture 2

# Carbohydrate Metabolism 1

# Overview of Catabolism



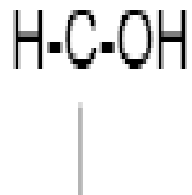
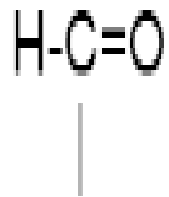
Dietary carbohydrates

# Carbohydrates

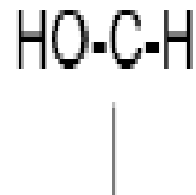
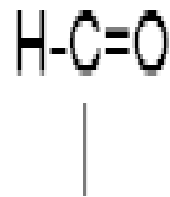
- They have the formula  $(CH_2O)_n$
- Contain  $-CHO$  or  $-C=O$  groups and several  $-OH$  groups
- Classified as mono, di and poly carbohydrates
- Constitutes the major part of our diet

# Monosaccharides

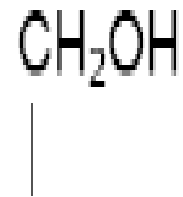
- May be trioses, pentoses, hexoses or others



D-glyceraldehyde



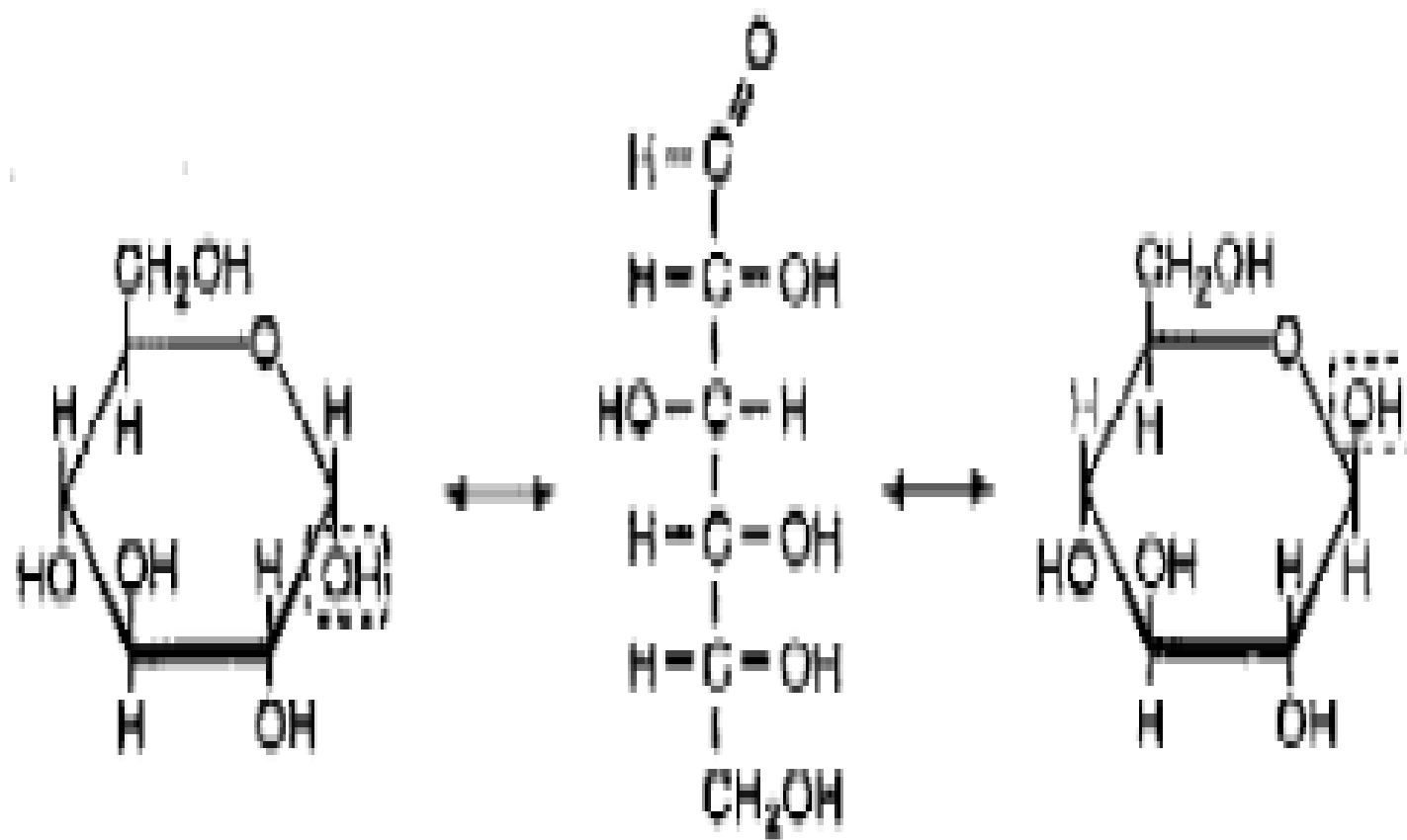
L-glyceraldehyde



dihydroxyacetone

# Monosaccharides

- They have at least one asymmetric carbon atom, accordingly they are classified into D and L isomers
- May contain 3, 4, 5, 6, 7, 8 or 9 carbon atoms
- Form ring structures
- Hydrophilic, do not readily cross cell membran
- May be partially oxidized, need less O<sub>2</sub>



$\alpha$ -D-glucose (ring)    D-glucose (open chain)     $\beta$ -D-glucose (ring)



# Most important Saccharides for human

- Monohexoses  
Glucose, Fructose and Galactose
- Disaccharides  
Maltose, Lactose and Sucrose
- Polysaccharides  
Starch and Glycogen

# Stage 1 of Carbohydrate metabolism: (Digestion and absorption)

## Digestion

- Start in oral cavity by salivary amylase
- Continued in the duodenum by pancreatic amylase
- Completed in duodenum and jejunum by maltase, lactase, isomaltase and others

# Absorption

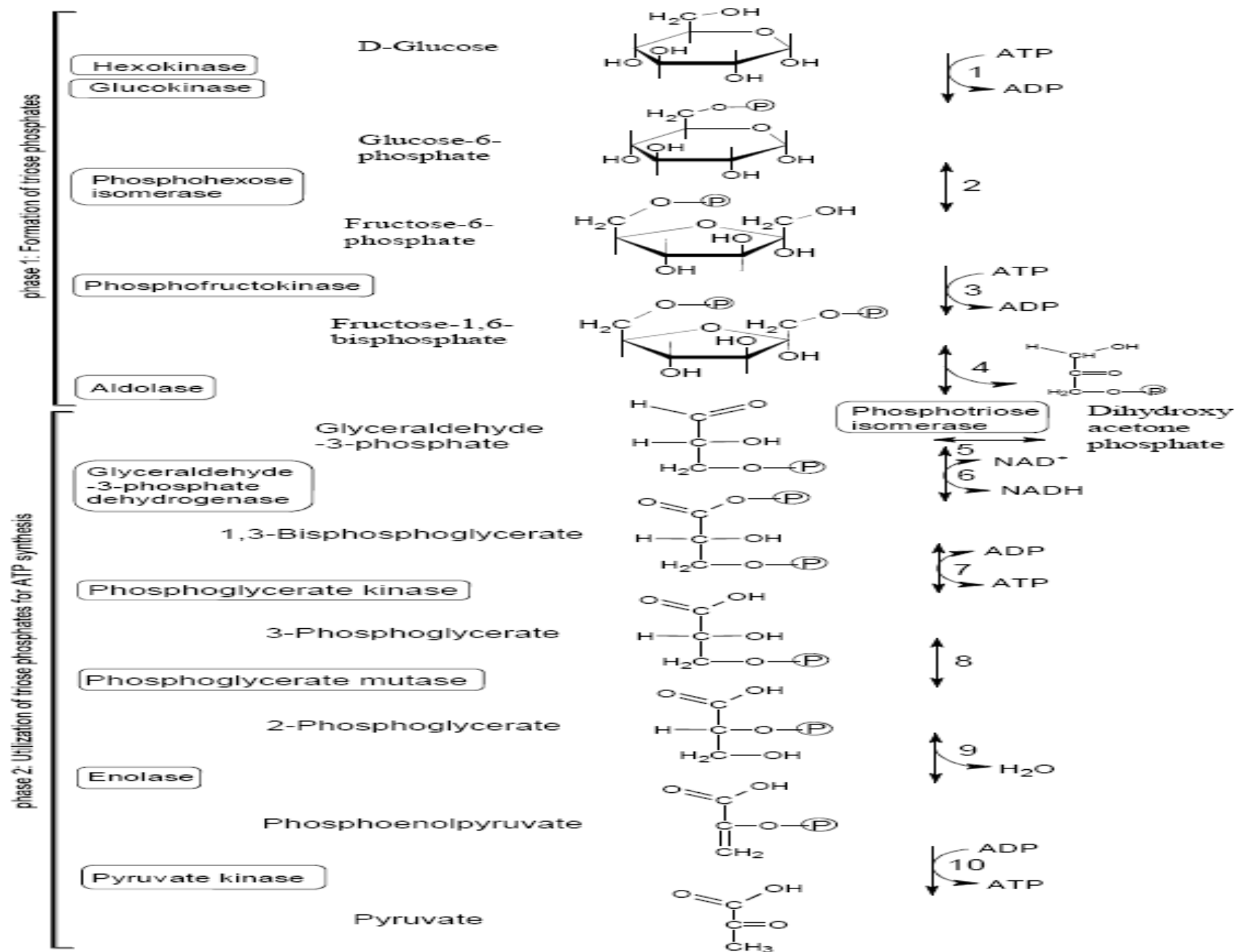
- It is carried out from the gut to the absorptive cells by active transport
- From the absorptive cells to other cells by facilitated diffusion Which need glucose transporters (GLUT 1 to 5)
- Synthesis of some transporters are is enhanced by insulin (GLUT 4) in muscles and adipose tissues

# Stage 2 of Carbohydrate Metabolism

Starts with glycolysis

It is characterized by:

- Ten reactions
- In the cytosol
- The function of glycolysis is to produce energy (ATP) and provide cells with essential metabolites, in particular trioses.



**Fig 1: Glycolysis**

# Glycolysis

- Three of them are irreversible, 7 reversible
- May be aerobic or anaerobic
- Conversion of glucose to G-6-P is achieved by 2 enzymes

Glucokinase in liver

Hexokinase in other tissues

# Glycolysis

- Phosphorylation of glucose is important step due to
  - Makes glucose anionic
  - Increase the reactivity of sugare
  - Makes high energetic compounds

# Glycolysis

- Insulin Induces glucose uptake in several tissues in particular muscles and adipose tissues, in other it could not do so
- In red blood cells, the first site of ATP formation may be bypassed. 1,3- bisphosphoglycerate is converted to 2,3-BPG by BPG mutase. 2,3-BPG can bind to hemoglobin, decreasing its affinity for oxygen, and making it available to tissues in some circumstances for example high altitude areas.



# Control of glycolysis

- HK is inhibited by G-6-P
- PFK is inhibited by citrate and by normal cellular concentration of ATP (negative allosteric effector), and induced by 5-AMP (positive allosteric effector). It is also regulated hormonally in liver (insulin stimulates and glucagon inhibits). Reaction 3 is the first reaction unique to glycolysis. It is known as the committing step since it commits glucose to metabolism by glycolysis.
- PK is regulated by covalent modification, thus phosphorylation deactivates this enzyme.

# Significance of lactate production

