

**CARBOHYDRATE
METABOLISM**

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- ✓ Introduction
- ✓ Classification of Carbohydrates
- ✓ Glycolysis
- ✓ Glycogenolysis
- ✓ Glycogenesis
- ✓ Citric acid cycle
- ✓ Pentose phosphate pathway
- ✓ Applied aspects
- ✓ Regulation of Blood glucose

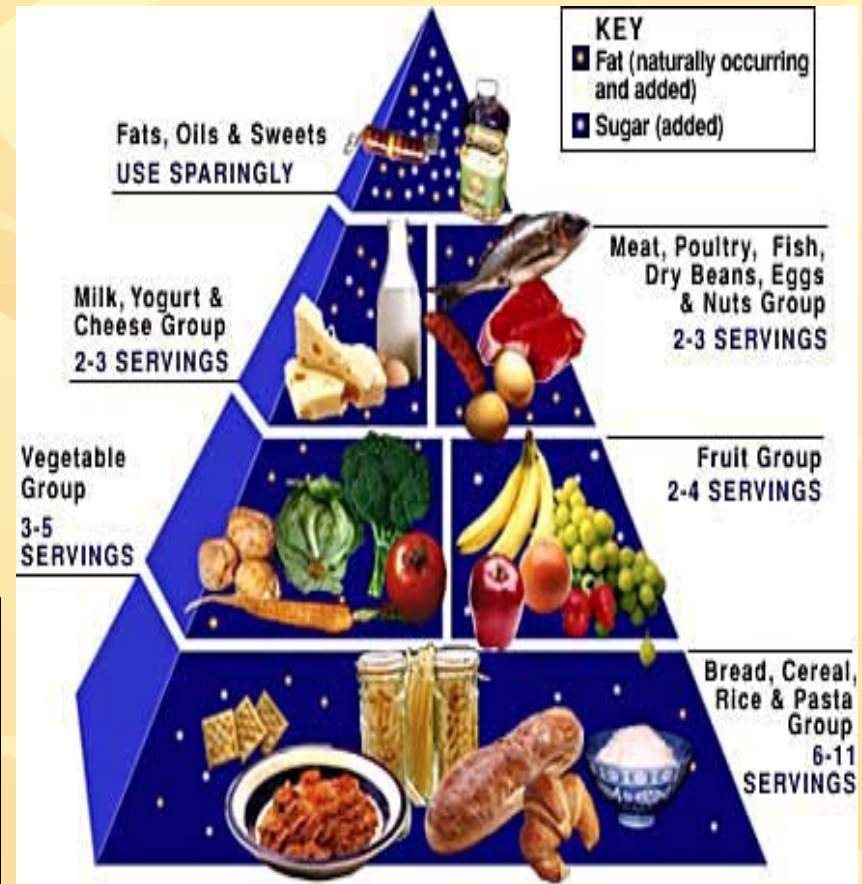
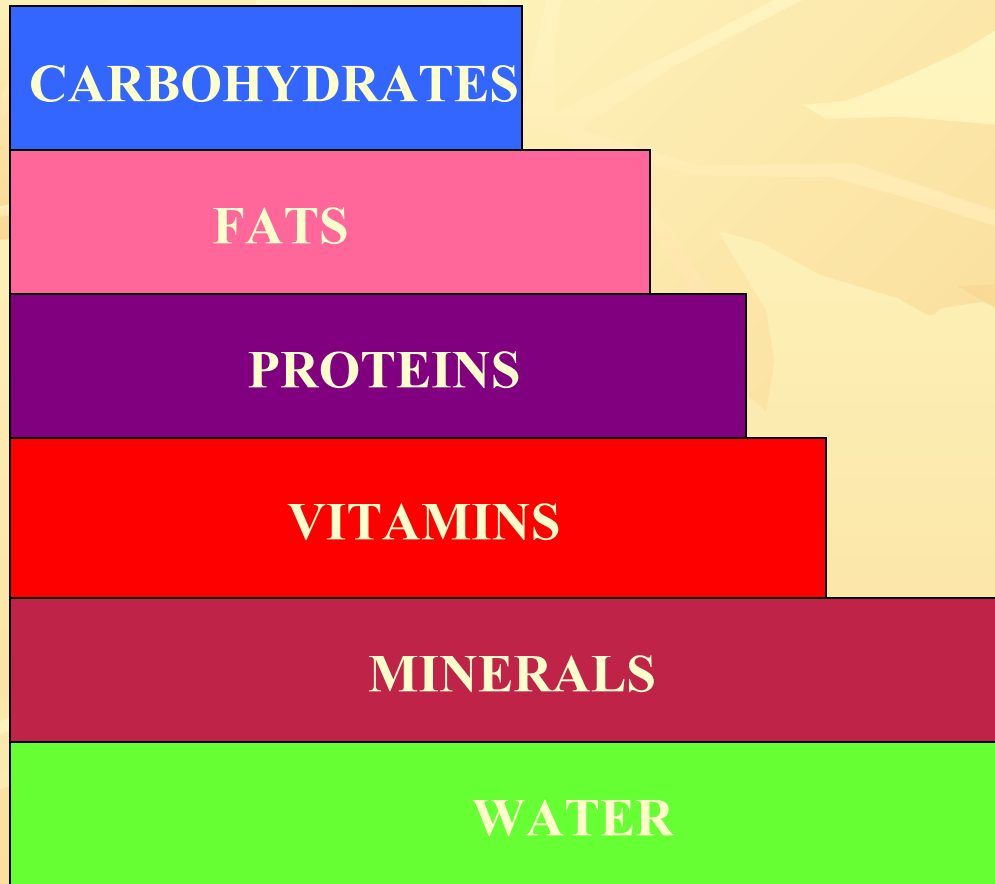


NUTRITION

Nutrition is defined as *“the science of how the body utilizes food to meet requirements for development growth, repair and maintenance”*



NUTRIENTS



Introduction

In plants,

Carbondioxide+water



Glucose

(stored as starch or
converted to cellulose)

In Animals,

Fat + protein



carbohydrate

Biomedical Importance

Glucose is a major carbohydrate

It is a major fuel of tissues

It is converted into other carbohydrates

- ✓ Glycogen for storage.
- ✓ Ribose in nucleic acids.
- ✓ Galactose in lactose of milk.
- ✓ They form glycoproteins & proteoglycans
- ✓ They are present in some lipoproteins (LDL) .
- ✓ Present in plasma membrane:glycocalyx.
- ✓ Glycophorin is a major intergral membrane glycoprotein of human erythrocytes.

Carbohydrates

```
graph TD; Carbohydrates --> Monosaccharides; Carbohydrates --> Disaccharides; Carbohydrates --> Oligosaccharides; Carbohydrates --> Polysaccharide;
```

Monosaccharides

Disaccharides

Oligosaccharides

Polysaccharide

Monosaccharides



Depending on carbon
atoms

- **Trioses:** Glycerose-Aldo
Dihydroxyacetone-Ketone
- **Tetroses** Erythrose (A)
Erythrulose (K)
- **Pentoses:** Ribose (A)
Ribulose (K)
- **Hexoses:** Glucose (A)
Fructose (K)

Depending on aldehyde or
ketone group

• **Aldoses**

• **Ketoses**

• **Disaccharides**

- Maltose
- Sucrose

Oligosaccharides

- Maltotriose

Polysaccharides

- Linear - Starch
- Branched- Dextrin

METABOLISM

The entire spectrum of chemical reactions, occurring in the living system are referred as “**Metabolism**”.

Types of metabolic pathways

- Anabolic pathways: Protein synthesis.
- Catabolic Pathways: Oxidative phosphorylation.
- Amphibolic pathways: Citric acid cycle.

Food molecules → simpler molecules

Amphibolic pathway

Anabolic

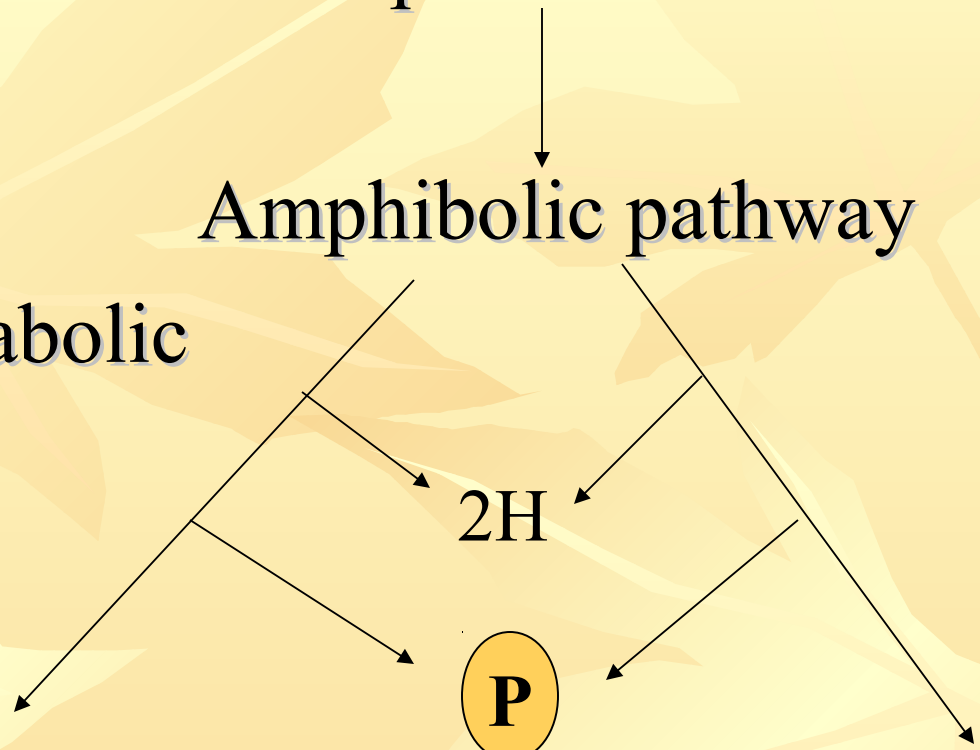
Catabolic

2H

P

Proteins, carbohydrates,
lipids, nucleic acids etc.

CO₂+H₂O



Metabolic pathways may be studied at different levels of organisation.

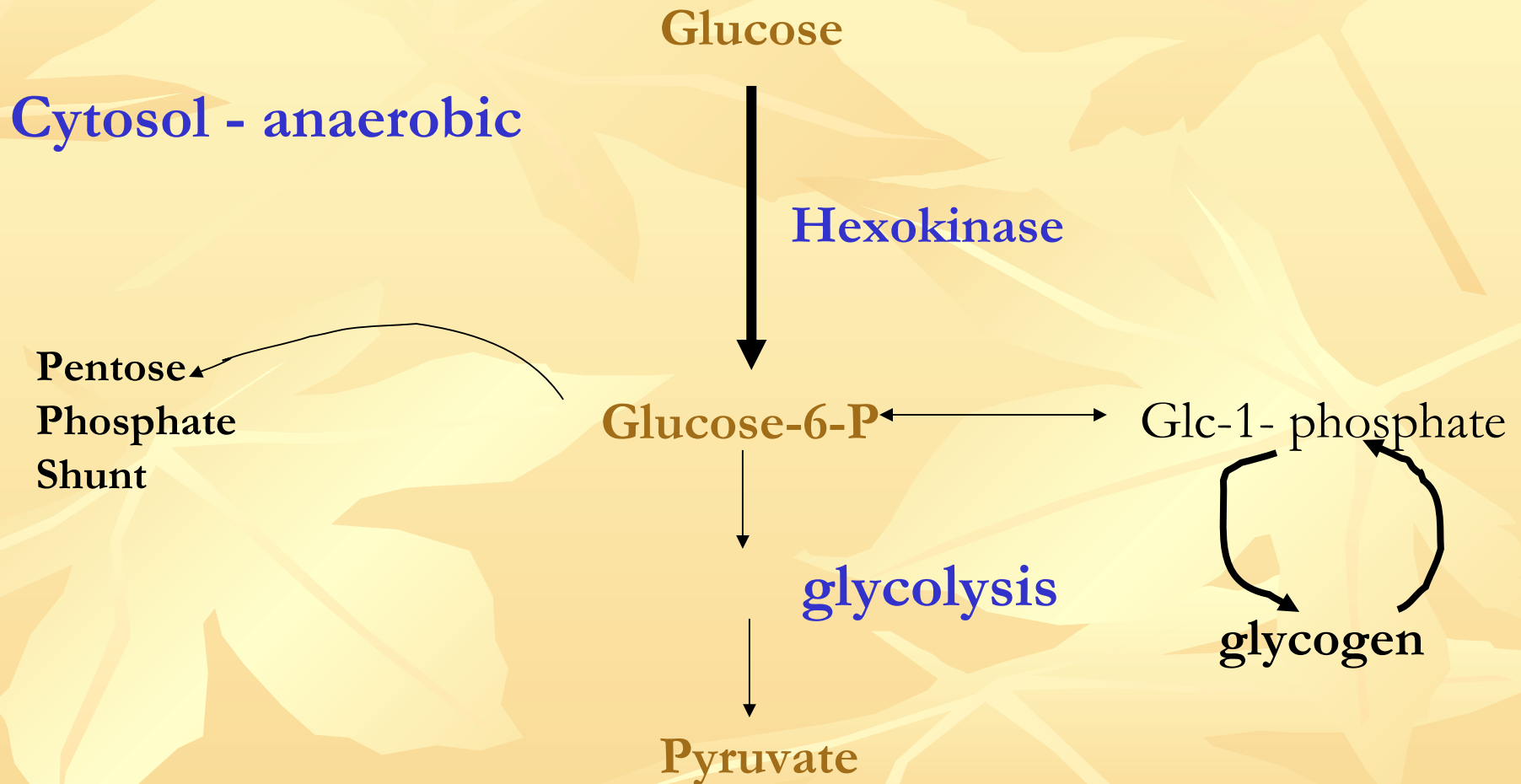
- At tissue level
- At subcellular level

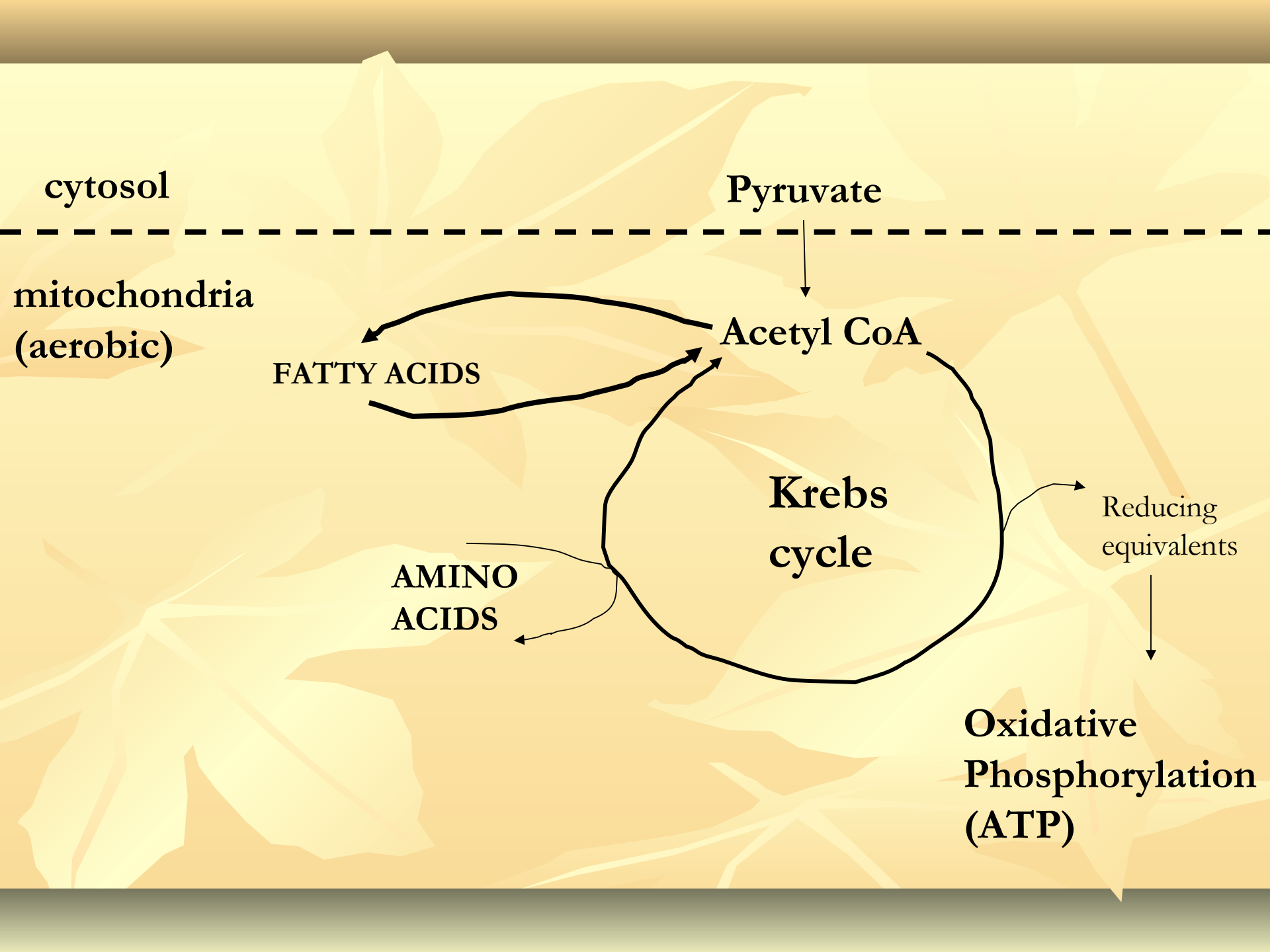


Overview of Carbohydrate Metabolism

Carbohydrates

- Serve as primary source of energy in the cell
- Central to all metabolic processes





cytosol

Pyruvate

mitochondria
(aerobic)

FATTY ACIDS

Acetyl CoA

Krebs
cycle

AMINO
ACIDS

Reducing
equivalents

Oxidative
Phosphorylation
(ATP)



GLYCOLYSIS

Glycolysis

Defn: It is defined as sequence of reactions of glucose to lactate & pyruvate with the production of ATP.

It is derived from greek word *glycose* -sweet or sugar, *lysis*- dissolution.

Site: Cytosolic fraction of cell

GLYCOLYSIS

STAGE I

Glucose

Hexokinase



Glucose-6-phosphate

Phosphoglucose
isomerase



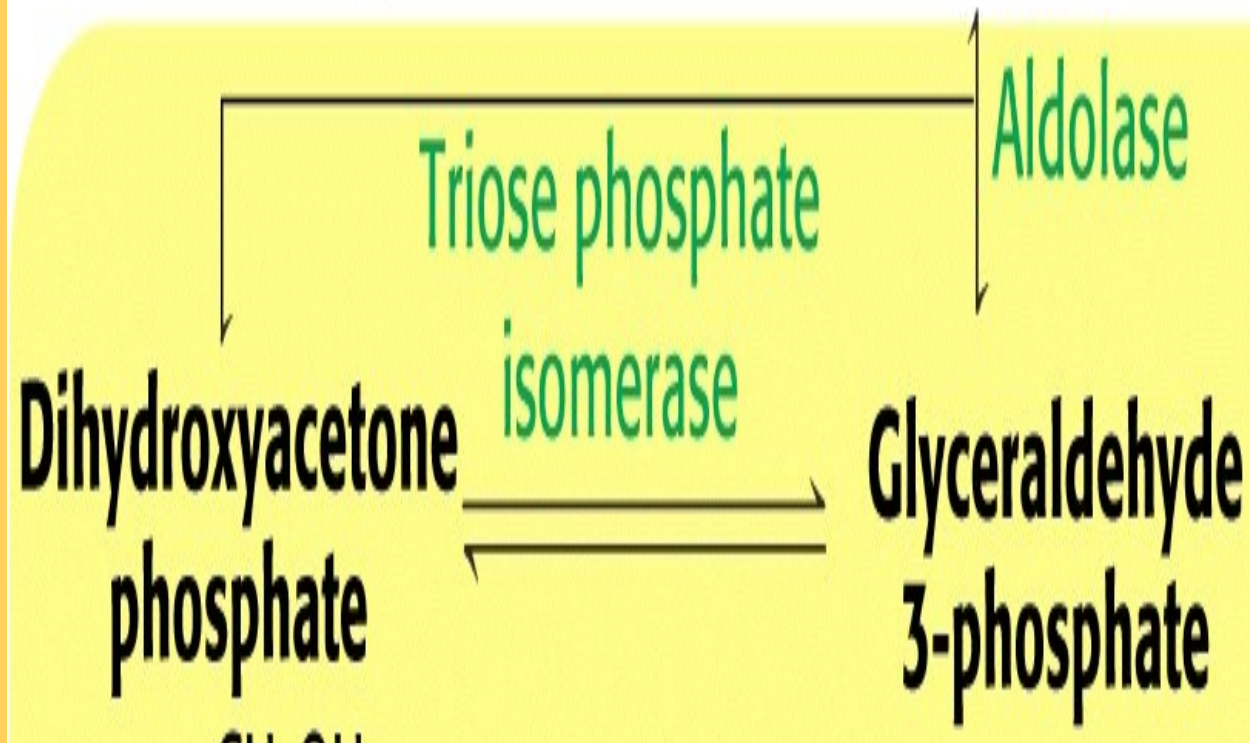
Fructose-6-phosphate

Phospho-
fructokinase

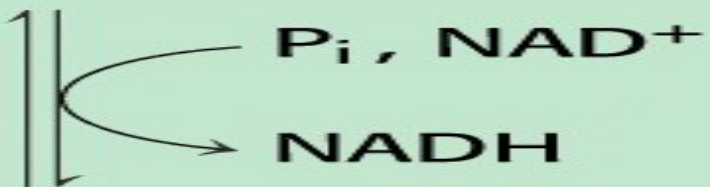


Fructose-1,6-bisphosphate

STAGE II



Glyceraldehyde
3-phosphate
dehydrogenase



1,3-Bisphosphoglycerate

Phosphoglycerate
kinase



3-Phosphoglycerate

Phosphoglycerate
mutase



STAGE III

2-Phosphoglycerate

Enolase



Phosphoenolpyruvate

Pyruvate kinase



Pyruvate

Bioenergetics in Glycolysis:

Total of 8 ATP is formed in glycolysis.

Oxidation of glucose in aerobic condition: 38 ATP

Anaerobic condition: 2 ATP

Biomedical importance of Glycolysis

- Principal route of metabolism.
- Production of acetyl coA in citric acid cycle.
- Metabolism of fructose & galactose.
- Provides ATP in absence of Oxygen.

Clinical Aspects

- Hemolytic Anaemias: Inherited aldolase A & pyruvate kinase deficiencies.
- Skeletal muscle fatigue
- Inherited Pyruvate dehydrogenase deficiency-
Lactic acidosis
- Fast growing cancer cells glycolysis proceeds at faster rate – increased acidic environment-
implication in certain types of cancer.

Metabolism of Glycogen

- ✓ Major storage form of carbohydrate.
- ✓ Glycogenesis: occurs in muscle & liver.

Biomedical importance

- Liver glycogen largely concerned with transport & storage of hexose units.
- For maintenance of blood glucose mainly between meals.

Clinical aspects

Glycogen storage diseases

Type of disorder

Type I (Von Gierke's disease)

Type II (Pompe's disease)

Type III (Cori's disease)

Type IV (Andersen's disease)

Type V (McArdle's disease)

Cause of disorder

Glucose-6-phosphatase deficiency.

Acid maltase deficiency.

Debranching enzyme deficiency.

Branching enzyme deficiency.

Muscle phosphorylase deficiency.

Type VI (Her's disease)

**Liver phosphorylase
deficiency.**

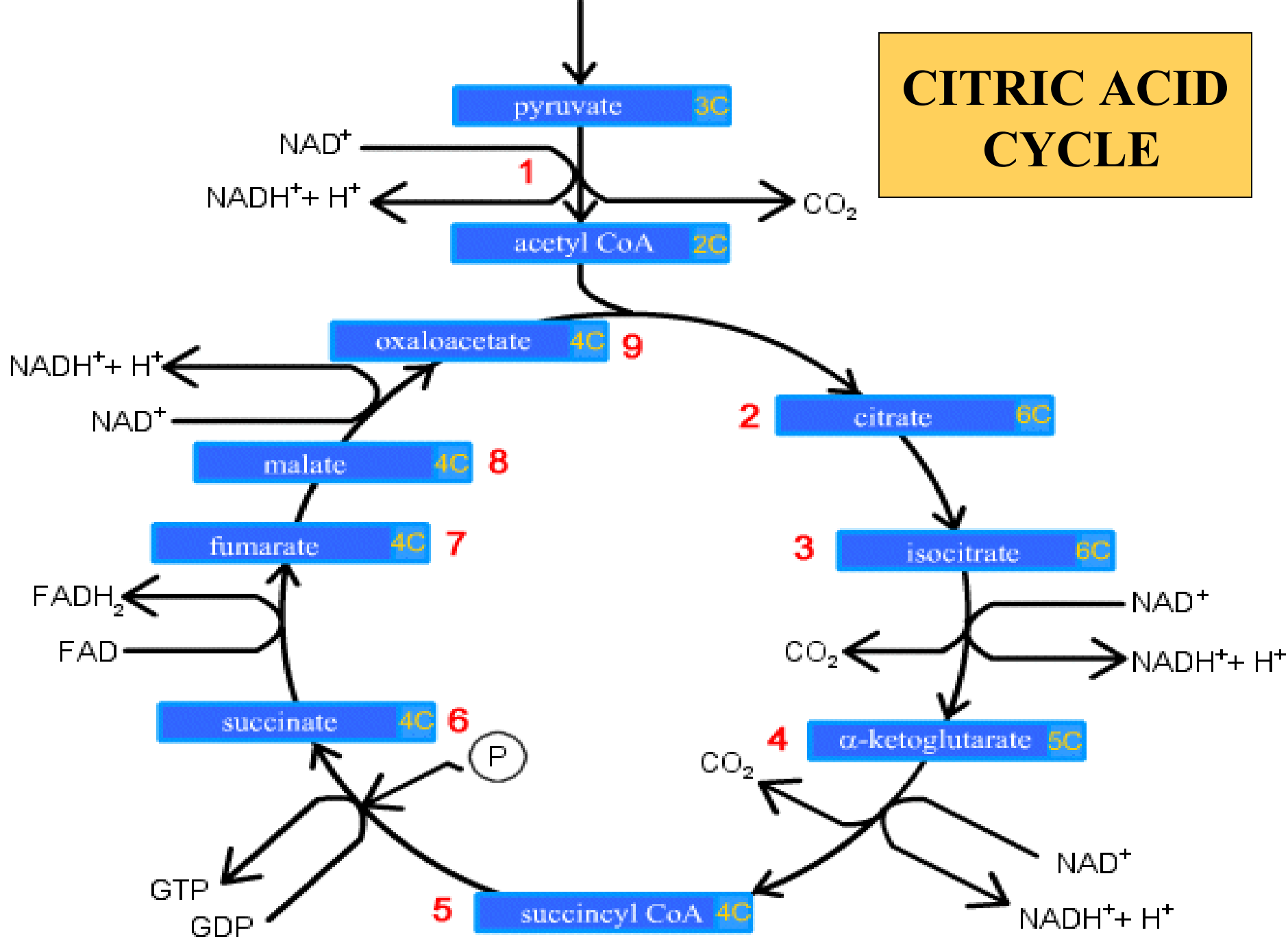
**Type VII (Tarui's
disease)**

**Phosphofructokinase
deficiency**

Type VIII

•
**Liver phosphorylase
kinase.**

CITRIC ACID CYCLE



Biomedical importance

- Final common pathway for oxidation of carbohydrates, lipids , & proteins.
- Major role in gluconeogenesis, transamination, deamination & lipogenesis.
- Vitamins play a key role in this cycle

Eg; Riboflavin – FAD.

Niacin – NAD.

Thiamine.

Pantothenic acid as a part of co-A.

Bioenergetics :12 ATP per cycle.

Pentose Phosphate Pathway

Alternative route for metabolism of glucose

It occurs in cytosol

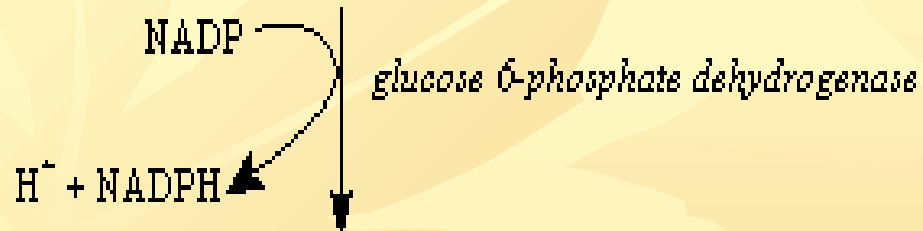
Sequence of reactions occur in two phases

1. Oxidative non reversible phase-Forms

NADPH

2. Non oxidative reversible phase.- Forms ribose precursors for nucleotide synthesis.

Glucose 6-phosphate



6-phosphoglucono-1,5-lactone

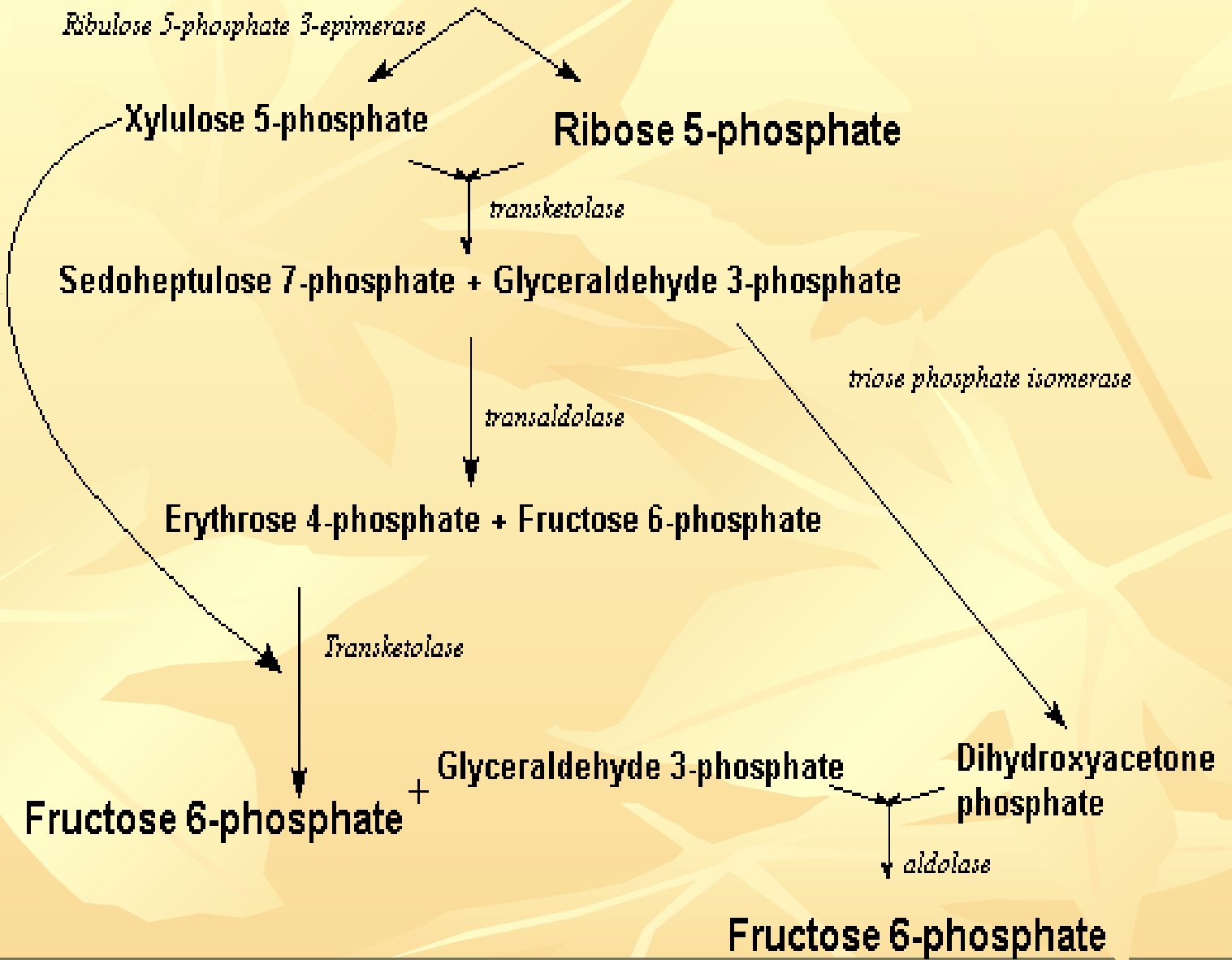
gluconolactonase

6-phosphogluconate



Ribulose 5-phosphate

Ribulose 5-phosphate



Biomedical importance

- Glutathione peroxidase protects erythrocytes against hemolysis.
- Pentose useful in synthesis of DNA & RNA.
- NADPH is required for reductive biosynthesis of fatty acids & steroids.
- NADPH is required in synthesis of amino acids.
- Microsomal cytochrome P450 system brings detoxification of drugs & foreign compounds.

Clinical aspects

- Erythrocyte hemolysis
- Impairment of generation of NADPH manifests as hemolysis when given drugs like Antimalarial- Primaquine aspirin or sulfonamides.

(G6 PD) Deficiency:

- ✓ It makes red cells susceptible to hemolysis
- ✓ X linked inheritance
- ✓ Onset of Anaemia is rapid
- ✓ Mild jaundice

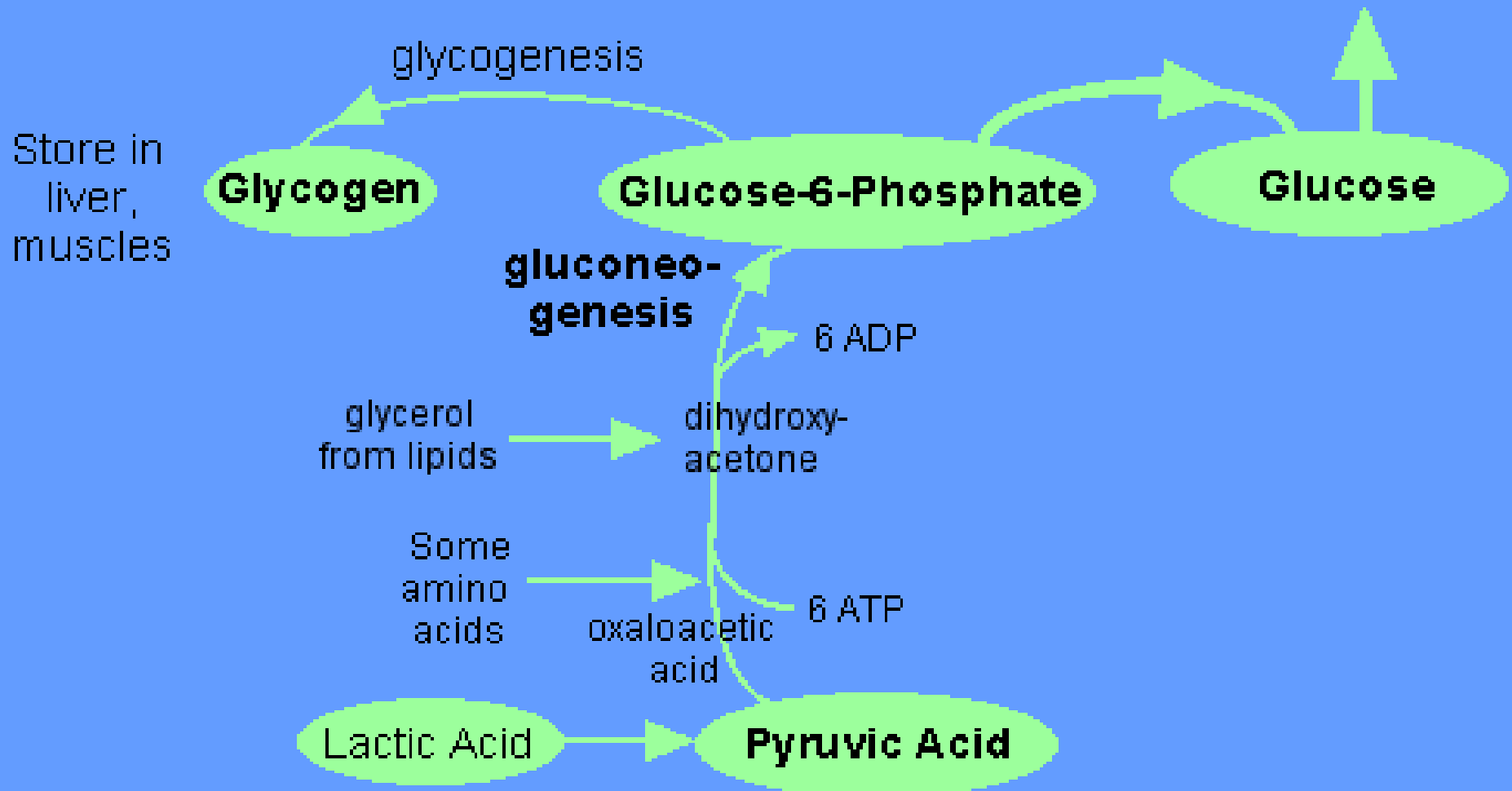
- Defects in Fructose metabolism
- Lack of hepatic fructokinase causes Fructosuria.
- Absence of Hepatic aldolase-Hereditary fructose intolerance.
 - ✓ Hypoglycemia, vomiting, sweating.
 - ✓ Albuminuria, aminoaciduria.
 - ✓ Reduced caries incidence.
 -
- Fructose & sorbitol in lens associated with diabetic cataract.

Gluconeogenesis

- Synthesis of glucose from non carbohydrate compounds is called “gluconeogenesis”
- Site : Mainly occurs in Liver & kidney matrix in cytosol.

Gluconeogenesis

Occurs mainly in the liver
to make glucose for the blood



Regulation of gluconeogenesis

- Influence of Glucagon.
- Availability of substrates.
- Alcohol inhibits gluconeogenesis.

Proteoglycans & Glycosaminoglycans

Seven glycosaminoglycans

- 1 Hyaluronic acid
- 2 Chondroitin sulfate
- 3 Keratan sulfate I
- 4 Keratan sulfate II
- 5 Heparin
- 6 Heparan sulfate
- 7 Dermatan sulfate

Mucopolysaccharidoses

■ MPS

MPS I (Hurler syndrome)

MPS II (Hunter syndrome)

MPS IIIA (Sanfilippo A)

MPS IIIB (Sanfilippo B)

MPS IIIC (Sanfilippo C)

■ Defect

Alpha-L-Iduronidase

Iduronate sulfatase

Heparan sulfate N sulfatase

Alpha-Acetylglucosaminidase

Acetyl transferase

- MPS IVA (Morquio A)
- MPS IVB (Morquio B)
- MPS VI (Maroteaux Lamy syndrome)
- MPS VII (Sly)
- Galactose-6-sulfatase
- Beta galactosidase
- N acetylgalactosamine 4 sulfatase
- Beta glucuronidase

Hunter's syndrome



Functions of glycoaminoglycans

- Structural components of extracellular matrix.
- Act as sieves in extracellular matrix.
- Facilitate cell migration.
- Corneal transparency.
- Anticoagulant (Heparin).
- Components of synaptic & other vesicles.

Glycoproteins

Oligosaccharide (glycan) covalently attached to their polypeptide backbones.

Glycoprotein

Collagen

Mucins

Transferrin &

Ceruloplasmin

Immunoglobulin molecule

Alkaline phosphatase

Functions

Structural molecule

Lubricant &
protective agent

Transport molecule.

Immunity

Enzymatic activity

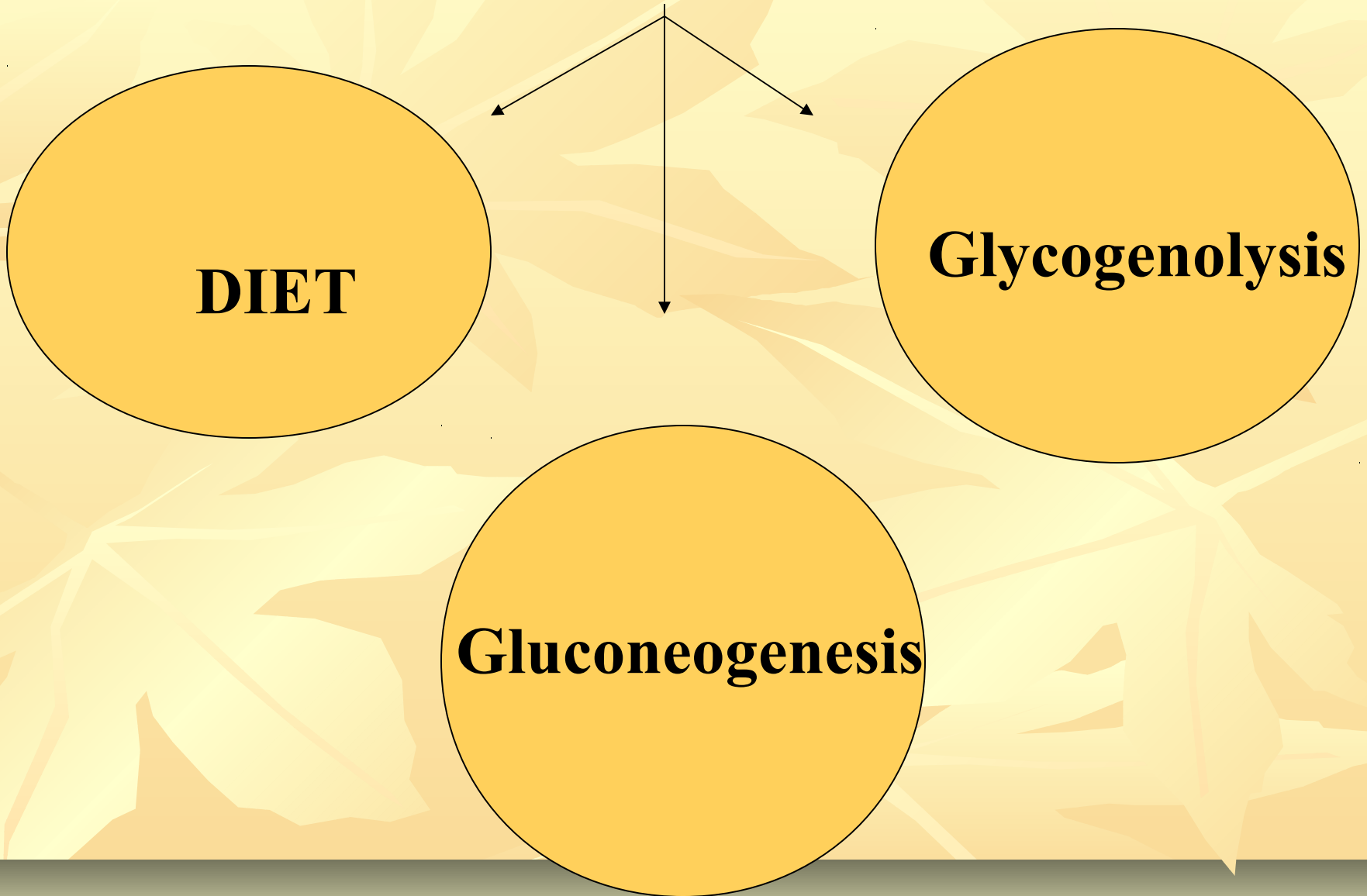
Regulation of Blood glucose

Postabsorptive state: Blood glucose is 4.5-5.5mmol/L.

After carbohydrate meal: 6.5-7.2mmol/L

During fasting : 3.3-3.9mmol/L

Blood Glucose



Metabolic & hormonal mechanisms regulate blood glucose level

Maintenance of stable levels of glucose in blood is by

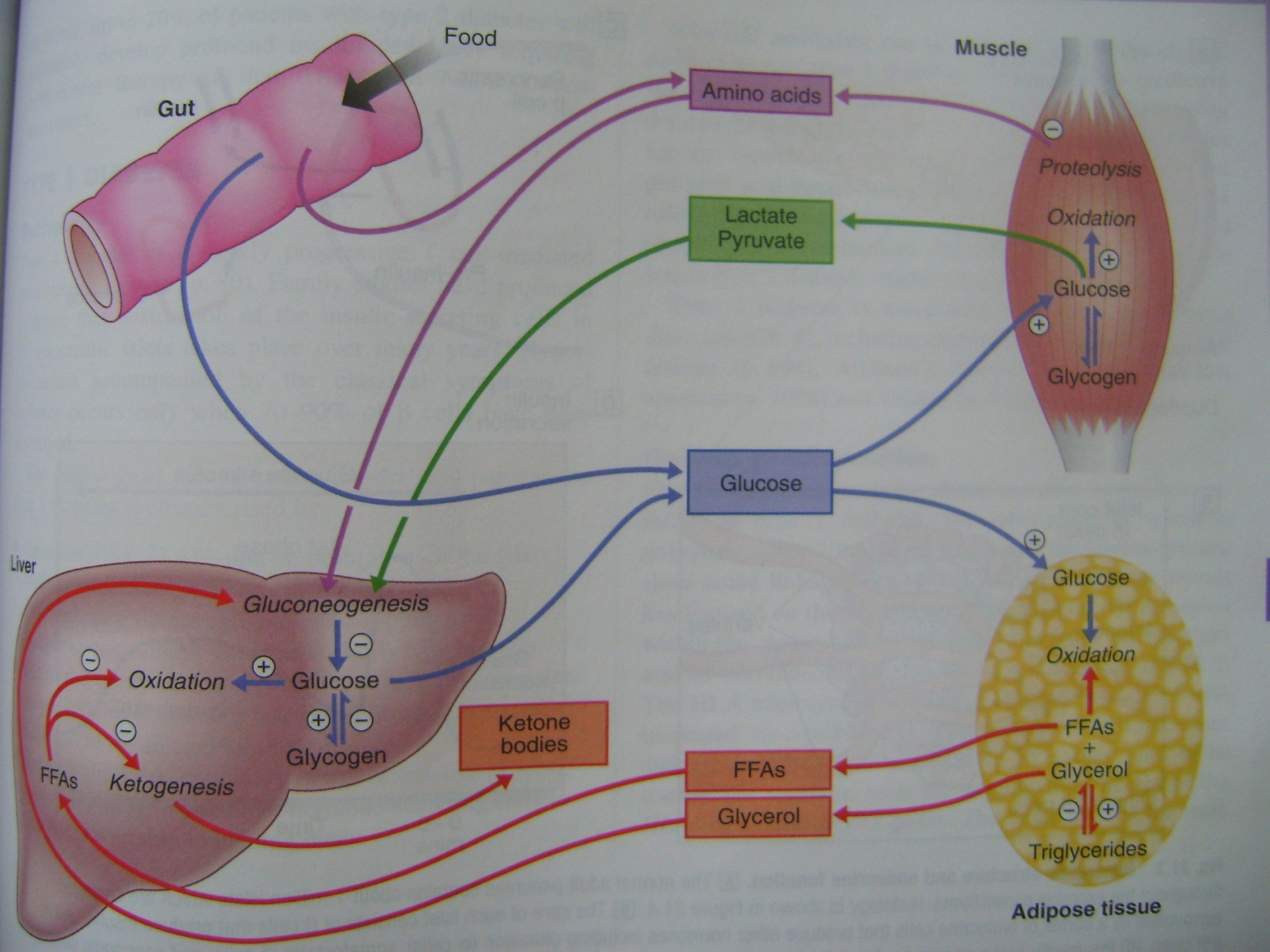
- ✓ Liver.
- ✓ Extrahepatic tissues.
- ✓ Hormones .

Liver

- Freely permeable to glucose via GLUT-2 transporter.
- Passage through cell membrane is rate limiting step.
- Glucose is phosphorylated by hexokinase on entry into cell

Extrahepatic tissues

- Relatively impermeable to glucose.
- Passage is facilitated through various enzymes.
- It has direct effect on entry of glucose into the cell.





Role Of Insulin

Regulation of blood glucose levels

Insulin

Anabolic in response to hyperglycemia

Liver

- Stimulates glycogen synthesis, glycolysis, and fatty acid synthesis

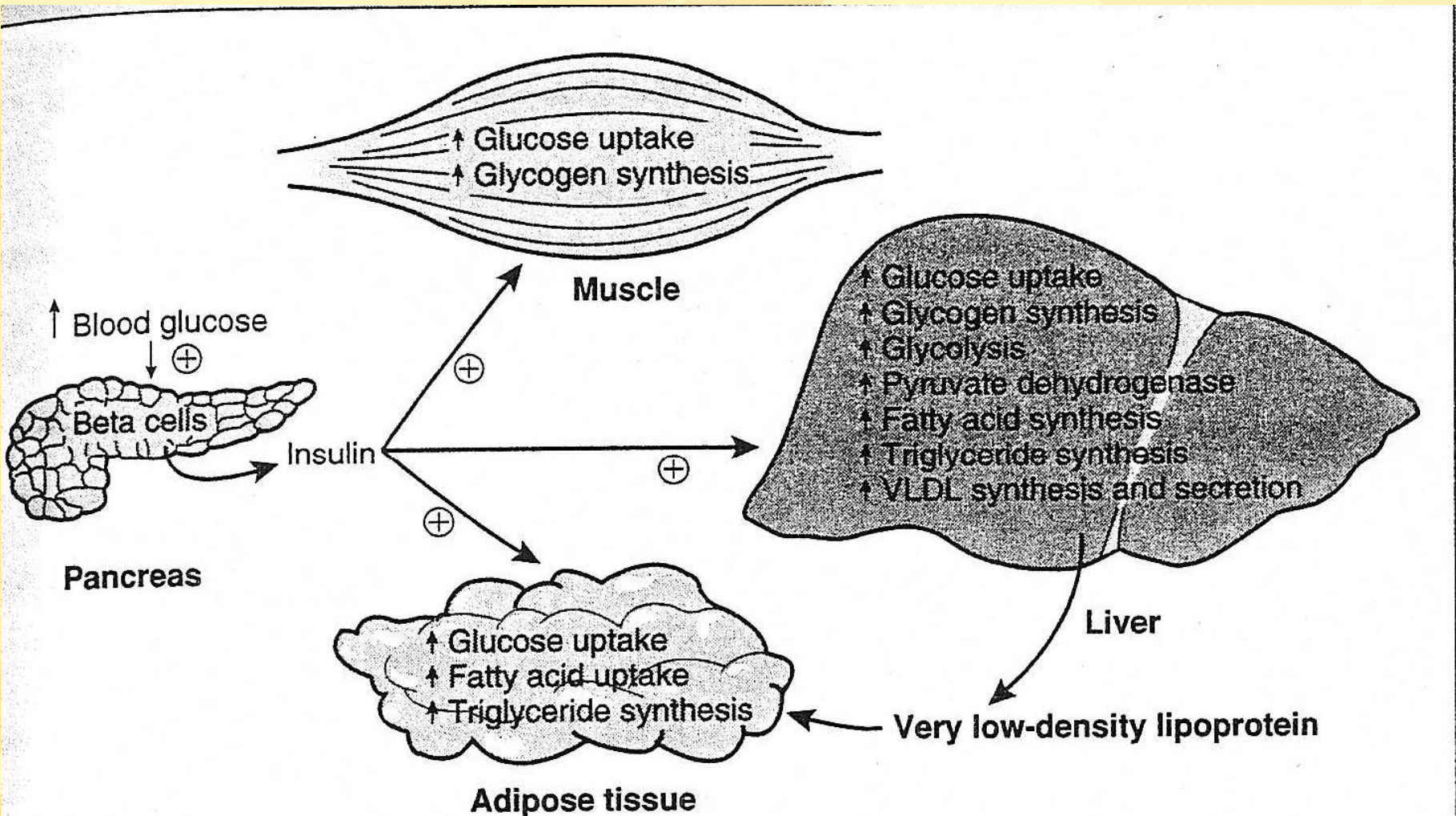
Muscle

- Stimulates glycogen synthesis

Adipose tissue

- Stimulates lipoprotein lipase resulting in uptake of fatty acids from chylomicrons and VLDL
- Stimulates glycolysis for glycerol phosphate synthesis (precursor to triglycerides)

Role in insulin in lowering blood glucose



Glucagon

- ✓ Produced by A cells of islets of langerhans of pancreas
- ✓ Actions opposite to Insulin.
- ✓ Its secretion is stimulated by hypoglycemia.
- ✓ It stimulates glycogenolysis & gluconeogenesis from amino acids & lactate.

Regulation of blood glucose levels by Glucagon

Catabolic, in response to hypoglycemia

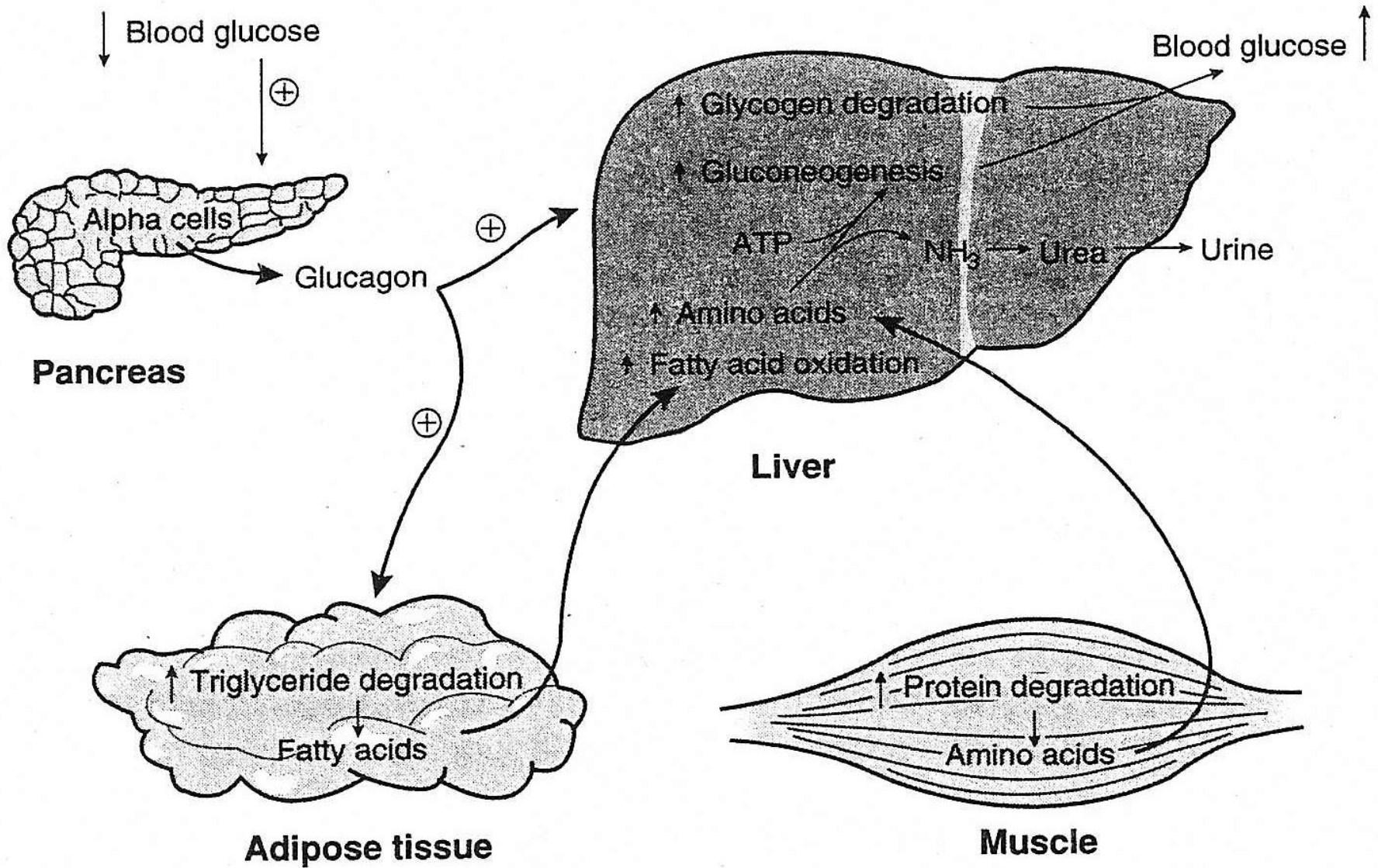
Liver

- Activates glycogen degradation, gluconeogenesis

Adipose tissue

- Stimulates lipolysis and release of fatty acids

Role of glucagon



Role of thyroid hormone

It stimulates glycogenolysis & gluconeogenesis.

Hypothyroid

- Fasting blood glucose is lowered.
- Patients have decreased ability to utilise glucose.
- Patients are less sensitive to insulin than normal or hyperthyroid patients.

Hyperthyroid

- Fasting blood glucose is elevated
- Patients utilise glucose at normal or increased rate

Glucocorticoids

- ✓ Glucocorticoids are antagonistic to insulin.
- ✓ Inhibit the utilisation of glucose in extrahepatic tissues.
- ✓ Increased gluconeogenesis .

Epinephrine

- ✓ Secreted by adrenal medulla.
- ✓ It stimulates glycogenolysis in liver & muscle.
- ✓ It diminishes the release of insulin from pancreas.

Other Hormones

Anterior pituitary hormones

Growth hormone:

- ✓ Elevates blood glucose level & antagonizes action of insulin.
- ✓ Growth hormone is stimulated by hypoglycemia (decreases glucose uptake in tissues)
- ✓ Chronic administration of growth hormone leads to diabetes due to B cell exhaustion.

SEX HORMONES

- ✓ Estrogens cause increased liberation of insulin.
- ✓ Testosterone decrease blood sugar level.

Hyperglycemia

- Thirst, dry mouth
- Polyuria
- Tiredness, fatigue
- Blurring of vision.
- Nausea, headache,
- Hyperphagia
- Mood change

Hypoglycemia

- Sweating
- Trembling, pounding heart
- Anxiety, hunger
- Confusion, drowsiness
- Speech difficulty
- Incoordination.
- Inability to concentrate

Clinical aspects

Glycosuria: occurs when venous blood glucose concentration exceeds 9.5-10.0mmol/L

Fructose-1,6-Biphosphatase deficiency causes lactic acidosis & hypoglycemia..

Diabetes Mellitus

A multi-organ catabolic response caused by insulin insufficiency

Muscle

- Protein catabolism for gluconeogenesis

Adipose tissue

- Lipolysis for fatty acid release

Liver

- Ketogenesis from fatty acid oxidation
- Gluconeogenesis from amino acids and glycerol

Kidney

- Ketonuria and cation excretion
- Renal ammoniagenesis.

Role of carbohydrates in dental caries

- Fermentable carbohydrates causes loss of caries resistance.
- Caries process is an interplay between oral bacteria, local carbohydrates & tooth surface

Bacteria + Sugars + Teeth \longrightarrow Organic acids



Caries

Role of carbohydrates in periodontal

disease

Abnormal
glucose metabolism



Diabetes Mellitus



Periodontal disease

Excessive carbohydrate
intake



Obesity



Periodontal disease

References

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Thank you