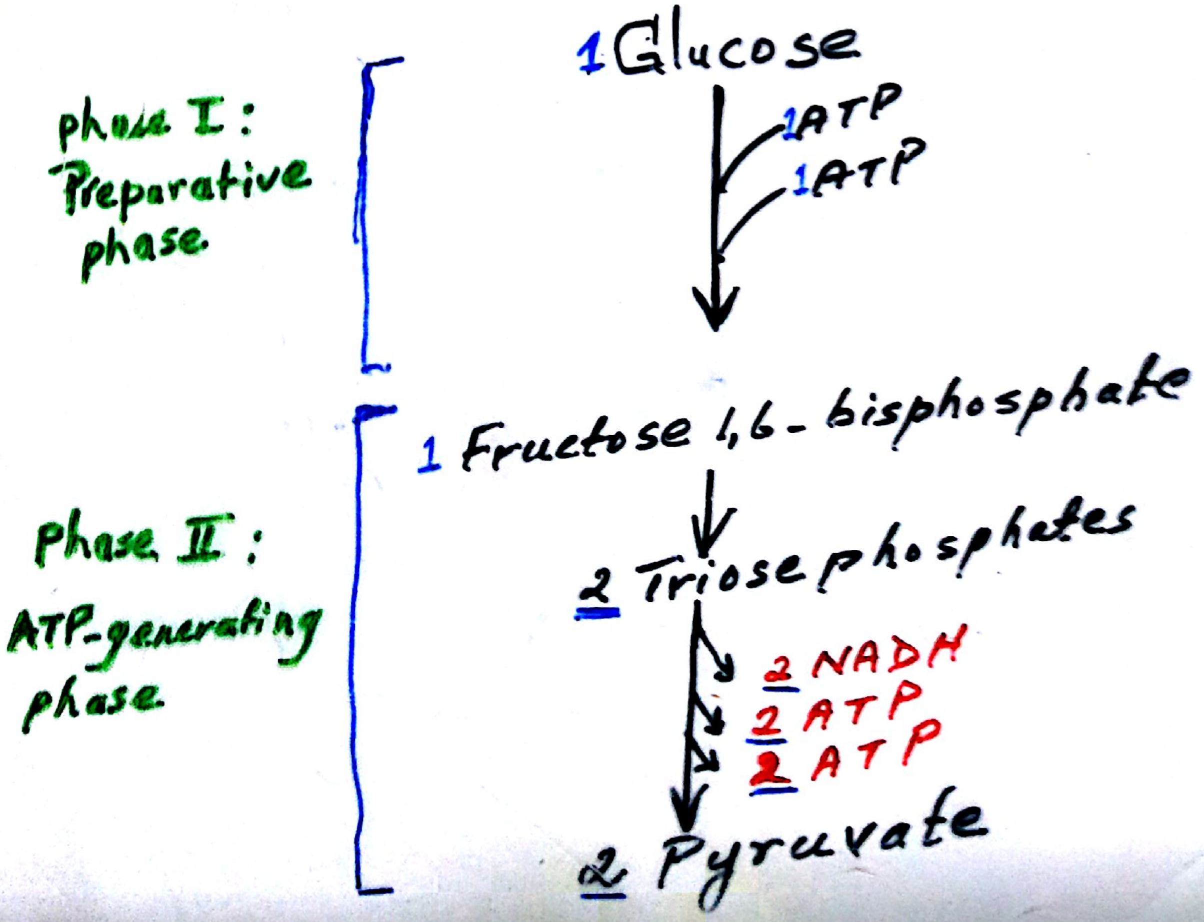
GLYCOLYSIS

- Universal Pathway in all cell types
- Generation of ATP with, and without, O_2
- Anabolic Pathway
  → biosynthetic precursors
- Phases of the glycolytic Pathway



GLYCOLYSIS :-

- Occurs in all Human Cells

Glucose ⟹ 2 Pyruvate —PDH→ 2-acetyl CoA → TCA → 4 CO_2

2 Pyruvate ⇌ 2-lactate

PDH → 2 CO_2

No O_2-requirement for glycolysis - anaerobic fermentation

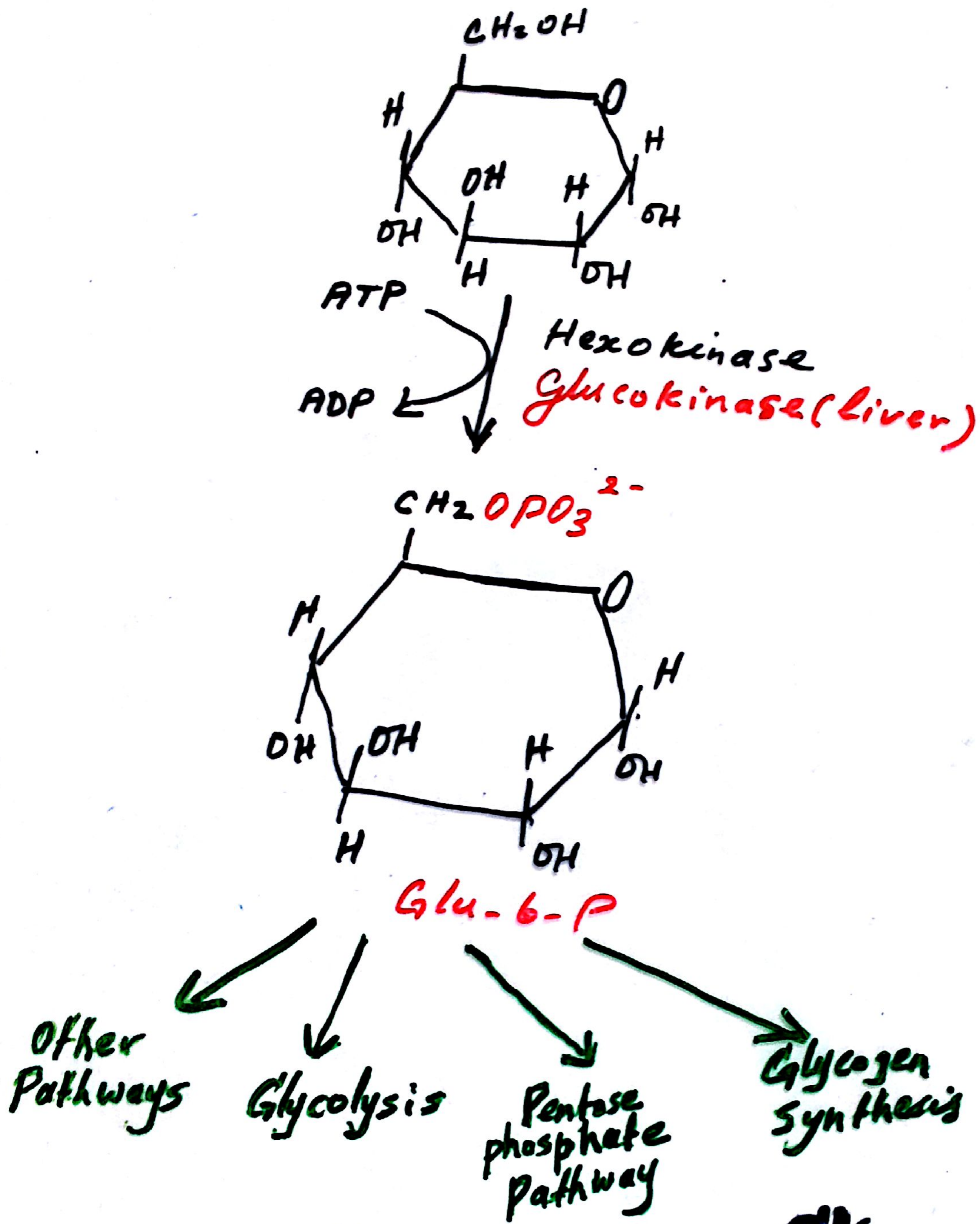
O_2-requirement for PDH & TCA activity

Glu + 2ADP + 2Pi → 2ATP + 2-lactate

Glu + 6O_2 + 38 ADP + 38 P_i + 38 H^+ ⟹ 6CO_2 + 6H_2O + 38 ATP

- Tissues that have an Absolute Requirement for Glucose
  - Brain
  - Red Blood Cells
  - Cornea, lens and retina
  - Kidney Medulla, testis, leukocyte and white muscle fibers

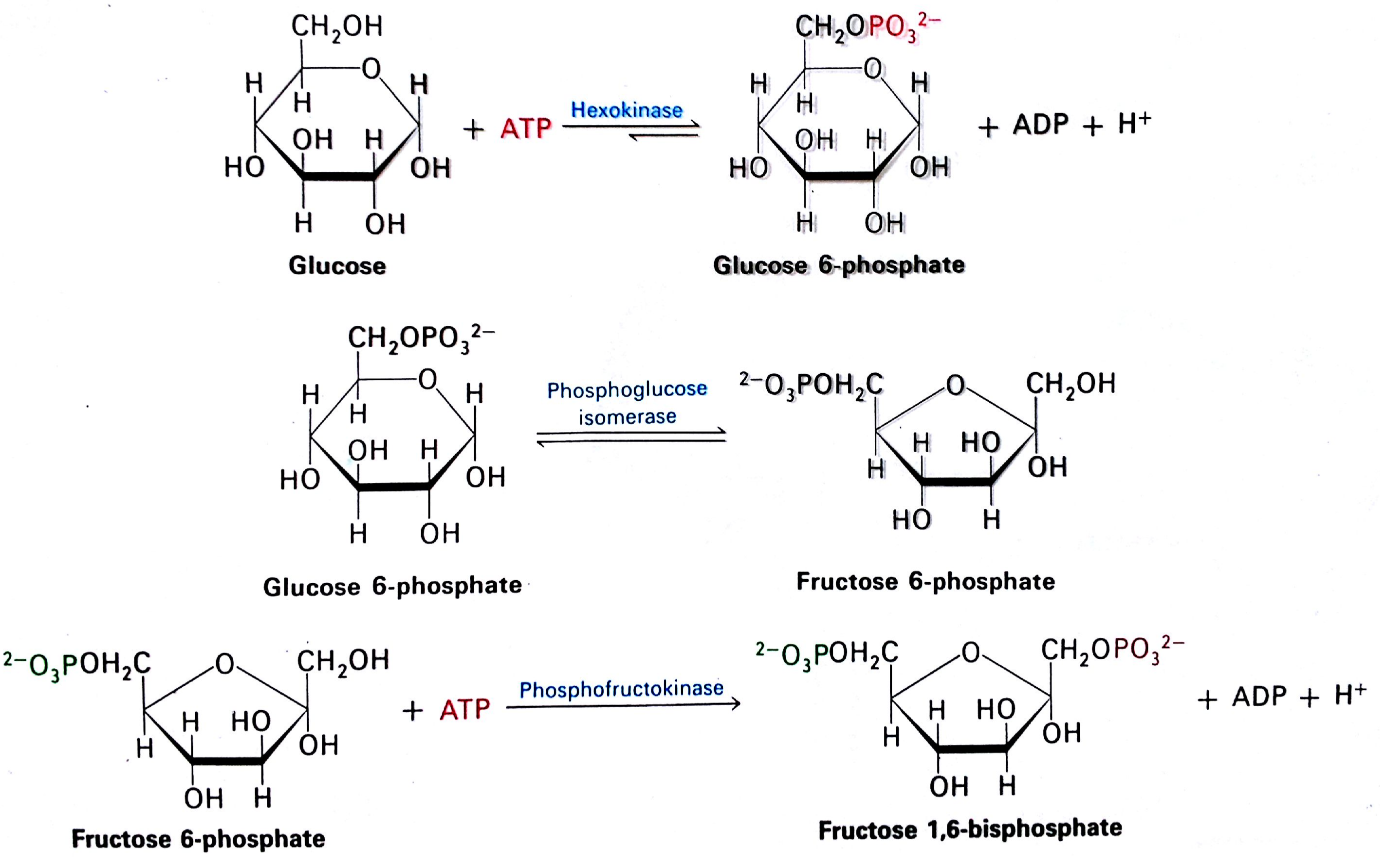
Glucose-6-phosphate Metabolism



	HK	GK
Occurrence	in all tissues	in Liver
Km	<0.02 mM	10 – 20 mM
Sp.	Glu, Fru, Man, Gal	Glu + others
Induction	Not induced	↑ insulin, Glu
Function	Even low blood Glu	only > 100 mg/dl

Reactions of GLYCOLYSIS

Ic

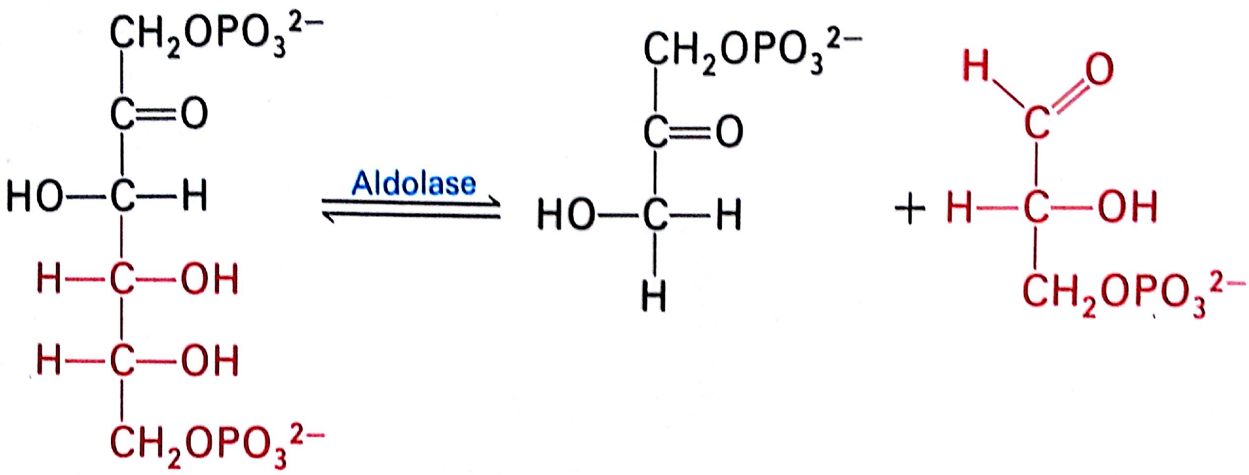


Assorted figures from pages 486 and 487

T-53

Stryer: *Biochemistry*, Fourth Edition

Set I



Fructose 1,6-bisphosphate | **Dihydroxyacetone phosphate** | **Glyceraldehyde 3-phosphate**

Bottom figure, page 487

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Set I

Glyceraldehyde 3-P dehydrogenase

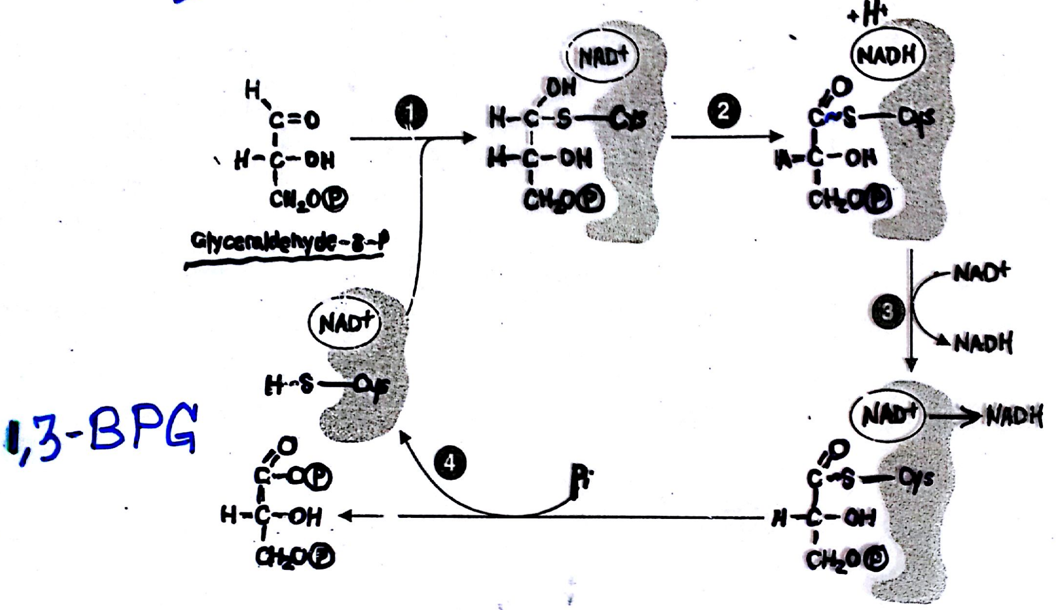
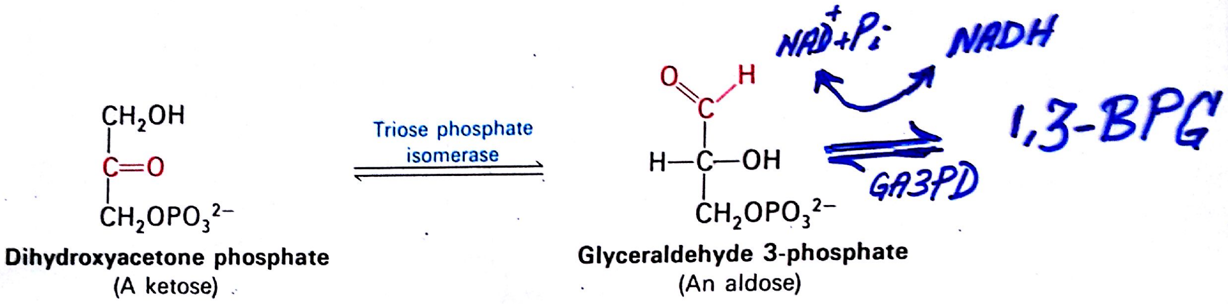
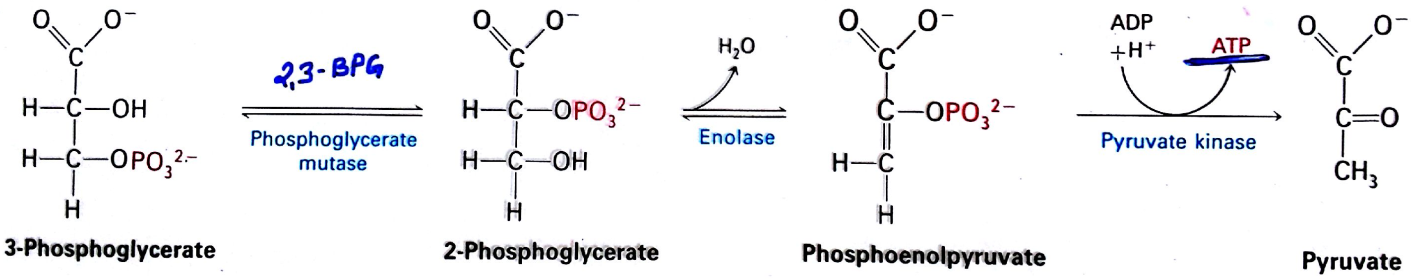


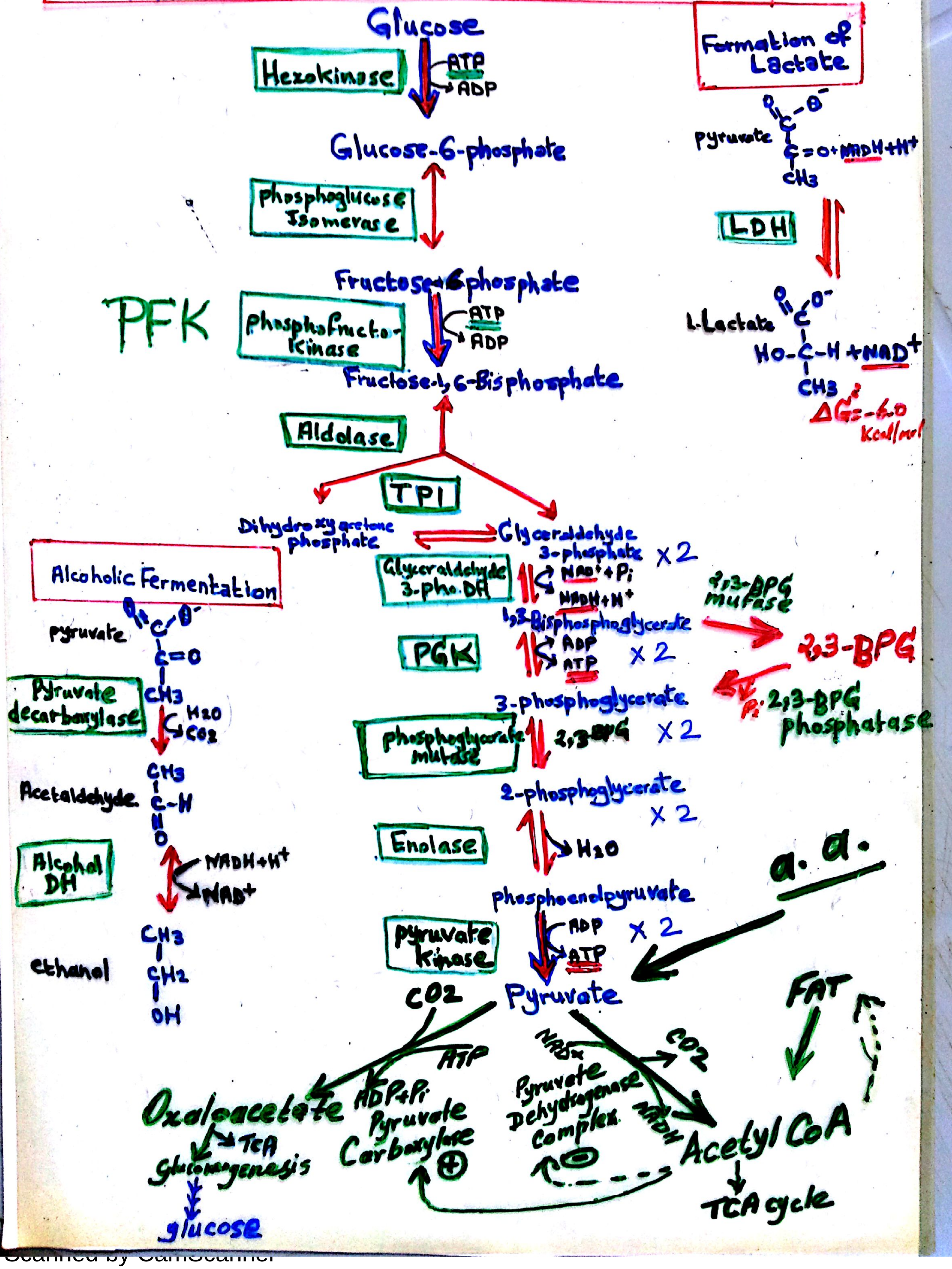
Fig. 22.17. Mechanism of the glyceraldehyde 3-phosphate dehydrogenase reaction. 1. The enzyme forms a covalent linkage with the substrate, using a cysteine group at the active site. The enzyme also contains bound NAD^+ close to the active site. 2. The substrate is oxidized, forming a high-energy thioester linkage (in blue), and NADH. 3. NADH has a low affinity for the enzyme and is replaced by a new molecule of NAD^+. 4. Inorganic phosphate attacks the thioester linkage, releasing the product 1,3 bisphosphoglycerate, and regenerating the active enzyme in a form ready to initiate another reaction.



1,3 BPG + ADP ⇌ 3-phosphoGlycerate + ATP (PGK)



The Glycolytic Pathway



Lactate is produced anaerobically to meet the following demands

1. Cells with low energy demand

2. To cope with increased energy demands in vigorously exercising muscle
   Lactate level is increased 5 to 10-fold

3. Hypoxia
   to survive brief episodes of hypoxia
   - but mixed blessings

Lactic Acidosis:- → lactate > 5mM (0.4 – 1.8mM) Ref. range
→ pH < 7.2 (7.35 – 7.45)

is the most common cause of metabolic acidosis

→ . increased production of lactic acid
. decreased utilization " " "

Most common cause is impairment of oxidative metabolism resulting from
Collapse of Circulatory System:-
. Impaired O_2 transport
  e.g. myocardial infarction

. Respiratory Failure
  e.g. Pulmonary embolism

- Uncontrolled hemorrhage
- Direct inhibition of Oxidative-phosphorylation

Other Causes :-
- Hypoxia in any tissue
- Alcohol intoxication → ↑↑ NADH/NAD

V. rare
- ↓ gluconeogenesis
- ↓ Pyruvate dehydrogenase e.g. inherited deficiency
  - thiamine deficiency
- ↓ TCA activity
- ↓ Pyruvate Carboxylase deficiency

Regulation of the Glycolytic Pathway

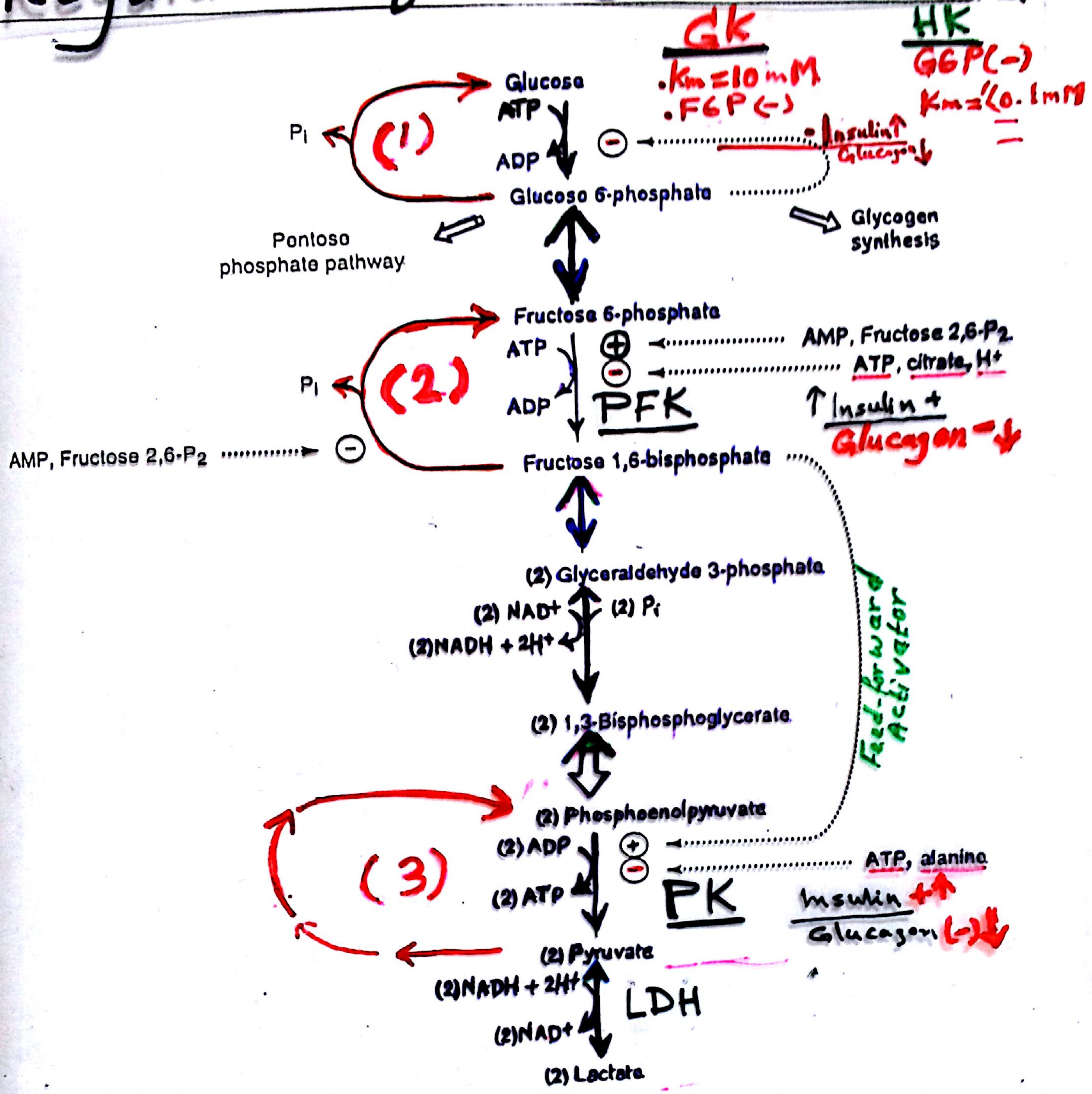


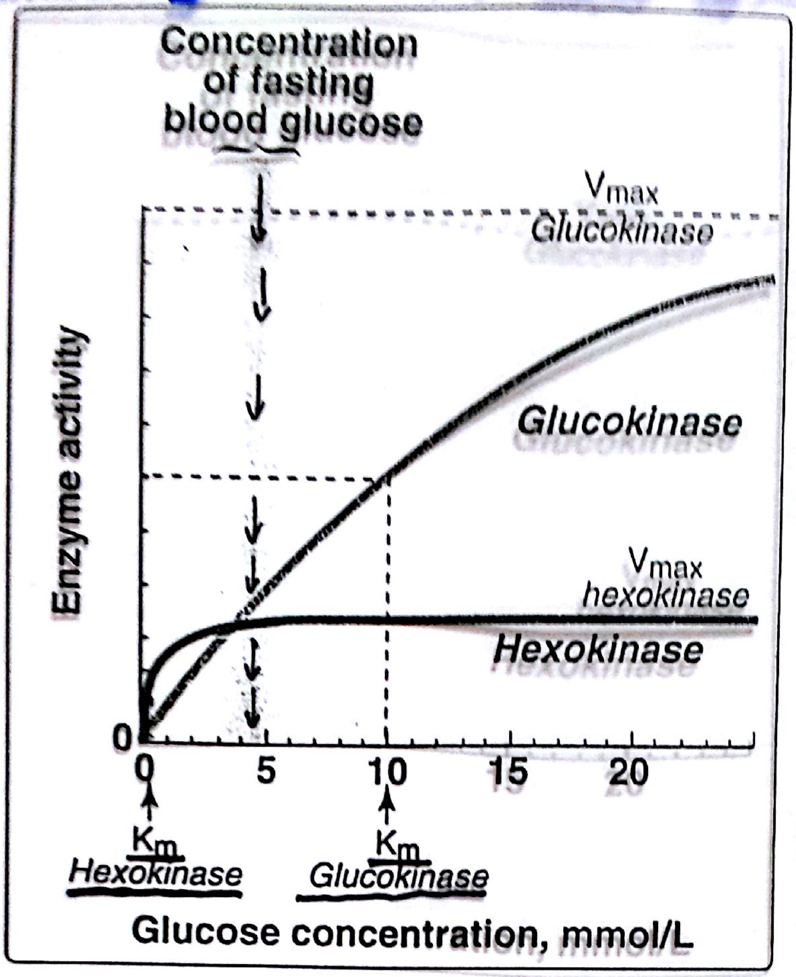
FIGURE 7.13
Important regulatory features of the glycolytic pathway. Because of differences in isoenzyme distribution, not all tissues of the body have all of the regulatory mechanisms shown here.

- Regulation of Liver PK by phosphorylation – Dephosphorylation

PK —— PK–P

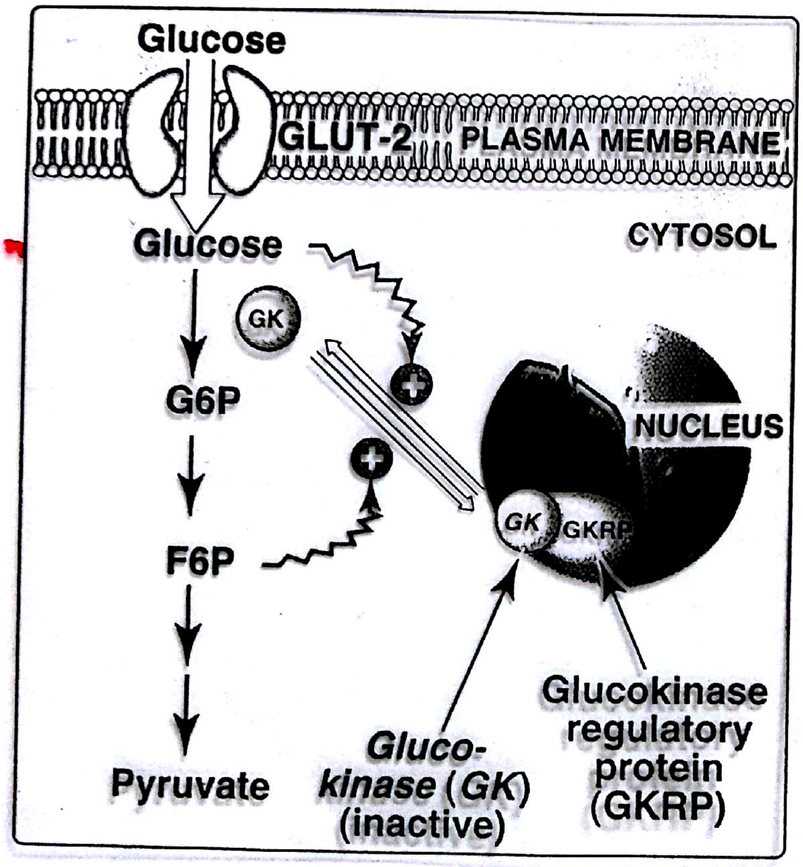
Active Inactive

Effect of [Glucose] on HK and GK.

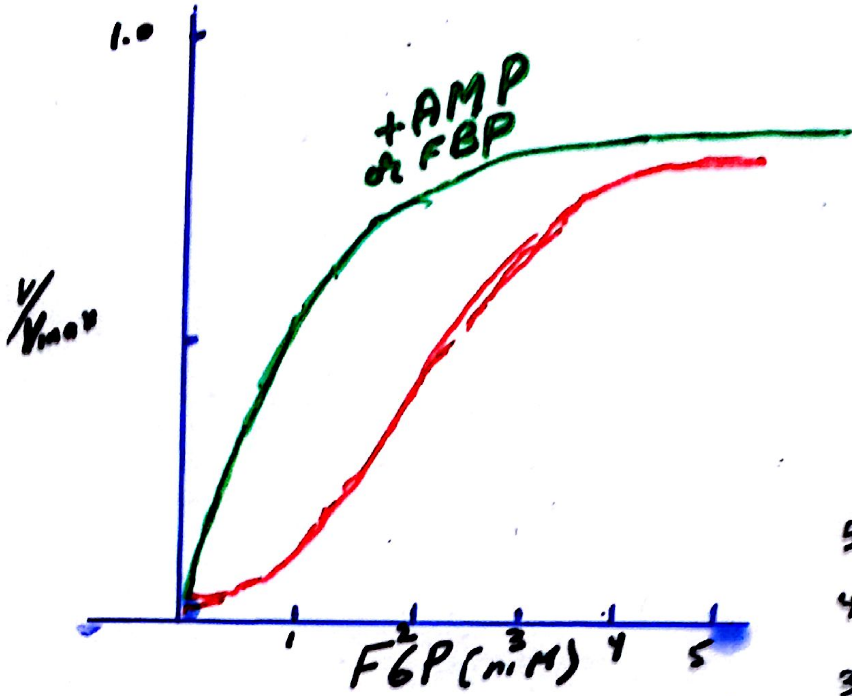


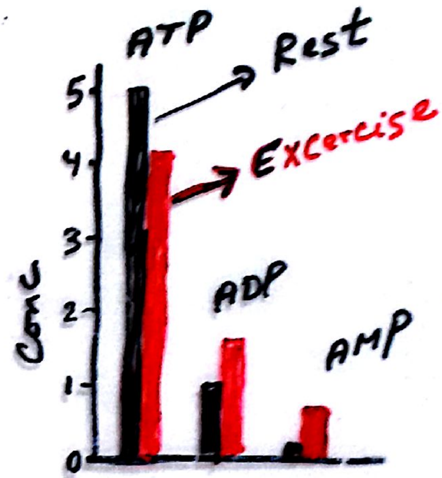
Regulation of GK by "(1)" GKRP

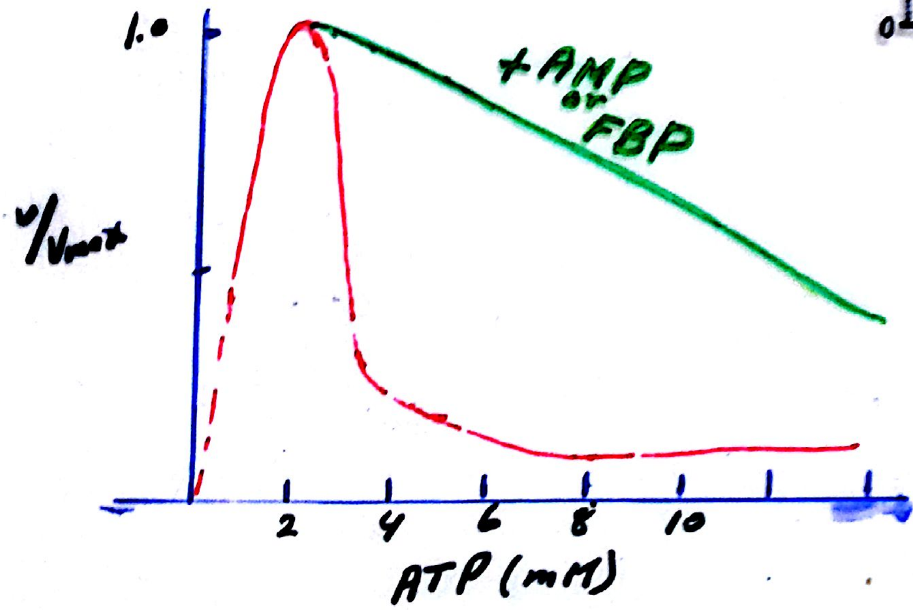
2) Insulin → ↑ GK transcription



Regulation of PFK by AMP and ATP



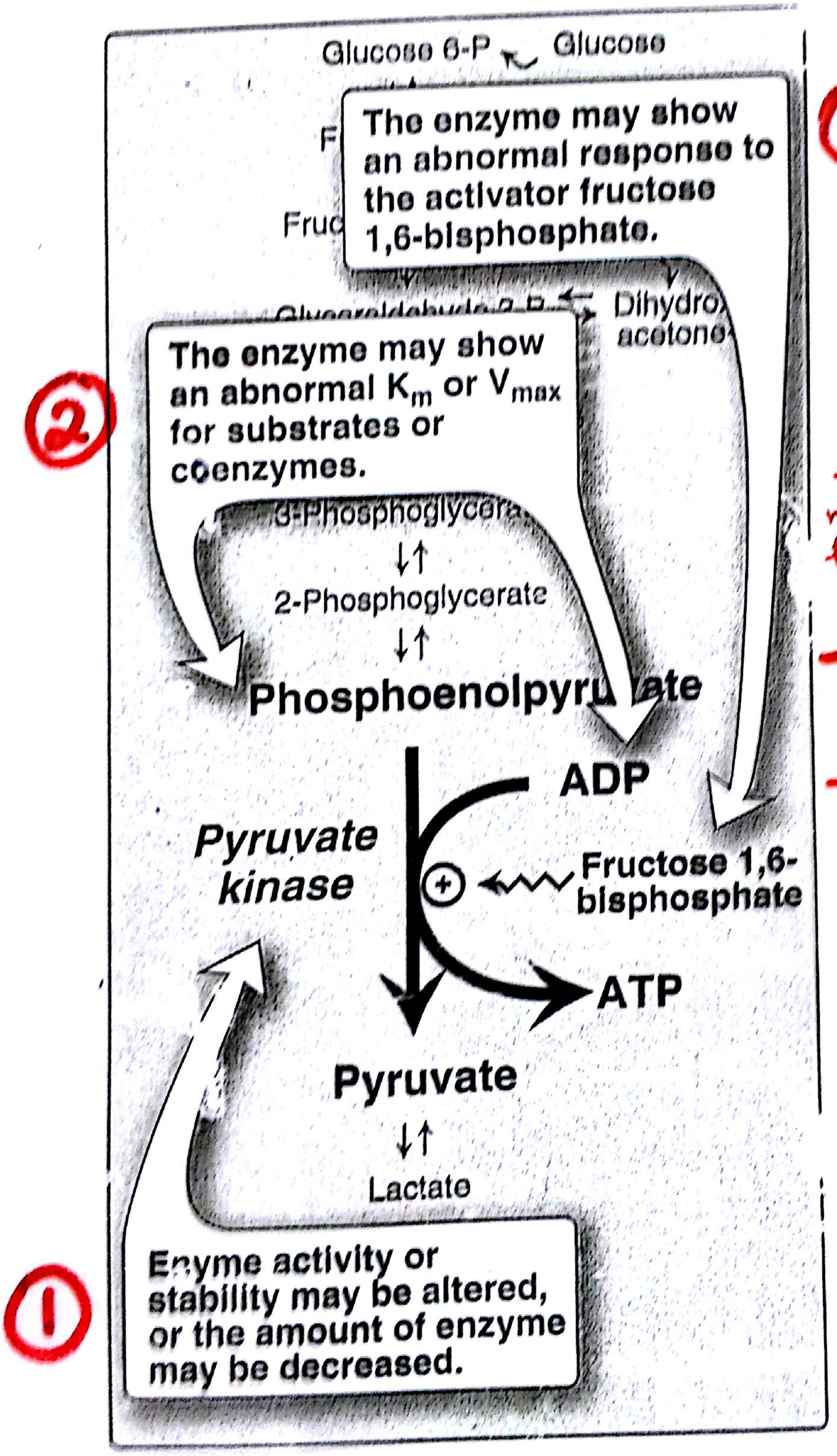




$$F6P + ATP \xrightarrow[PFK]{} F1,6BP + ADP$$

- Pyruvate Kinase Deficiency

95% of glycolytic enz deficiency cases



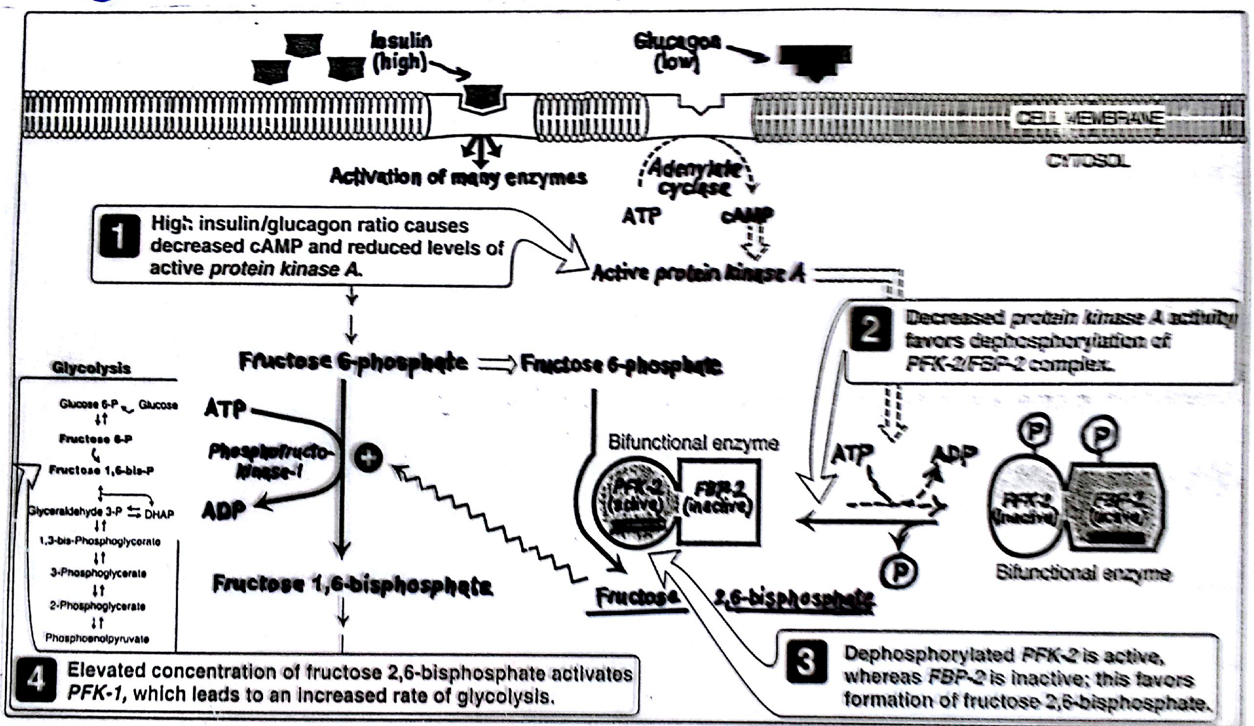
- severe deficiency requires blood transfusion

→ ↑ 2,3-BPG

→ ↓ ATP

- PGI (4% of glycolytic cases)

Regulation of Fru-2,6-BP Level



- Regulation of PK by phosphorylation - Dephosph