Fig. 17-CO, p.463

Glycolysis (해당)
= EMP 회로
(Embden-Meyerhof-Panas pathway)

① Glycos (sugar) + Lysis --> Glycolysis

② Glucose ----------> Pyruvate

③ 세포질에서 일어난다.

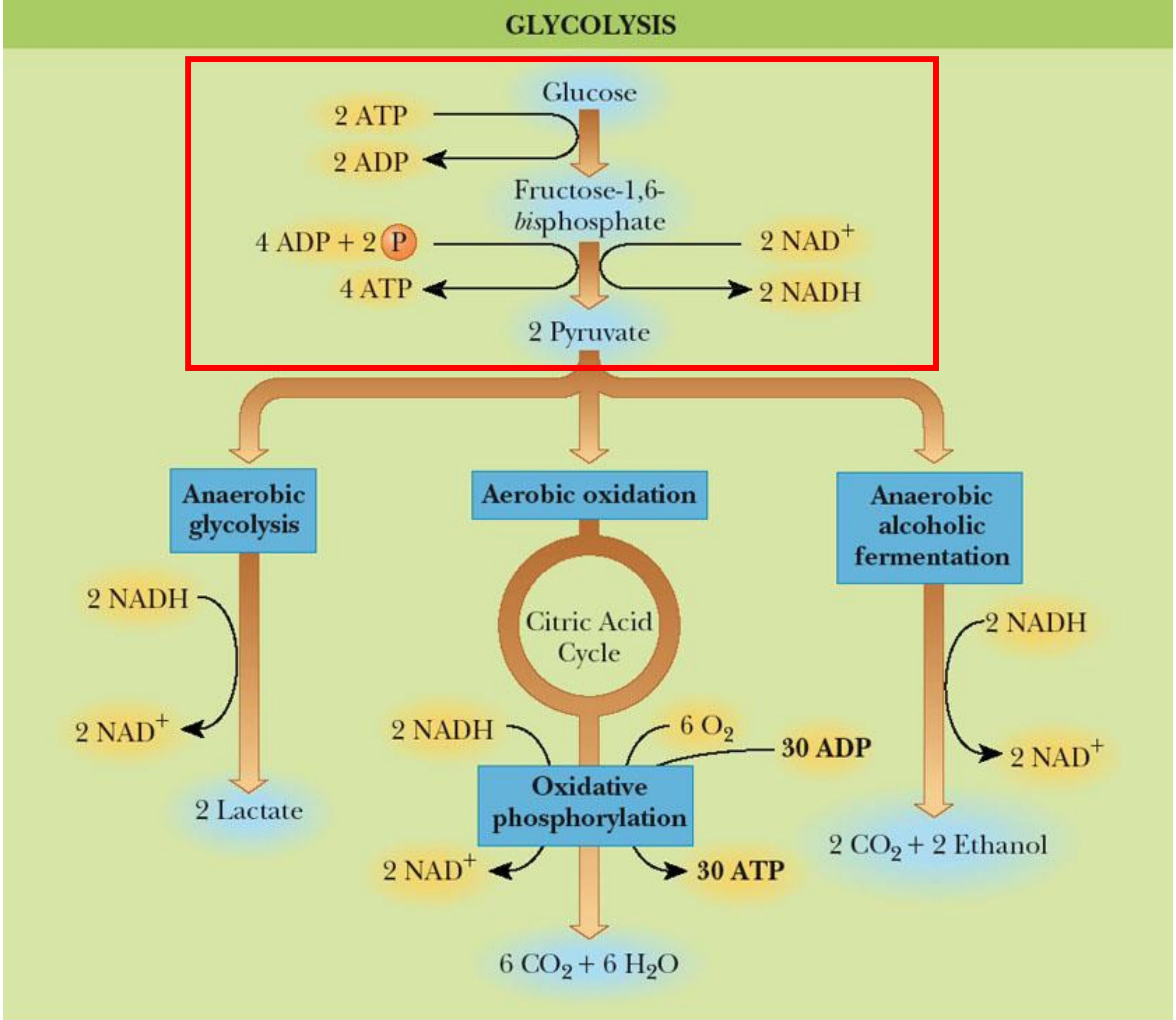

GLYCOLYSIS
Glucose
2 ATP
2 ADP
Fructose-1,6-
*bis*phosphate
4 ADP + 2 P
4 ATP
2 NAD+
2 NADH
2 Pyruvate
Anaerobic glycolysis
Aerobic oxidation
Anaerobic alcoholic fermentation
2 NADH
2 NAD+
2 Lactate
Citric Acid Cycle
2 NADH
6 O2
30 ADP
Oxidative phosphorylation
2 NAD+
30 ATP
6 CO2 + 6 H2O
2 NADH
2 NAD+
2 CO2 + 2 Ethanol

Fig. 17-1, p.464

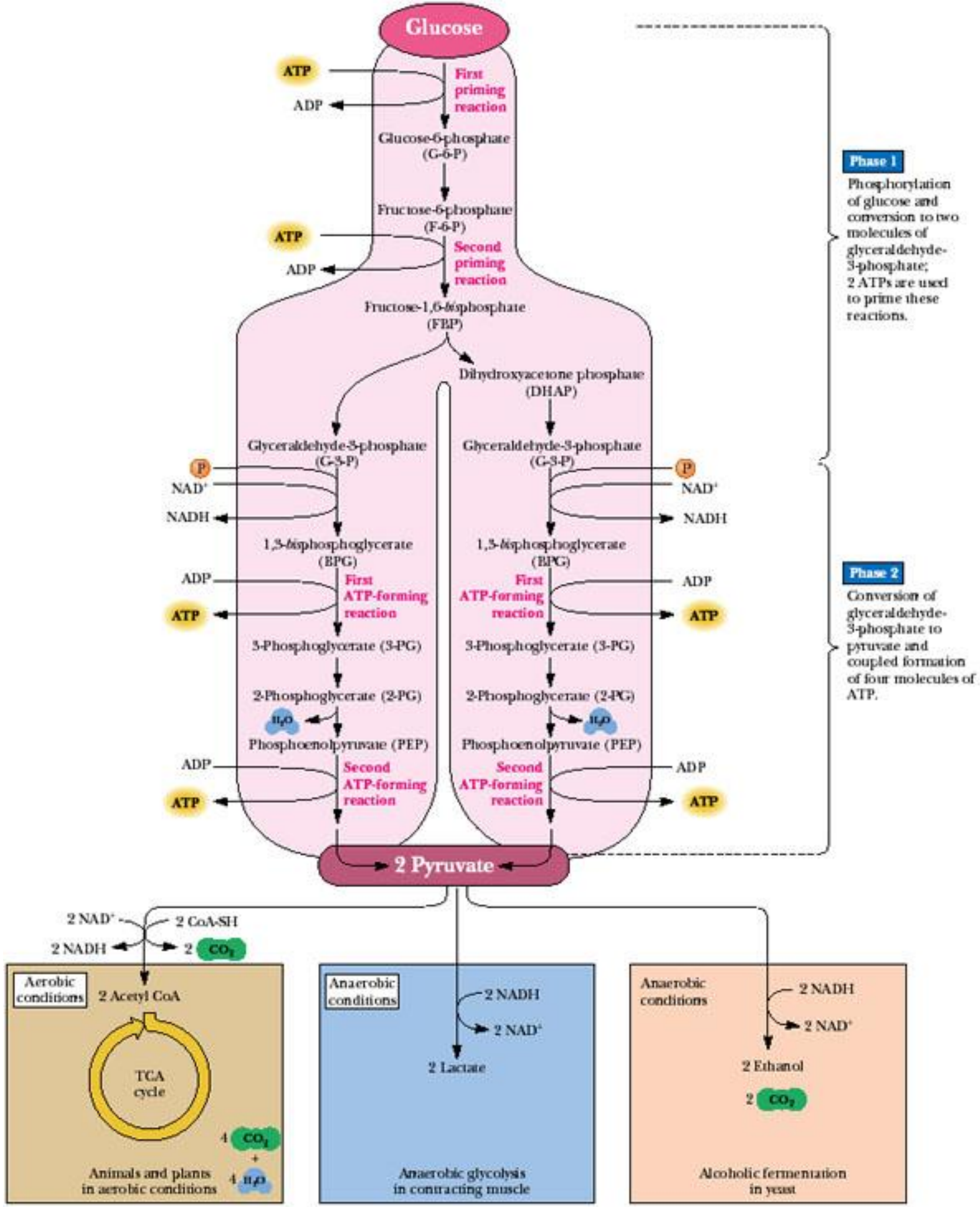

Glucose
ATP
ADP
First priming reaction
Glucose-6-phosphate (G-6-P)
Fructose-6-phosphate (F-6-P)
ATP
ADP
Second priming reaction
Fructose-1,6-bisphosphate (FBP)
Dihydroxyacetone phosphate (DHAP)
Glyceraldehyde-3-phosphate (G-3-P)
Glyceraldehyde-3-phosphate (G-3-P)
P
NAD+
NADH
P
NAD+
NADH
1,3-bisphosphoglycerate (BPG)
1,3-bisphosphoglycerate (BPG)
ADP
ATP
First ATP-forming reaction
First ATP-forming reaction
ADP
ATP
3-Phosphoglycerate (3-PG)
3-Phosphoglycerate (3-PG)
2-Phosphoglycerate (2-PG)
2-Phosphoglycerate (2-PG)
H2O
H2O
Phosphoenolpyruvate (PEP)
Phosphoenolpyruvate (PEP)
ADP
ATP
Second ATP-forming reaction
Second ATP-forming reaction
ADP
ATP
2 Pyruvate
Phase 1
Phosphorylation of glucose and conversion to two molecules of glyceraldehyde-3-phosphate; 2 ATPs are used to prime these reactions.
Phase 2
Conversion of glyceraldehyde-3-phosphate to pyruvate and coupled formation of four molecules of ATP.
2 NAD+
2 CoA-SH
2 NADH
2 CO2
Aerobic conditions
2 Acetyl CoA
TCA cycle
4 CO2
+
4 H2O
Animals and plants in aerobic conditions
Anaerobic conditions
2 NADH
2 NAD+
2 Lactate
Anaerobic glycolysis in contracting muscle
Anaerobic conditions
2 NADH
2 NAD+
2 Ethanol
2 CO2
Alcoholic fermentation in yeast

Fig. 17-2, p.465

The Overall Pathway of Glycolysis

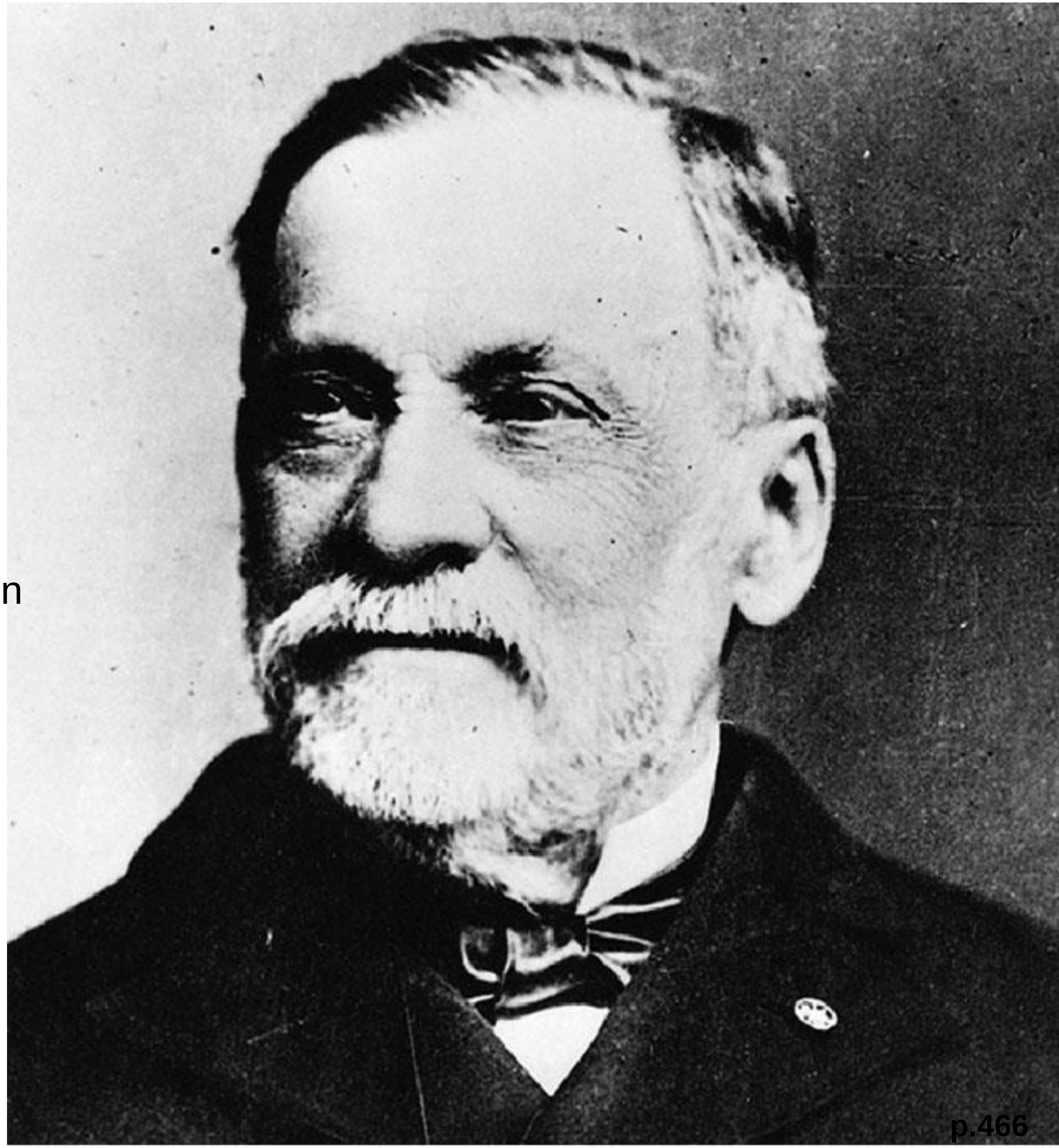
- **Glycolysis** is the first stage of glucose metabolism
- One molecule of glucose is converted to fructose-1,6-bisphosphate, which gives rise to two molecules of pyruvate
- It plays a key role in the way organisms extract energy from nutrients
- Once pyruvate is formed, it has one of several fates

루이 파스퇴르

혐기적, 호기적대사 미생물의 역할 발견

자연발생설 비판-세균설

가열살균법 - pasteurization



p.466

해당의 기능

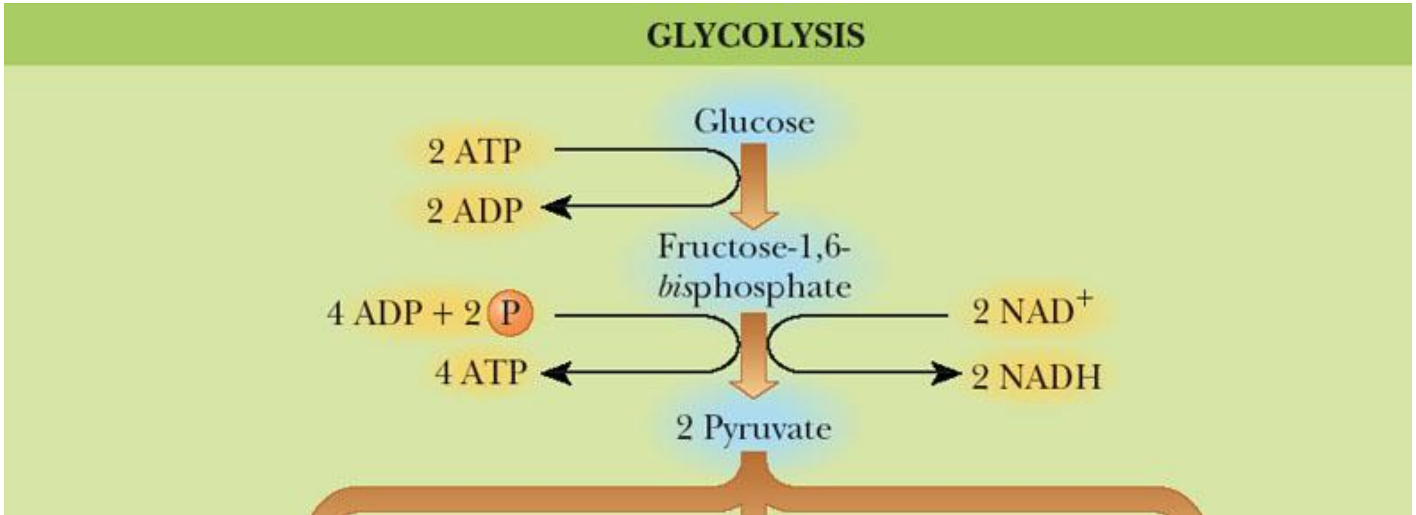
① **ATP 형성**

② **Precursor (전구체) 생성**

㉠ **C6 units**

㉡ **C3 units**

㉢ 중간물질들은 인산에 모두 에스테르화되어있다



해당과정의 주요반응

① 인산기 전달 (phosphoryl transfer) :
ATP로부터 인산기 전달

② 인산기 이동 (Phosphoryl shift) : 한 분자 내에서
인산기가 다른 산소원자로 이동

③ 이성질화 (Isomerization) : 구조식은 같으나 다른
모양의 화합물로 변화

④ 탈수 (Dehydration) : 물 분자의 제거

⑤ 알돌 분해 (Aldol cleavage) : 탄소-탄소 결합의 분해

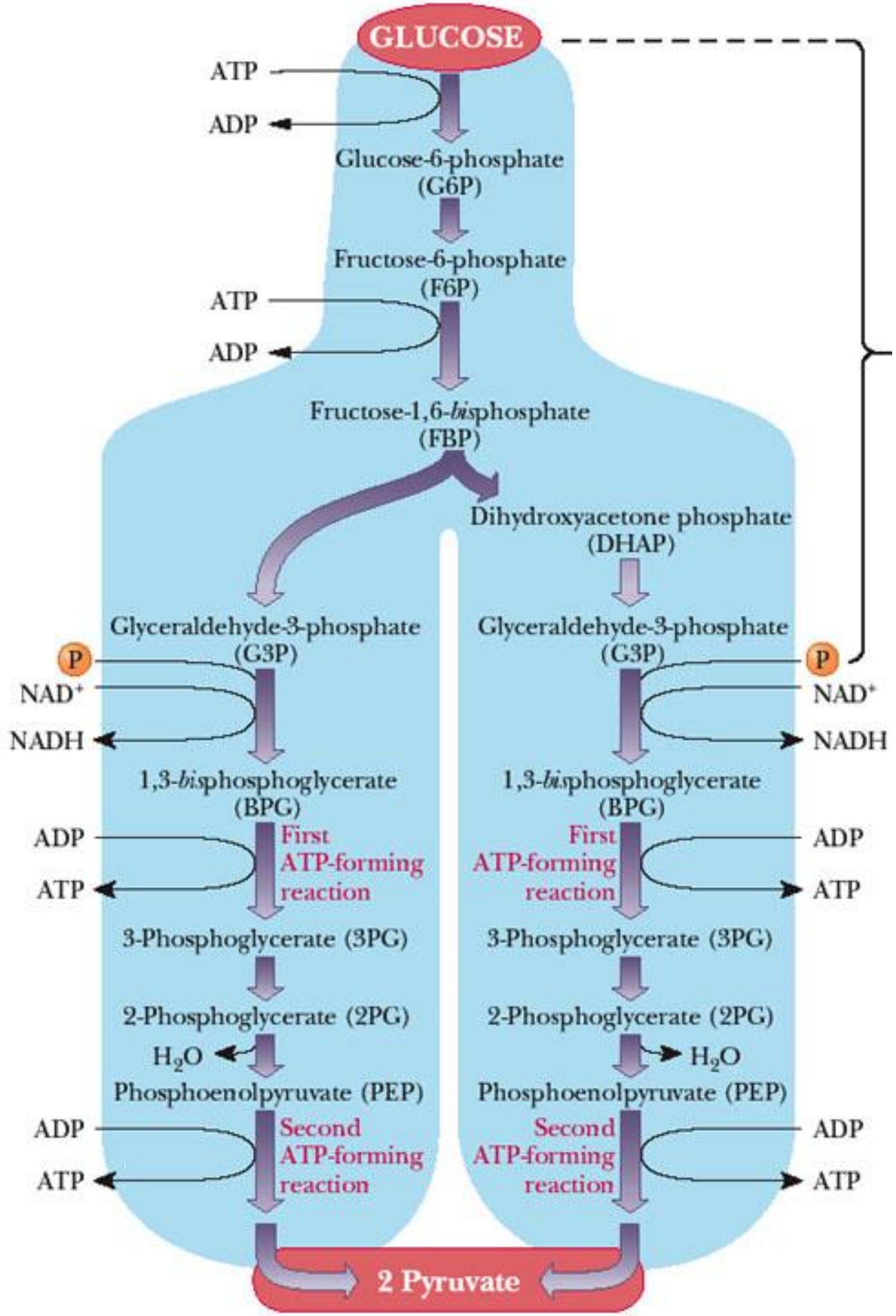
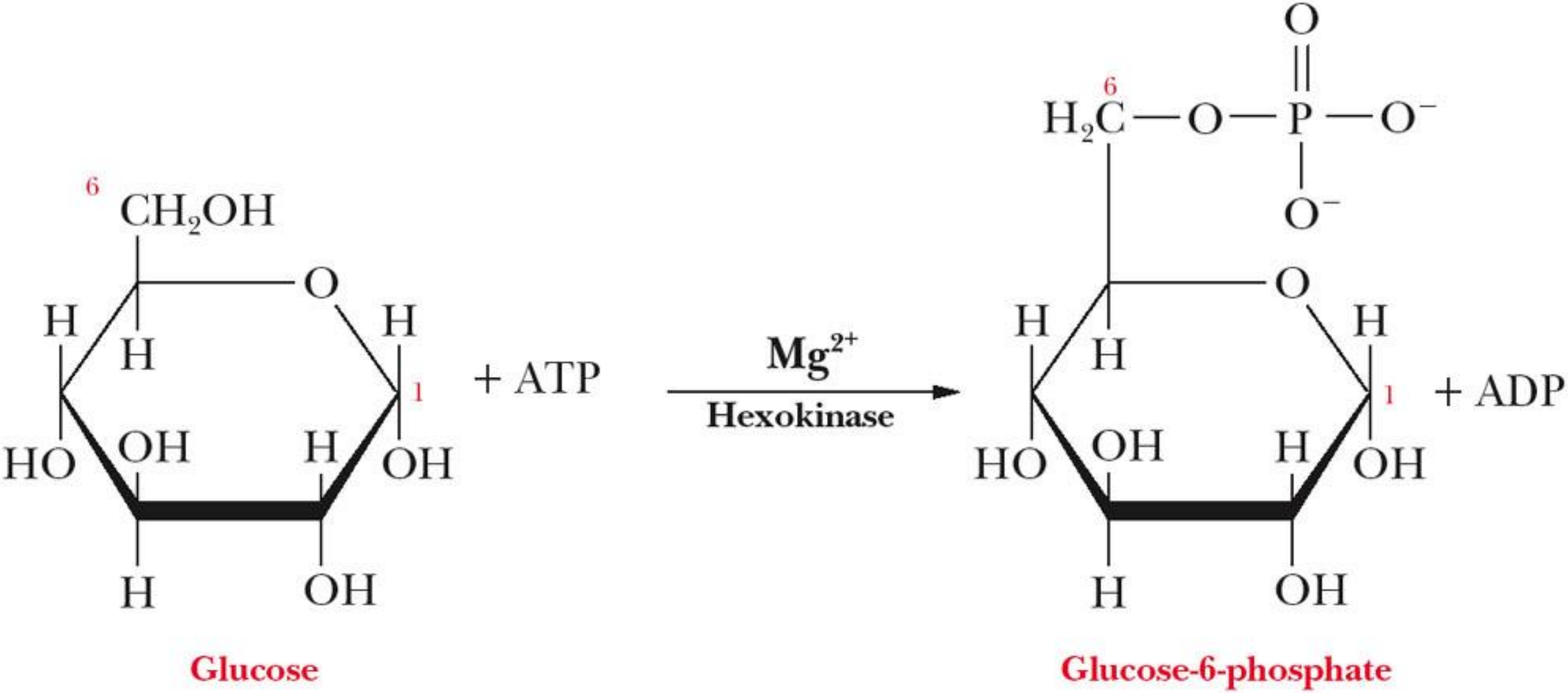


Fig. 17-3a, p.468

육탄당 인산화효소


6
CH2OH
O
H
H
H
1
HO
OH
H
OH
H
OH
+ ATP
Mg2+
Hexokinase
6
H2C—O—P—O−
O
O−
+ ADP
Glucose
Glucose-6-phosphate

Induced-fit의 예 (hexokinase)

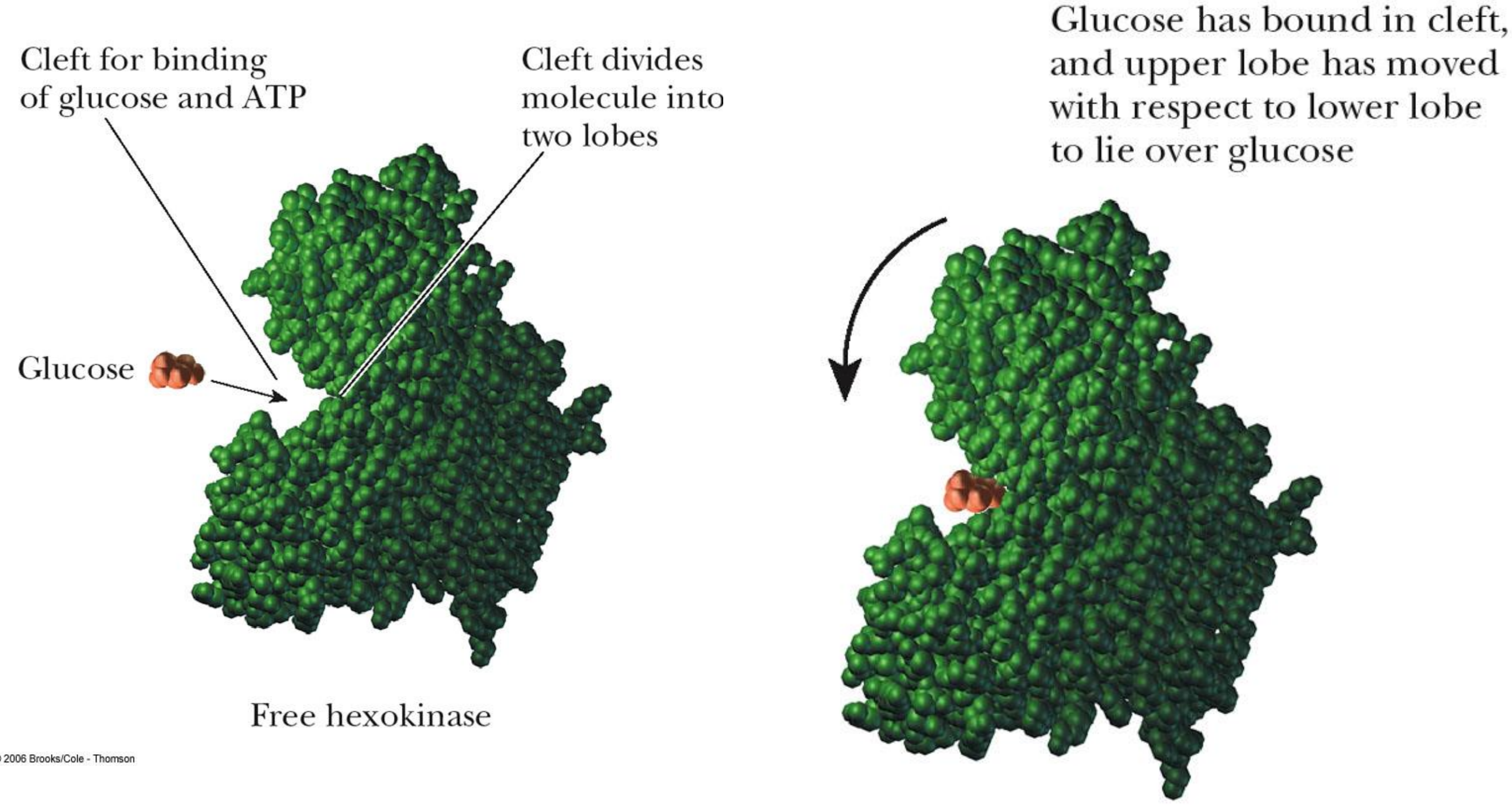
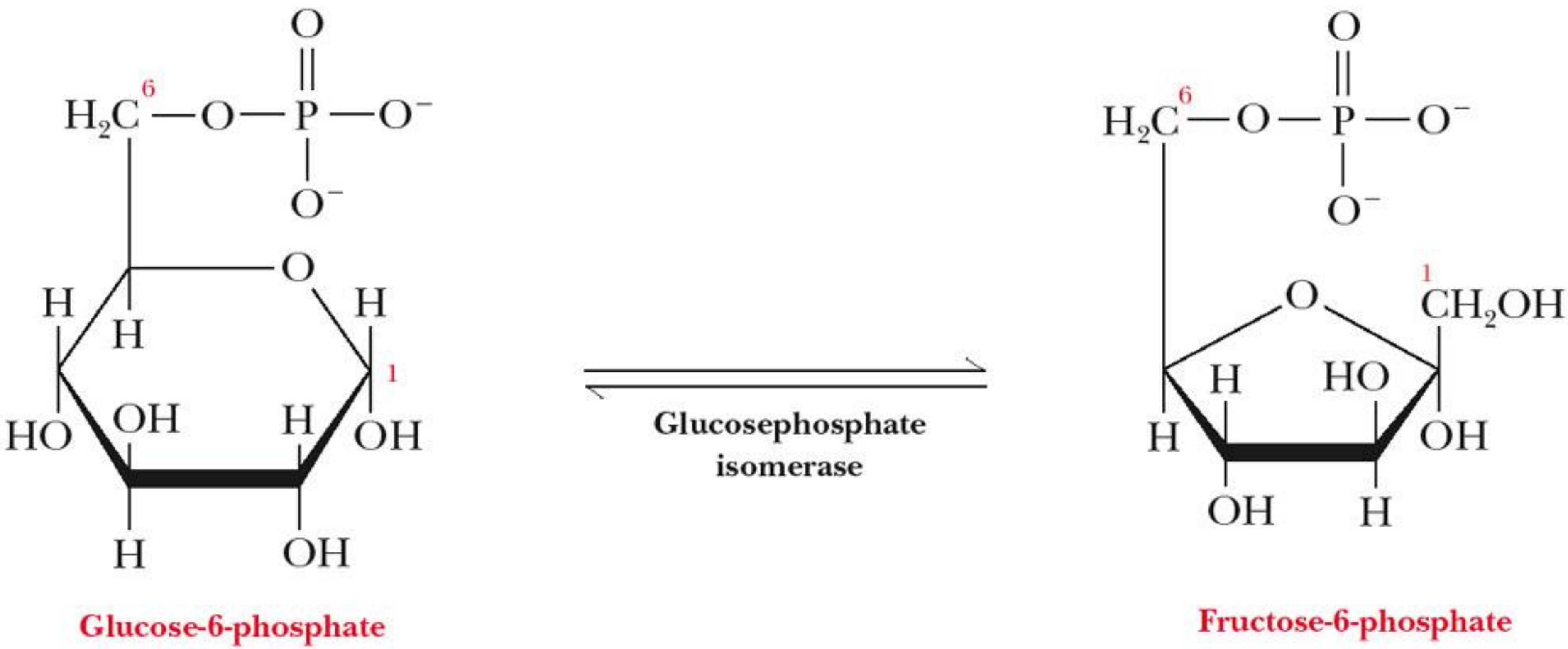
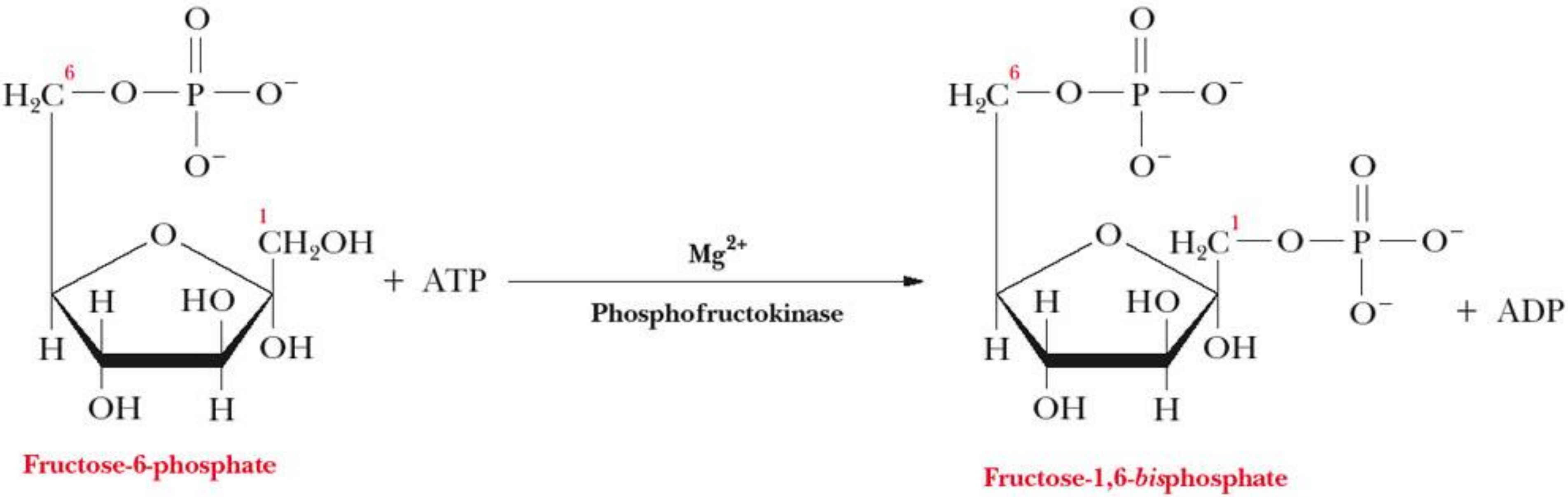


Fig. 17-4a, p.470

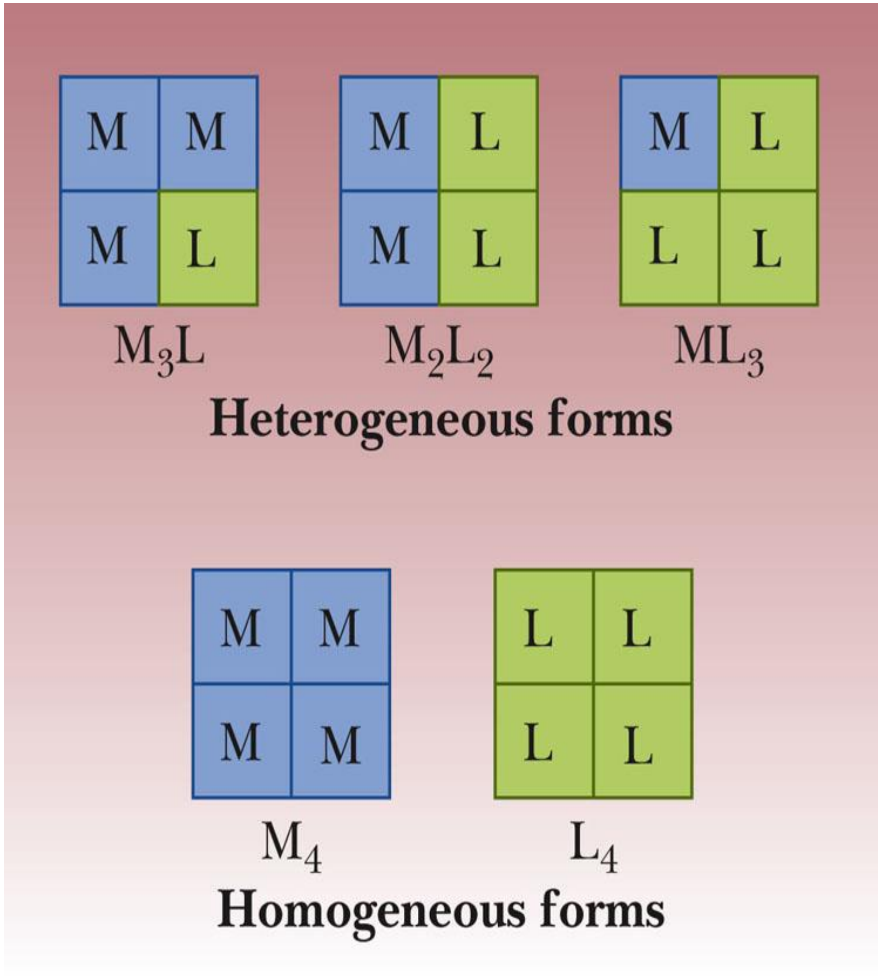
글루코오즈인산 이성화효소



포스포프락토오즈 인산화효소



PFK can exist in Many Isozyme Forms



- Exists as a tetramer.
- Muscles are rich in M_4.
- Liver is rich in L_4.
- subject to allosteric feedback.
- ATP is an allosteric effector.
- high levels inhibit the enzyme, low levels activate it.

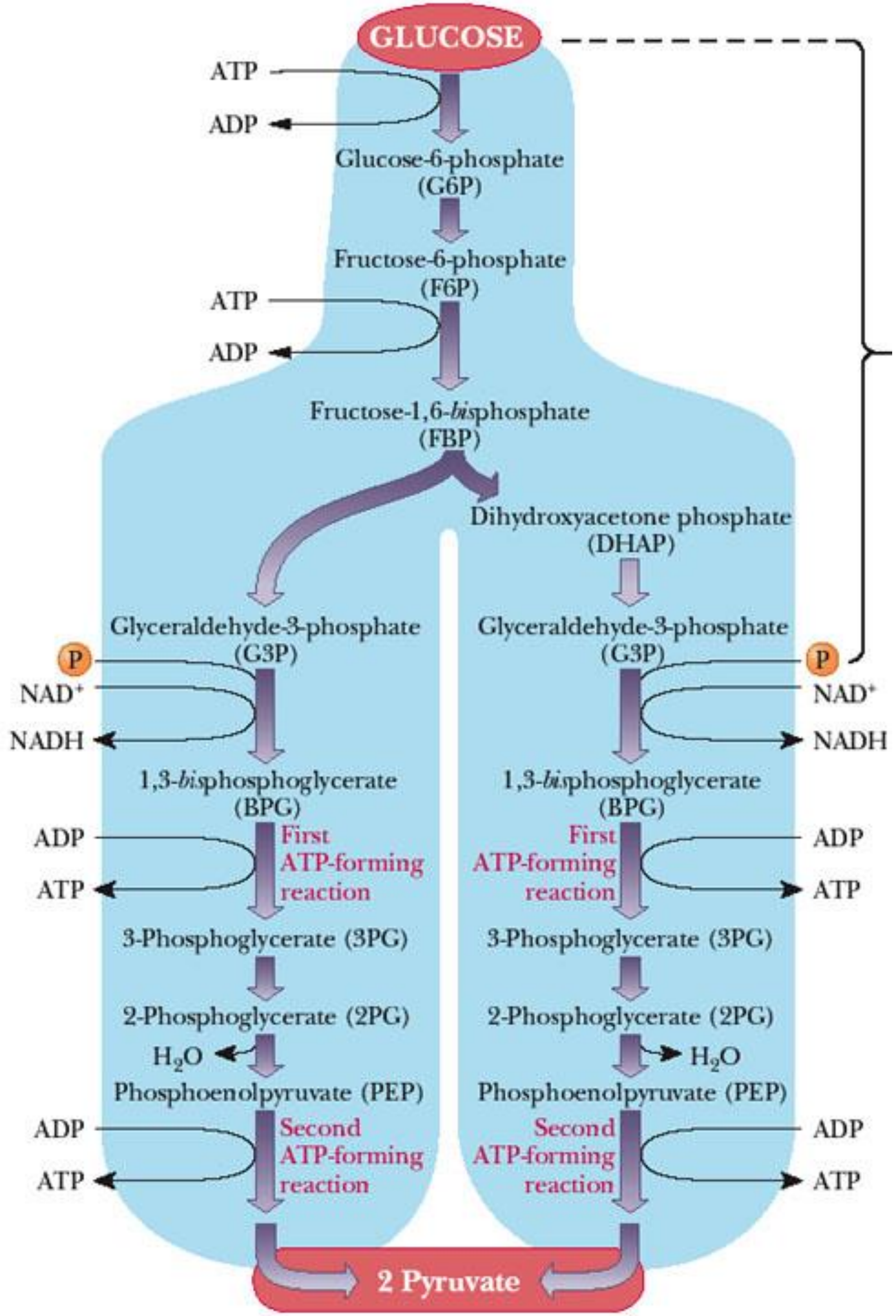
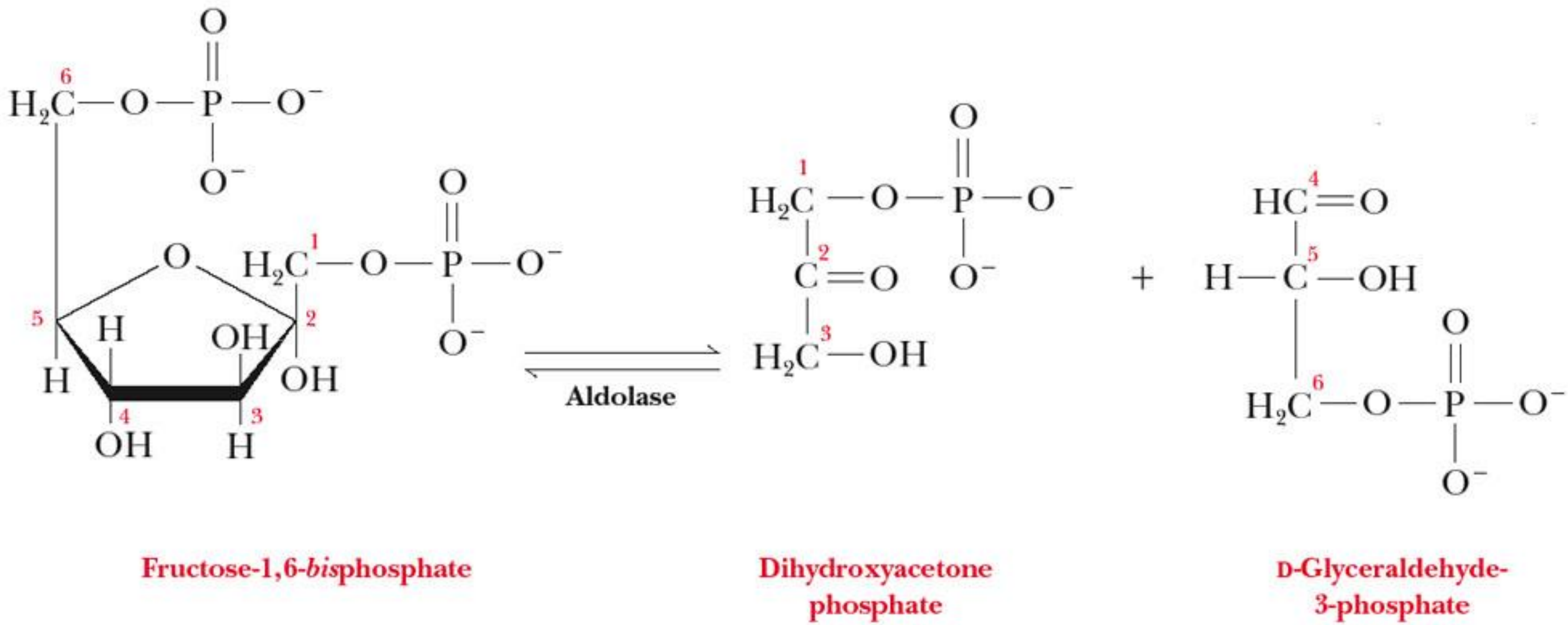


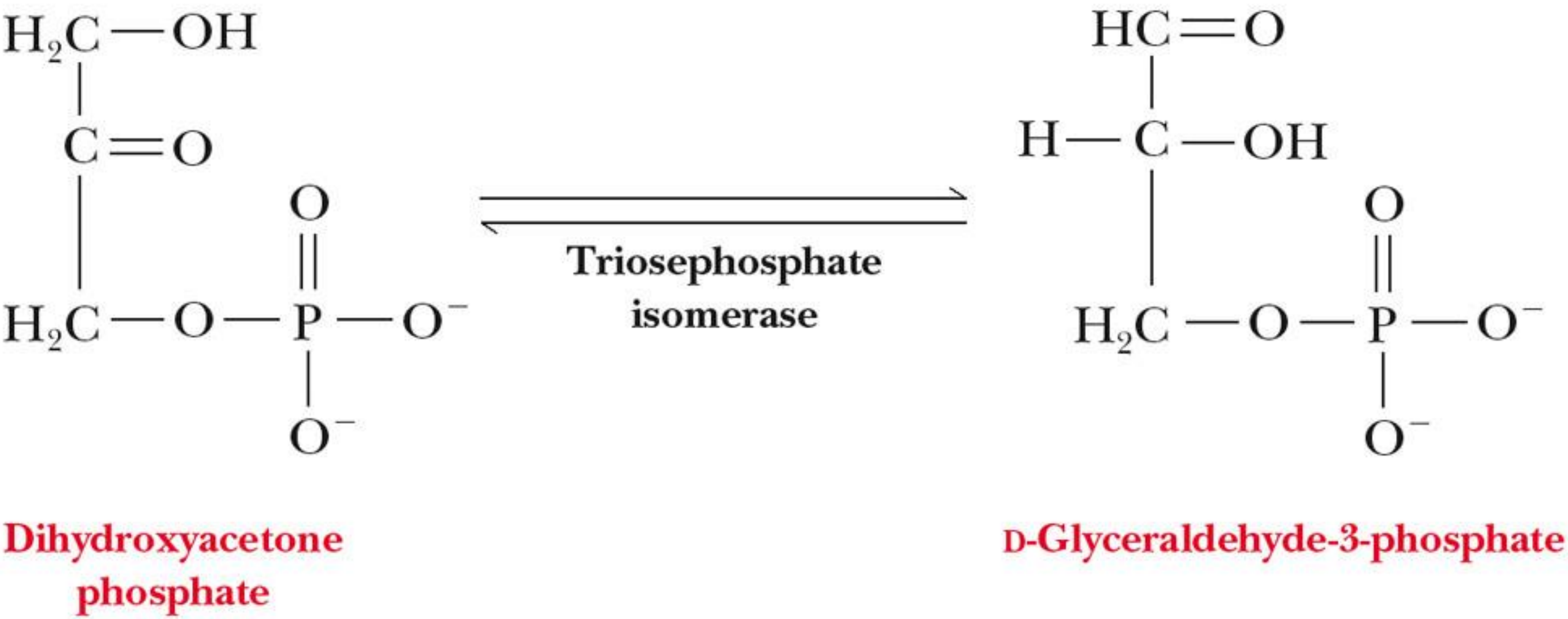
Fig. 17-3a, p.468

알돌레이즈



Aldolase
Fructose-1,6-*bis*phosphate
Dihydroxyacetone phosphate
D-Glyceraldehyde-3-phosphate

3탄당인산 이성화효소



p.471b

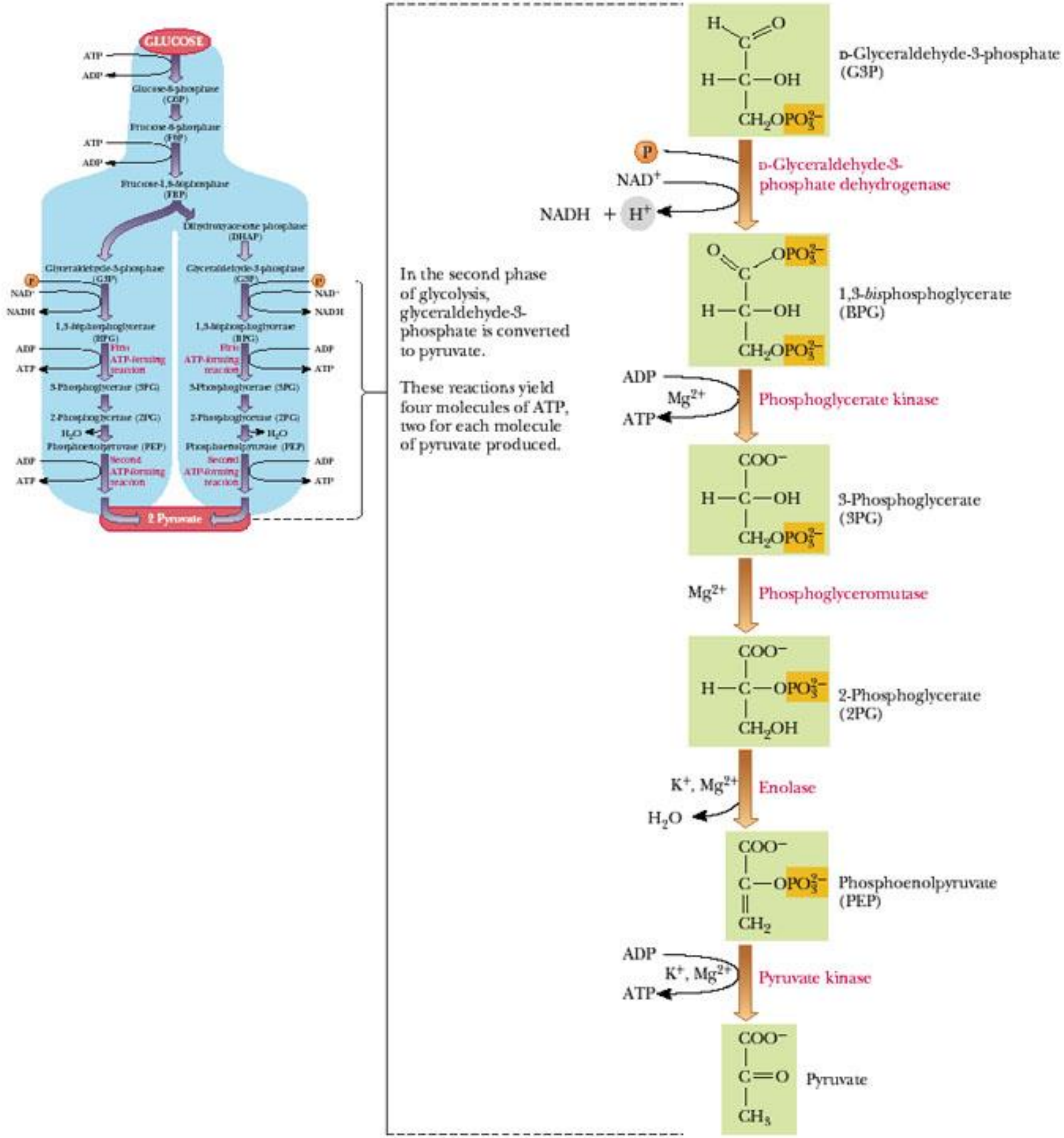
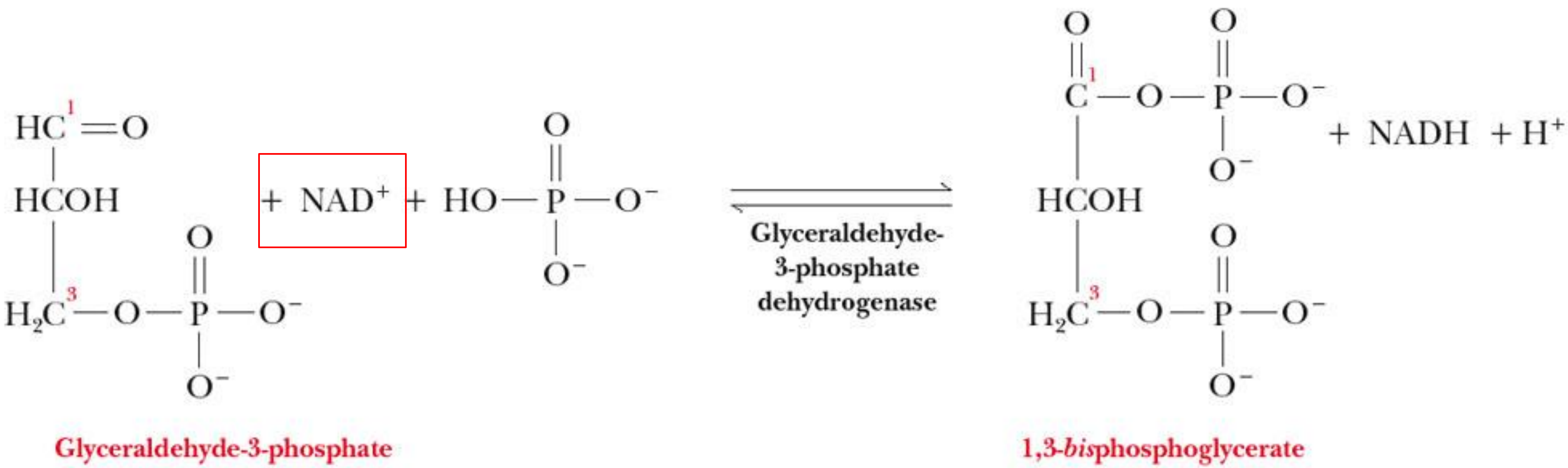
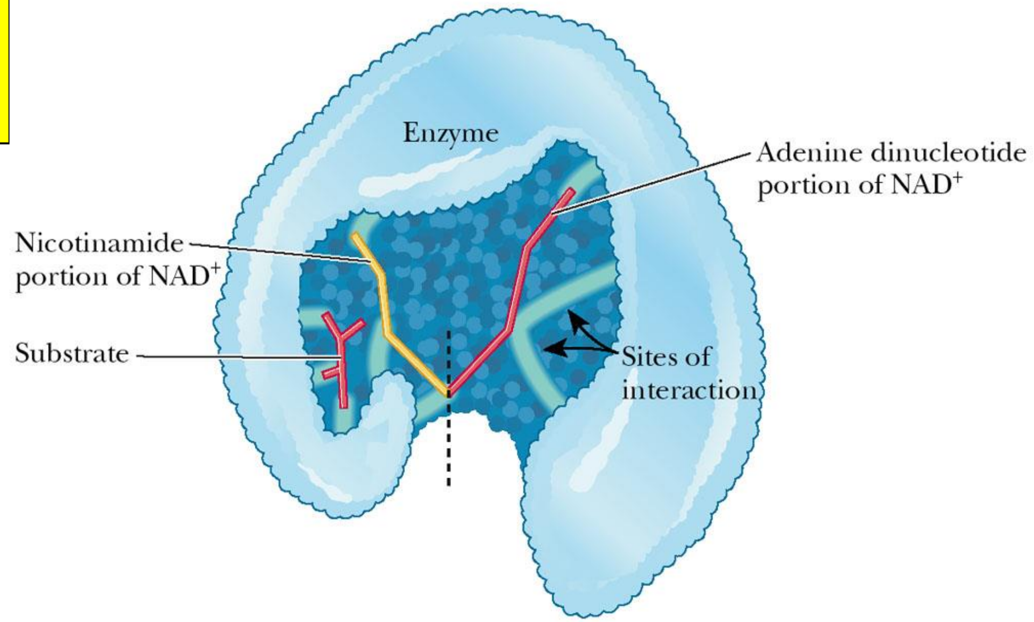

GLUCOSE
2 Pyruvate
In the second phase of glycolysis, glyceraldehyde-3-phosphate is converted to pyruvate.
These reactions yield four molecules of ATP, two for each molecule of pyruvate produced.
D-Glyceraldehyde-3-phosphate (G3P)
D-Glyceraldehyde-3-phosphate dehydrogenase
NAD+
NADH + H+
1,3-bisphosphoglycerate (BPG)
ADP
Mg2+
ATP
Phosphoglycerate kinase
3-Phosphoglycerate (3PG)
Mg2+
Phosphoglyceromutase
2-Phosphoglycerate (2PG)
K+, Mg2+
Enolase
H2O
Phosphoenolpyruvate (PEP)
ADP
K+, Mg2+
ATP
Pyruvate kinase
Pyruvate

Fig. 17-7, p.473

글리세르알데히드-3-인산 탈수소효소



산화 환원 반응



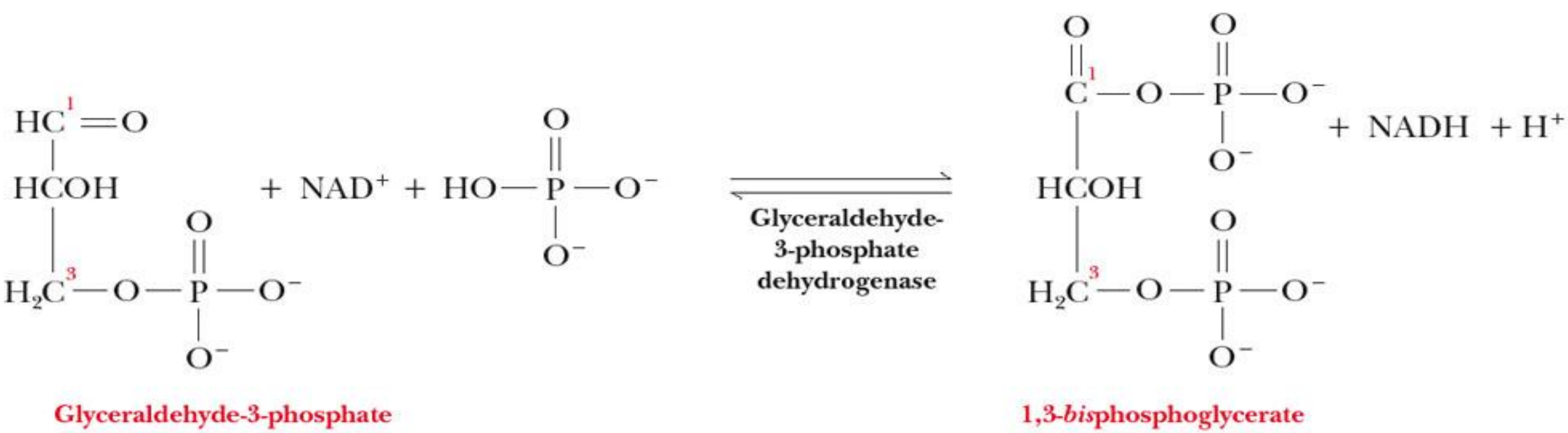
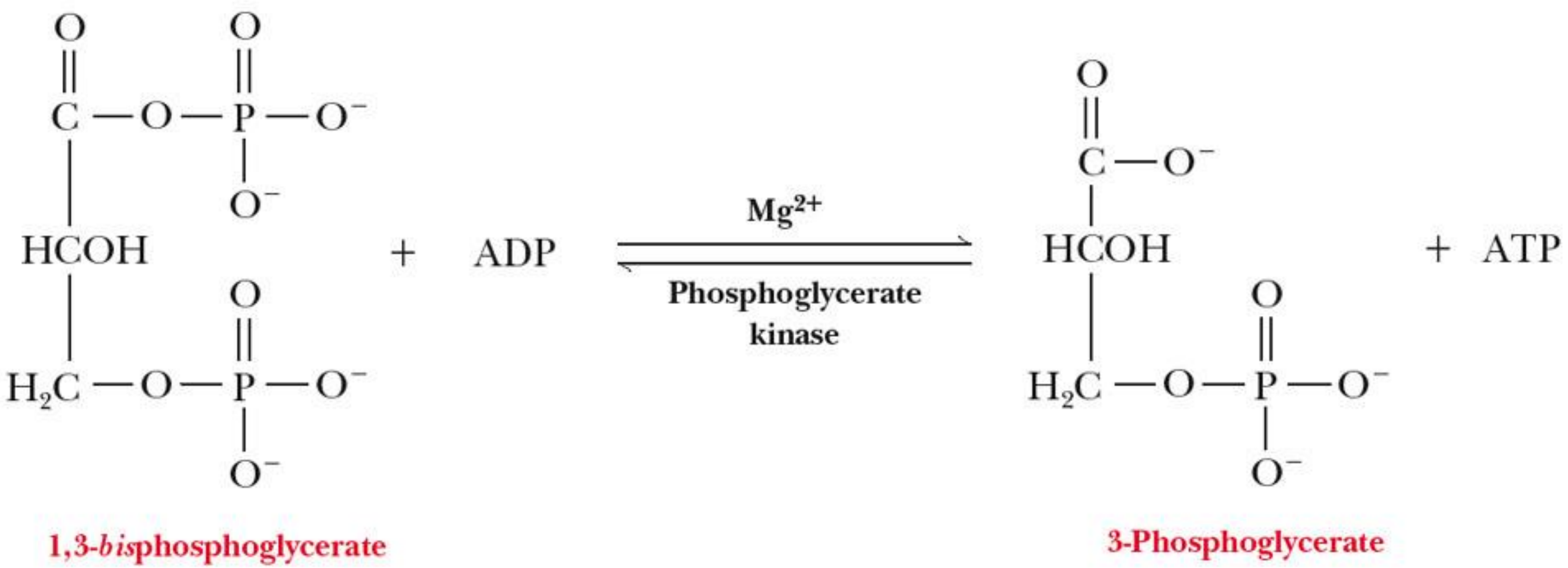


Fig. 17-8, p.475

포스포글리세르산 인산화효소



기질수준인산화

기질수준인산화와 산화적인산화

- 기질수준인산화:

  반응물의 에너지 수준이 높을 때 ATP (7.4 kcal) 로 직접 전달된다.

- 산화적 인산화 :

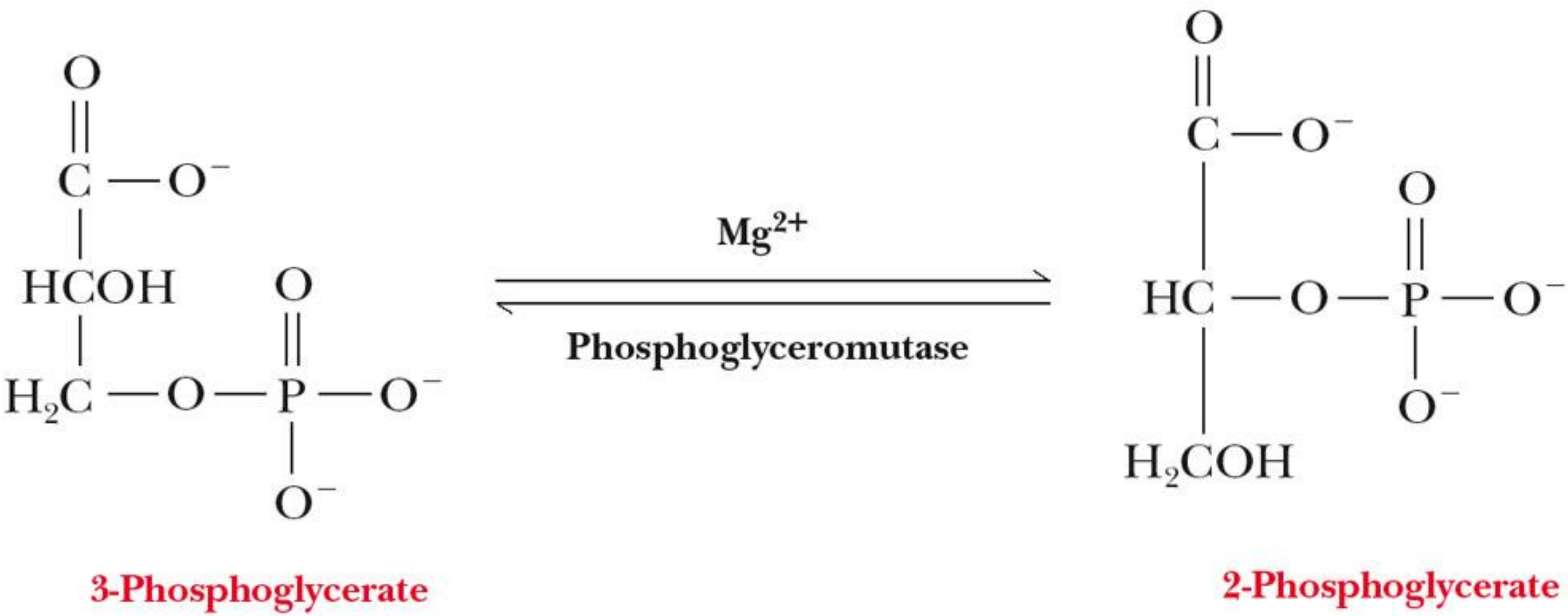
  산소로 전자를 전달하는 과정에서 ATP가 생성된다.

Table 17.1

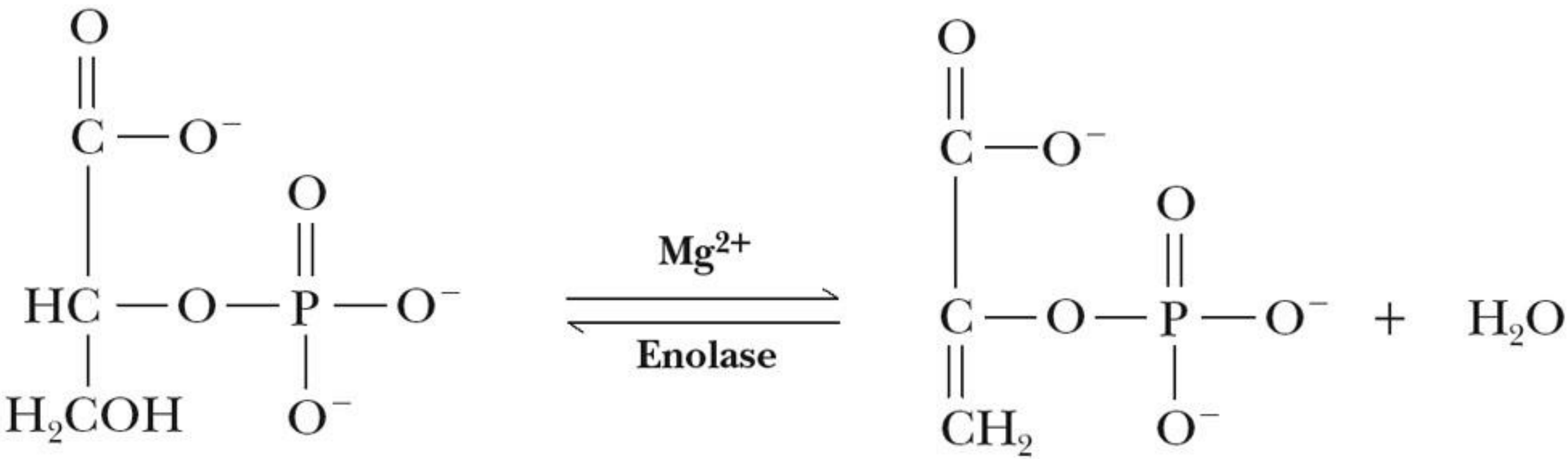
The Reactions of Glycolysis and Their Standard Free-Energy Changes

Step	Reaction	Enzyme	$\Delta G^{\circ\prime}$*	
			kJ mol^{-1}	kcal mol^{-1}
1	Glucose + ATP $\rightarrow$ Glucose-6-phosphate + ADP	Hexokinase/Glucokinase	−16.7	−4.0
2	Glucose-6-phosphate $\rightarrow$ Fructose-6-phosphate	Glucose phosphate isomerase	+1.67	+0.4
3	Fructose-6-phosphate + ATP $\rightarrow$ Fructose-1,6-*bis*phosphate + ADP	Phosphofructokinase	−14.2	−3.4
4	Fructose-1,6-*bis*phosphate $\rightarrow$ Dihydroxyacetone phosphate + Glyceraldehyde-3-phosphate	Aldolase	+23.9	+5.7
5	Dihydroxyacetone phosphate $\rightarrow$ Glyceraldehyde-3-phosphate	Triose phosphate isomerase	+7.56	+1.8
6	2(Glyceraldehyde-3-phosphate + NAD^+ + P_i $\rightarrow$ 1,3-*bis*phosphoglycerate + NADH + H^+)	Glyceraldehyde-3-P dehydrogenase	2(+6.20)	2(+1.5)
7	2(1,3-*bis*phosphoglycerate + ADP $\rightarrow$ 3-Phosphoglycerate + ATP)	Phosphoglycerate kinase	2(−18.8)	2(−4.5)
8	2(3-Phosphoglycerate $\rightarrow$ 2-Phosphoglycerate)	Phosphoglyceromutase	2(+4.4)	2(+1.1)
9	2(2-Phosphoglycerate $\rightarrow$ Phosphoenolpyruvate + H_2O)	Enolase	2(+1.8)	2(+0.4)
10	2(Phosphoenolpyruvate + ADP $\rightarrow$ Pyruvate + ATP)	Pyruvate kinase	2(−31.4)	2(−7.5)
Overall	Glucose + 2 ADP + 2 P_i + NAD^+ $\rightarrow$ 2 Pyruvate $\rightarrow$ 2 ATP + NADH + H^+	Lactate dehydrogenase	−73.3	−17.5
	2 Pyruvate + NADH + H^+ $\rightarrow$ Lactate + NAD^+		2(−25.1)	2(−6.0)
	Glucose + 2 ADP + 2 P_i $\rightarrow$ 2 Lactate + 2 ATP		−123.5	−29.5

포스포글리세르산 뮤테이즈



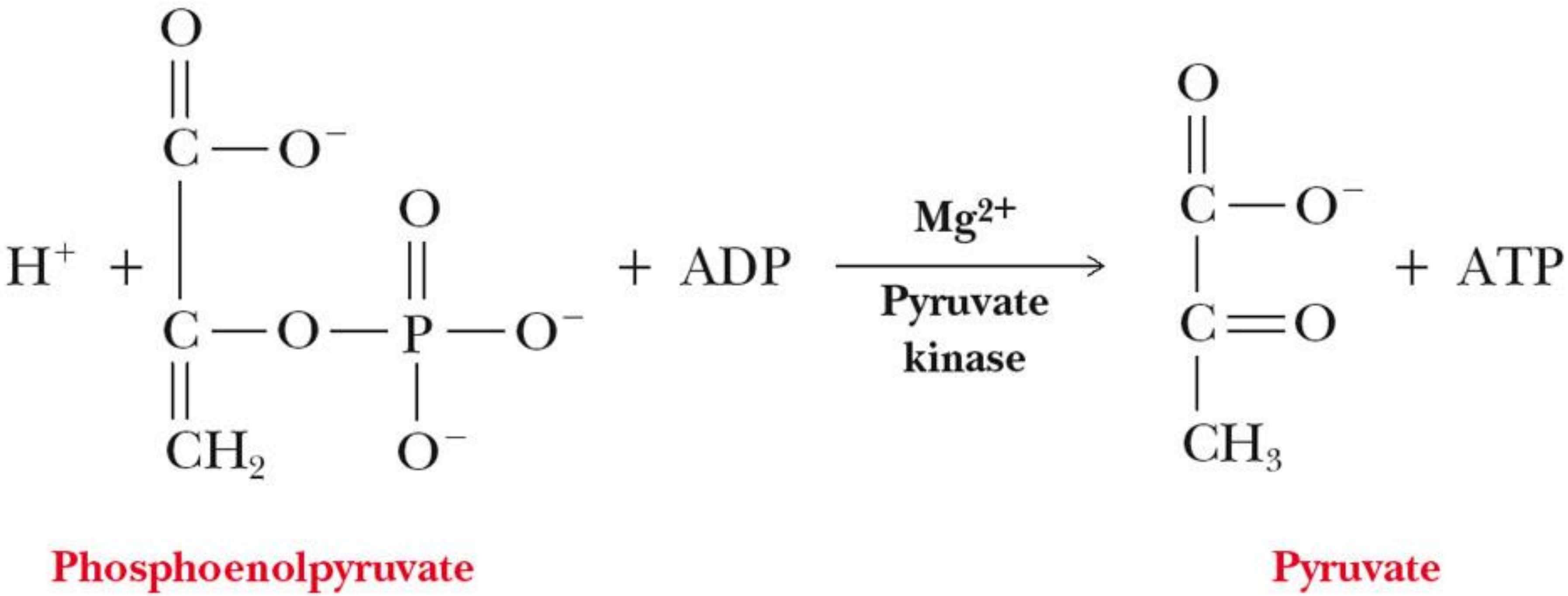
엔올레이즈



2-Phosphoglycerate

Phosphenolpyruvate (PEP)

피루브산 인산화효소



기질수준인산화

해당과정의 에너지 수득율

Glucose + 2 NAD+ + 2 Pi + 2 ADP

---> 2 pyruvate + 2 ATP + 2 NADH

+ 2 H^+ + 2 H_2O

Δ G'= -17.5 kcal/mole

해당과정의 자유에너지 변화

Table 17.1

The Reactions of Glycolysis and Their Standard Free-Energy Changes

Step	Reaction	Enzyme	$\Delta G^{\circ\prime}$* kJ mol^{-1}	$\Delta G^{\circ\prime}$* kcal mol^{-1}	ΔG** kJ/mol
1	Glucose + ATP → Glucose-6-phosphate + ADP	Hexokinase/Glucokinase	−16.7	−4.0	−33.9
2	Glucose-6-phosphate → Fructose-6-phosphate	Glucose phosphate isomerase	+1.67	+0.4	−2.92
3	Fructose-6-phosphate + ATP → Fructose-1,6-*bis*phosphate + ADP	Phosphofructokinase	−14.2	−3.4	−18.8
4	Fructose-1,6-*bis*phosphate → Dihydroxyacetone phosphate + Glyceraldehyde-3-phosphate	Aldolase	+23.9	+5.7	−0.23
5	Dihydroxyacetone phosphate → Glyceraldehyde-3-phosphate	Triose phosphate isomerase	+7.56	+1.8	+2.41
6	2(Glyceraldehyde-3-phosphate + NAD^+ + P_i → 1,3-*bis*phosphoglycerate + NADH + H^+)	Glyceraldehyde-3-P dehydrogenase	2(+6.20)	2(+1.5)	2(−1.29)
7	2(1,3-*bis*phosphoglycerate + ADP → 3-Phosphoglycerate + ATP)	Phosphoglycerate kinase	2(−18.8)	2(−4.5)	2(+0.1)
8	2(3-Phosphoglycerate → 2-Phosphoglycerate)	Phosphoglyceromutase	2(+4.4)	2(+1.1)	2(+0.83)
9	2(2-Phosphoglycerate → Phosphoenolpyruvate + H_2O)	Enolase	2(+1.8)	2(+0.4)	2(+1.1)
10	2(Phosphoenolpyruvate + ADP → Pyruvate + ATP)	Pyruvate kinase	2(−31.4)	2(−7.5)	2(−23.0)
Overall	Glucose + 2 ADP + 2 P_i + NAD^+ → 2 Pyruvate → 2 ATP + NADH + H^+	Lactate dehydrogenase	−73.3	−17.5	−98.0
	2 Pyruvate + NADH + H^+ → Lactate + NAD^+		2(−25.1)	2(−6.0)	2(−14.8)
	Glucose + 2 ADP + 2 P_i → 2 Lactate + 2 ATP		−123.5	[illegible]	[illegible]

Table 17-1, p.469

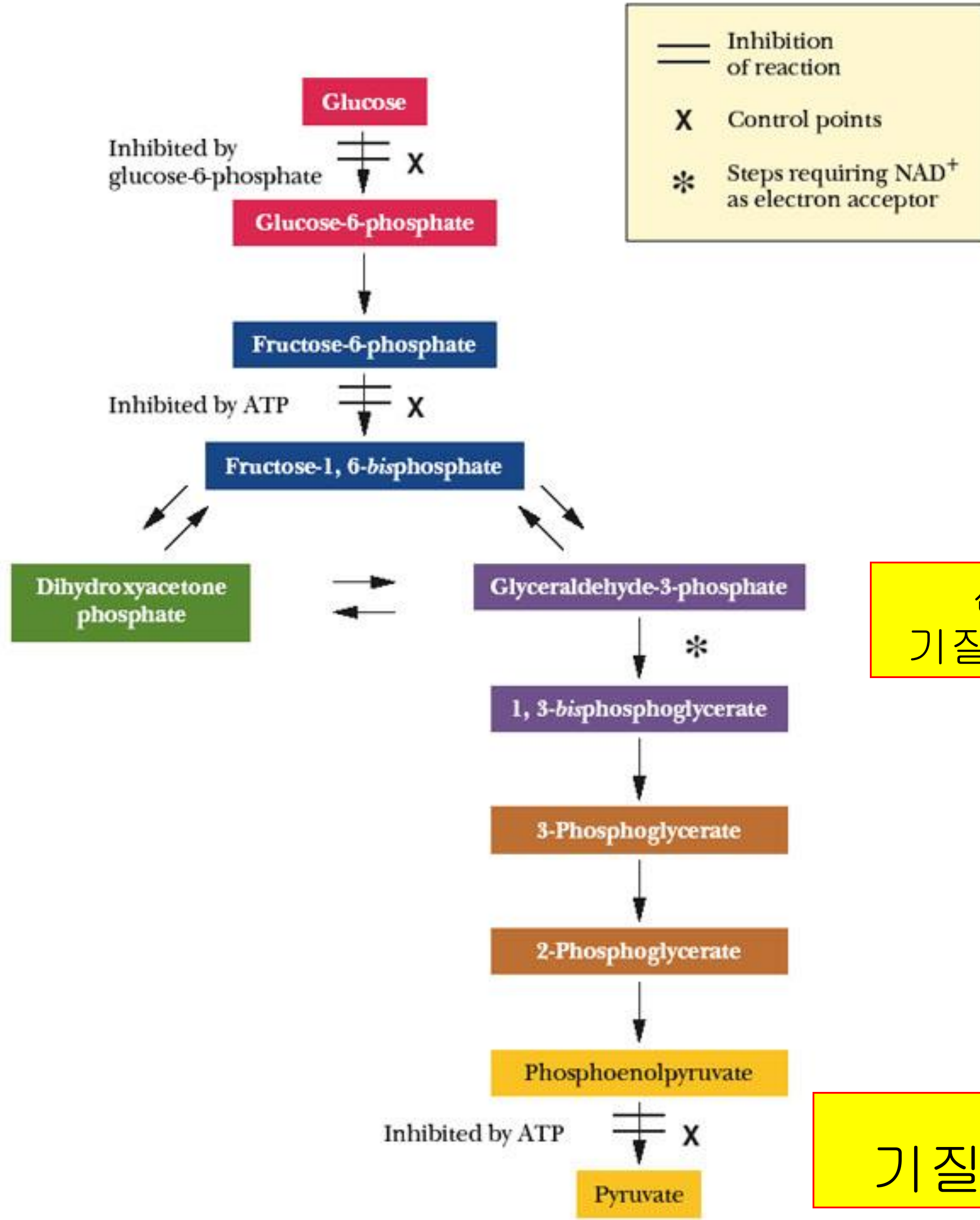
해당과정은 언제 활발할까?

Regulation of glycolysis

① 특정 효소의 양 조절

- Feedback inhibition
- Covalent modification

② 에너지 부하에 의해 조절



산화반응
기질수준인산화

기질수준인산화

해당과정을 조절하는 효소

- **Hexokinase (HK)**

- **Phosphofructokinase (PF1K)**
  ㉠ **regulated in all tissues**
  ㉡ **key regulatory site in glycolysis**
  ㉢ **inhibited by ATP, citrate**
  ㉣ **activated by AMP**

- **Pyruvate kinase**

Hexokinase

㉠ regulated in brain and RBC , not in muscle (적혈구의 포도당 농도 5mM)

㉡ inhibited by glucose-6-phosphate

- 적혈구에서 해당과정이 손상되면 산소운반에 영향을 미친다.
- 왜냐하면 적혈구에는 mitochondria 가 없어 해당과정만 발생하기 때문이다.

Hexokinase와 glucokinase의 비교

㉠ **HK: glucose-6-phosphate 생산**
GK: glucose-1-phosphate 생산

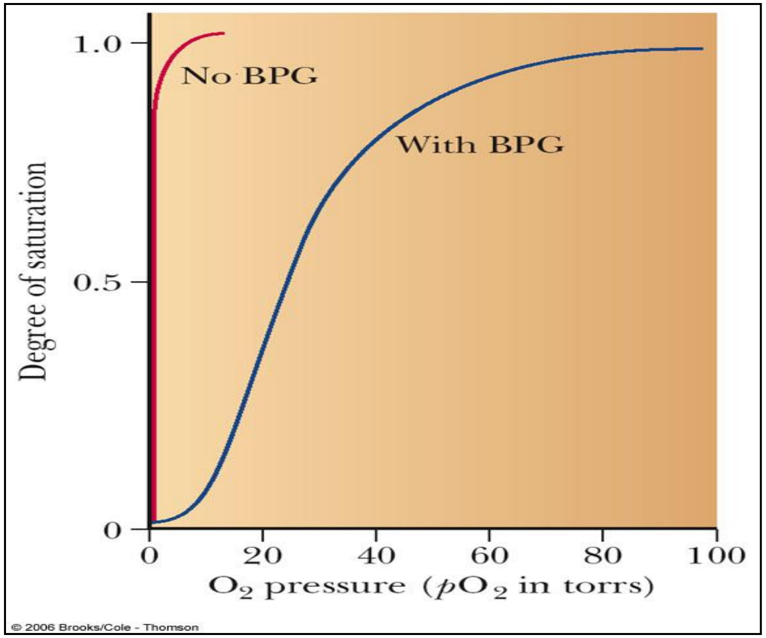
㉡ **HK: 해당과정에서 작용**
GK: glycogen 합성

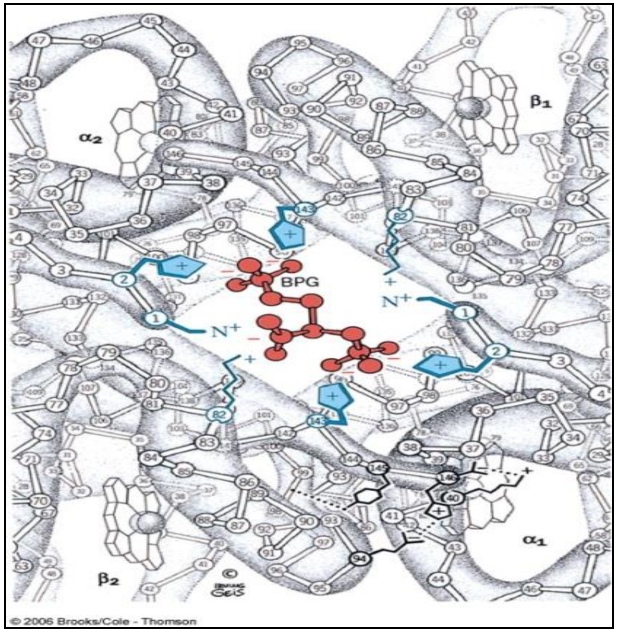
GK의 특성

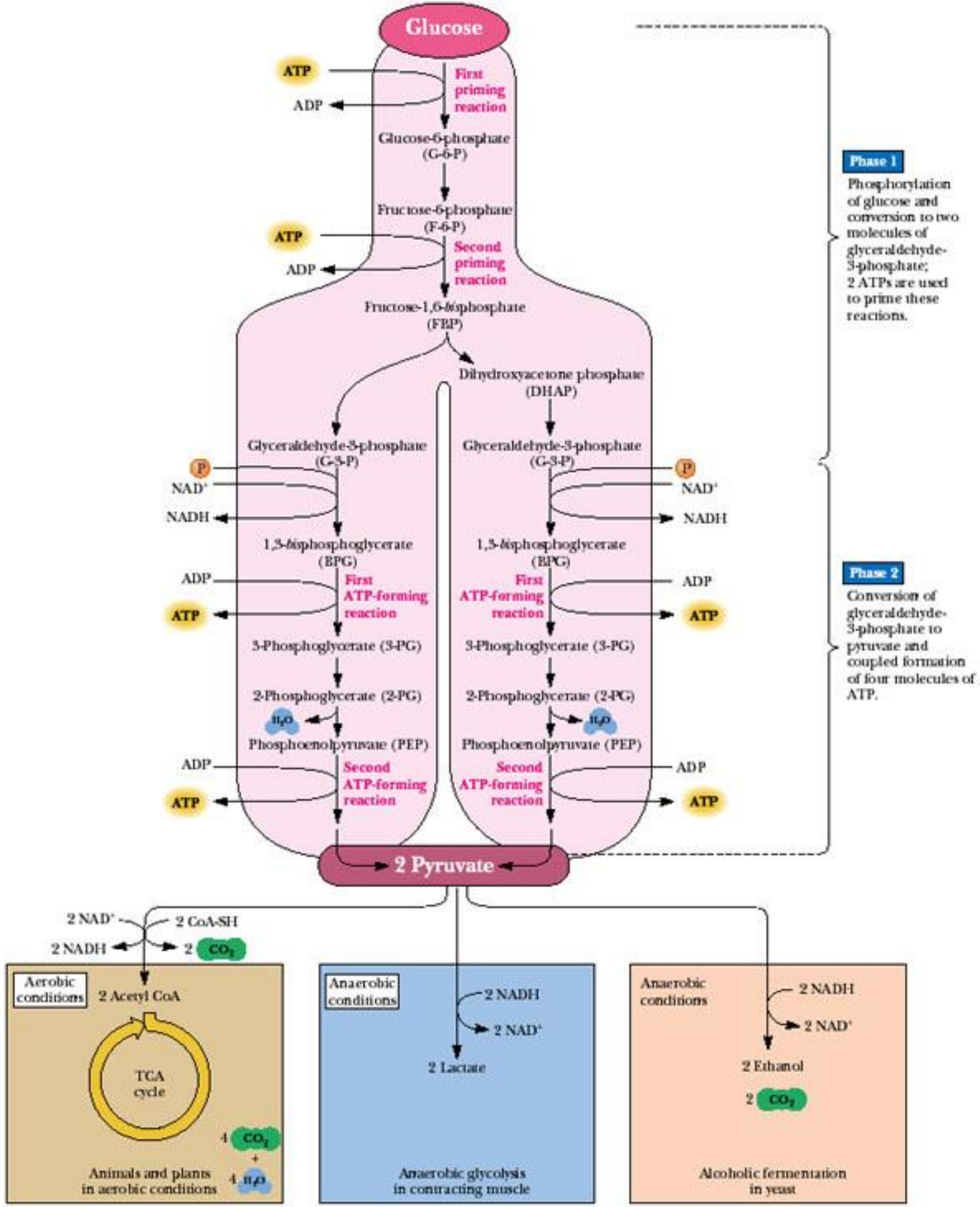
Ⓐ **effective when glucose is abundant → glucose-1-p → glycogen 합성 가능**
Ⓑ 인슐린에 의해 유도되는 효소
Ⓒ 생성물에 의해 방해되지 않는다

해당과정의 중요성

- 1,3-BPR로부터 2,3-BPG 생성
- 2,3-BPG 가 결여되면 헤모글로빈이 높은 산소친화력을 지녀 말초조직에 산소 운반을 어렵게 한다.







Glucose
ATP
ADP
First priming reaction
Glucose-6-phosphate (G-6-P)
Fructose-6-phosphate (F-6-P)
ATP
ADP
Second priming reaction
Fructose-1,6-bisphosphate (FBP)
Dihydroxyacetone phosphate (DHAP)
Glyceraldehyde-3-phosphate (G-3-P)
Glyceraldehyde-3-phosphate (G-3-P)
P
NAD+
NADH
1,3-bisphosphoglycerate (BPG)
ADP
ATP
First ATP-forming reaction
3-Phosphoglycerate (3-PG)
2-Phosphoglycerate (2-PG)
H2O
Phosphoenolpyruvate (PEP)
ADP
ATP
Second ATP-forming reaction
2 Pyruvate
Phase 1
Phosphorylation of glucose and conversion to two molecules of glyceraldehyde-3-phosphate; 2 ATPs are used to prime these reactions.
Phase 2
Conversion of glyceraldehyde-3-phosphate to pyruvate and coupled formation of four molecules of ATP.
2 NAD+
2 CoA-SH
2 NADH
2 CO2
Aerobic conditions
2 Acetyl CoA
TCA cycle
4 CO2
+
4 H2O
Animals and plants in aerobic conditions
Anaerobic conditions
2 NADH
2 NAD+
2 Lactate
Anaerobic glycolysis in contracting muscle
Anaerobic conditions
2 NADH
2 NAD+
2 Ethanol
2 CO2
Alcoholic fermentation in yeast

Fig. 17-2, p.465

Pyruvate는 어떻게 활용되는가?

1) 젖산으로 전환

<pyruvate + NADH --> lactate + NAD+>

LDH (lactate dehydrogenase): **allosteric enzyme**

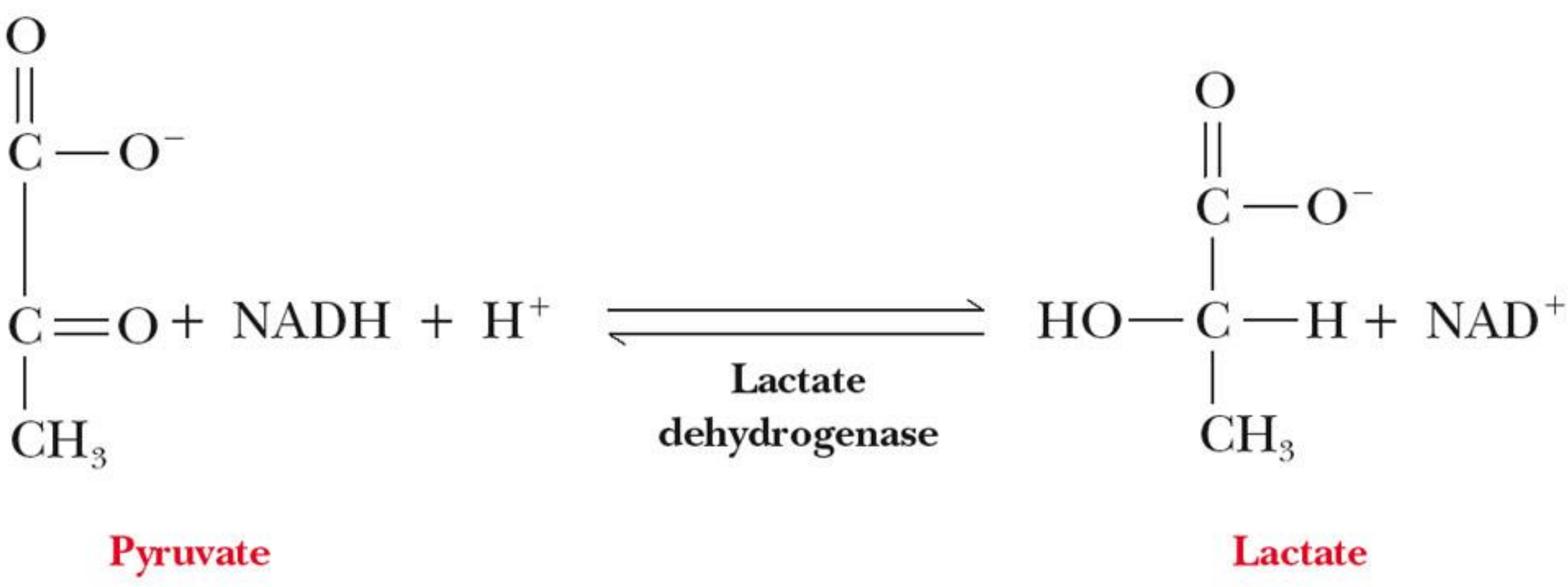
NAD+는 혐기적인 상황에서 해당과정을 지속시키는 원동력

2) 아세틸 CoA로 전환

3) Oxaloacetate나 malate로 전환됨

4) Alanine으로 전환

1) 젖산으로 전환



O
C — O⁻
C = O + NADH + H+
CH3
Lactate
dehydrogenase
O
C — O⁻
HO — C — H + NAD+
CH3
Pyruvate
Lactate

(b) Lactic acid fermentation

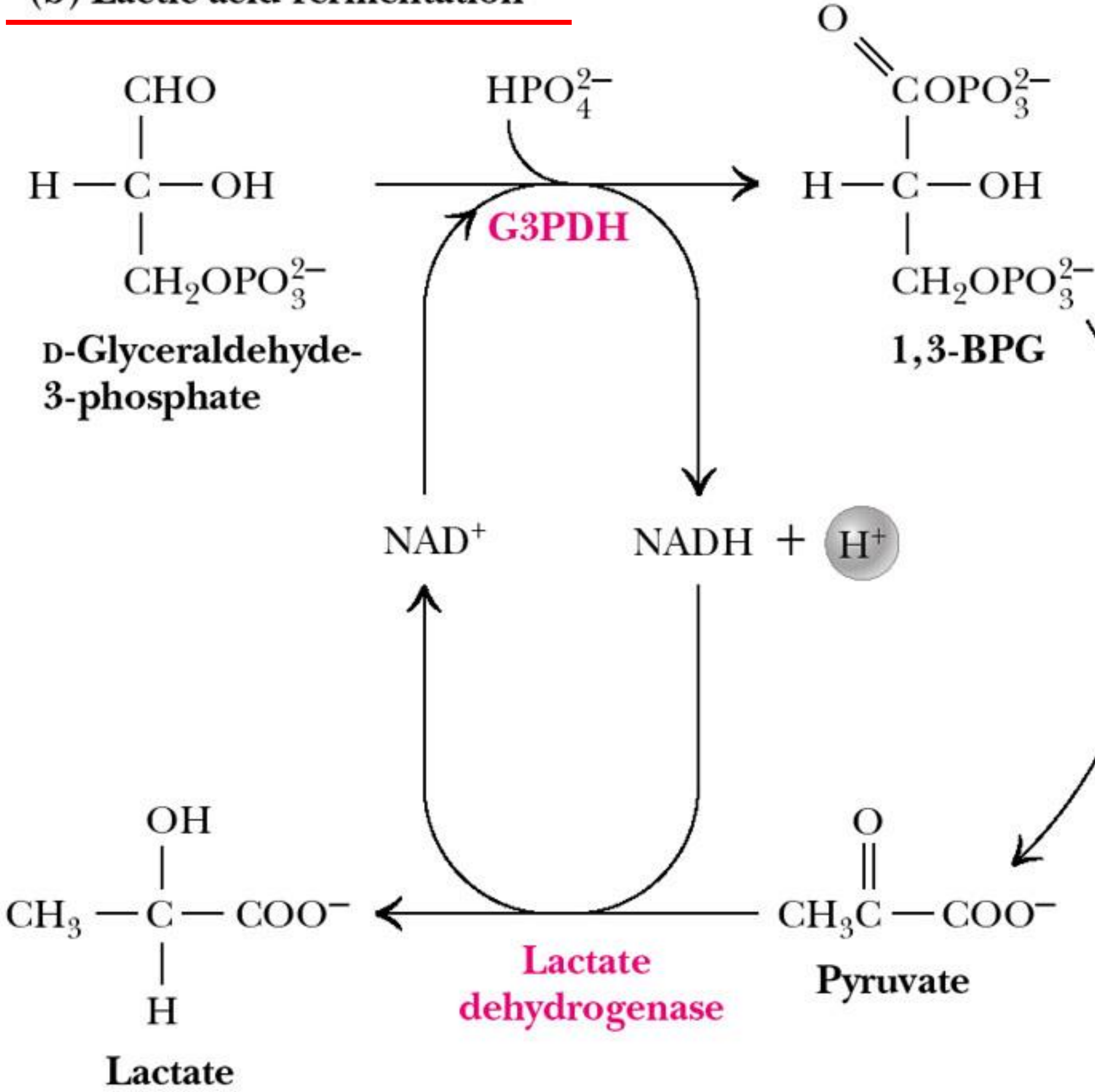


Fig. 17-11b, p.481

Pyruvate는 어떻게 활용되는가?

5) 알콜로 발효

<pyruvate--> acetadehyde--->ethanol>

Glucose + 2 ADP+ + pi ---> 2 ethanol + 2 ATP + 2 CO_2 + 2 H_2O

(a) Alcoholic fermentation

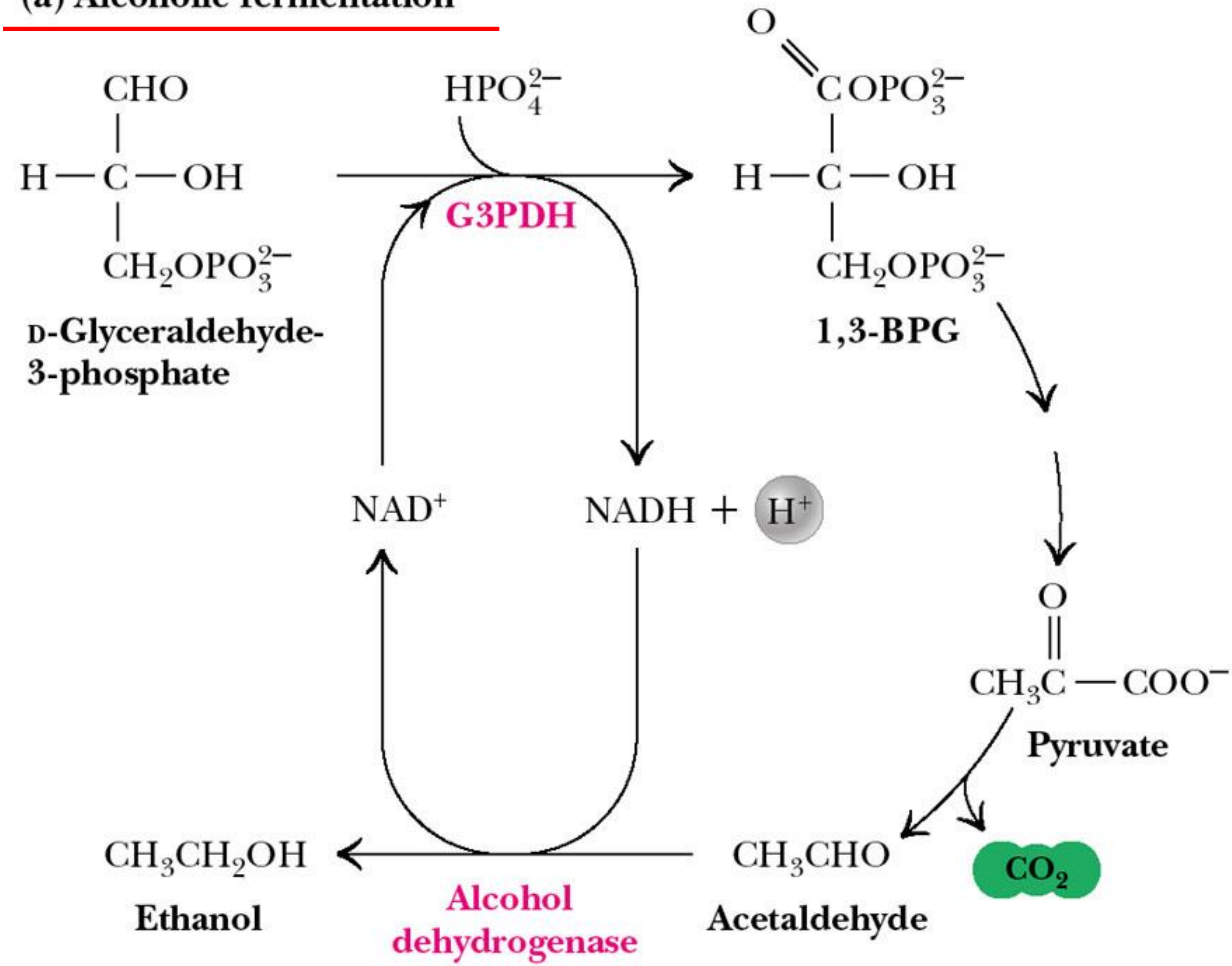
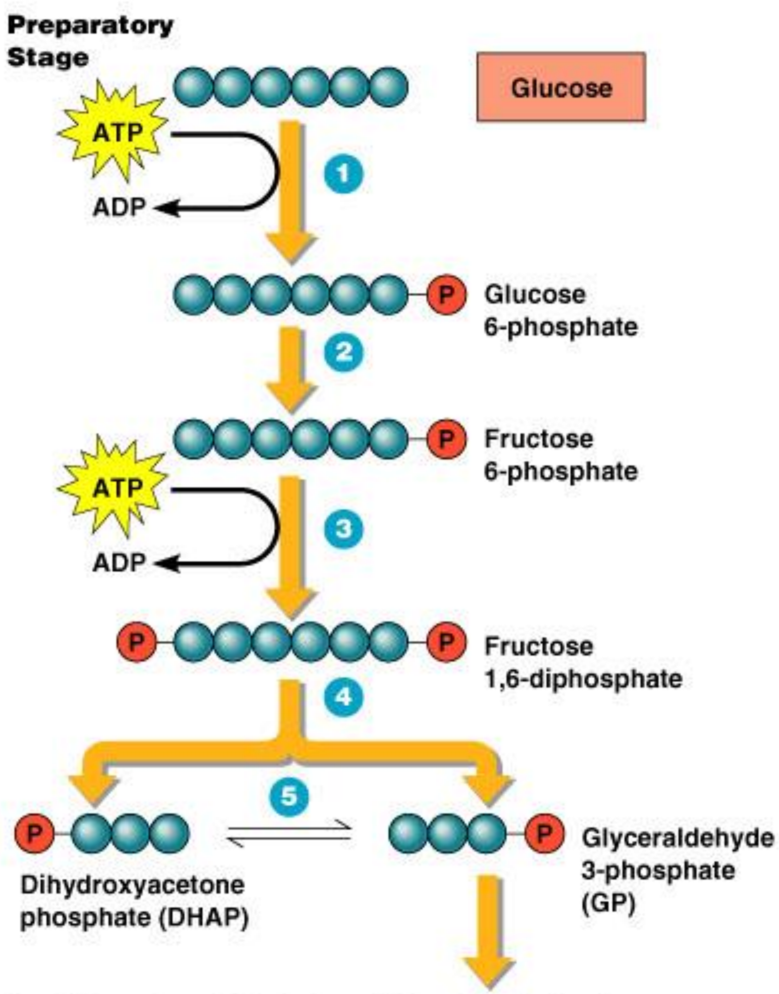
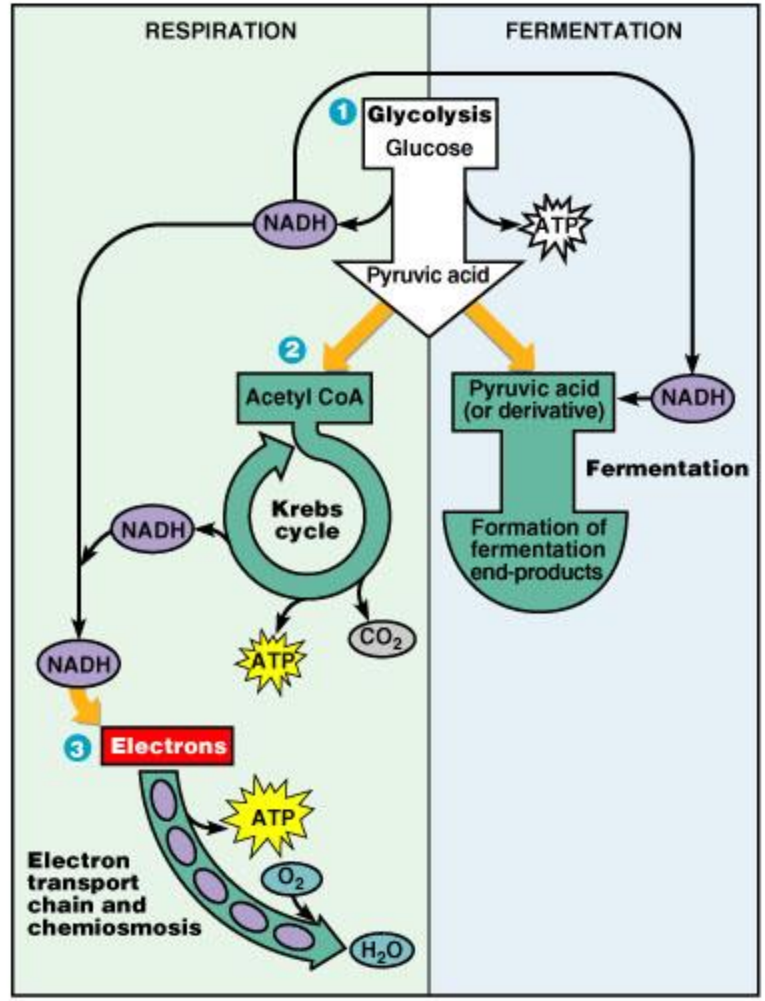


Fig. 17-11a, p.481


Preparatory Stage
Glucose
ATP
ADP
1
Glucose 6-phosphate
2
Fructose 6-phosphate
ATP
ADP
3
Fructose 1,6-diphosphate
4
5
P
Dihydroxyacetone phosphate (DHAP)
Glyceraldehyde 3-phosphate (GP)


RESPIRATION
FERMENTATION
1 Glycolysis
Glucose
NADH
ATP
Pyruvic acid
2
Acetyl CoA
Pyruvic acid (or derivative)
NADH
Fermentation
Krebs cycle
NADH
Formation of fermentation end-products
NADH
ATP
CO_2
3 Electrons
ATP
O_2
H_2O
Electron transport chain and chemiosmosis

기타 단당류의 해당과정에의 이용

① Mannose
→ M-6-P → F-6-P →→ → 해당

② Fructose
→ F-6-P → F-1,6 –BP → → → 해당 (minor) by hexokinase
→ F-1-P → DHAP + Glyceraldehyde → → → 해당 (major)
by fructokinase

③ Galactose
→ Gal-1-P → glucose-1-P → → → Glycogen 합성에 이용
gal-1-P uridyl transferase

Galactosemia

gal-1-P uridyl transferase의 결여 시 galactitol 발생-->뇌 손상

치아 우식

- 해당과정
- 혐기적대사와 관련이 있다
- 젖산 = 유기산

태아알콜증후군 (Fetal Alcohol syndrome:FAS)

Summary

- In the first stages of glycolysis, glucose is converted to two molecules of glyceraldehyde-3-phosphate
- The key intermediate in this series of reactions is fructose-1,6-bisphosphate. The enzyme that catalyzes this reaction, phosphofructokinase, is subject to allosteric control.

Summary

- In the final stages of glycolysis, two molecules of pyruvate are produced for each molecule of glucose that entered the pathway

- These reactions involve electron transfer, and the net production of two ATP for each glucose

- There are three control points in the glycolytic pathway

Summary

- Pyruvate is converted to lactate in anaerobic tissues, such as actively metabolizing muscle. NAD+ is recycled in the process

- In some organisms, pyruvate is converted to ethanol in a process requiring thiamine pyrophosphate as a coenzyme

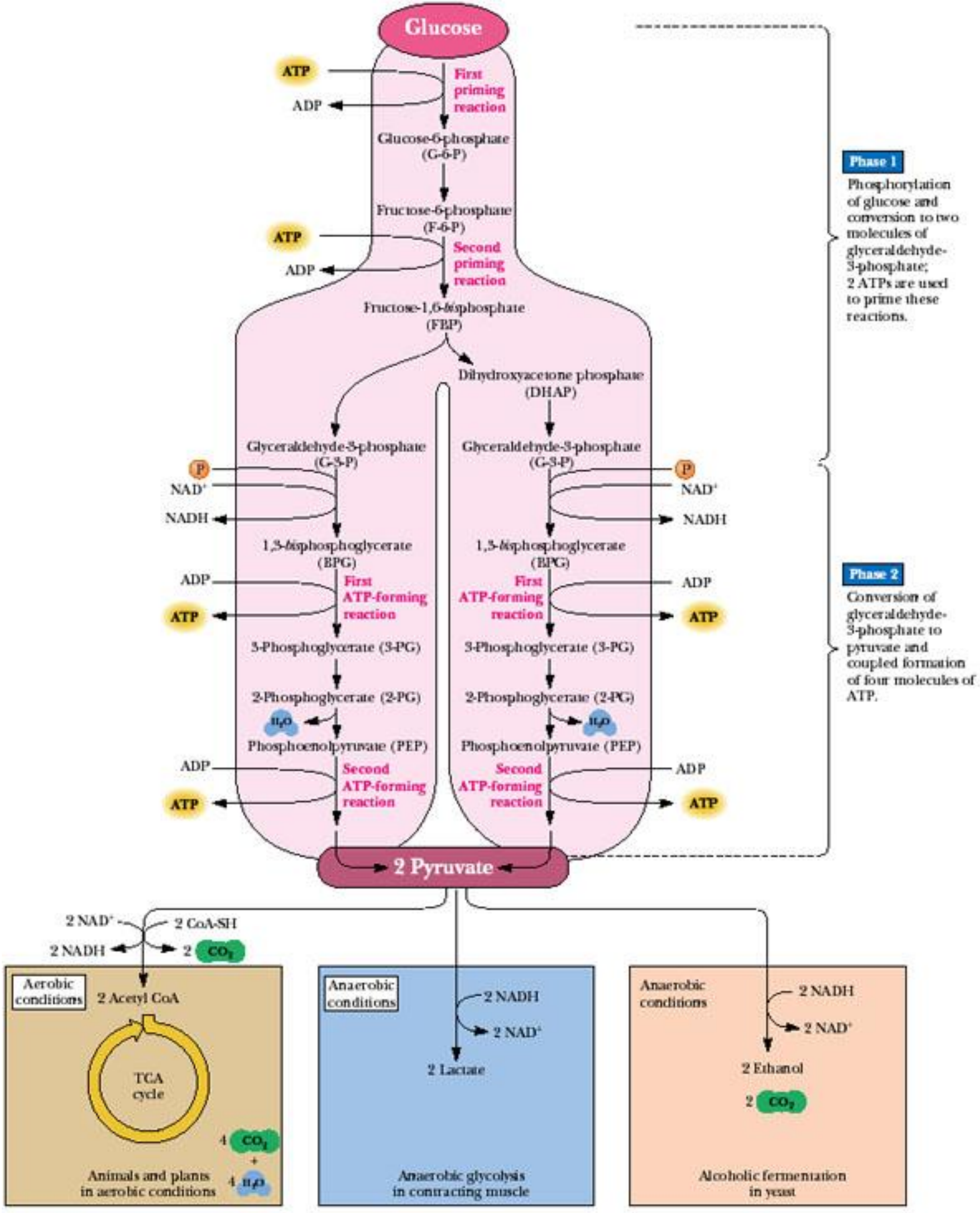

Glucose
ATP
ADP
First priming reaction
Glucose-6-phosphate (G-6-P)
Fructose-6-phosphate (F-6-P)
ATP
ADP
Second priming reaction
Fructose-1,6-bisphosphate (FBP)
Dihydroxyacetone phosphate (DHAP)
Glyceraldehyde-3-phosphate (G-3-P)
Glyceraldehyde-3-phosphate (G-3-P)
P
NAD+
NADH
P
NAD+
NADH
1,3-bisphosphoglycerate (BPG)
1,3-bisphosphoglycerate (BPG)
ADP
First ATP-forming reaction
ATP
ADP
First ATP-forming reaction
ATP
3-Phosphoglycerate (3-PG)
3-Phosphoglycerate (3-PG)
2-Phosphoglycerate (2-PG)
2-Phosphoglycerate (2-PG)
H2O
H2O
Phosphoenolpyruvate (PEP)
Phosphoenolpyruvate (PEP)
ADP
Second ATP-forming reaction
ATP
ADP
Second ATP-forming reaction
ATP
2 Pyruvate
Phase 1
Phosphorylation of glucose and conversion to two molecules of glyceraldehyde-3-phosphate; 2 ATPs are used to prime these reactions.
Phase 2
Conversion of glyceraldehyde-3-phosphate to pyruvate and coupled formation of four molecules of ATP.
2 NAD+
2 CoA-SH
2 NADH
2 CO2
Aerobic conditions
2 Acetyl CoA
TCA cycle
4 CO2
+
4 H2O
Animals and plants in aerobic conditions
Anaerobic conditions
2 NADH
2 NAD+
2 Lactate
Anaerobic glycolysis in contracting muscle
Anaerobic conditions
2 NADH
2 NAD+
2 Ethanol
2 CO2
Alcoholic fermentation in yeast

Fig. 17-2, p.465