Fig. 21-CO, p.568

지질대사

1. 지질의 분해과정
   - 중성지방
   - 인지질

2. 지질의 합성과정
   - 지방산의 합성
   - 복합지방의 합성
   - 콜레스테롤의 합성

3. 지질의 운반

지방의 기능

1) 세포막 구성
2) 에너지 저장형태 (reduced, anhydrous)
3) 호르몬---steroid hormone
4) 세포 내 전령---phosphatidyl inositol

Catabolism of Lipids

- TG → Glycerol + 3 Fatty acids
- 인지질 → glycerol + 지방산 + 인산 + 알콜

Catabolism of Lipids

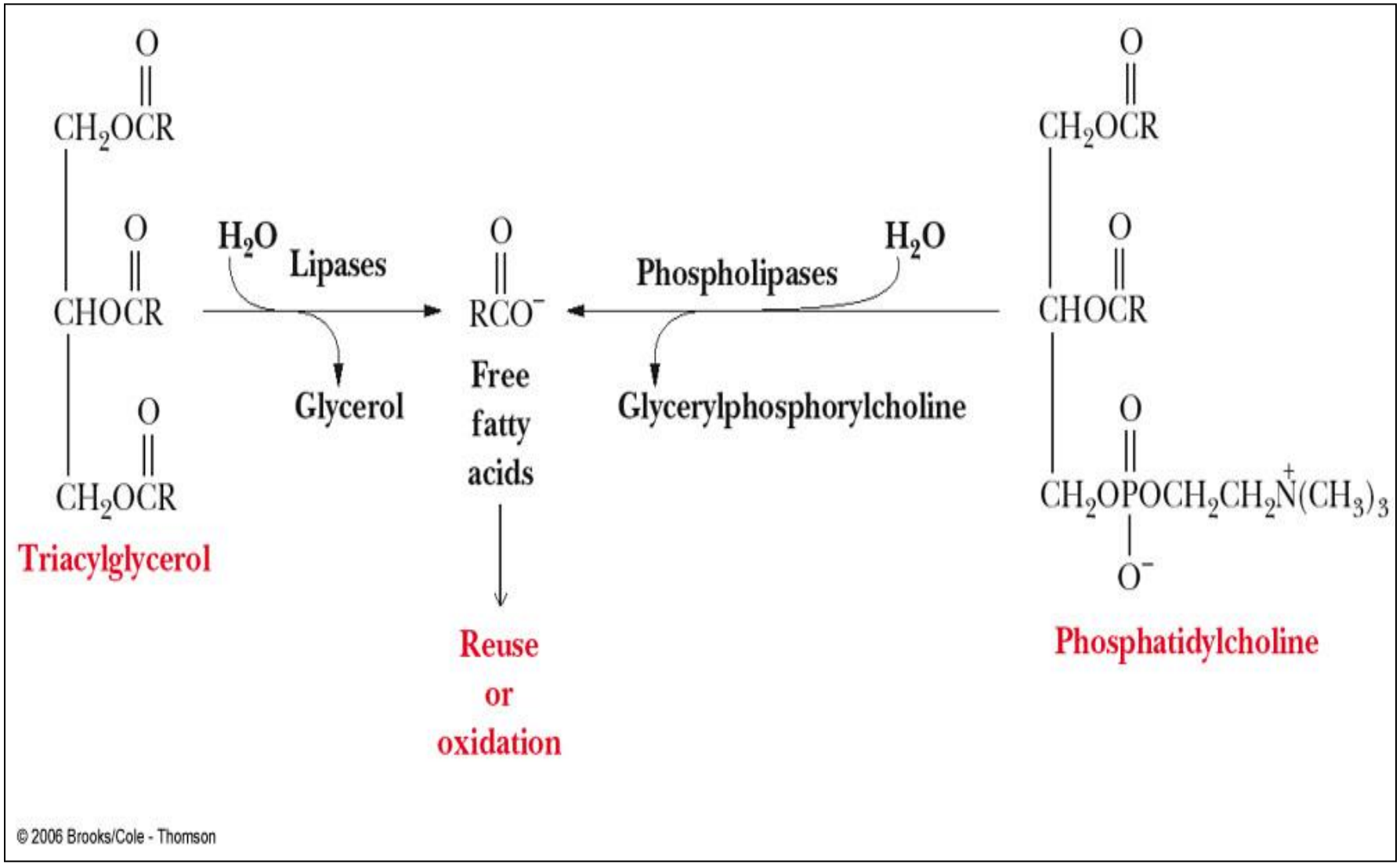
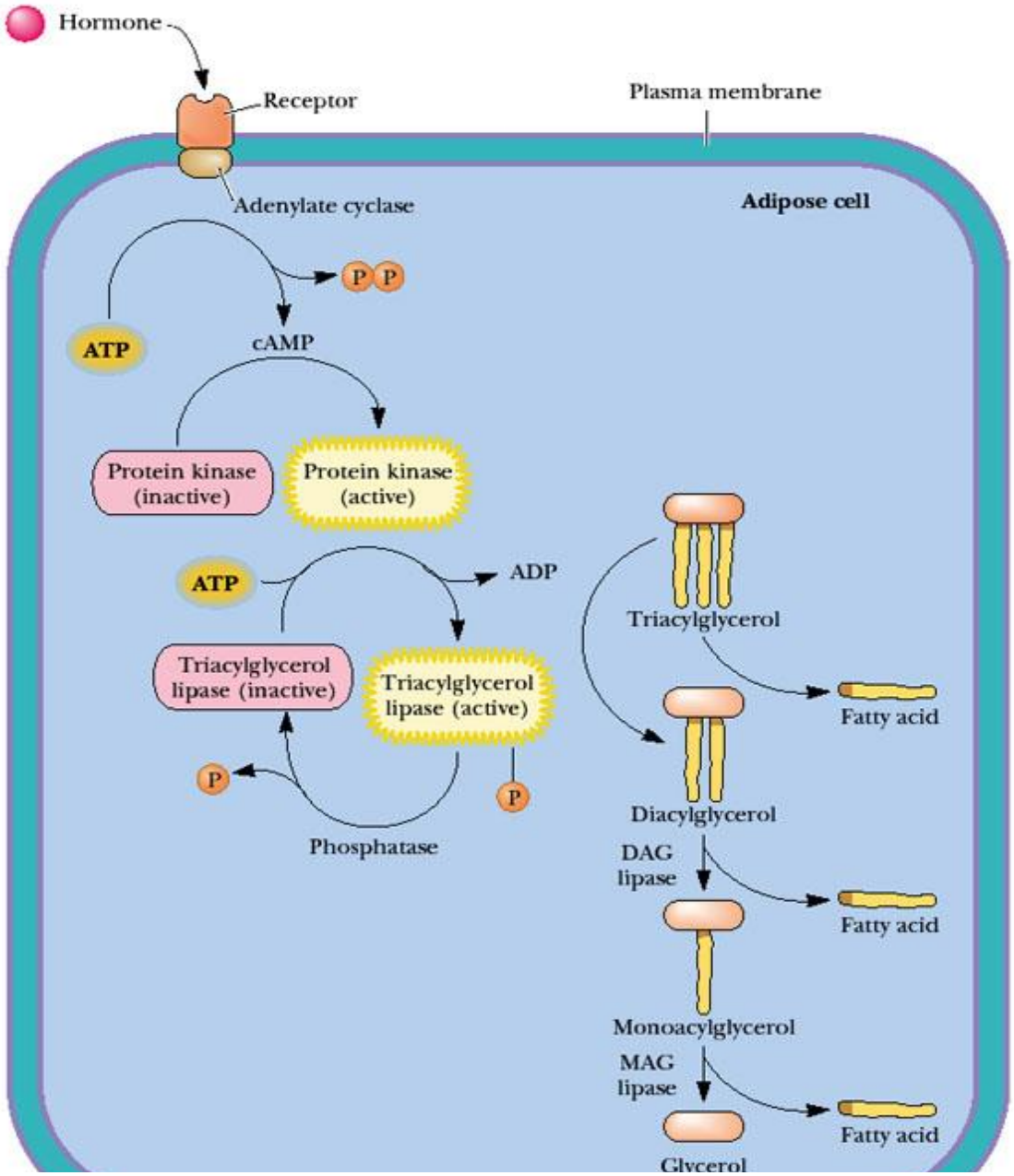


Fig. 21-1, p.569

지질 가수분해효소

- Lipases
  - pancreatic lipase
  - hepatic lipase
  - hormone sensitive lipase (epinephrine)
- Phospholipase
- Cholesteryl esterase



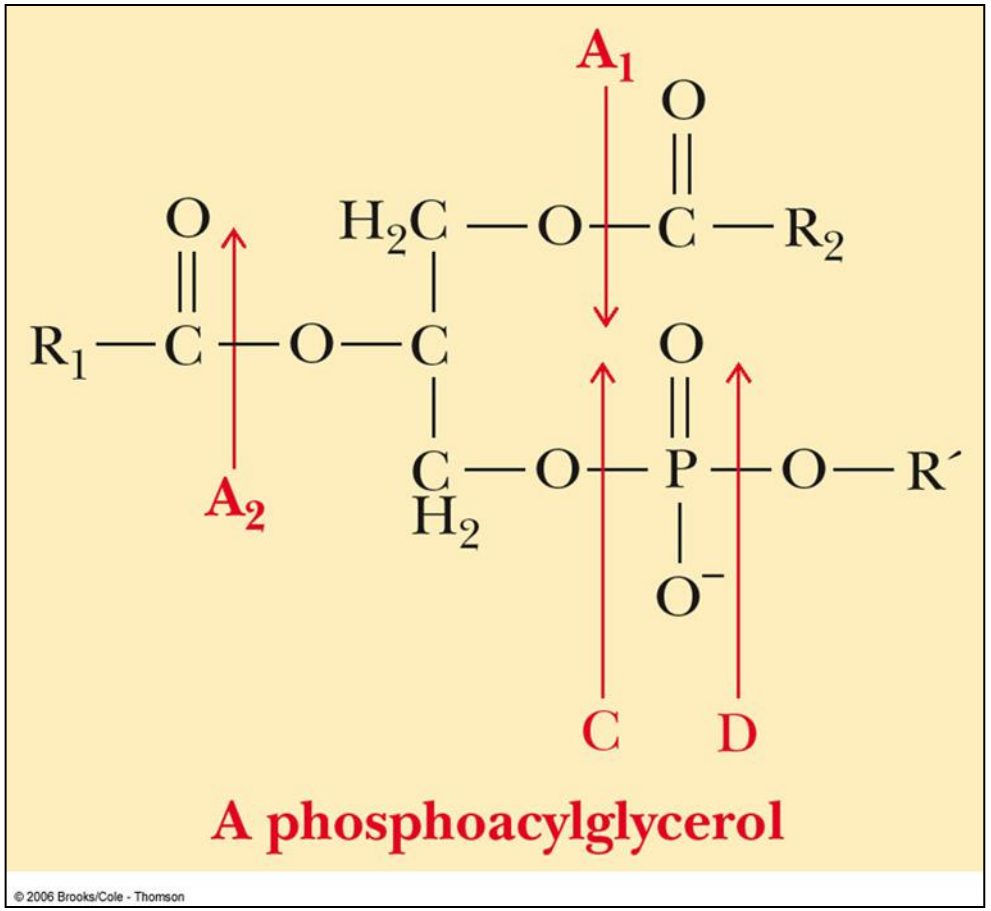
hormone sensitive lipase

Fig. 21-3, p.570

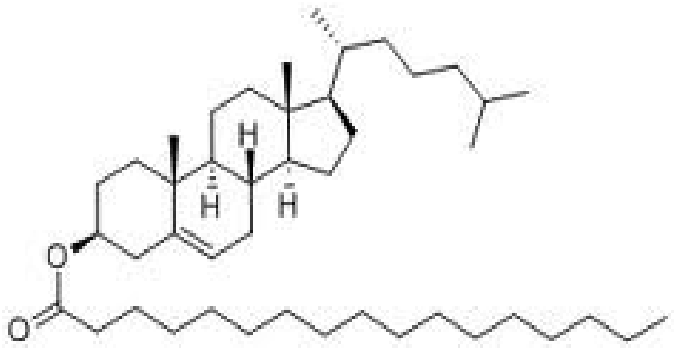
Phospholipases

Phospholipases

- A_1
- A_2
- C
- D



Cholesteryl esterase



Cholesterol + 지방산

지방산의 분해

① 첫 단계 (Activation 단계)

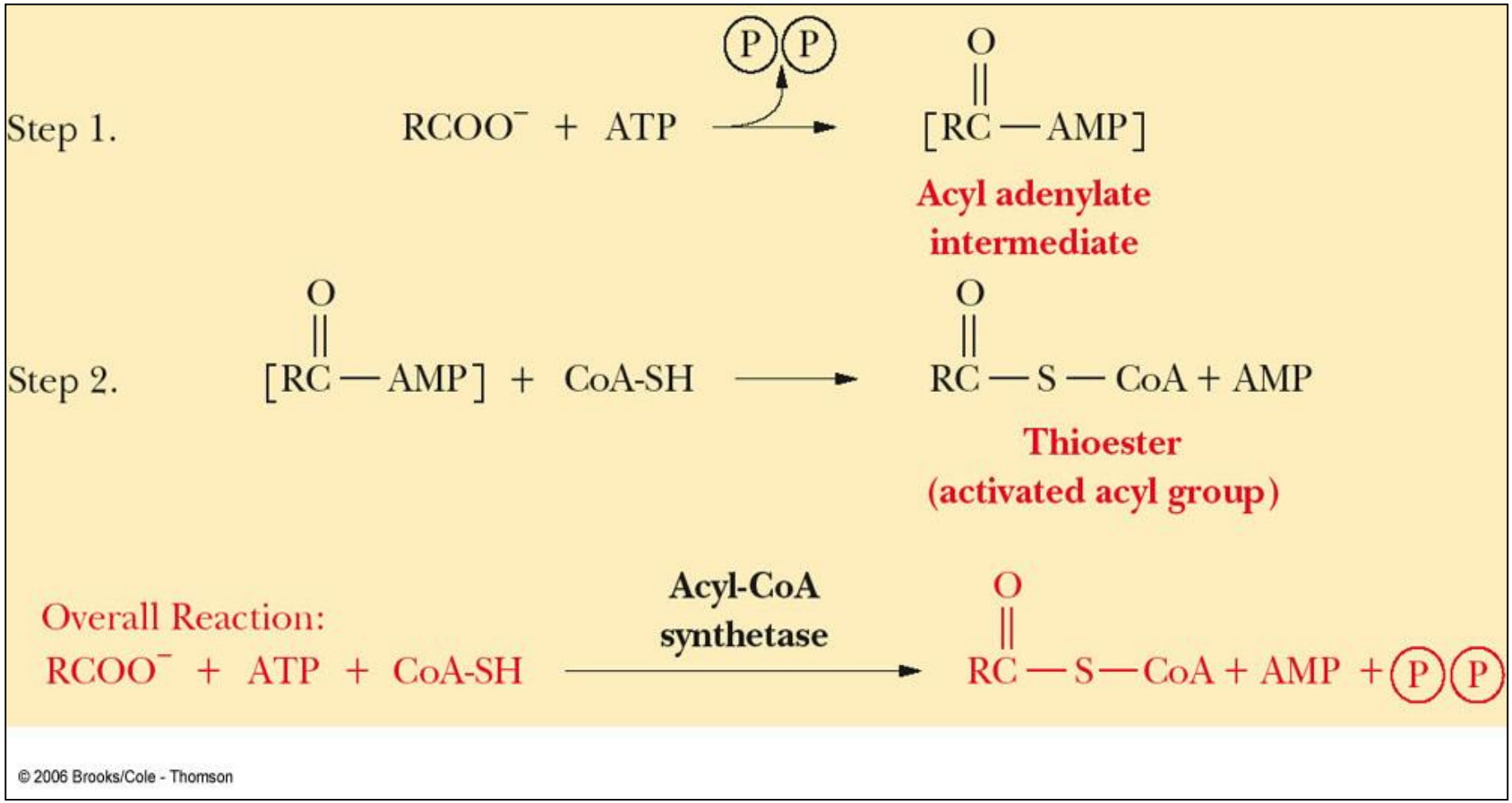


Fig. 21-4, p.570

지방산의 분해

② 2단계:미토콘드리아 기질내로의 이동

- carnitine이 도우미 역활

Acyl CoA + carnitine---->acylcarnitine---> 미토콘드리아---> Acyl CoA + Carnitine

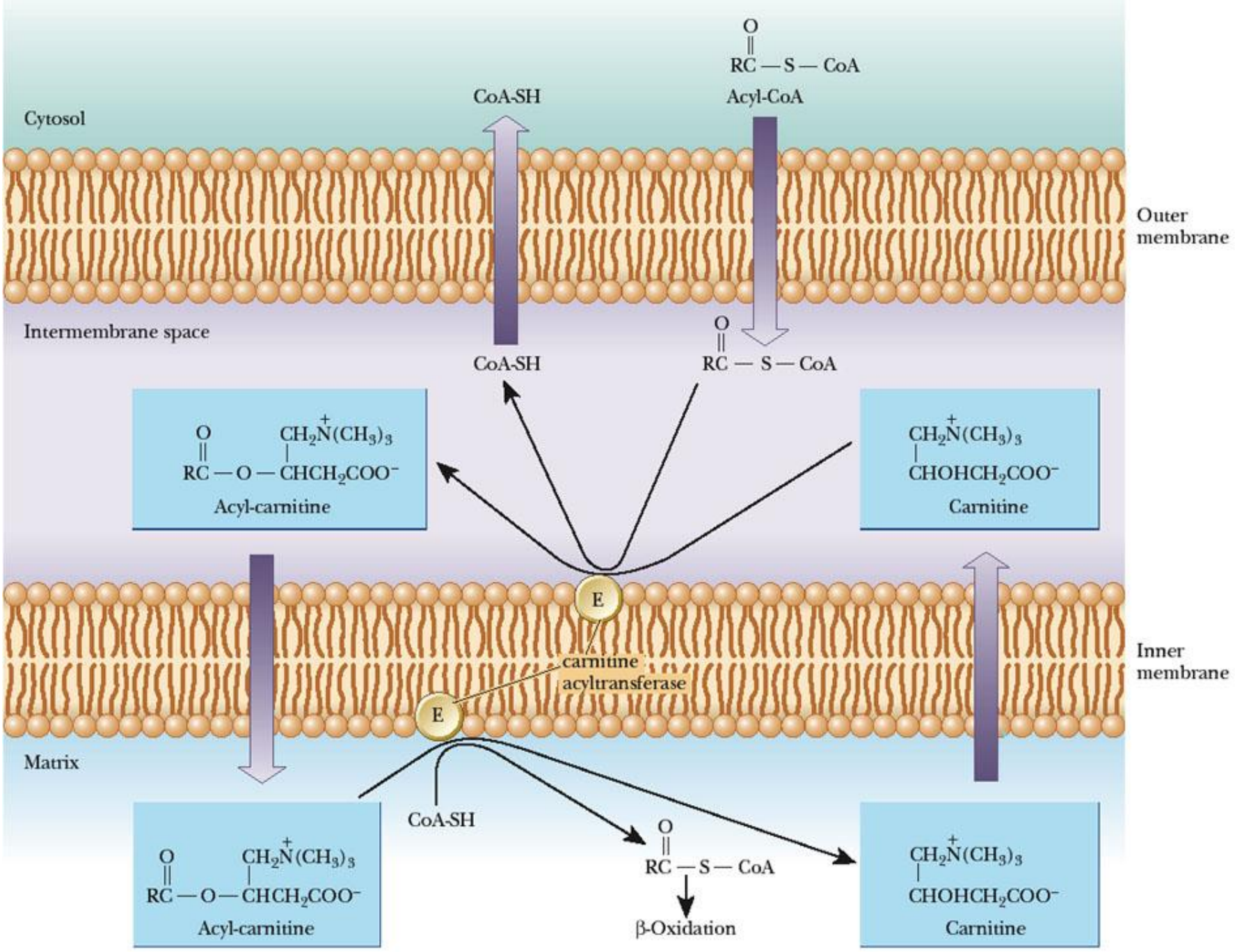


Fig. 21-5, p.571

지방산의 분해

③ 3단계: 4가지의 효소가 관여

① Acyl CoA dehydrogenase

② Enoyl CoA hydratase

③ 1,3-hydroxy-acyl CoA dehydrogenase

④ Thiolase

지방산의 분해

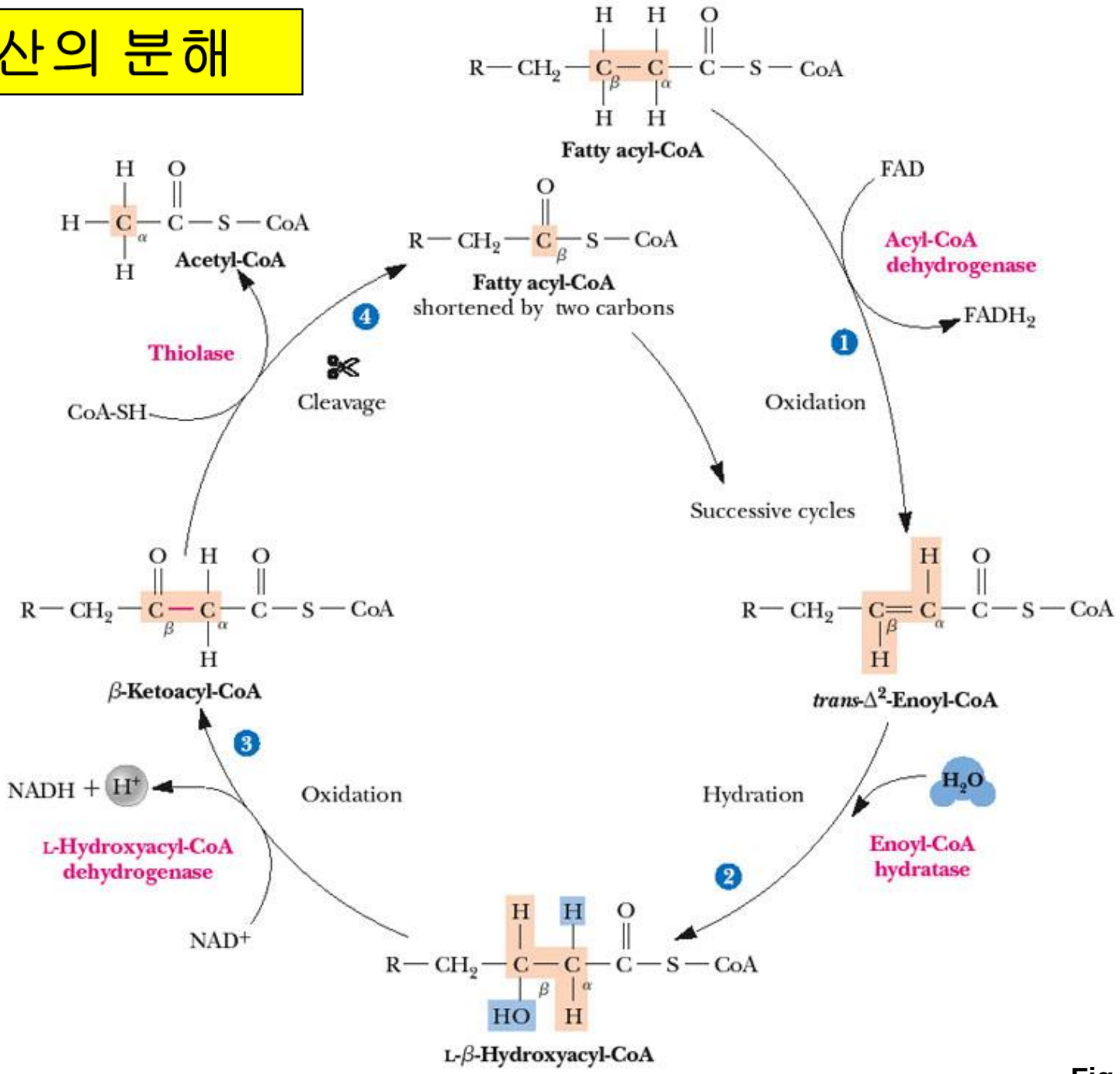
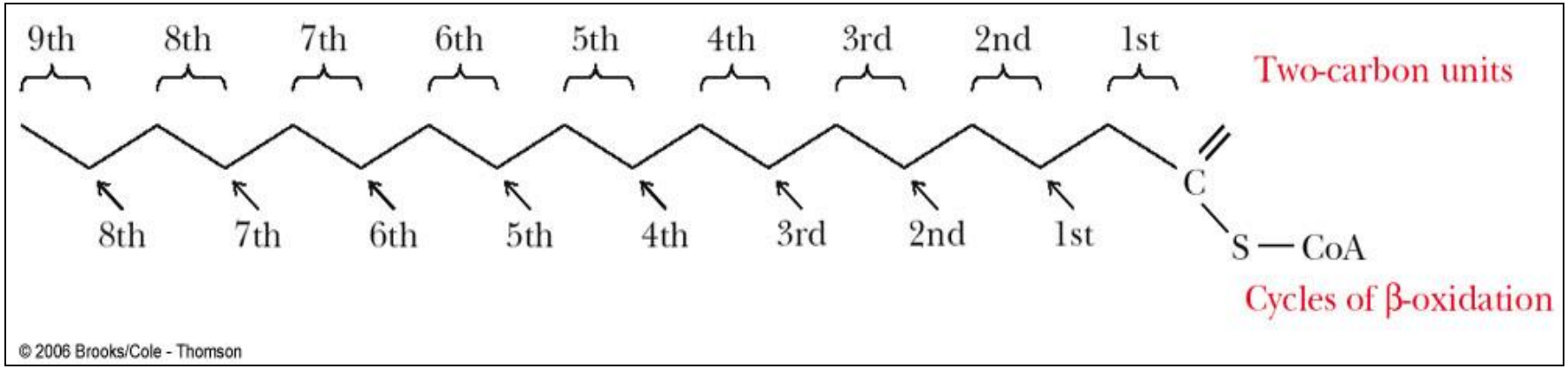


Fig. 21-6, p.572

지방산의 분해



- 지방산의 구조적 특성
  - ω end
  - carboxyl end

Fig. 21-7, p.573

Energetics of fatty acid

Palmitic acid + CoA + ATP ---->
Palmytoyl CoA + AMP + 2Pi (2ATP 소모)

Palmitoyl CoA + 7CoA + 7FAD + 7NAD---->
8 Acetyl CoA + 7FADH2 + 7NADH2

총 ATP= 8 x 12 + 7 x 2 + 7 x 3 = 131 - 2 ATP
= 129 ATP

Energetics of fatty acid

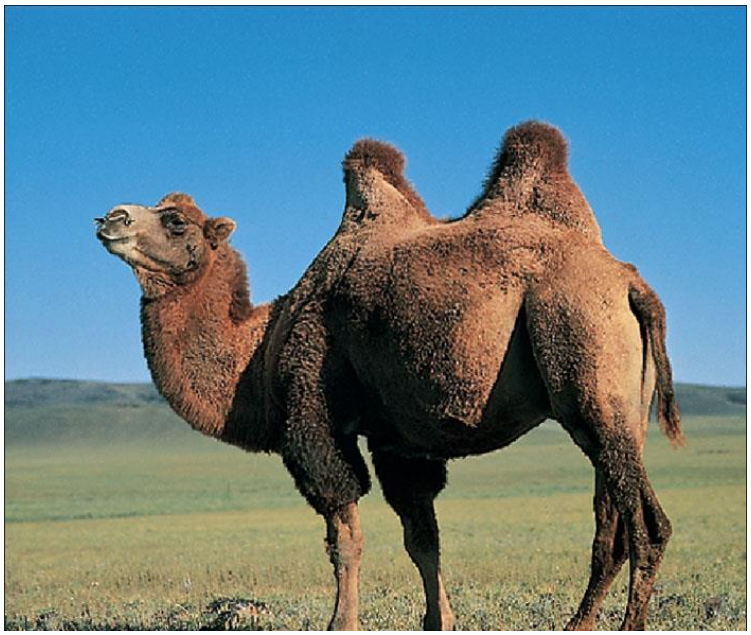
Table 21.1

The Balance Sheet for Oxidation of One Molecule of Stearic Acid

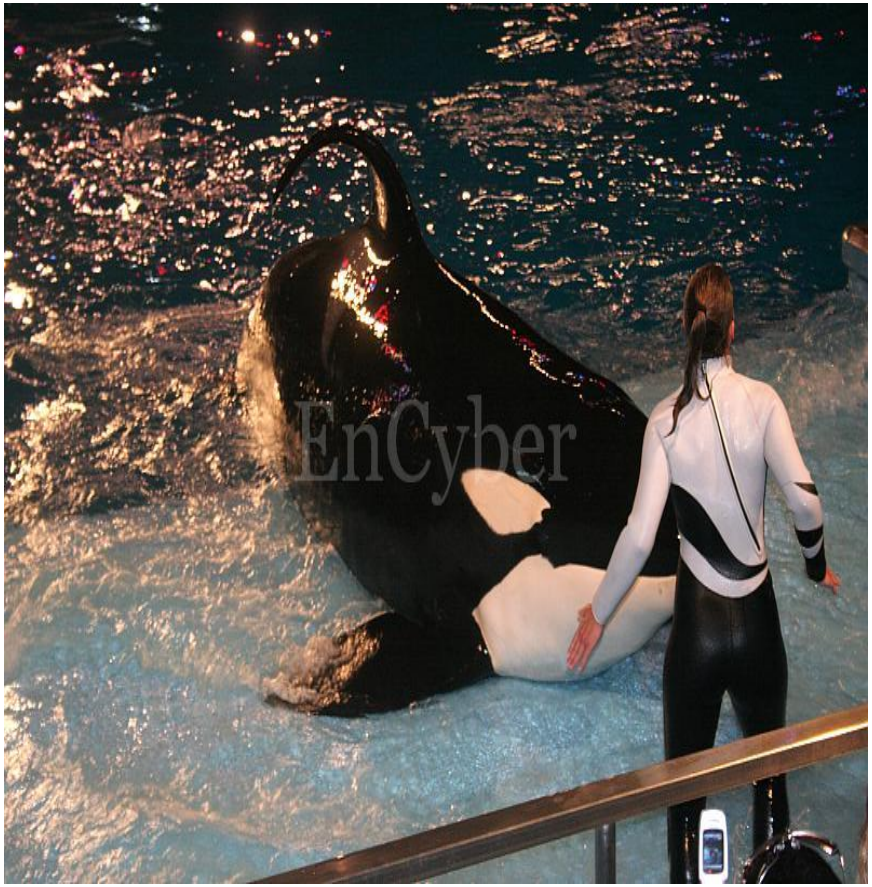
Reaction	NADH Molecules	$FADH_2$ Molecules	ATP Molecules
1. Stearic acid → Stearyl-CoA (activation step)			−2
2. Stearyl-CoA → 9 acetyl-CoA (8 cycles of β-oxidation)	+8	+8	
3. 9 Acetyl-CoA → 18 CO_2 (citric acid cycle); GDP → GTP (9 molecules)	+27	+9	+9
4. Reoxidation of NADH from β-oxidation cycle	−8		+20
5. Reoxidation of NADH from citric acid cycle	−27		+67.5
6. Reoxidation of $FADH_2$ from β-oxidation cycle		−8	+12
7. Reoxidation of $FADH_2$ from citric acid cycle		−9	+13.5
	0	0	+120

Table 21-1, p.575

지방산 산화는 대사수의 공급원



범고래



13번 문제

Glycerol의 분해

Glycerol + ATP --->glycerol 3-phosphate

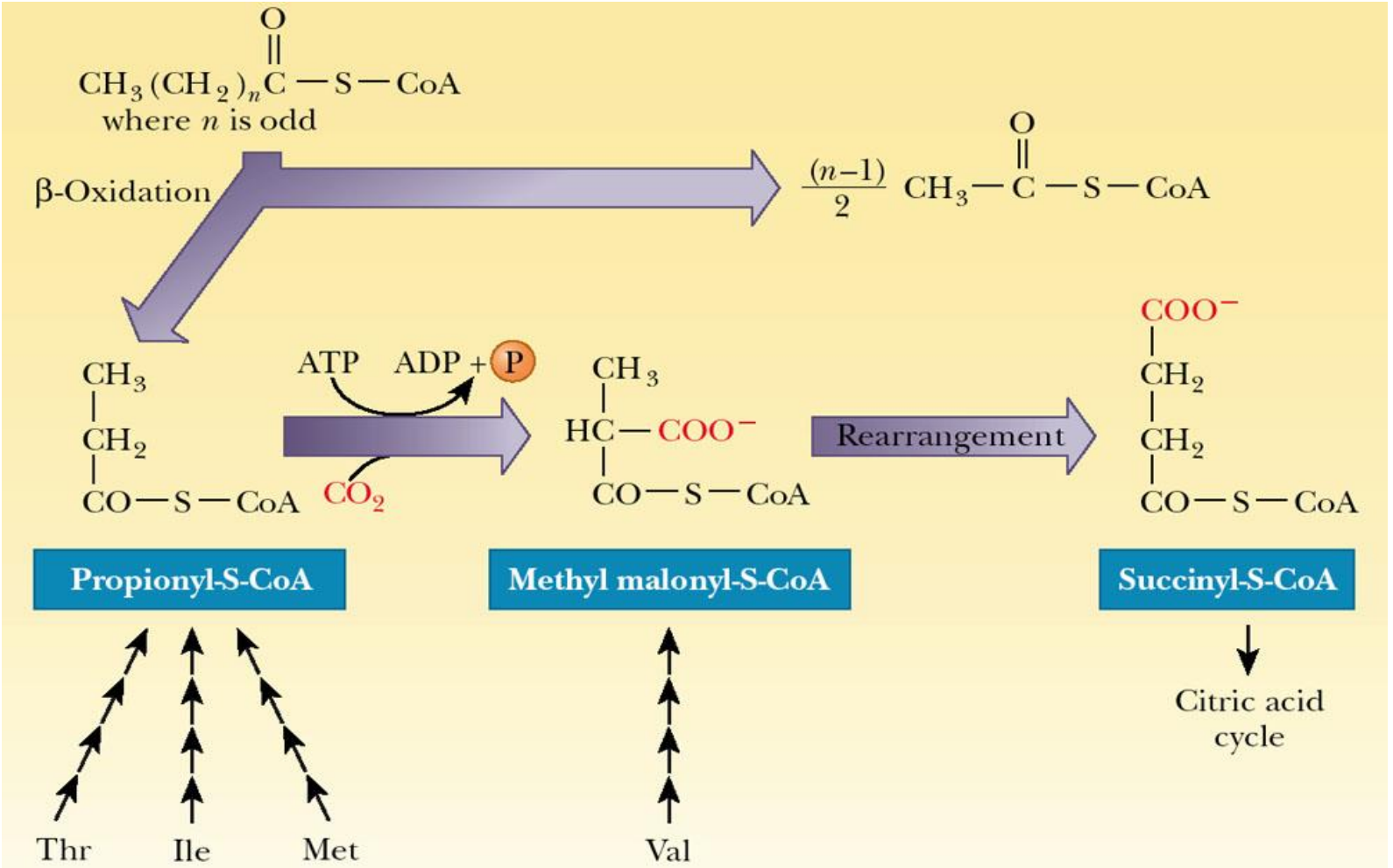
---> DHAP ---> 해당과정

홀수지방산의 산화

- 짝수지방산 산화과정과의 차이점을 살펴보자
- 종말물질로 propionyl CoA 생성 ---> succinyl CoA로 전환 → TCA 회로로 이동

<문제 21번, 22번>

홀수지방산의 산화



The catabolism of some amino acids also yields propionyl-CoA and methyl malonyl-CoA

Fig. 21-8, p.576

불포화지방산의 산화

- 포화지방산 산화과정과의 차이점을 살펴보자
- enoyl-CoA isomerase
- enoyl-CoA hydratase
- 2,4-dienoyl-CoA reductase

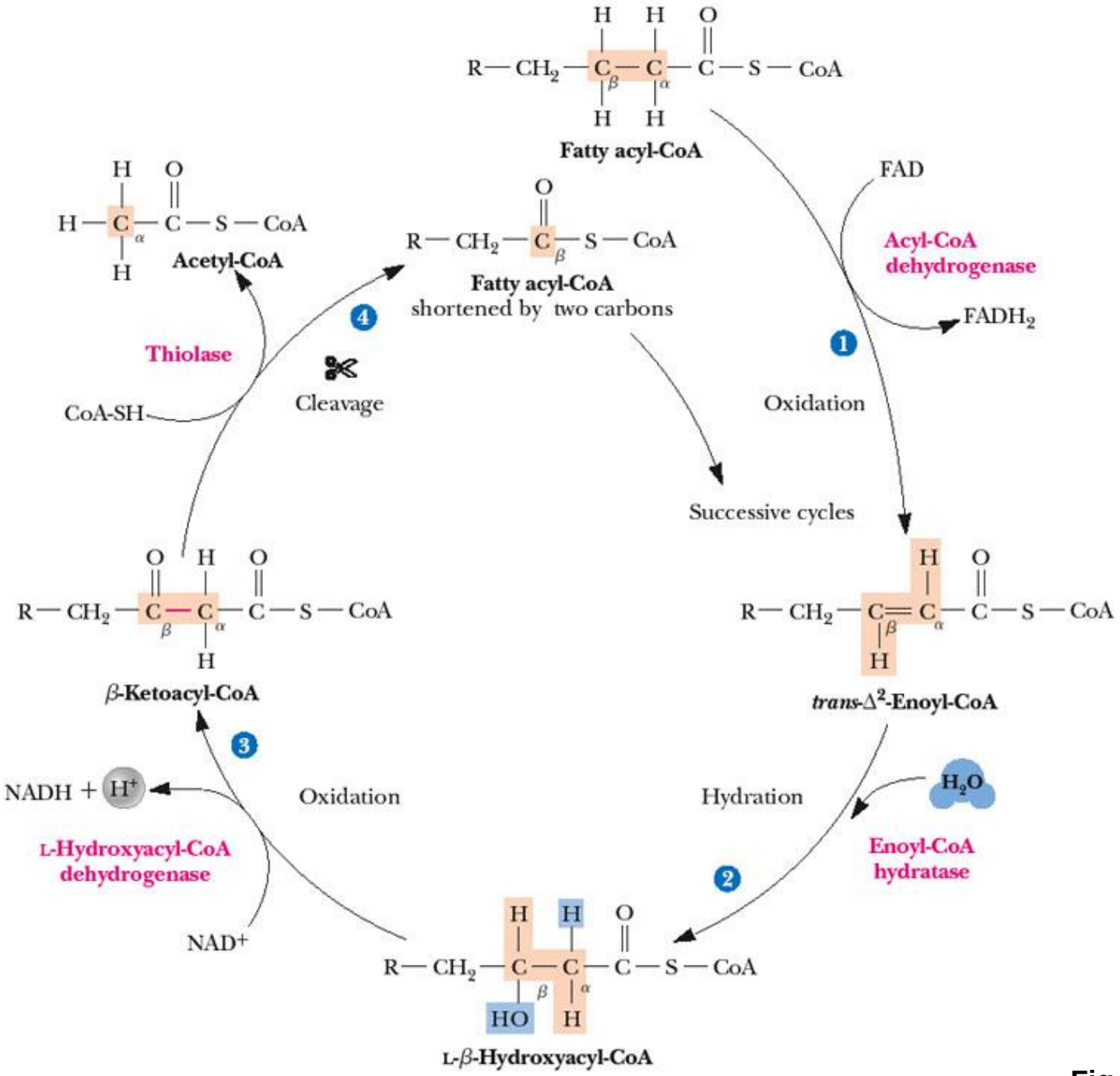


Fig. 21-6, p.572

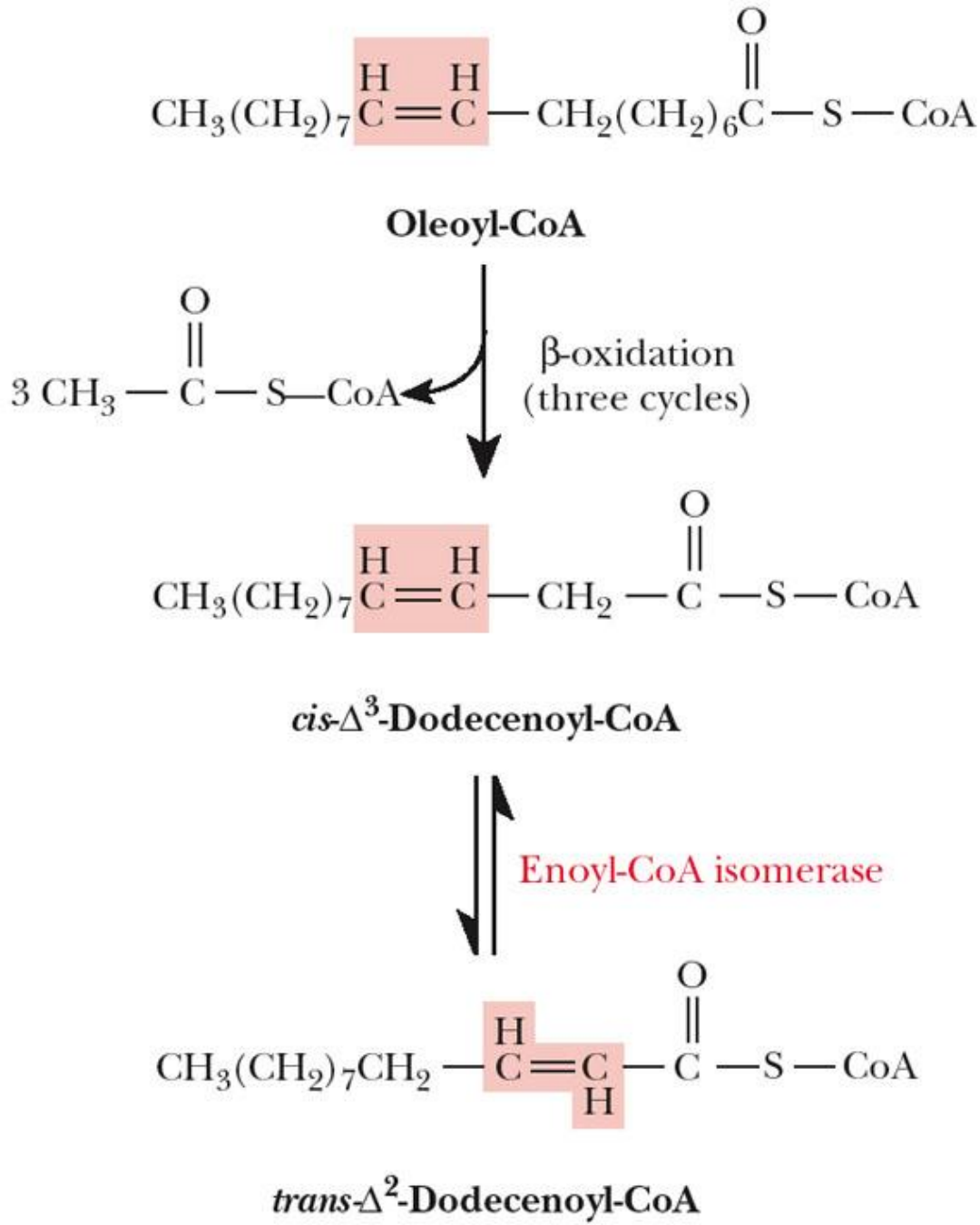


Fig. 21-9a, p.577

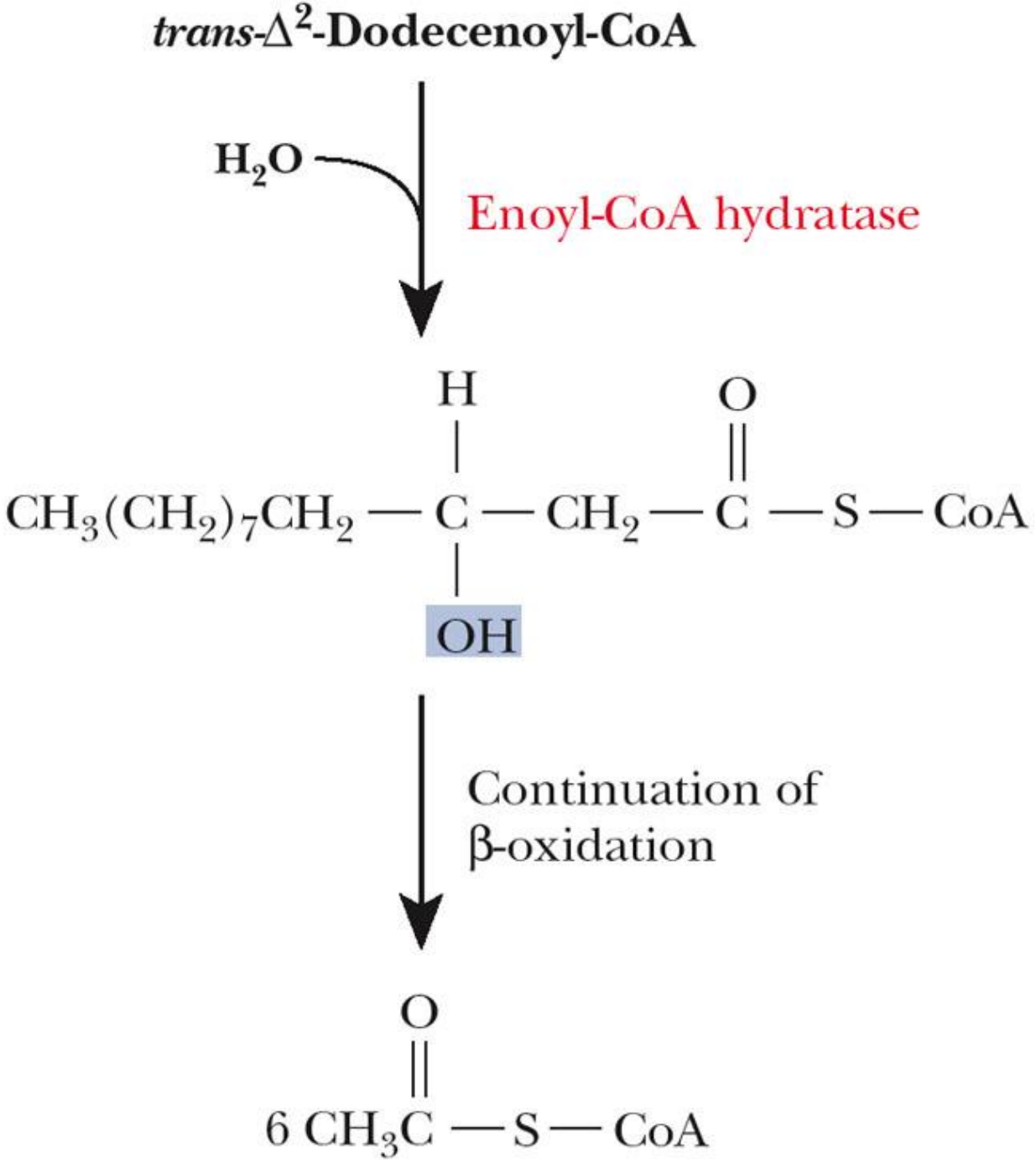


Fig. 21-9b, p.577

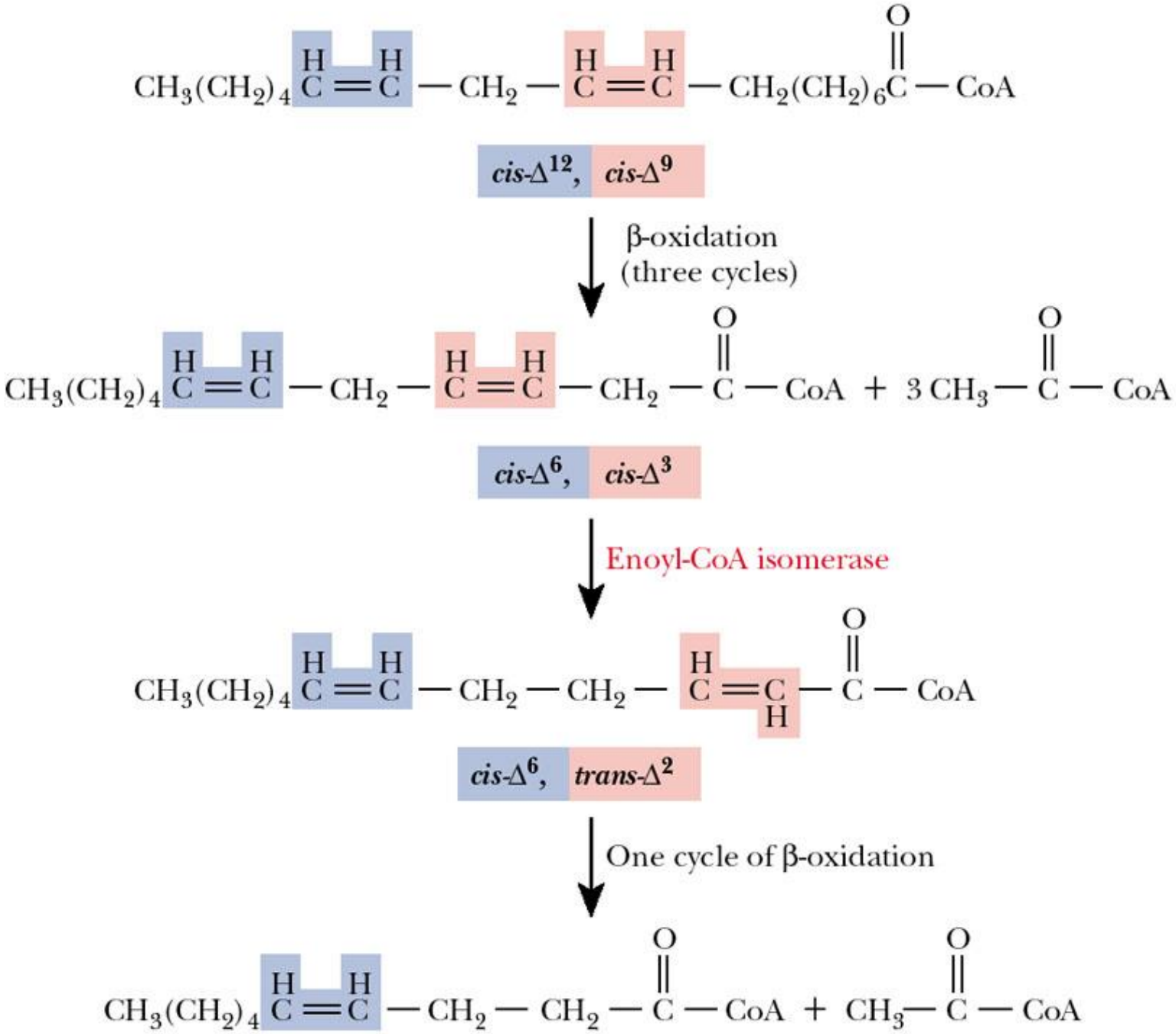


Fig. 21-10a, p.578

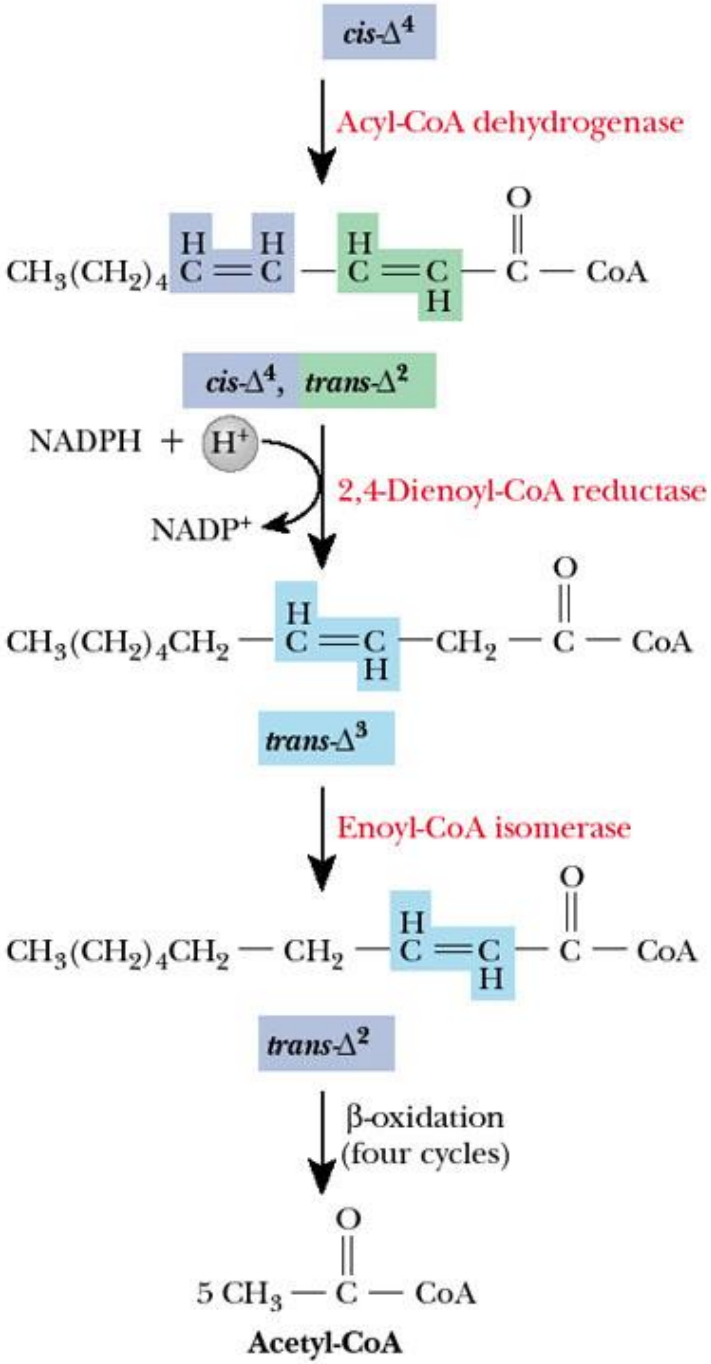


Fig. 21-10b, p.578

케톤체의 생성

- 간에서 생성
- acetoacetic acid
- β-hydroxy butyric acid
- acetone
- 케톤체의 과잉생성은 산독증을 유발
- 뇌세포에서는 케톤체를 분해하여 에너지를 얻는다

케톤체의 생성

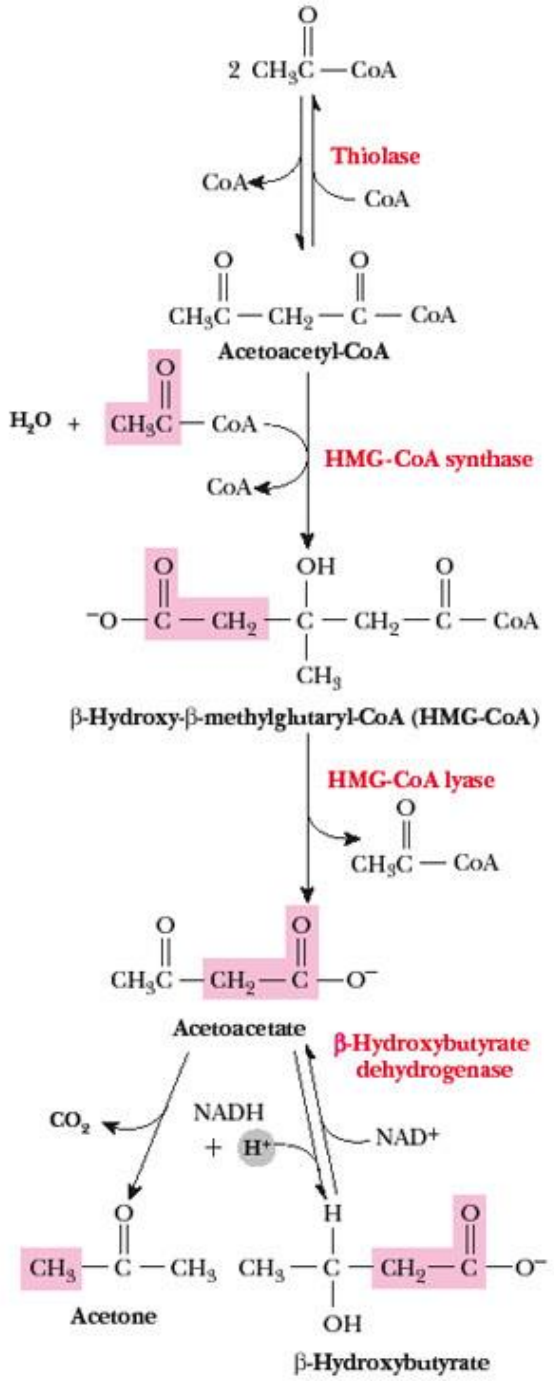


Fig. 21-11, p.580

- 문제 25번
- 문제 26번

케톤체와 효과적인 체중 조절

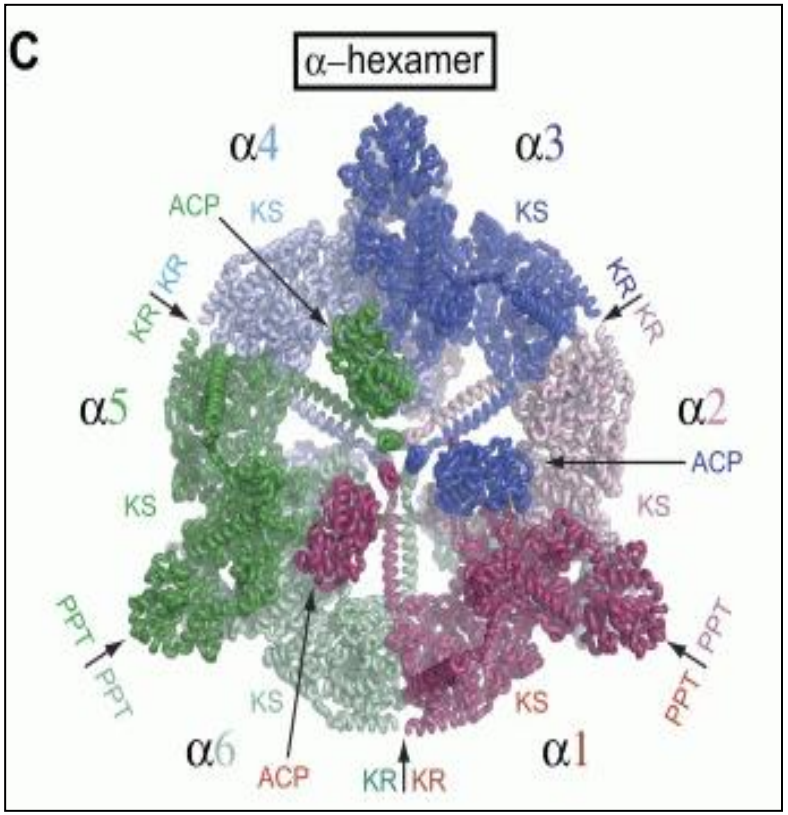
If you drink lots of fluids, your kidney will fulsh out the ketones in the urine to adjust body pH. You lose weight very efficiently at this point because you are literally putting excess calories “ down the drain”. The water in “Dr Stillman’s Water diet” was there for a reason.

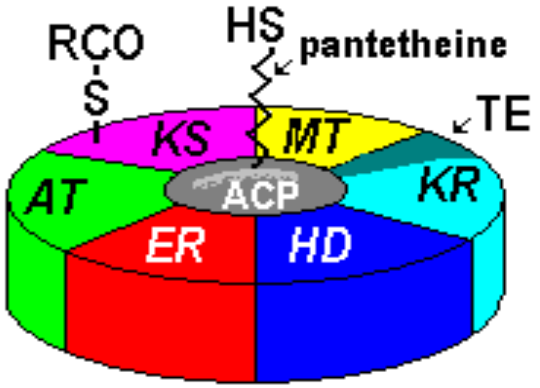
지방산 합성

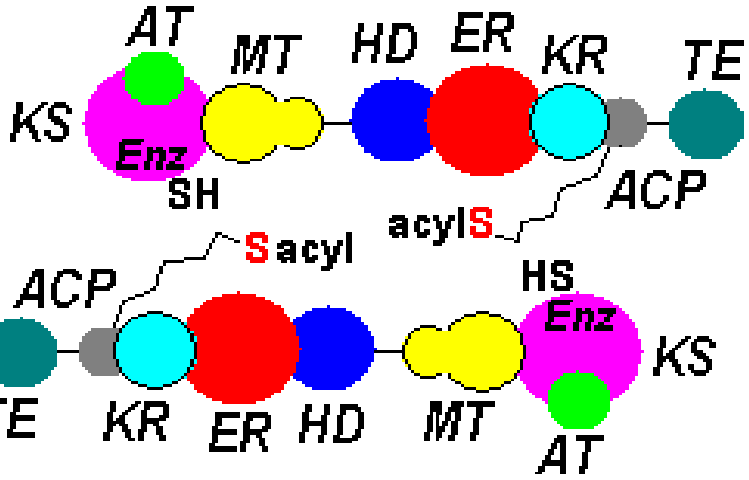
- 세포질에서 일어난다.
- ACP-linked fatty acids로 반응
  (Acyl carrier protein)
- NADPH 필요
- Multifunctional enzyme complex 관여
  (Fatty acid synthetase complex)
- ACP와 6개의 효소로 구성됨

Fatty acid synthetase (FAS)

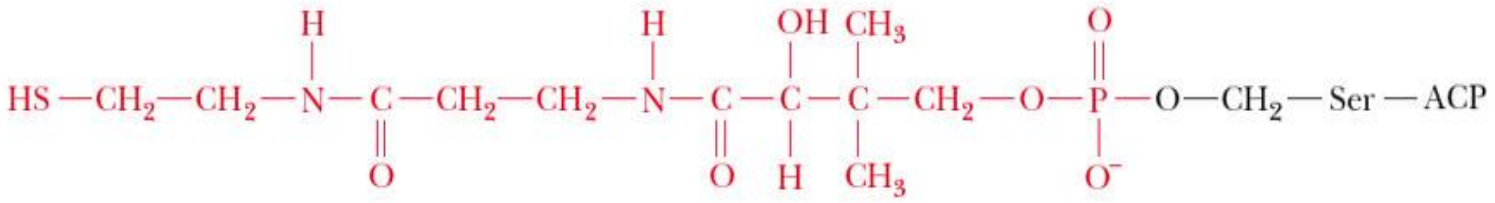
FAS: 2.6MDa



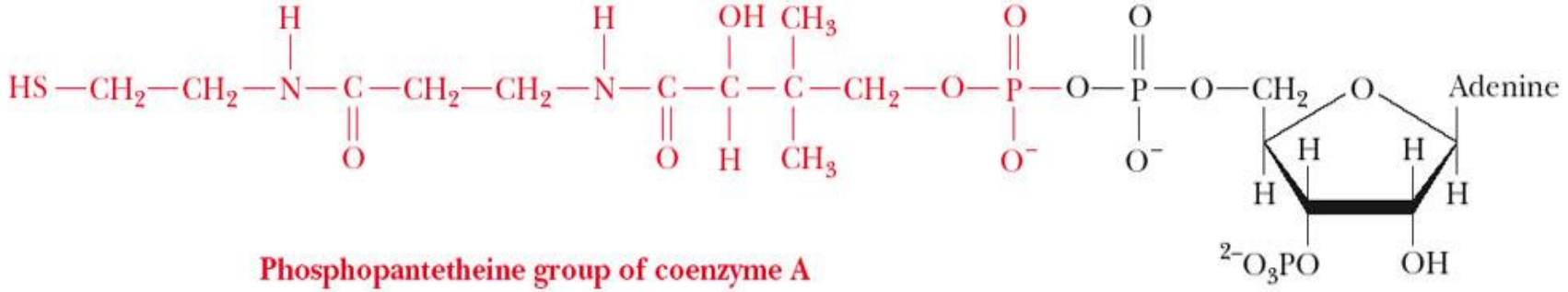




coenzyme A와 ACP의 구조적 유사성
phosphopantetheine group



Phosphopantetheine group of ACP



Phosphopantetheine group of coenzyme A

Fatty acid synthetase (FAS)

- malonyl CoA transferase (MT)
- Ketoacyl ACP synthase (KS)
- ketoacyl ACP reductase (KR)
- hydroxyacyl ACP dehydratase (HD)
- enoyl ACP reductase (ER)
- acyl transferase (AT)
- acyl carrier protein (ACP)

지방산 합성 1단계

1) Acetyl CoA의 이동

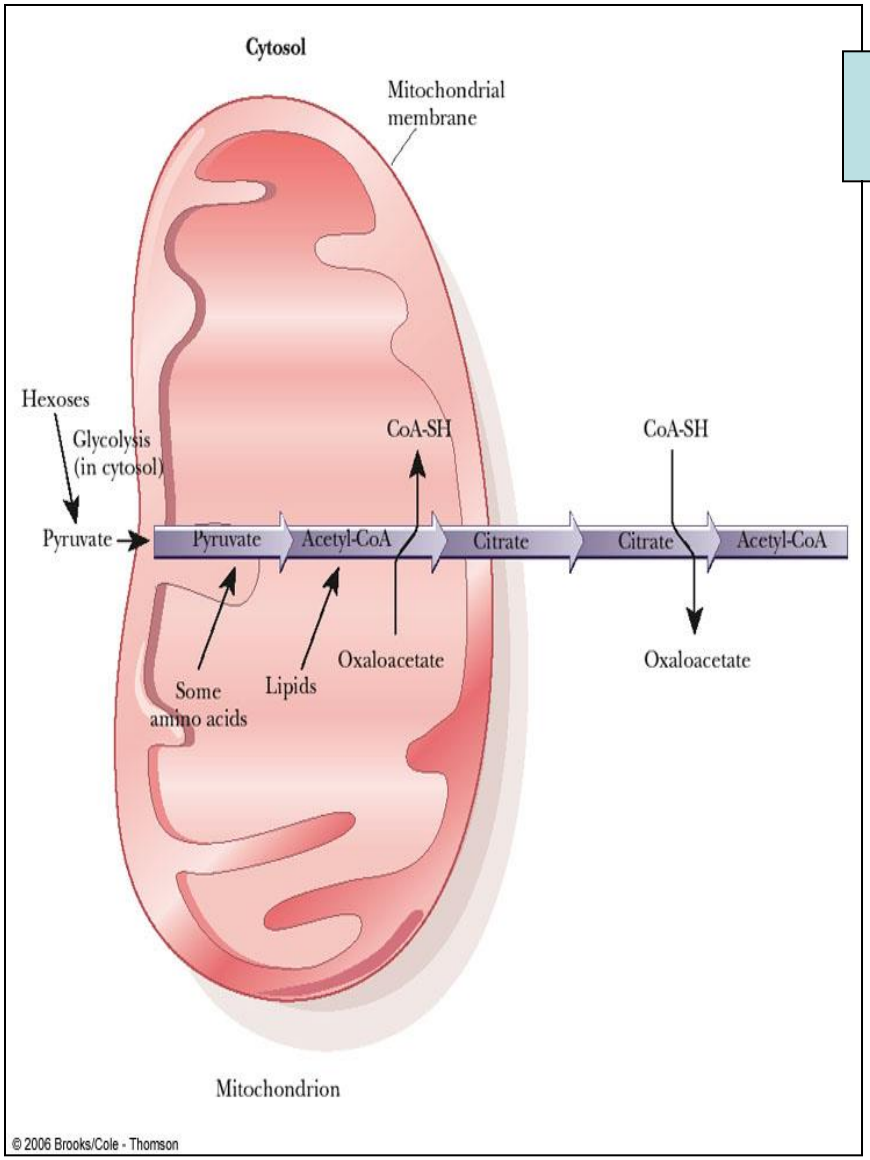
미토콘드리아 ---> 세포질로 이동

Citrate로 막을 통과하여

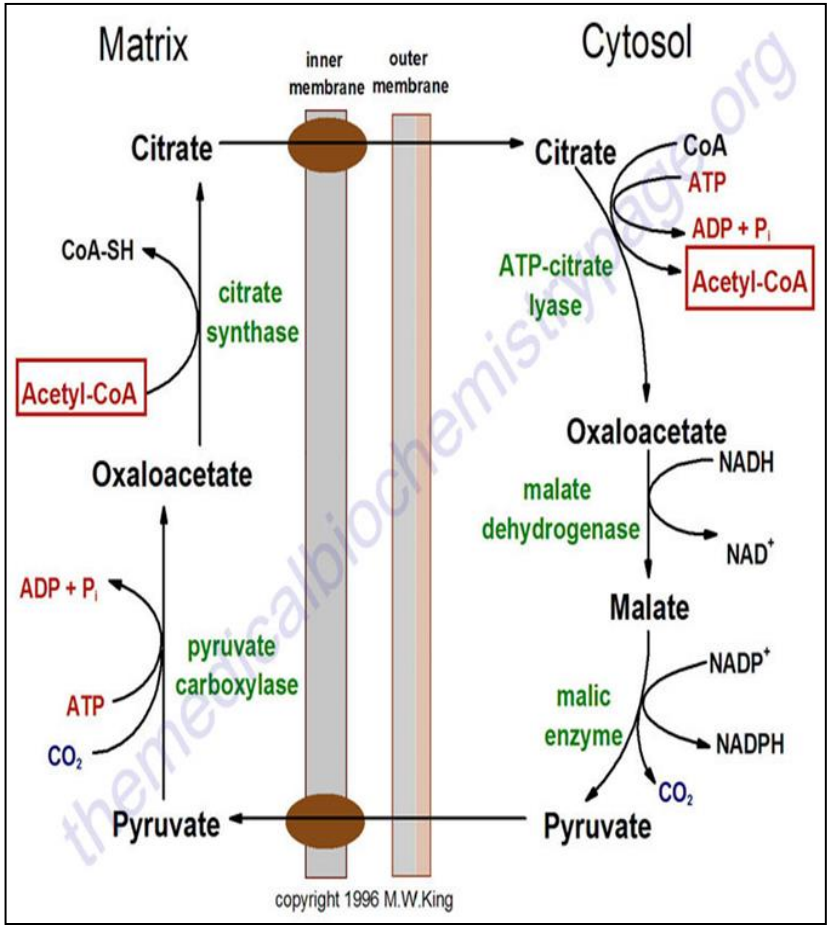
다시 acetyl CoA로 전환

(citrate-malate-pyruvate shuttle)

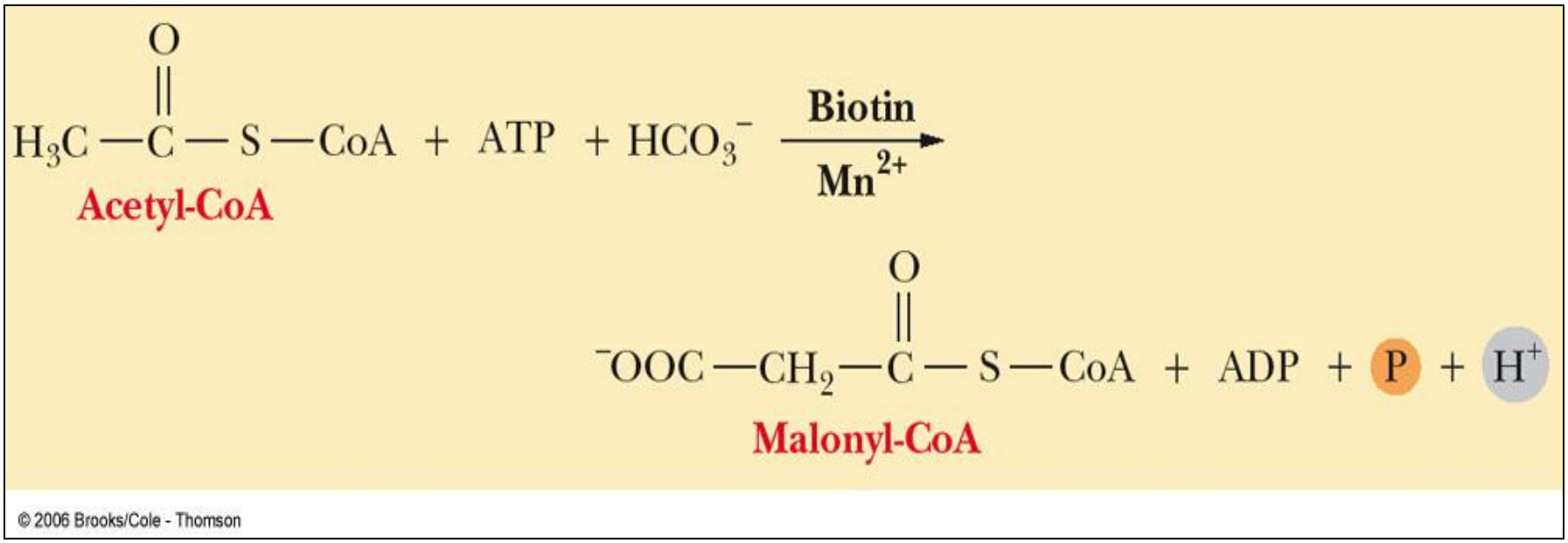
지방산 합성 1단계



acetyl groups from the mitochondrion to the cytosol.



지방산 합성 2단계



Acetyl CoA----------> malonyl CoA로 전환

Acetyl CoA carboxylase

지방산 합성의 속도 조절효소

Fig. 21-13, p.581

지방산 합성 2단계

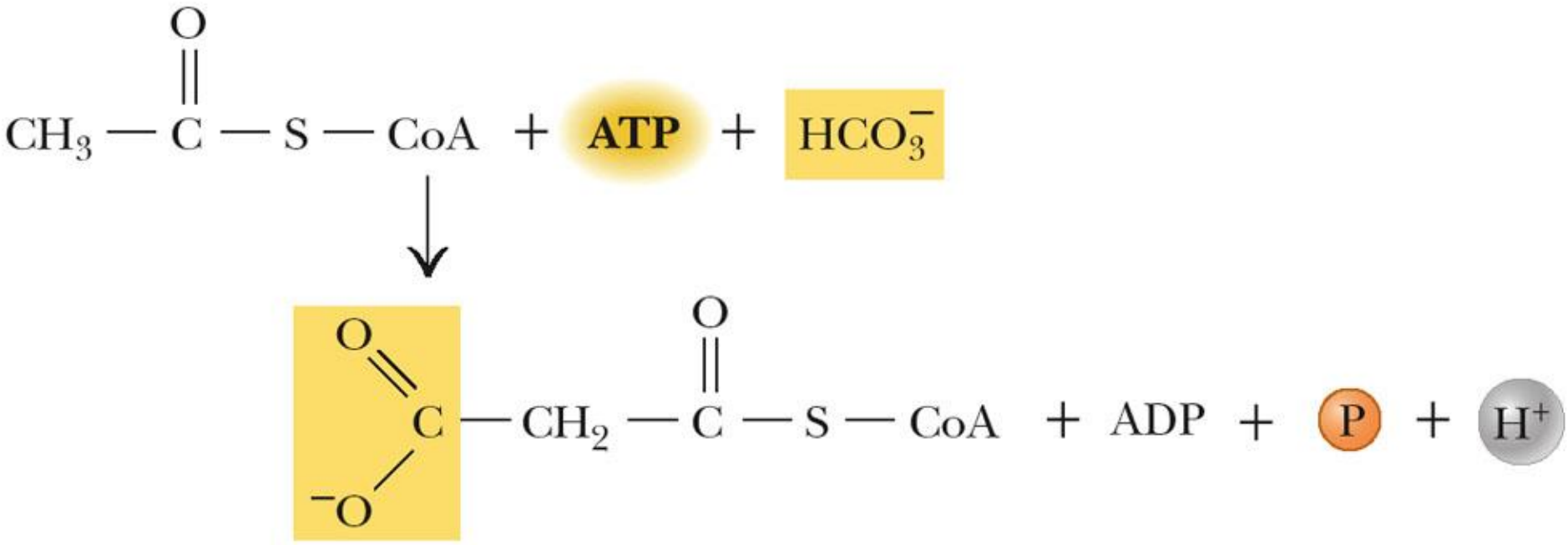


Fig. 21-14a, p.582

지방산 합성 2단계

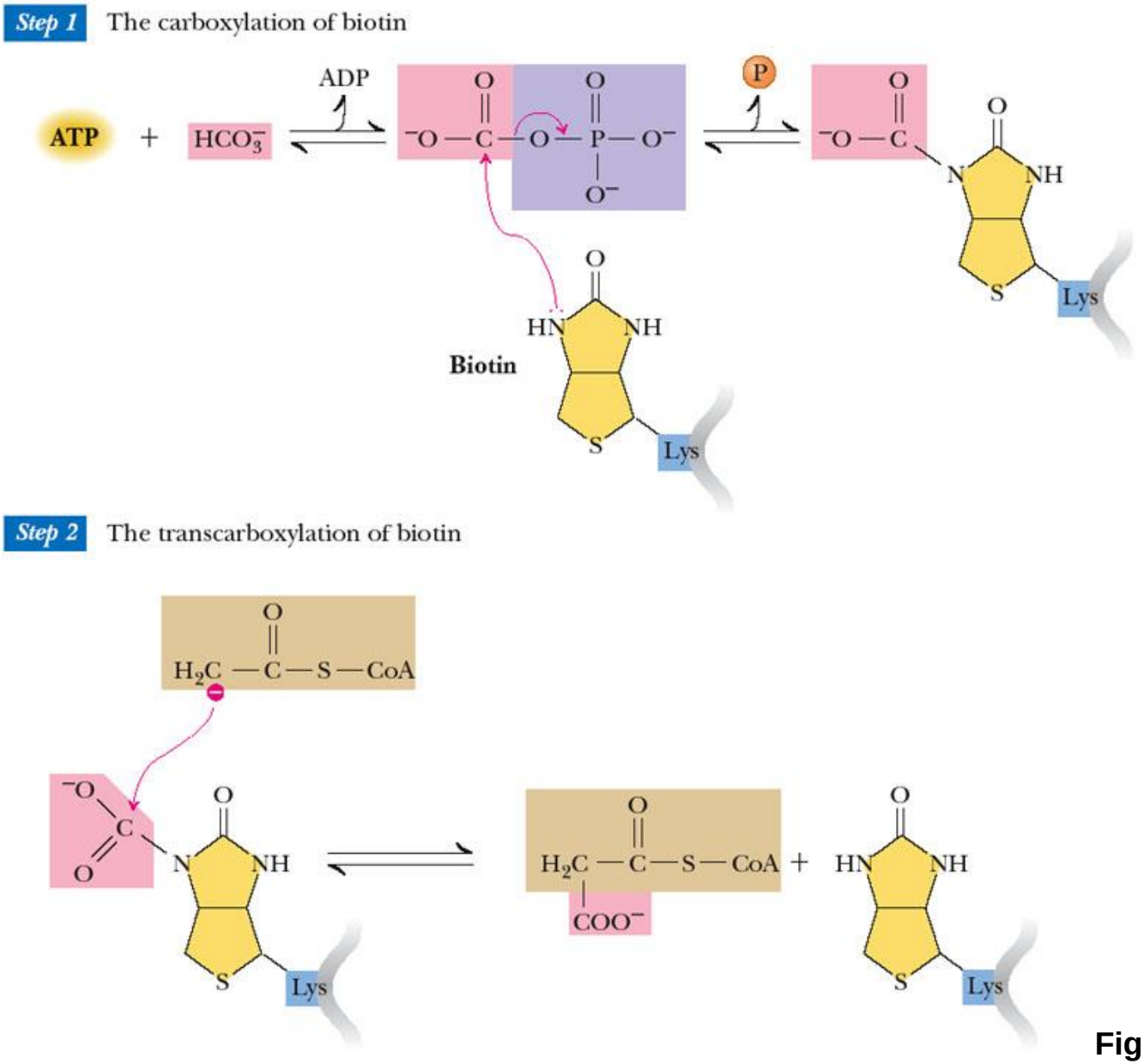


Fig. 21-14b, p.582

지방산 합성 3단계

- Fatty acid synthetase를 이용하여 합성됨
- Fatty acid synthetase는 여러 개의 효소가 결합된 복합효소임
- C_{16}까지만 Fatty acid synthetase를 이용하여 합성됨.

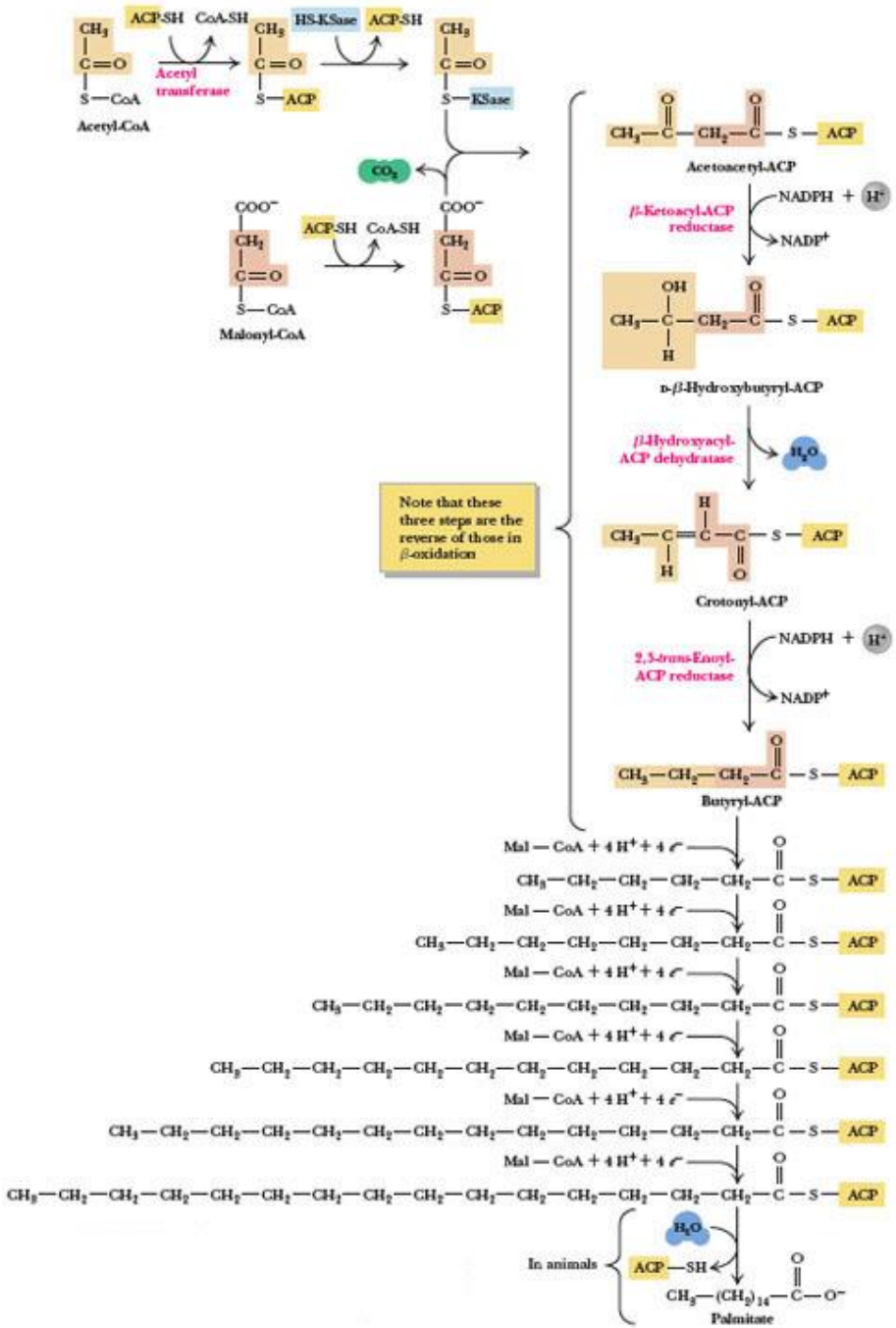


Fig. 21-15, p.583

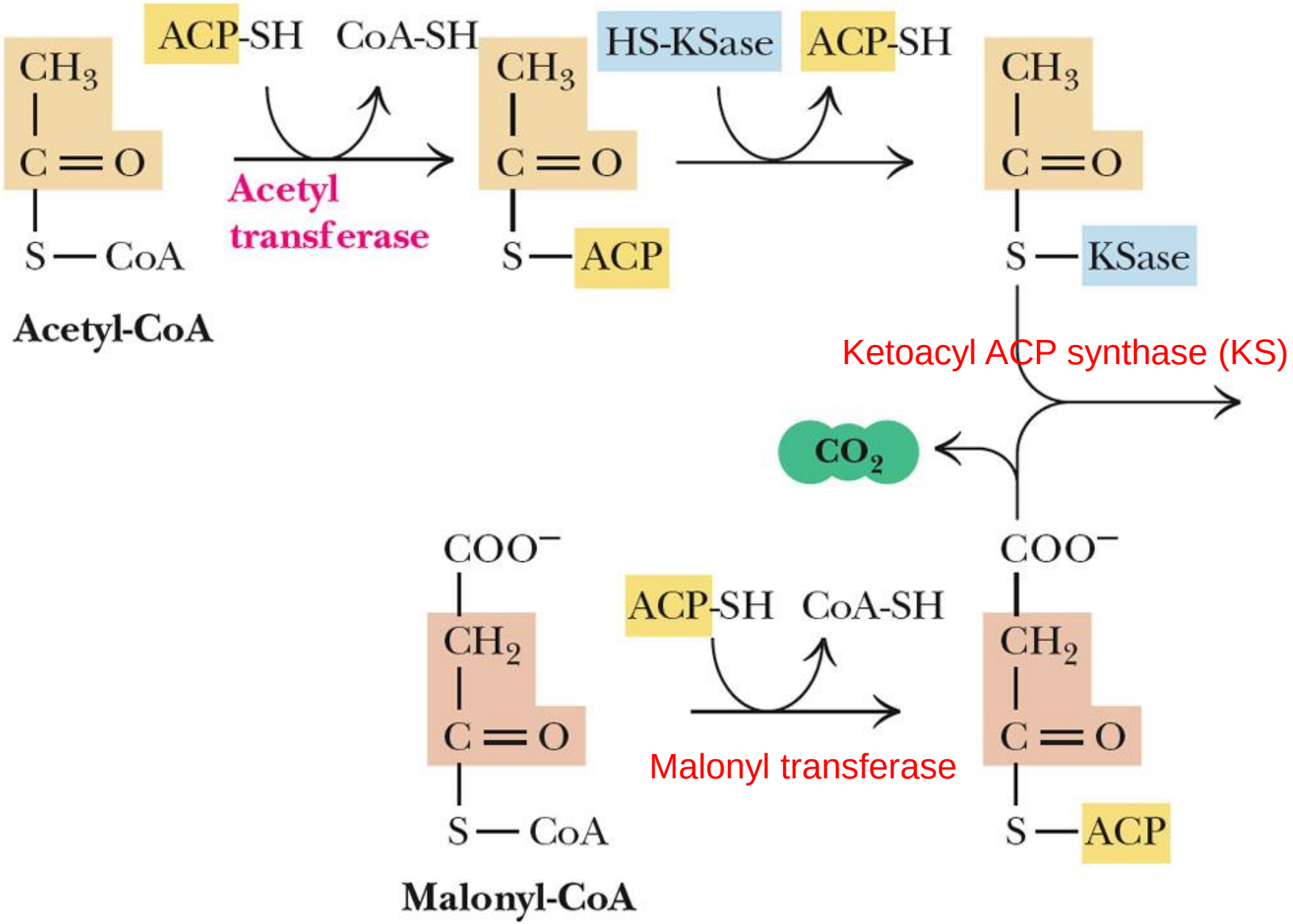


Fig. 21-15a, p.583

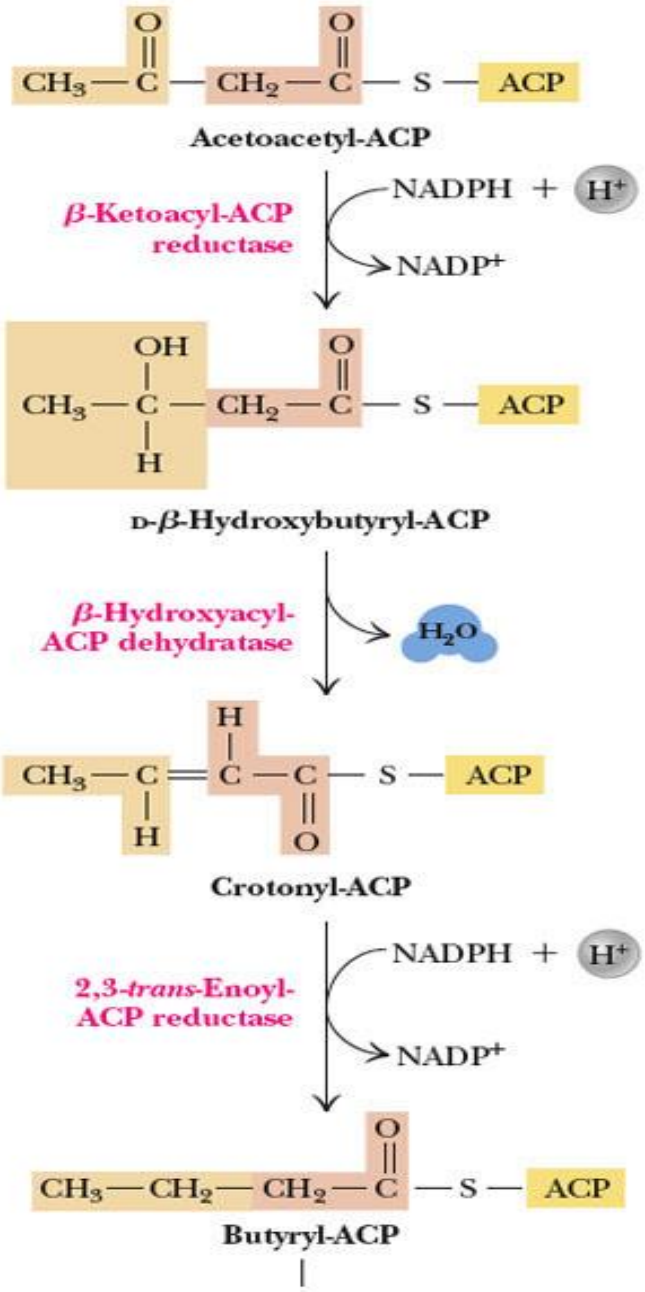


Fig. 21-15b, p.583

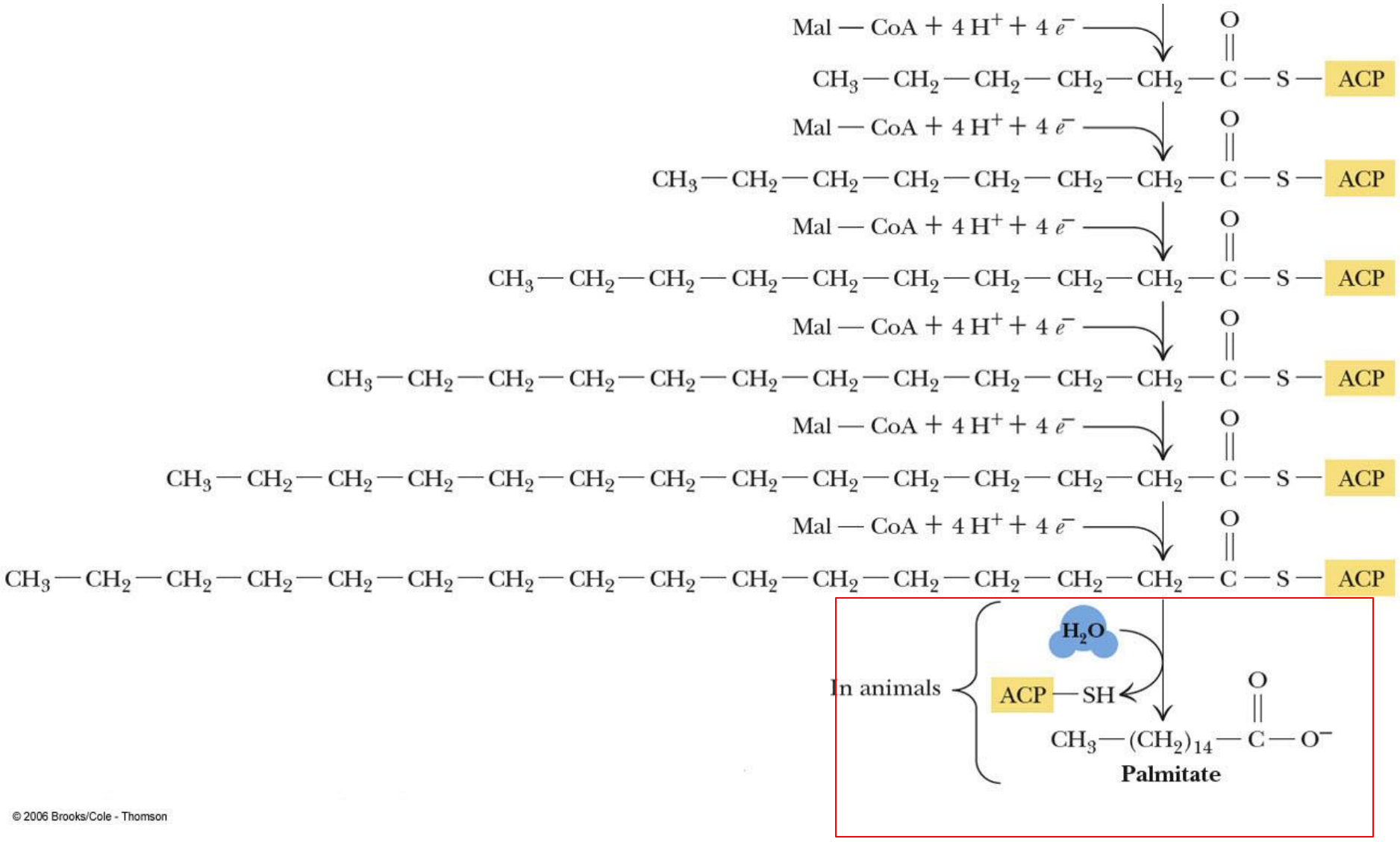


Fig. 21-15c, p.583

지방산 합성 equation

- acetyl-CoA + 7 malonyl-CoA + 14 NADPH → palmitate + 7 CO_2 + 8 HSCoA + 14 $NADP^+$ + 14 H^+ + 6 H_2O

- 7 acetyl-CoA + 7 ATP + 7 CO_2 + 7 H_2O →
  7 malonyl-CoA + 7 H+ + 7 ADP + 7 Pi

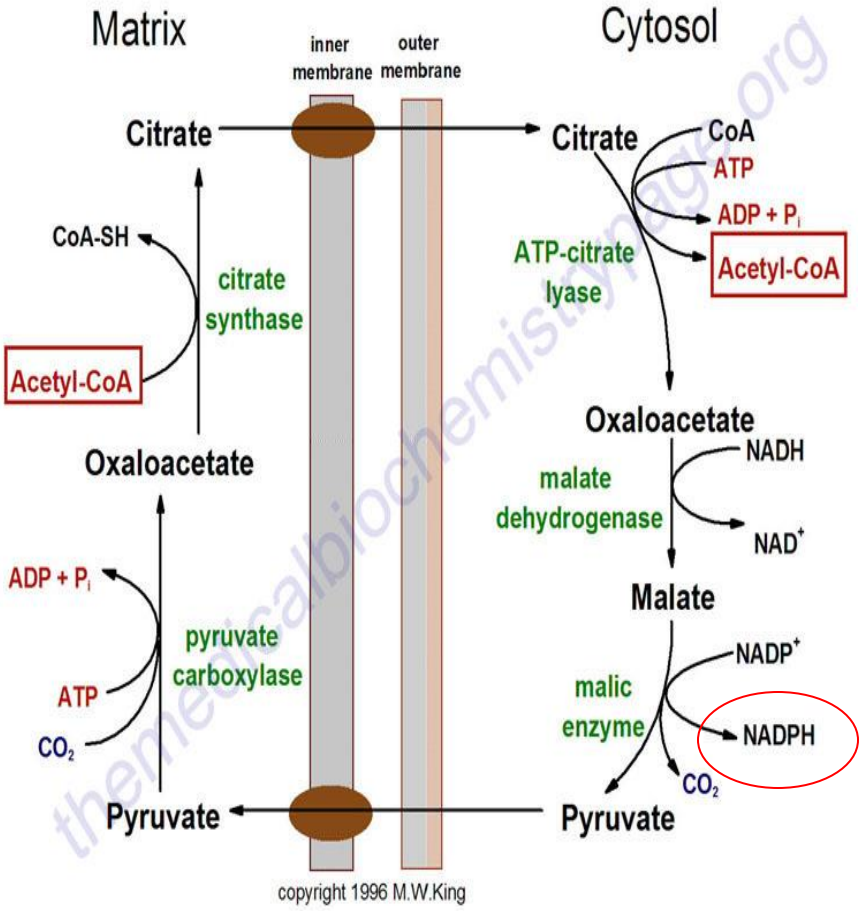
- 8 citrate + 8 ATP + 8 HSCoA →
  8 acetyl-CoA + 8 oxaloacetate + 8 ADP + 8 Pi

NADPH의 source

- The pentose phosphate cycle is a major source of NADPH.

- malate2 + NADP+

→ pyruvate + CO_2 + NADPH



지방산 합성과 분해과정의 비교

Table 21.2

A Comparison of Fatty Acid Degradation and Biosynthesis

Degradation	Biosynthesis
1. Product is acetyl-CoA	Precursor is acetyl-CoA
2. Malonyl-CoA is not involved; no requirement for biotin	Malonyl-CoA is source of two-carbon units; biotin required
3. Oxidative process; requires NAD^+ and FAD and produces ATP	Reductive process; requires NADPH and ATP
4. Fatty acids form thioesters with CoA-SH	Fatty acids form thioesters with acyl carrier proteins (ACP-SH)
5. Starts at carboxyl end (CH_3CO_2—)	Starts at methyl end (CH_3CH_2—)
6. Occurs in the mitochondrial matrix, with no ordered aggregate of enzymes	Occurs in the cytosol, catalyzed by an ordered multienzyme complex
7. β-Hydroxyacyl intermediates have the L configuration	β-Hydroxyacyl intermediates have the D configuration

Table 21-2, p.586

지방산의 연장 (elongation)

- Acyl CoA의 형태로 탄소수 길이가 연장됨
- 효소도 단일효소가 관여
- 미토콘드리아와 ER에서 일어난다
- Acetyl CoA (미토콘드리아) or malonyl coA(ER)의 형태로 관여한다

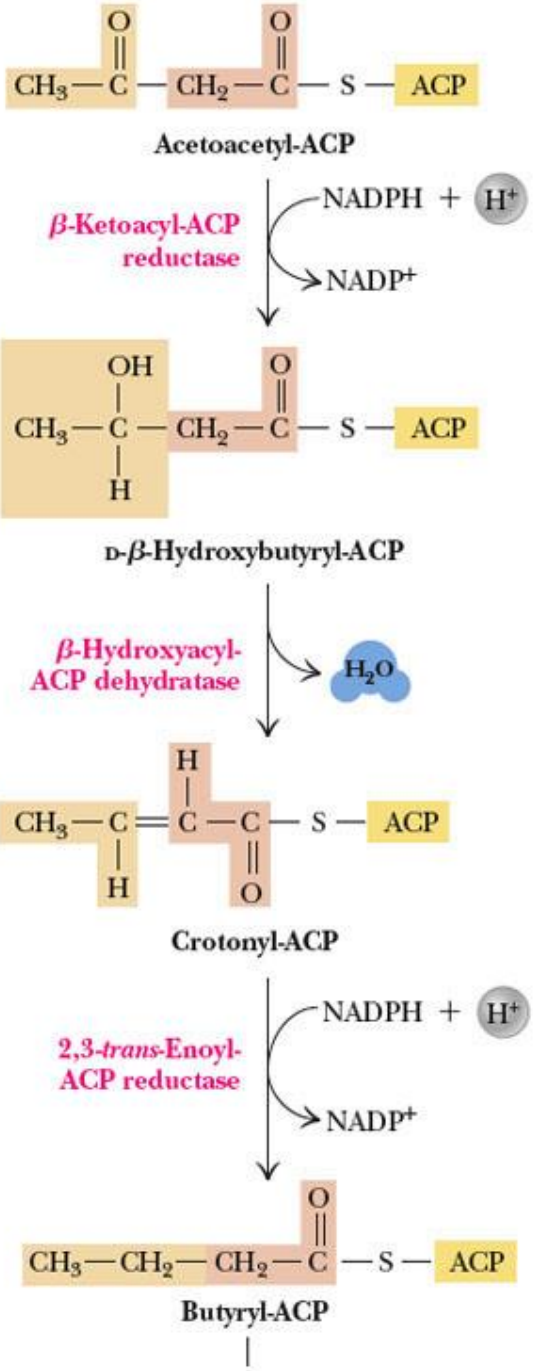


Fig. 21-15b, p.583

지방산의 불포화 (unsaturation)

- ER 막에 결합되어있는 세 가지 단백질이 관여
- desaturase
- cytochrome *b5* reductase
- cytochrome *b5*

필수지방산이란?

- W6 family-- linoleic acid (C18:2, 9,12)
  arachidonic acid (C20:4, 5,8,11,14)
- W3 family-- linolenic acid (C18:3, 9,12,15)

- 필수지방산은 동물에서 합성되지 않는다.
- Why? C9이상의 탄소위치에 이중결합을 만드는 효소가 없음

fatty-acid metabolism가 일어나는 장소

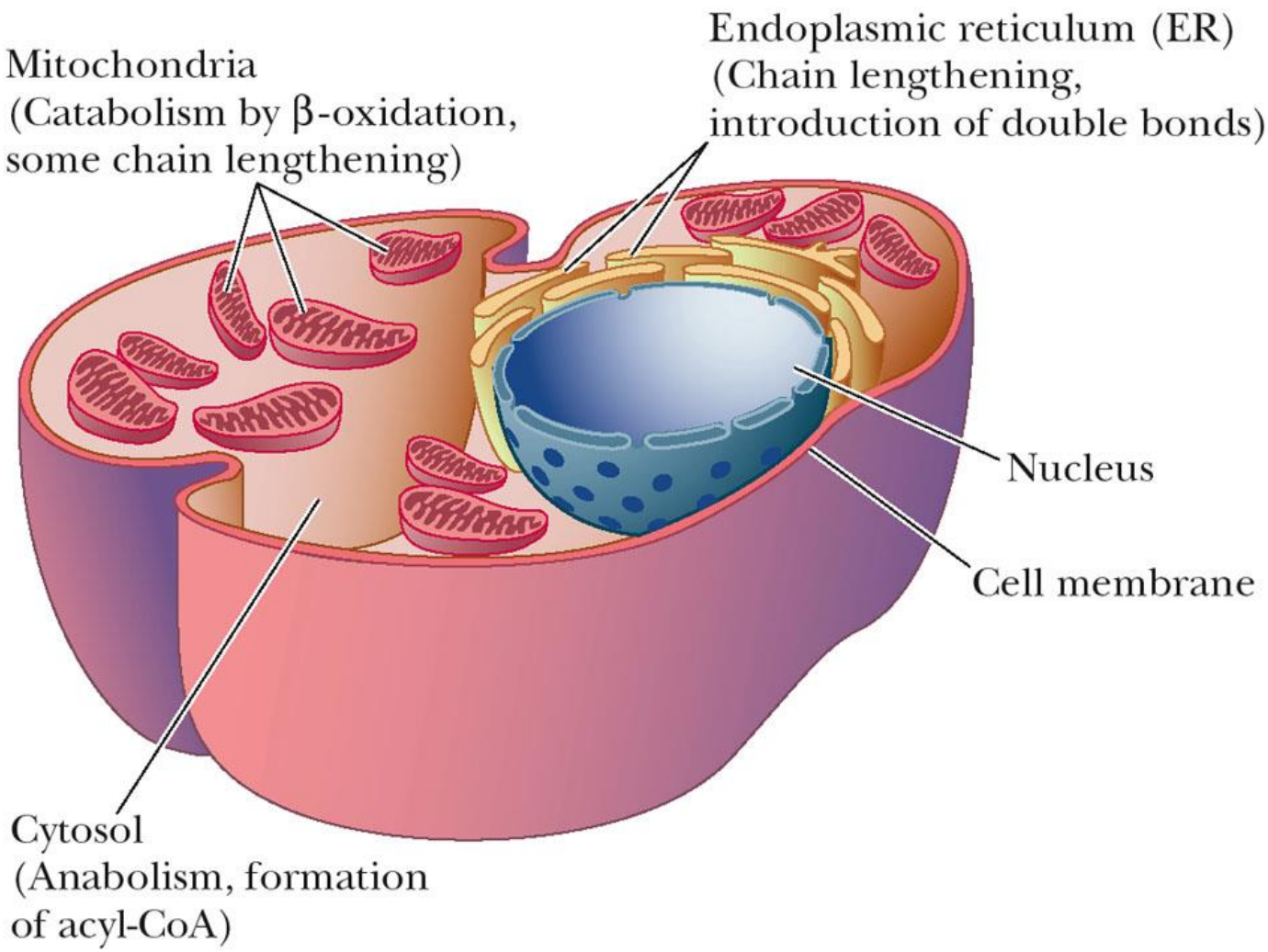


Fig. 21-17, p.586

지방산 대사의 조절

- 호르몬과 cAMP 는 acetyl CoA carboxylase (ACC)와 TG lipase 활성 촉진

Acetyl CoA Carboxylase

- A new target in the fight against obesity

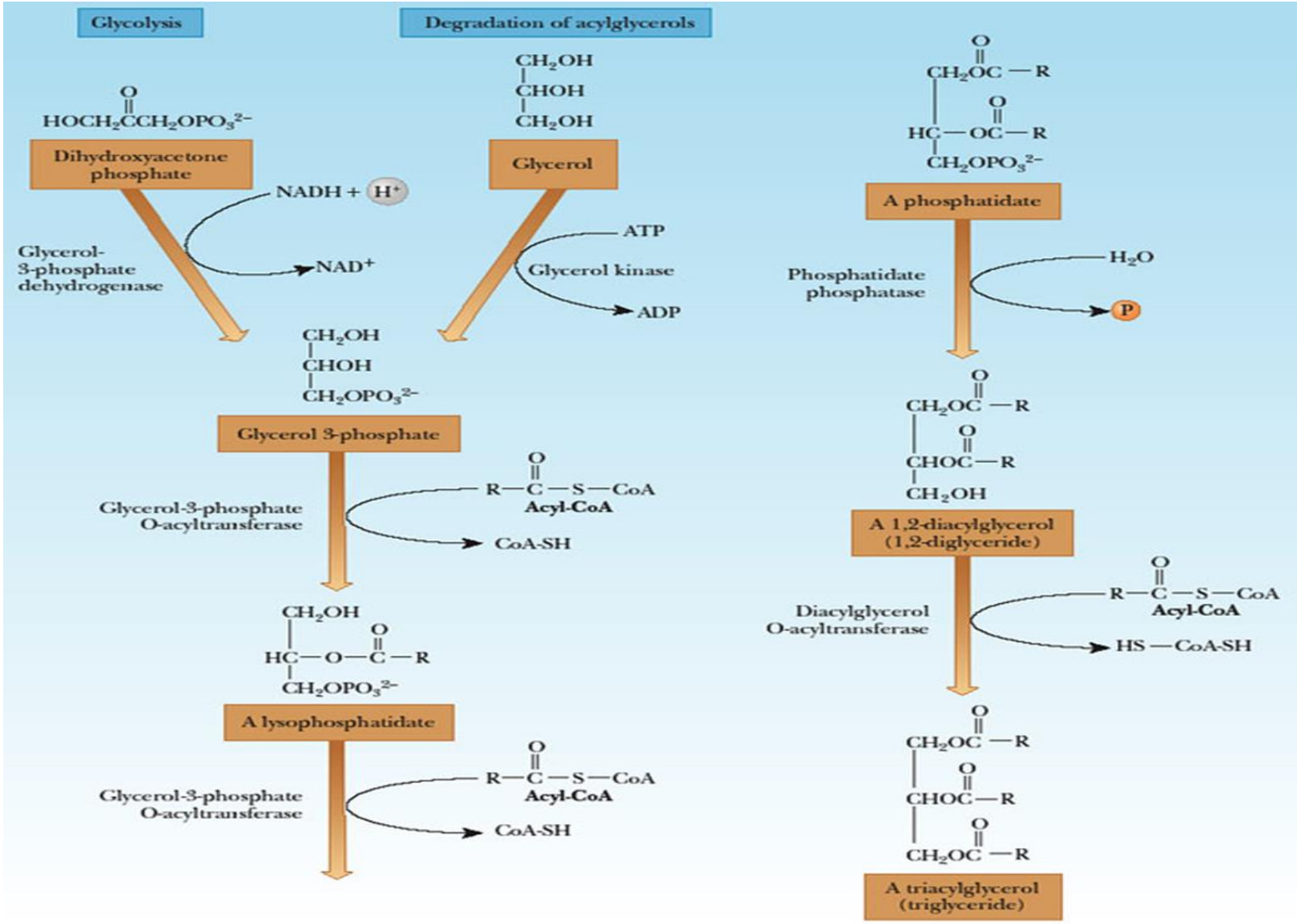
아이코사노이드의 생합성과 기능

- 국소호르몬(local hormone)이라고도 함.
- arachidonic acid을 비롯한 ω6,와 w3 지방산으로부터 만들어진다

① Prostaglandins: (PG) 염증반응과 관련
② Thromboxane: (Tx)
③ Leucotriene: (LT)

※ 아스피린의 효과
※ 비스테로이드성 항염증제

복합지방의 생합성



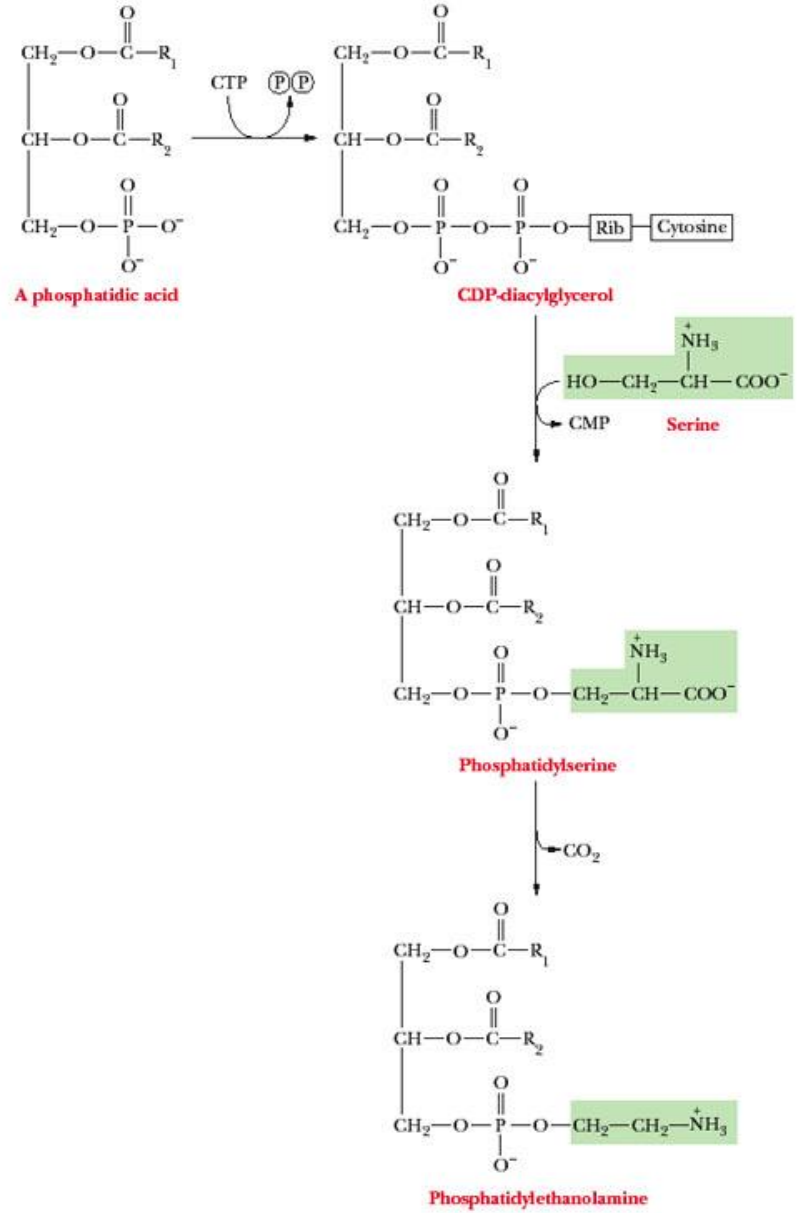


Fig. 21-19, p.589

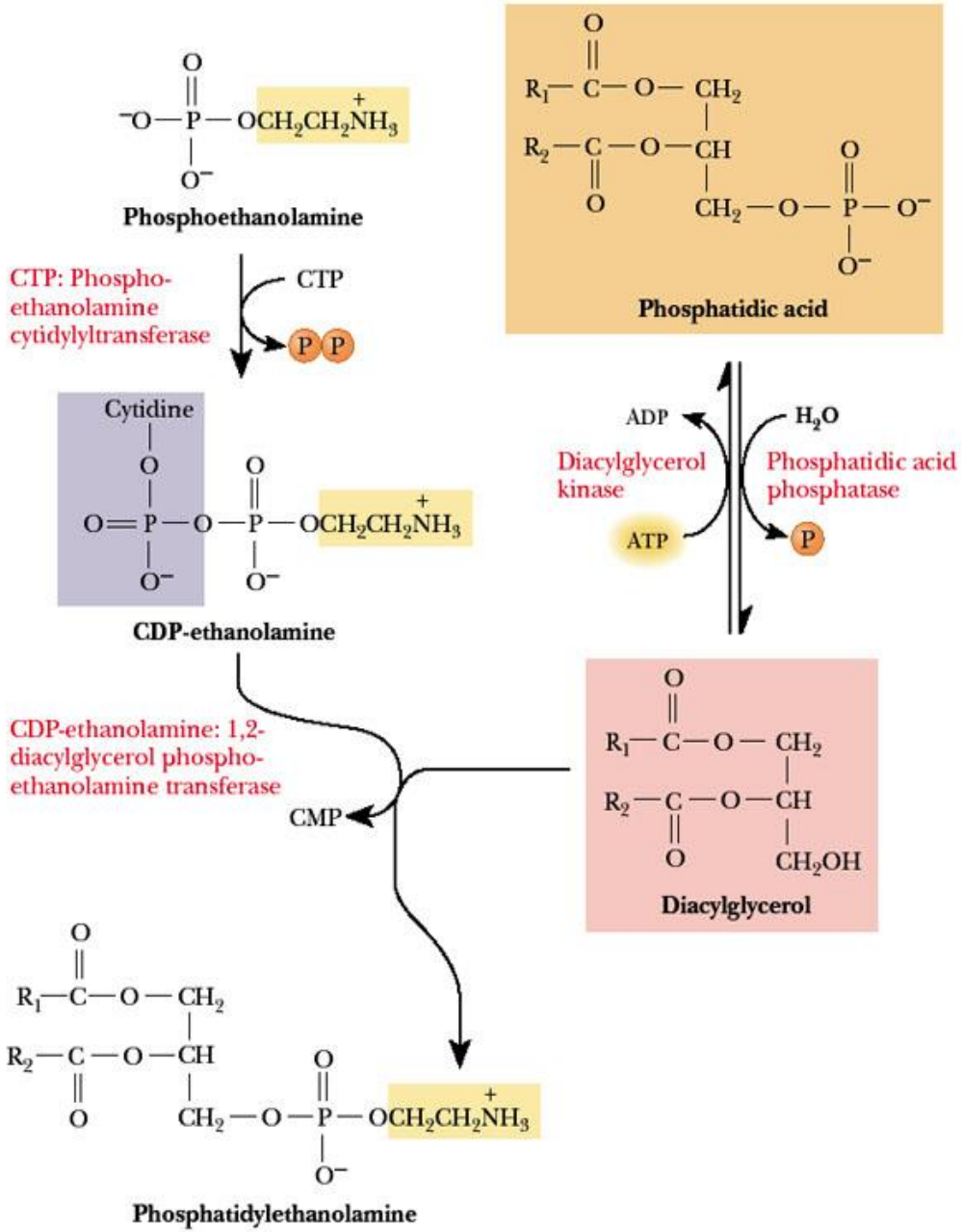


Fig. 21-20, p.590

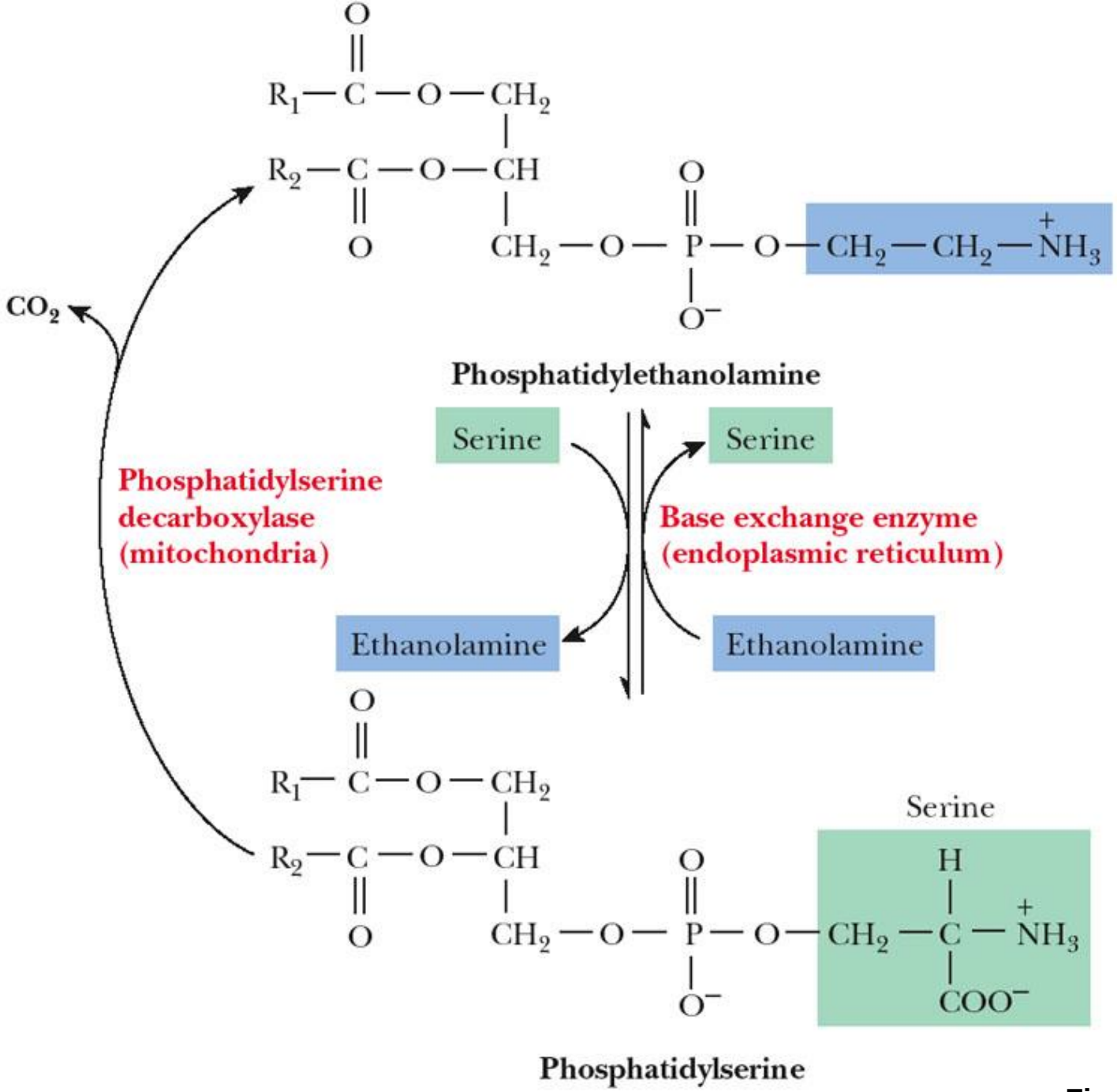
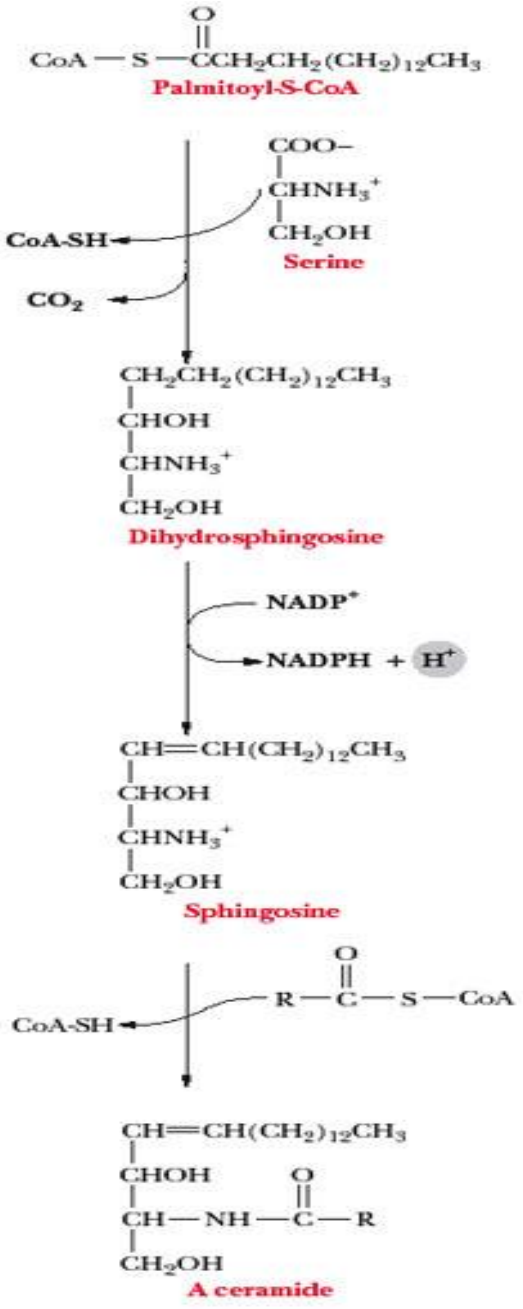


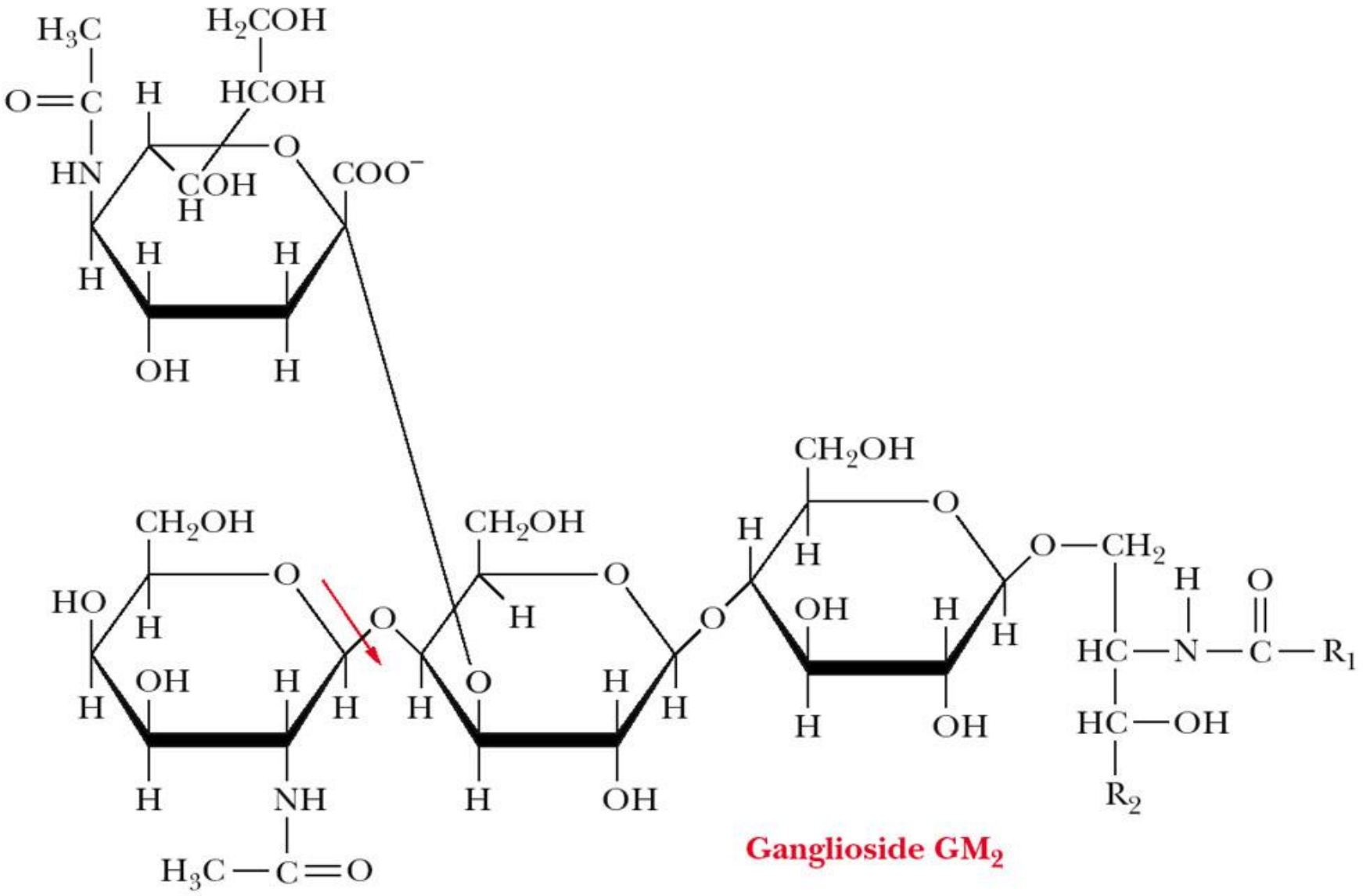
Fig. 21-21, p.591

The biosynthesis of sphingolipids



Sphingomyelins
Cerebrosides
gangliosides

Fig. 21-22, p.592



콜레스테롤의 생합성

- Acetyl CoA로부터 합성
- HMG CoA reductase ---콜레스테롤 합성속도를 조절하는 효소
- Squalene --- 중간생성물

콜레스테롤의 생합성

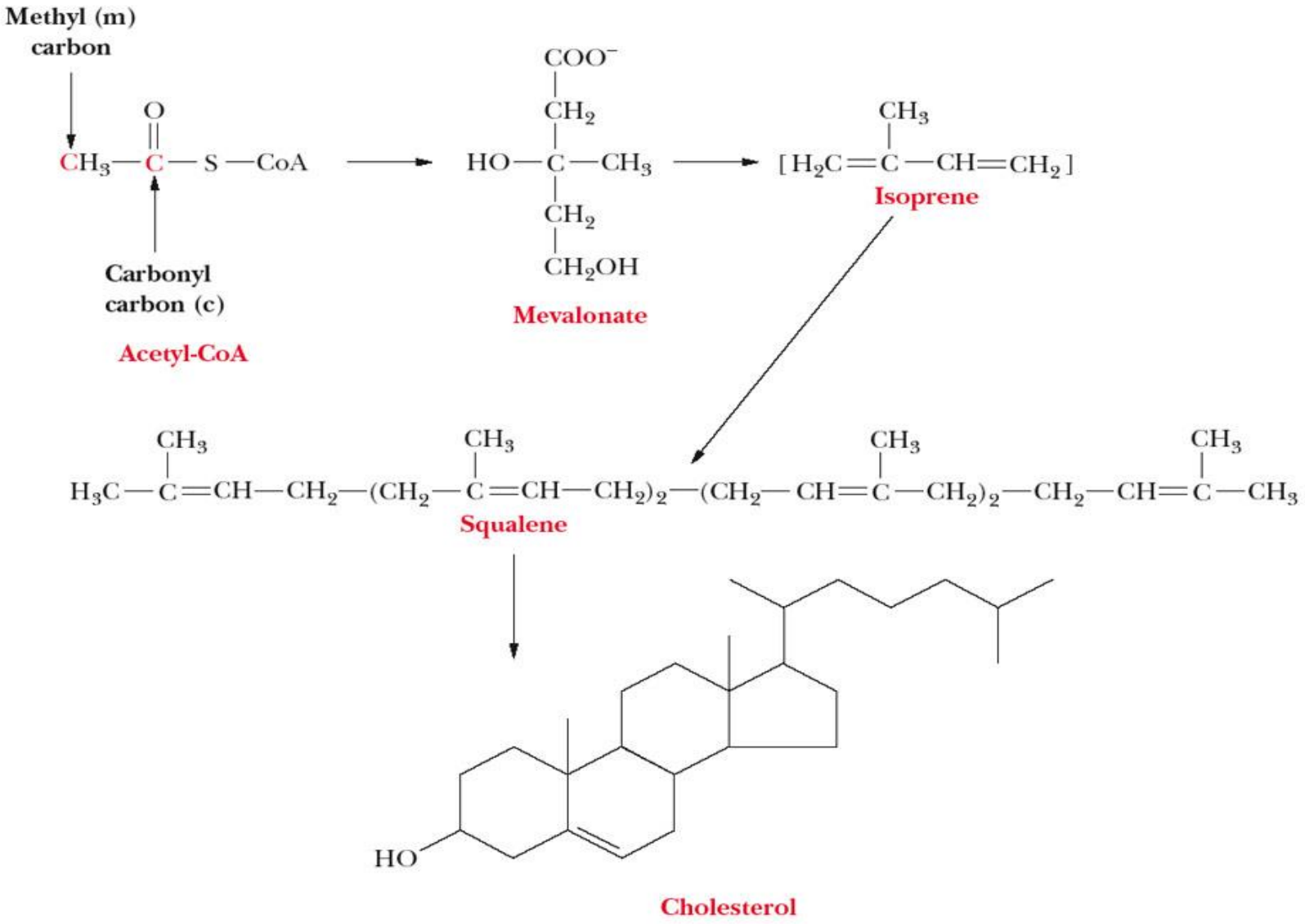


Fig. 21-23, p.593

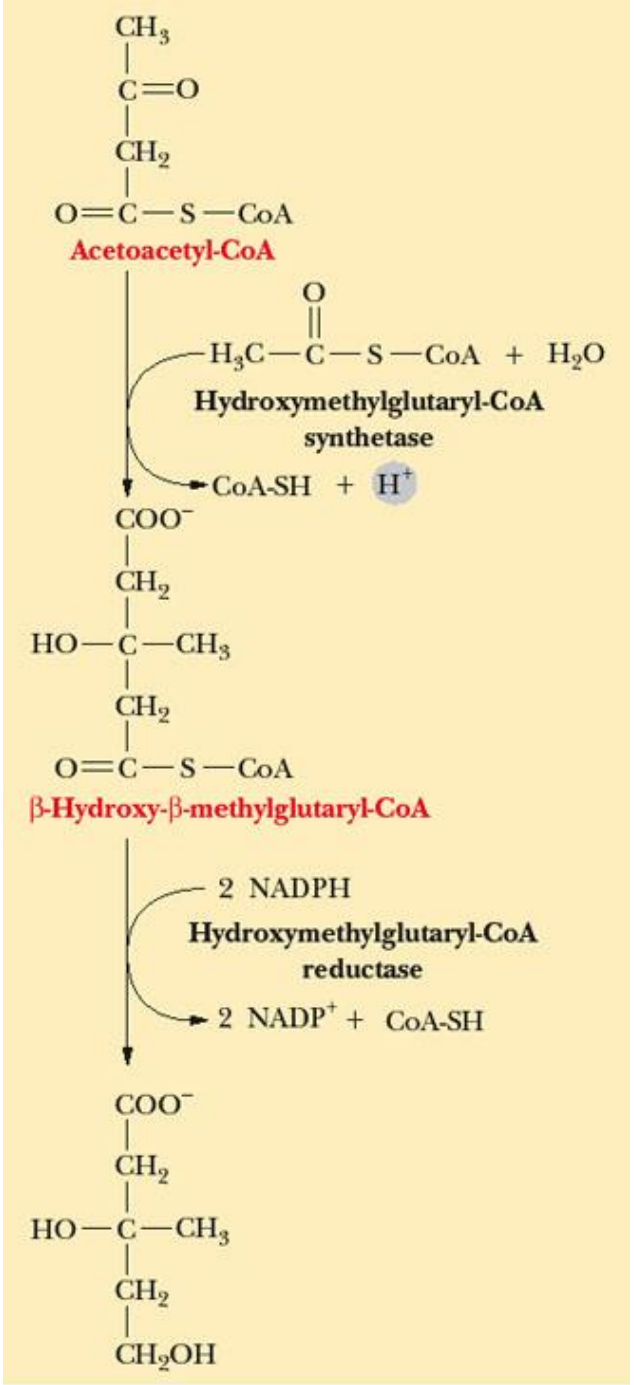


Fig. 21-25, p.594

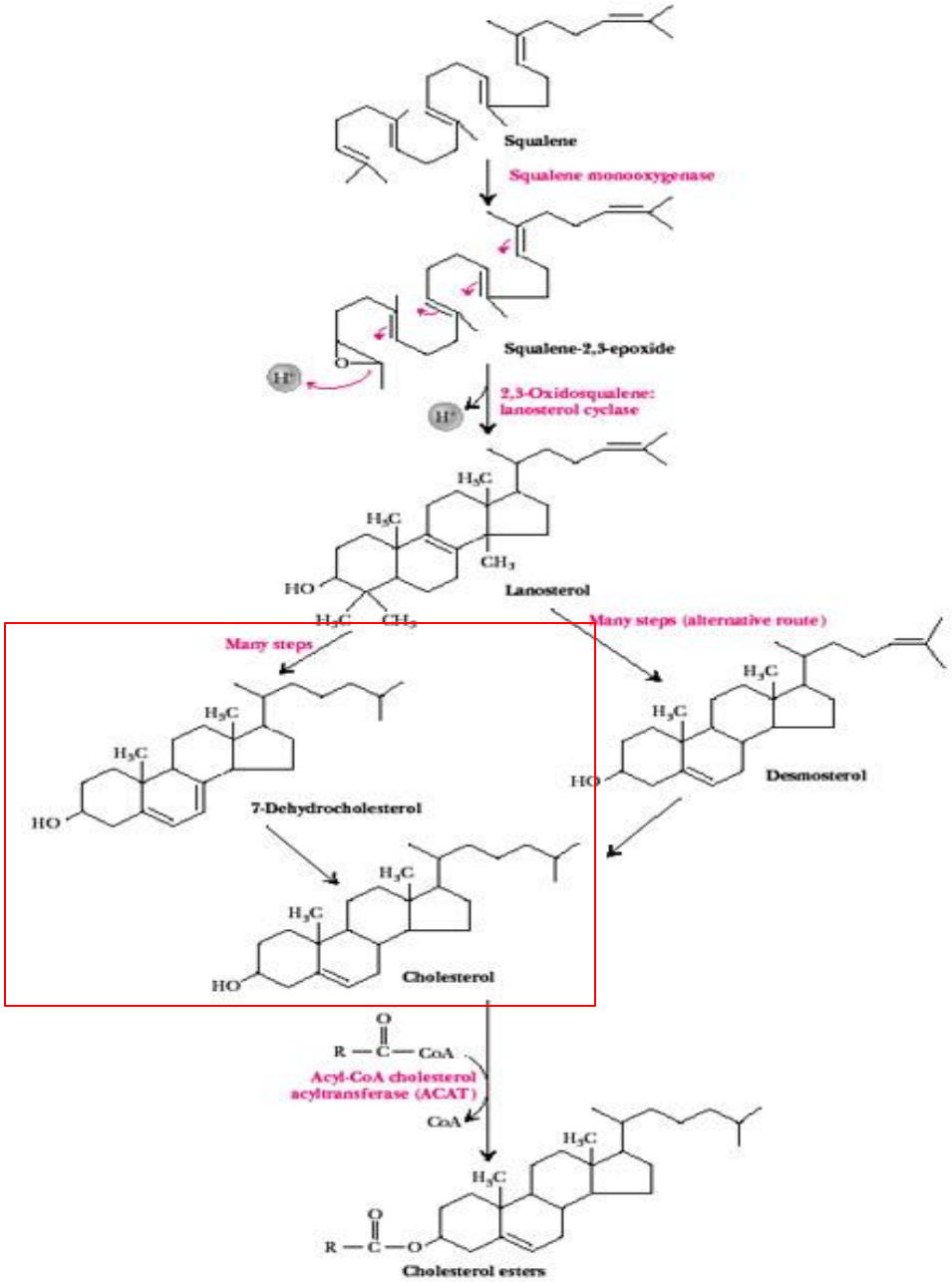


Fig. 21-28, p.596

콜레스테롤의 저장

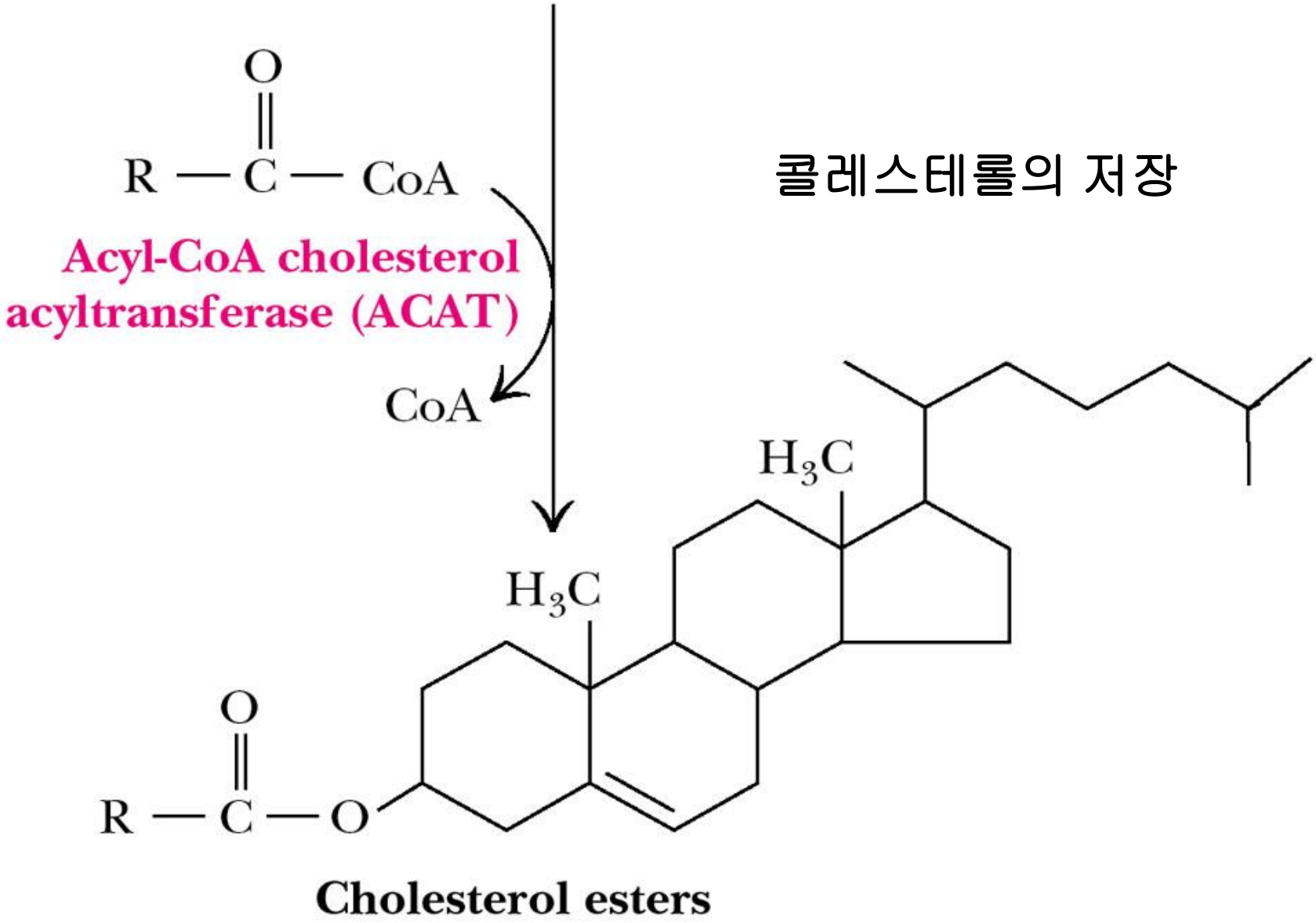


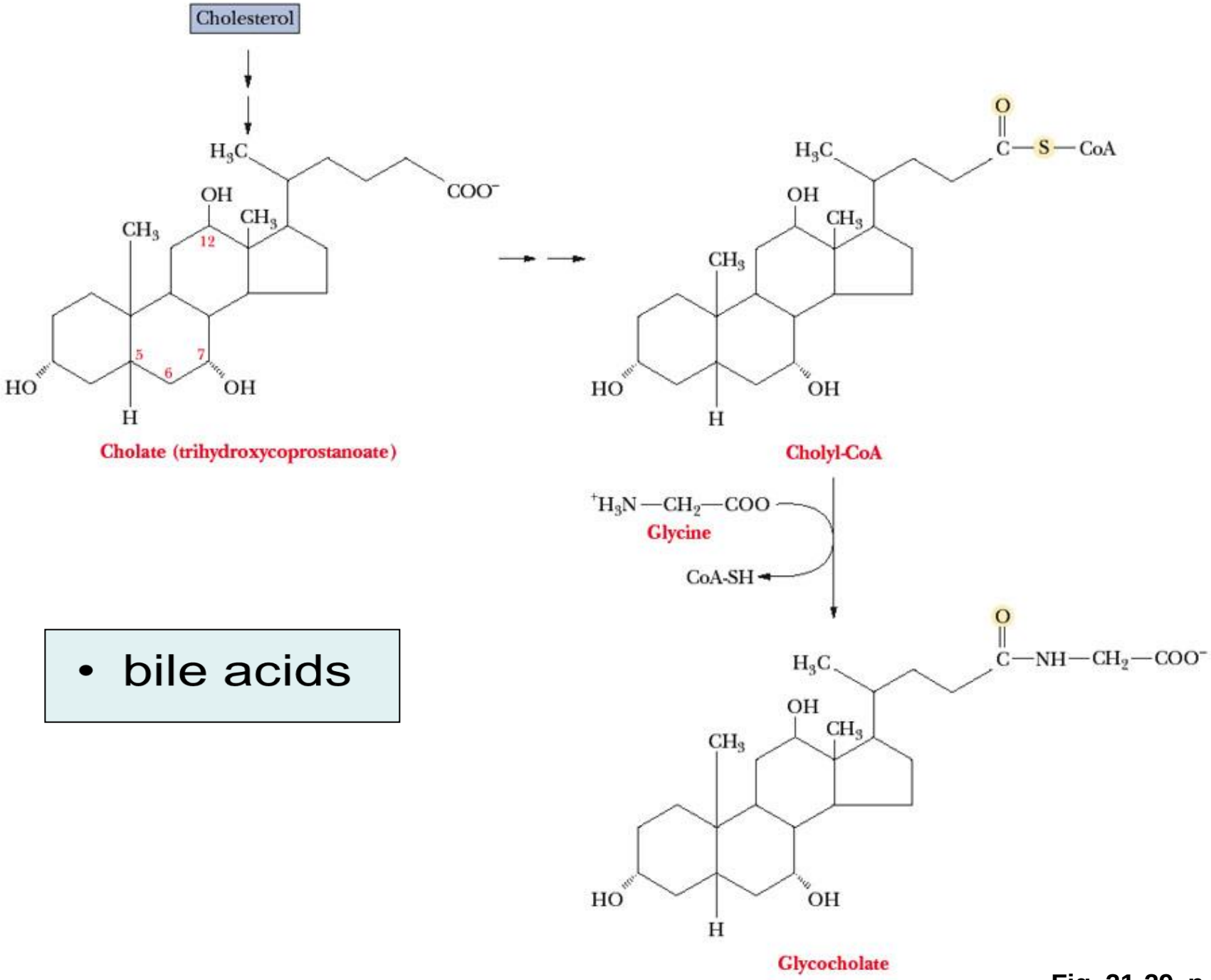
Fig. 21-28c, p.596

콜레스테롤로부터 합성되는 **steroid** 화합물

- bile acids
- 비타민 D
- steroid hormone

  - 성 호르몬 estrogen, androgen 등

  - 부신피질호르몬 aldosterone, corticoids



- bile acids

Fig. 21-29, p.597

The synthesis of steroid hormones from cholesterol

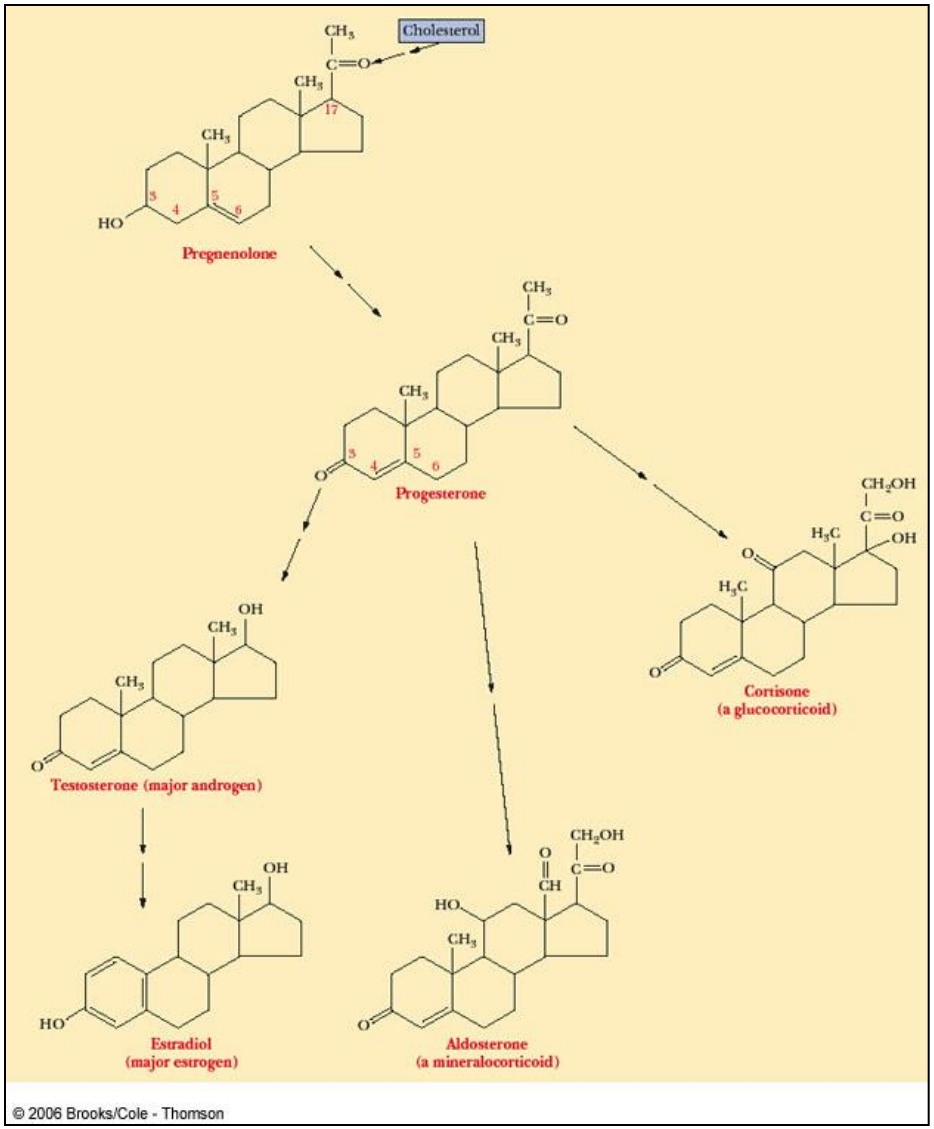


Fig. 21-30, p.598

스테로이드 호르몬의 기능 및 작용 기작

- 핵에서 전사 조절
- 생체대사 조절
- anabolic steroids

TG와 콜레스테롤의 운반

- 단백질, 인지질로 구성된 운반체가 존재
- 밀도차이에 따라 분류
- 단백질의 비율이 높을수록 밀도가 커짐

Table 21.3

Major Classes of Lipoproteins in Human Plasma

Lipoprotein class	Density (g mL^{-1})
Chylomicrons	<0.95
VLDL	0.95–1.006
IDL	1.006–1.019
LDL	1.019–1.063
HDL	1.063–1.210

LDL particle의 구조

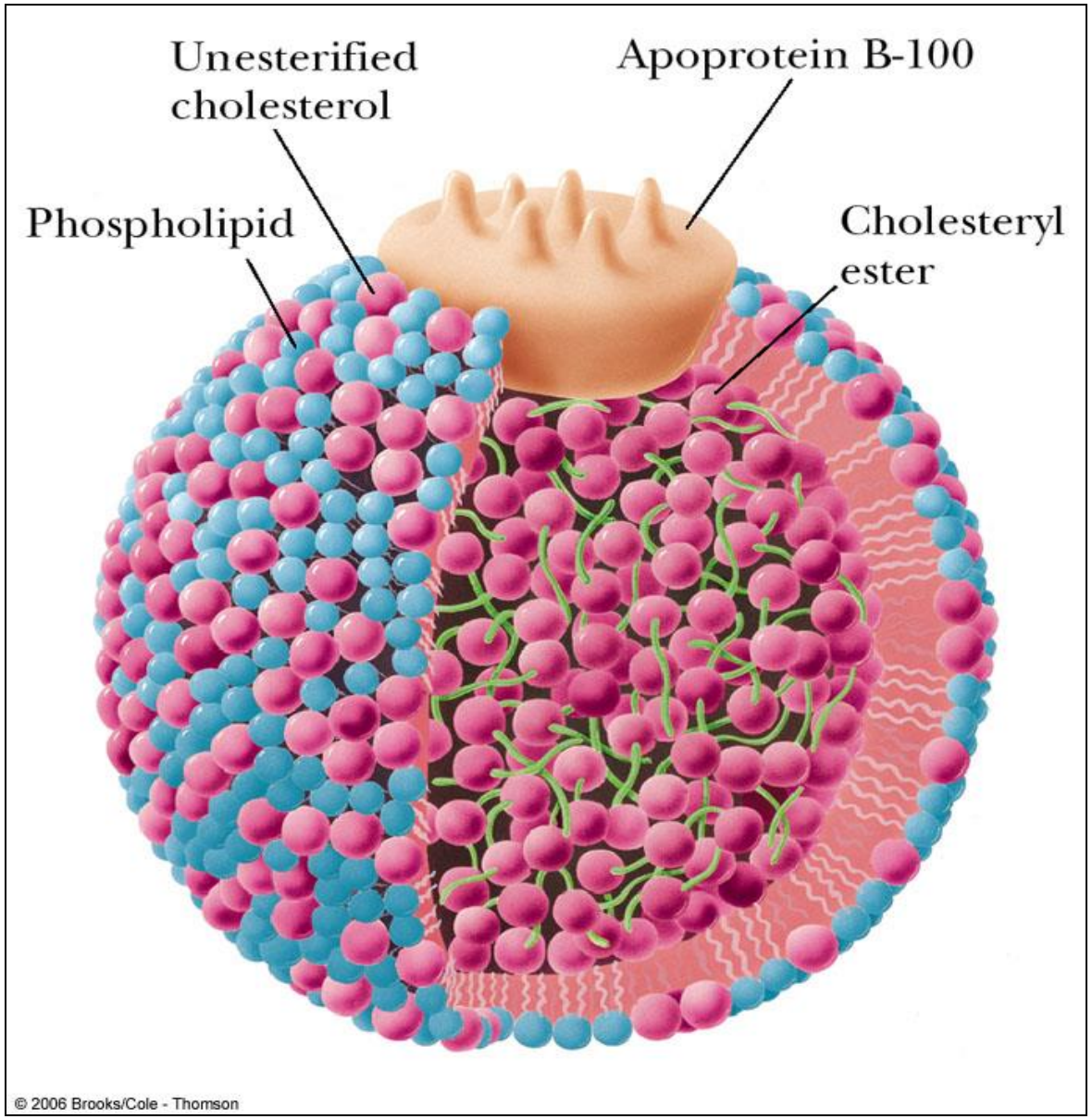


Fig. 21-31, p.599

The fate of cholesterol in the cell

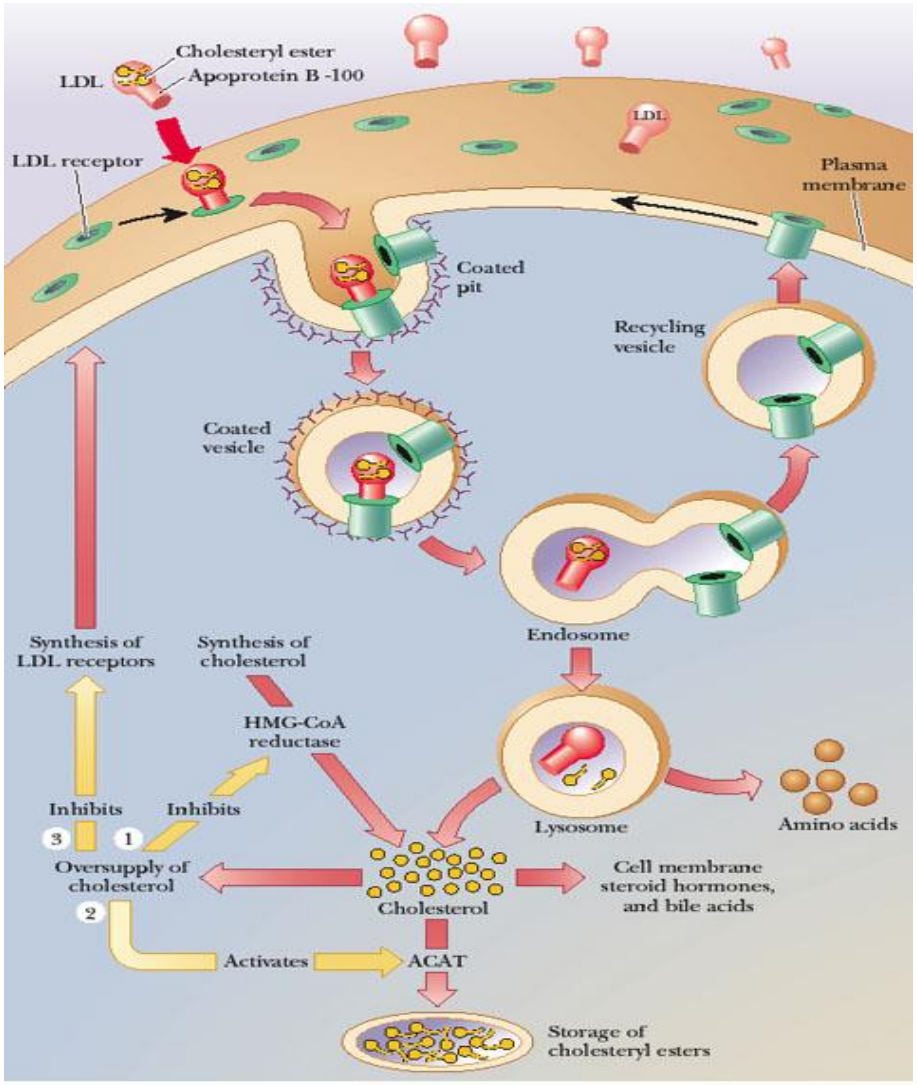


Fig. 21-32, p.600

문제풀기

- 문제 49번
- 문제 50번