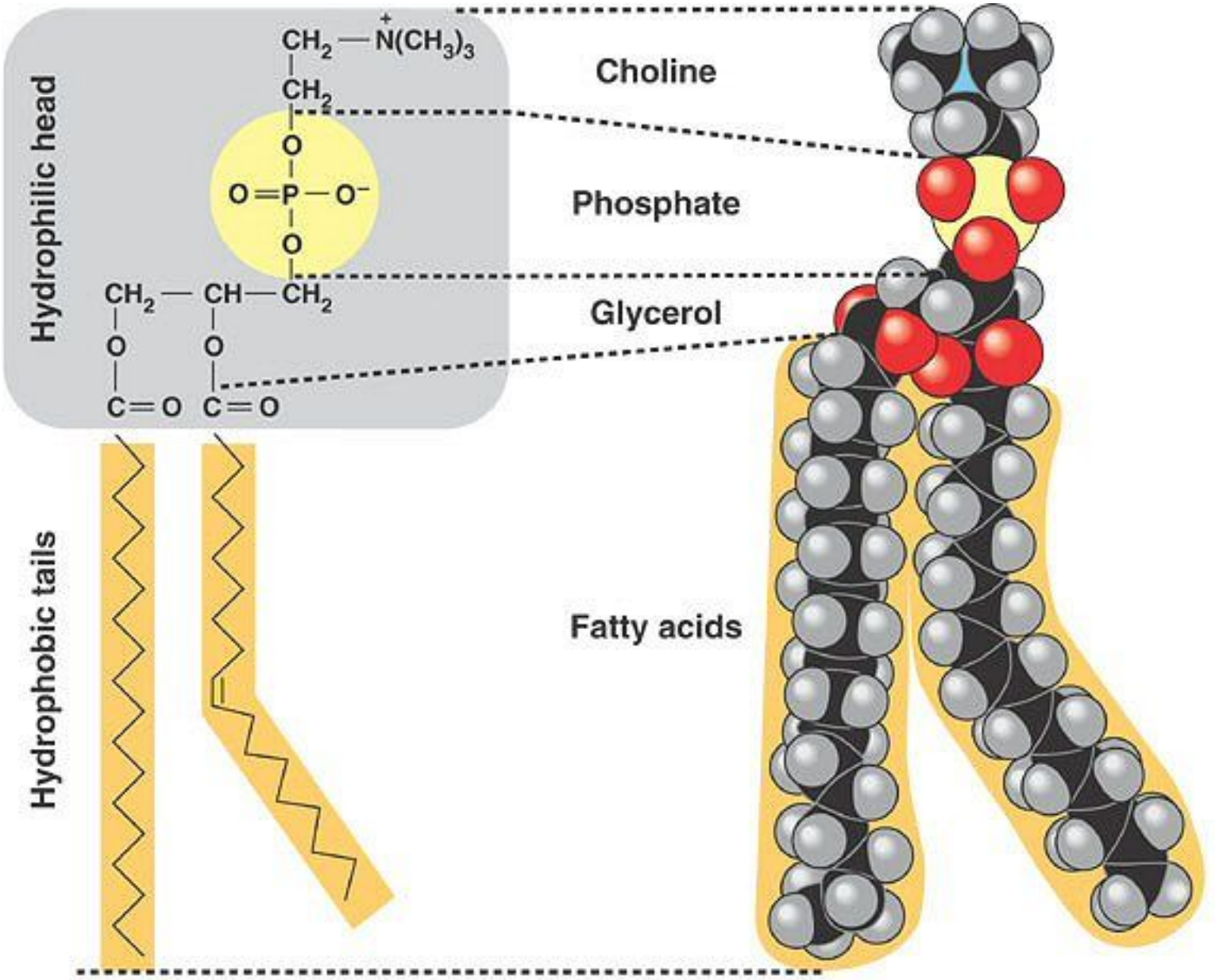
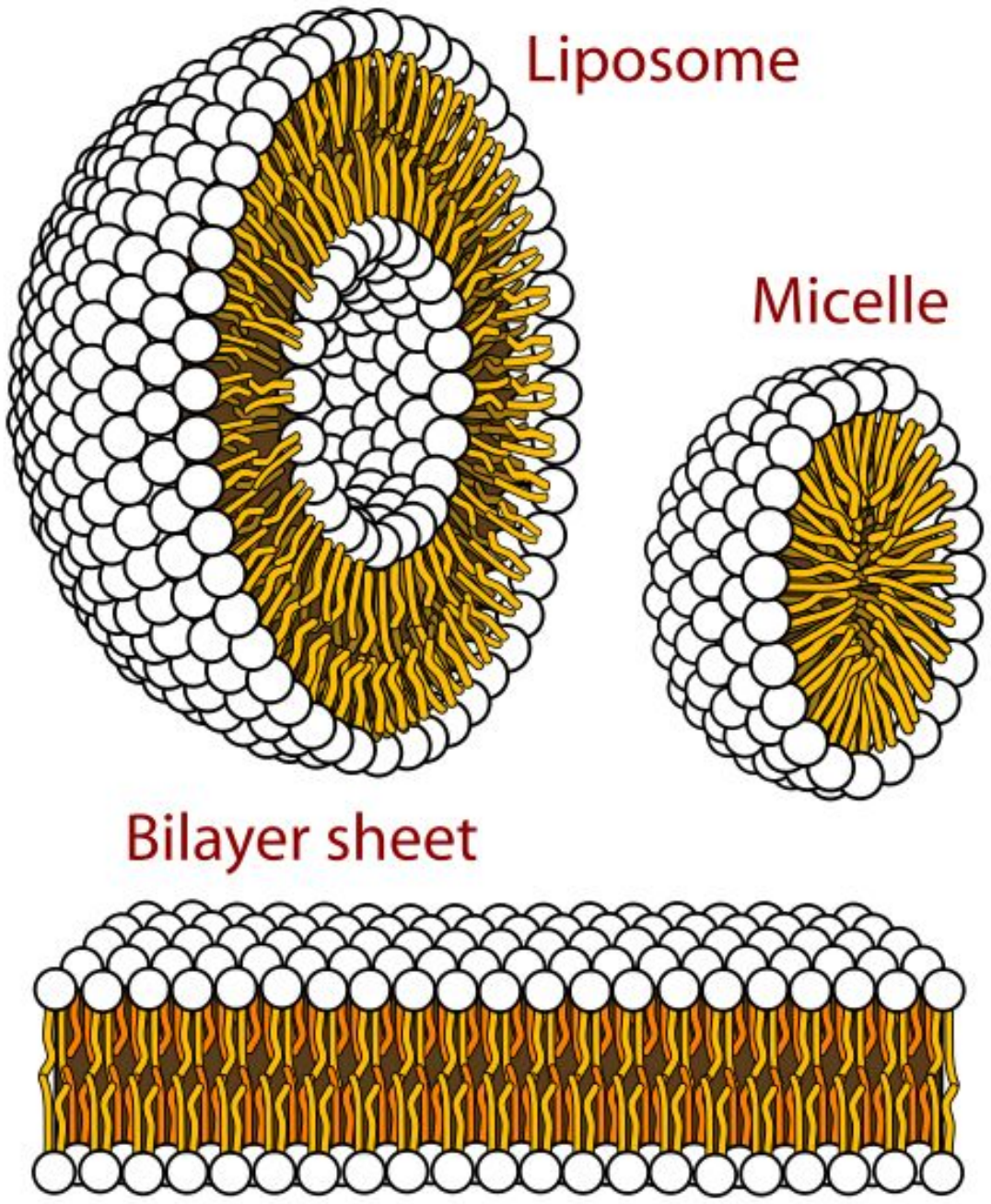
LIPID METABOLISM

Part 2

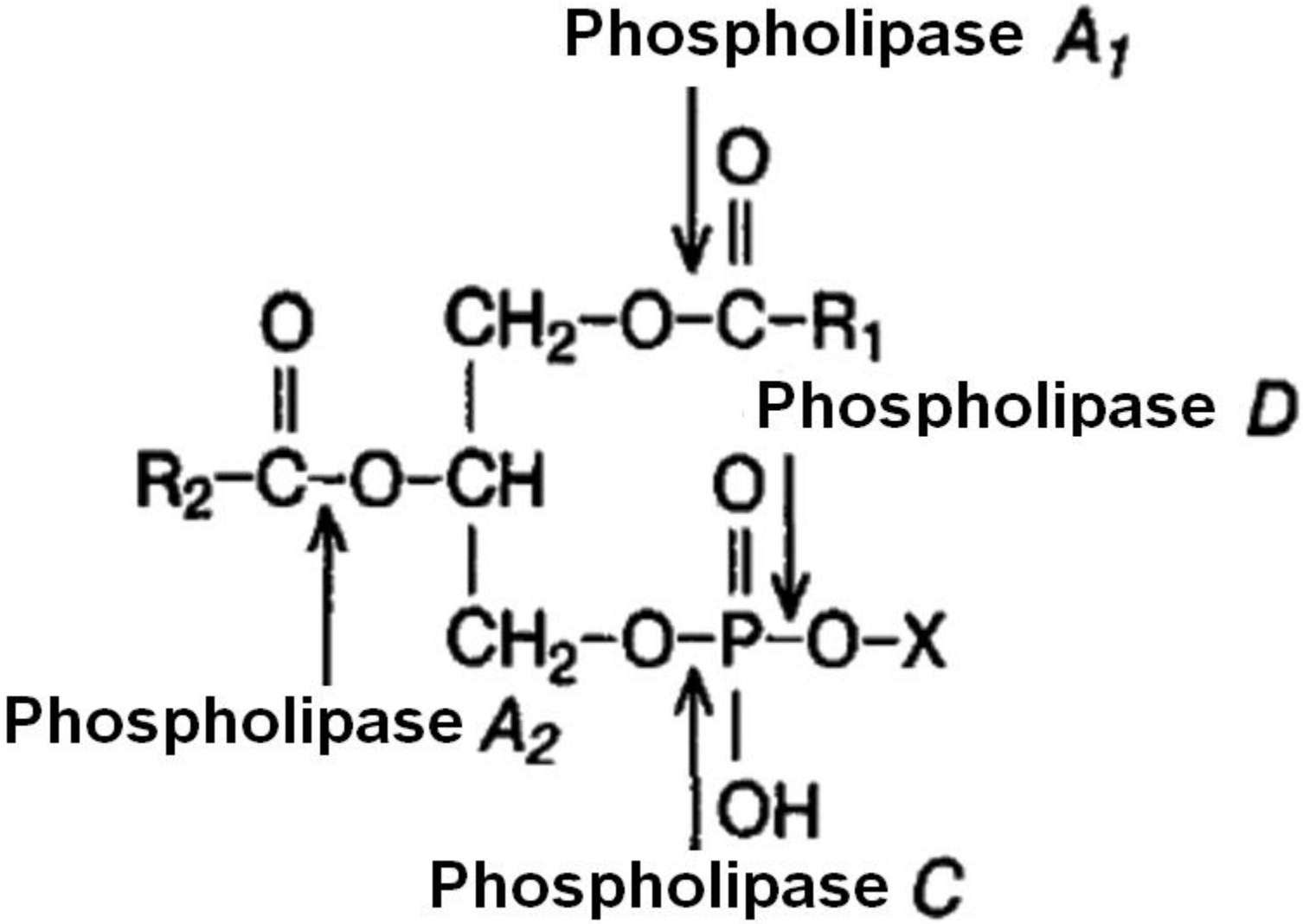
Phospholipid



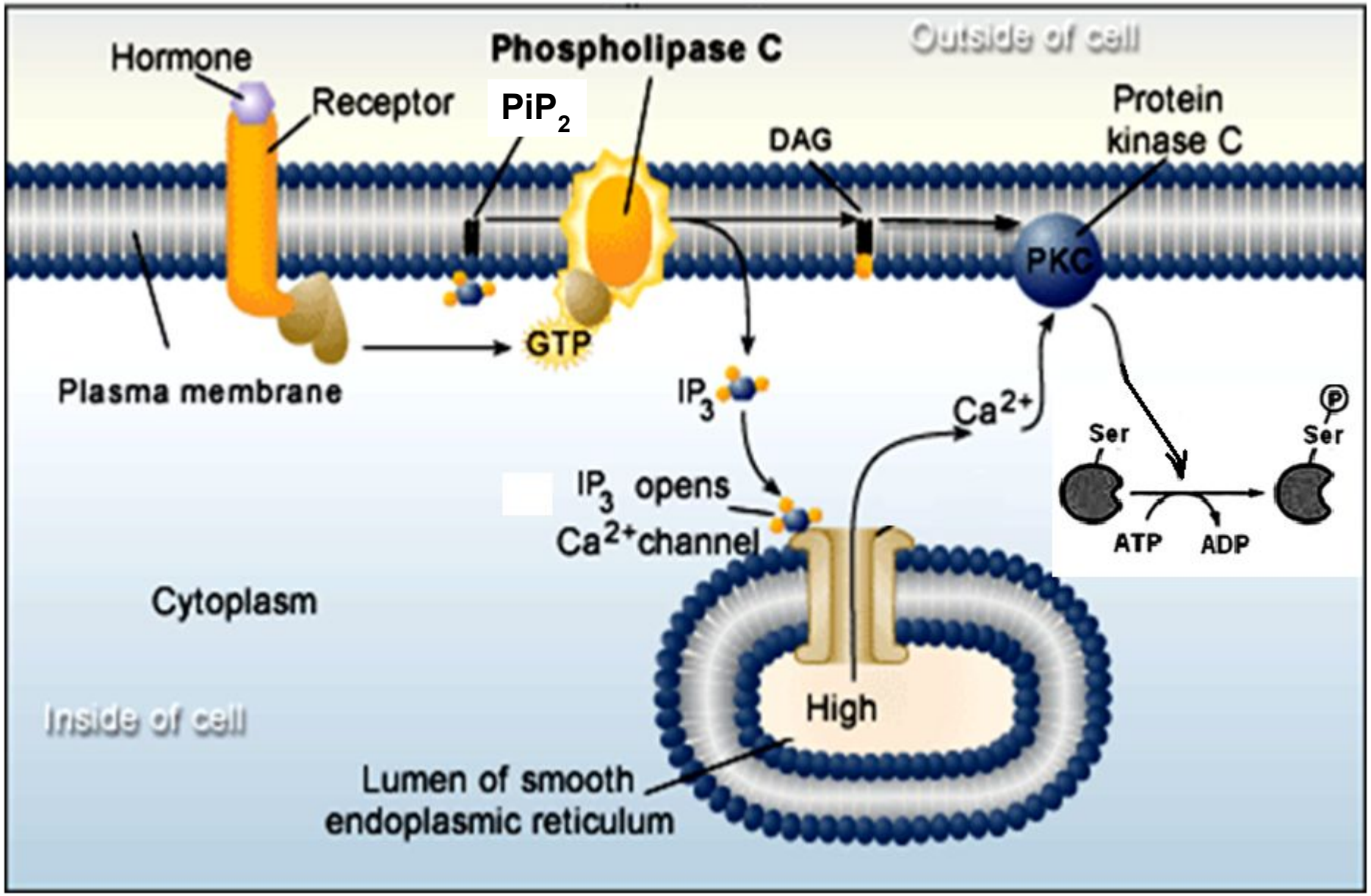
Self-organization of phospholipids



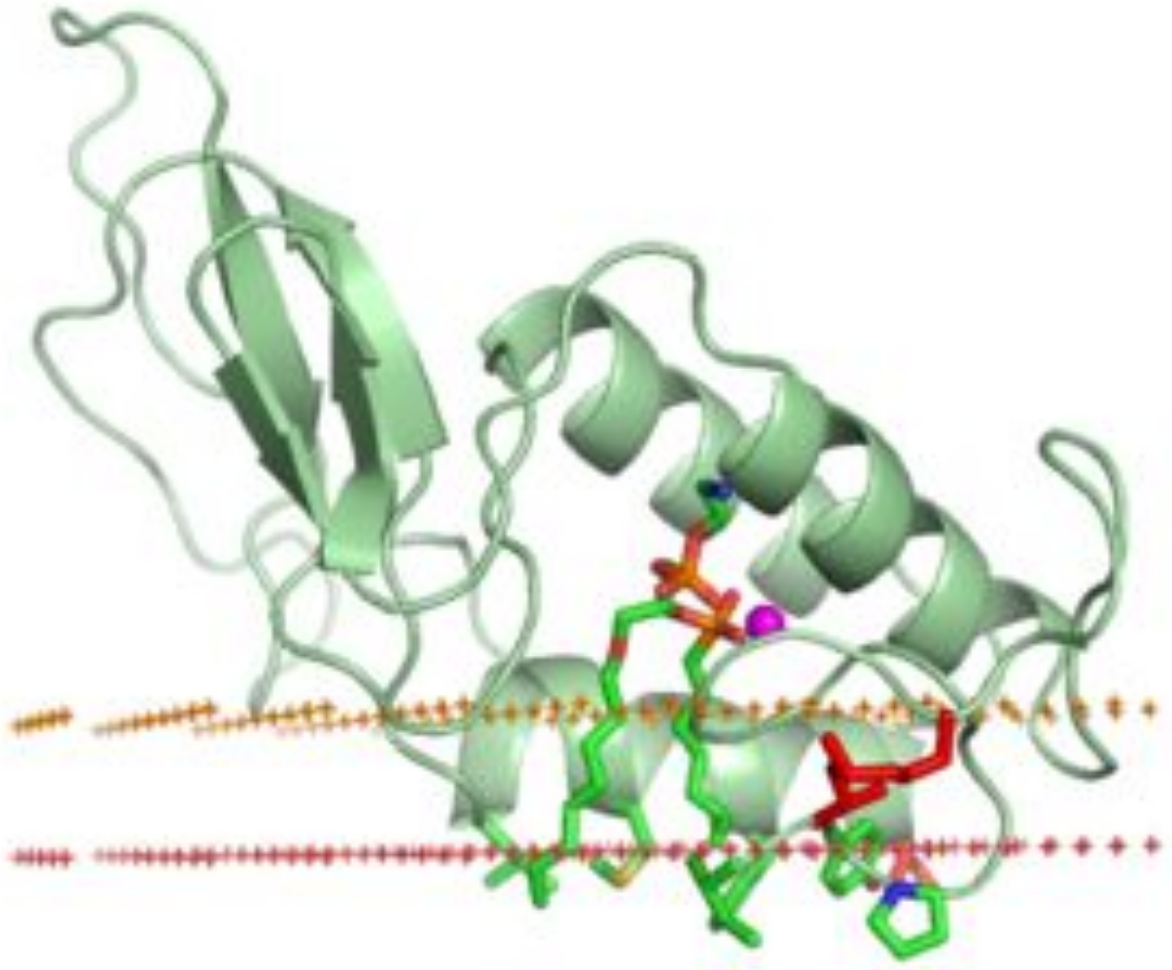
Cleavage sites of phospholipases



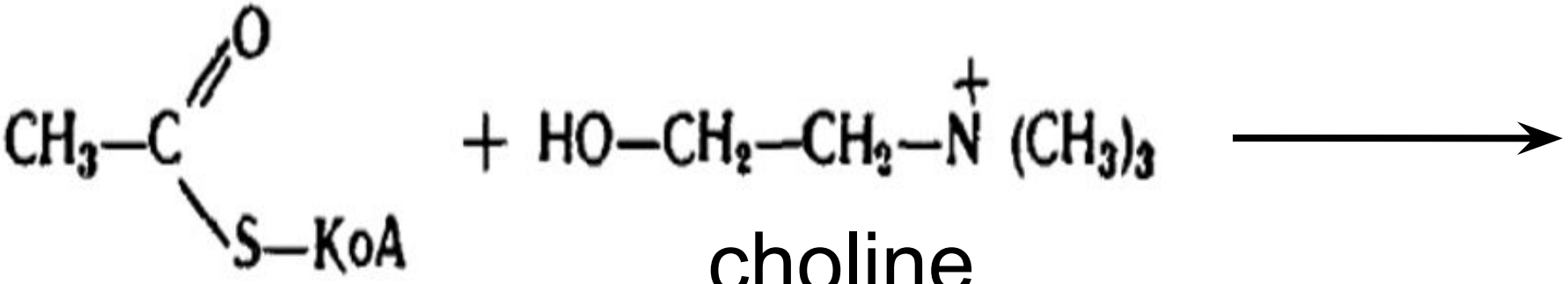
Phosphatidyl inositol calcium system



Phospholipase A_2 of bee venom

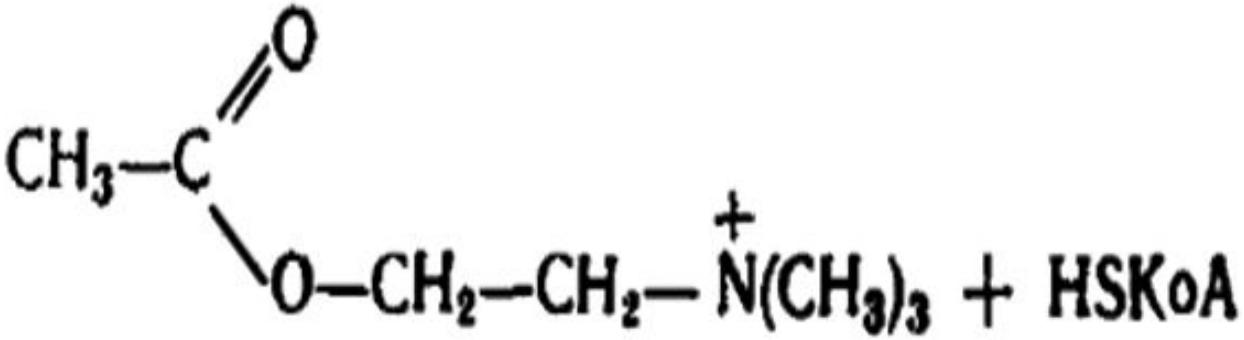


The synthesis of acetylcholine



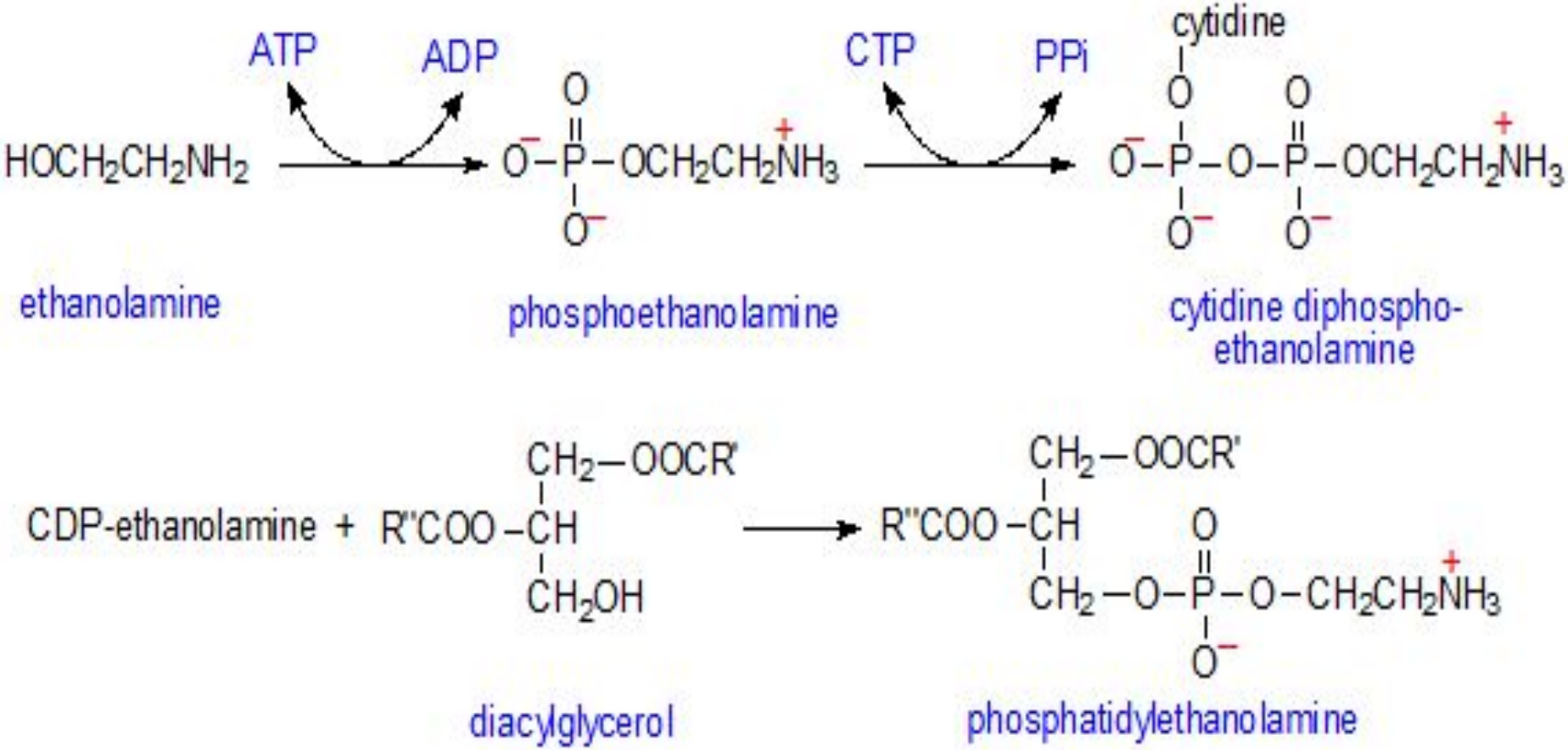
choline

Choline acetyl-transferase



acetylcholine

Phospholipid synthesis



Violations of complex lipid metabolism

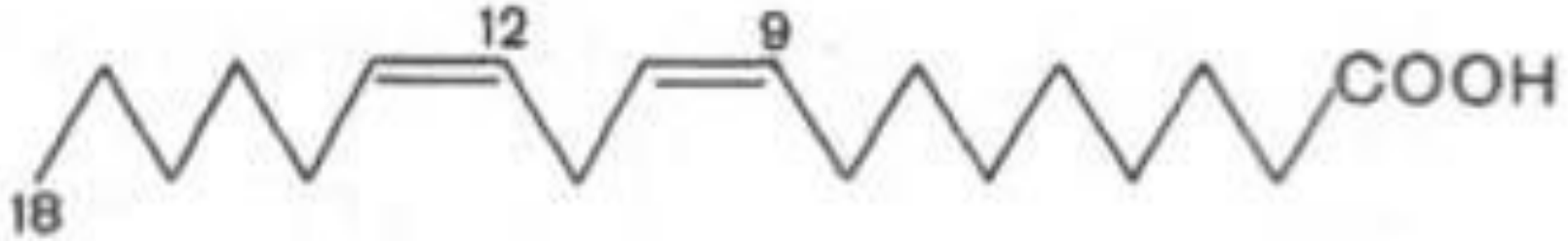
galactocerebroside

glucocerebroside ceramide sphingosine

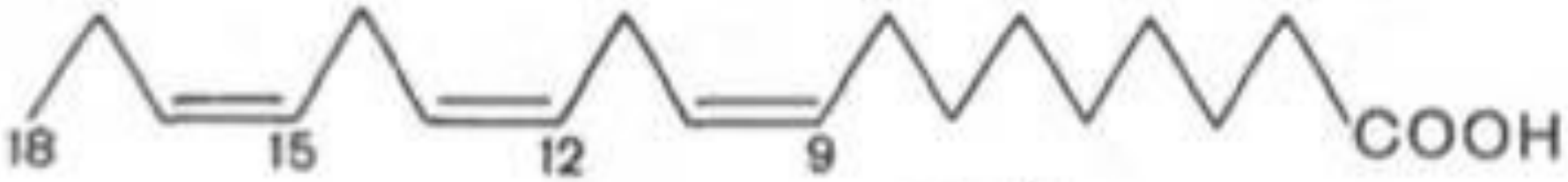
sphingomieline

1 - Gaucher disease (glucocerebrosidase deficiency)
2 - Krabbe disease (galactocerebrosidase deficiency)
3 - Farber disease (ceramidase deficiency)
4 - Niemann-Pick disease (sphingomielinidase deficiency)

Polyunsaturated fatty acids



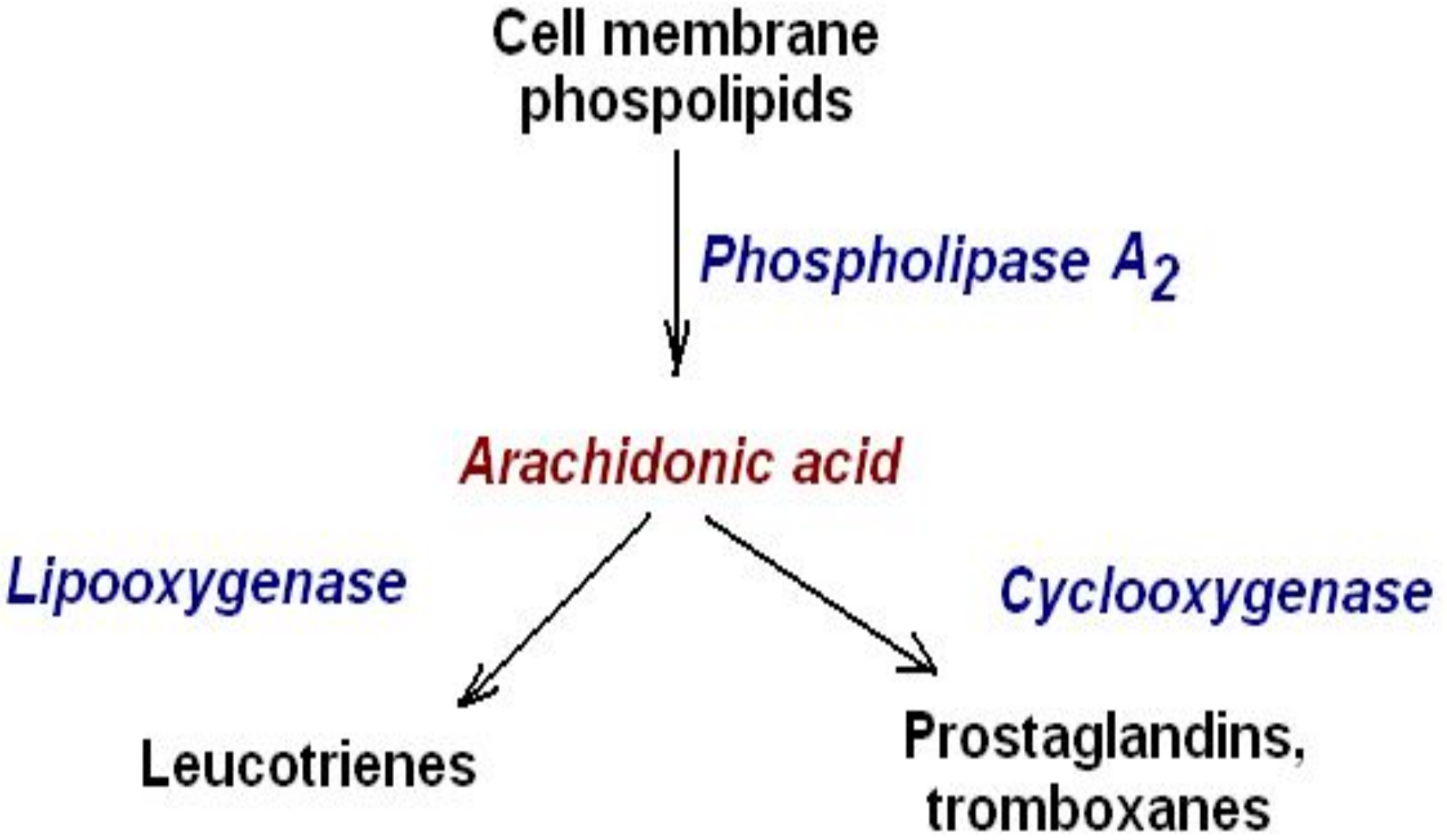
Linoleic acid (18:2;9,12)



Linolenic acid (18:3;9,12,15)

Arachidonic acid (20:4;5;8,11,14)

Eicosanoids synthesis



1982 Nobel Prize in Physiology or Medicine

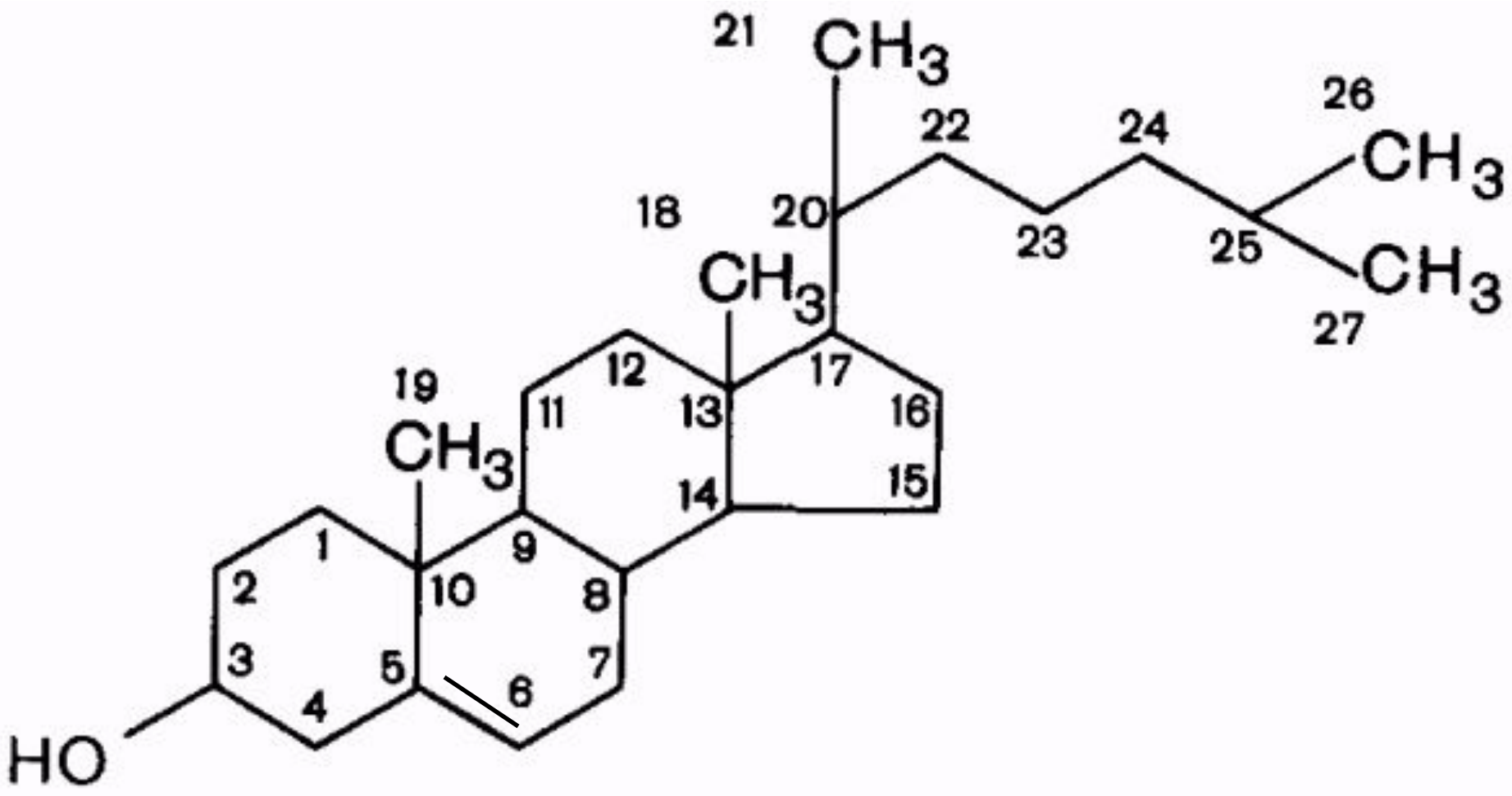
for their discoveries concerning prostaglandins
and related biologically active substances

Sune K. Bergström **Bengt I. Samuelsson** **Sir John R. Vane**

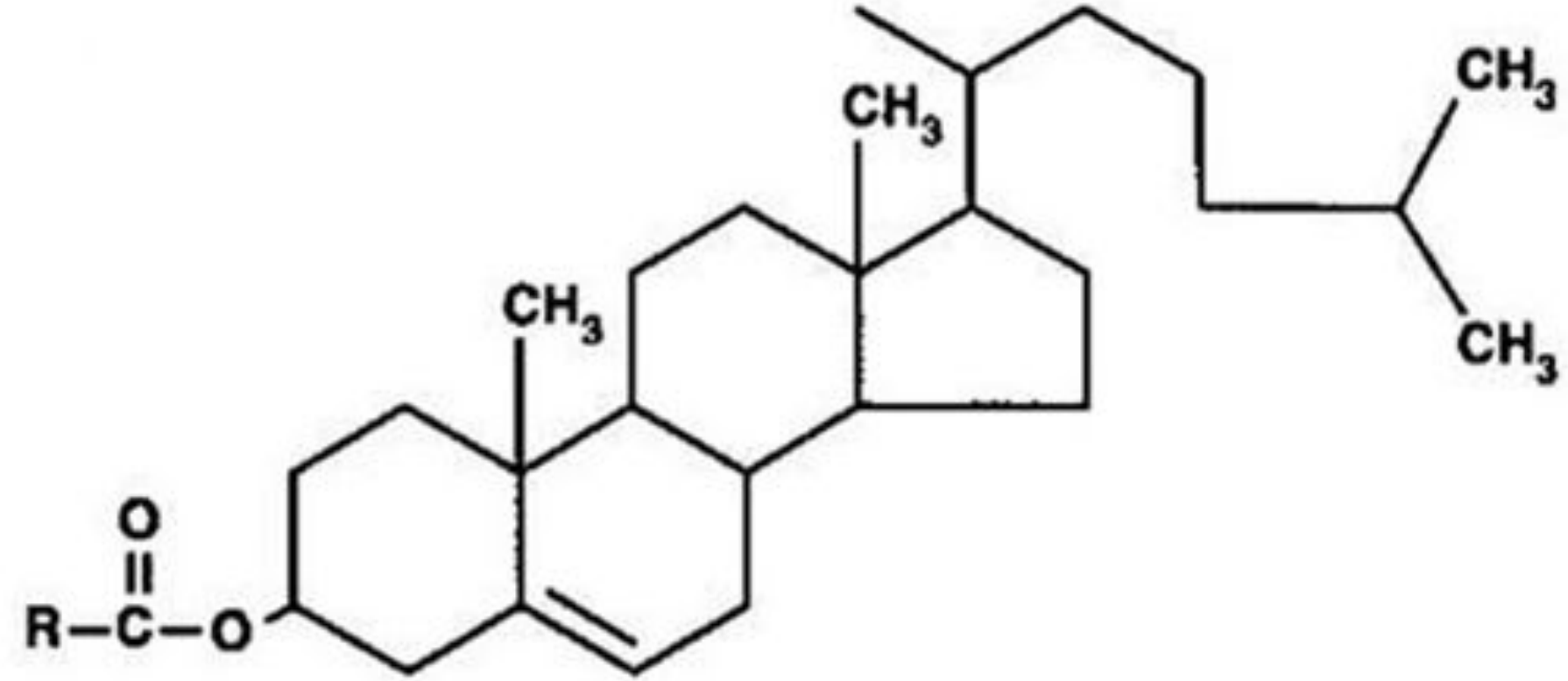
Ulf von Euler - 1970 Nobel Prize in Medicine and Physiology (identified prostaglandin)

Elias J. Corey - 1990 Nobel Prize in Chemistry (chemical synthesis of prostaglandin)

Cholesterol

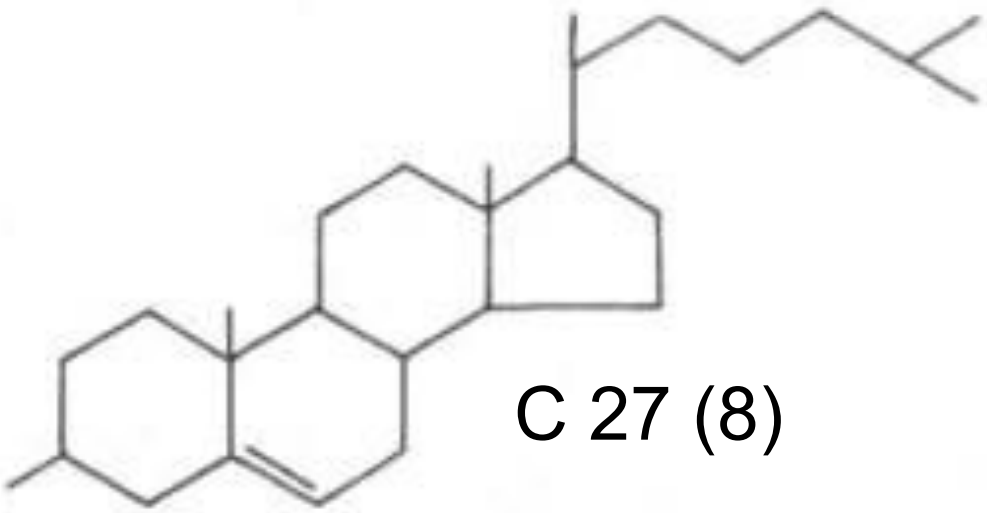


Cholesterol ester

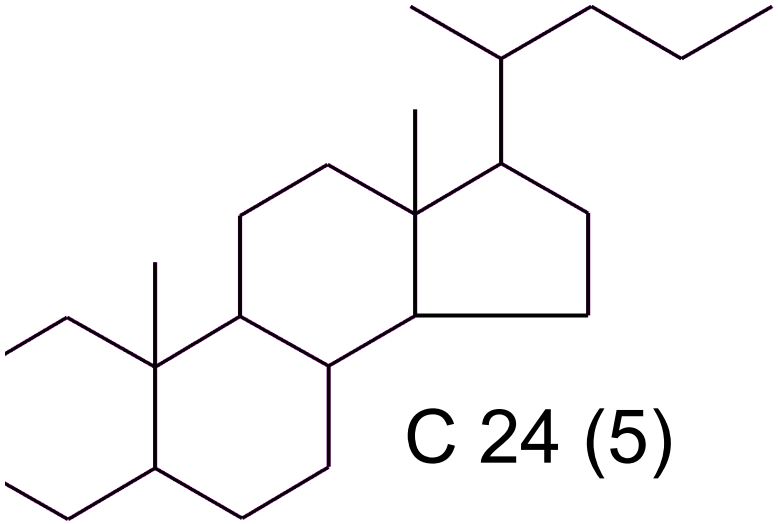


Fatty acid residue

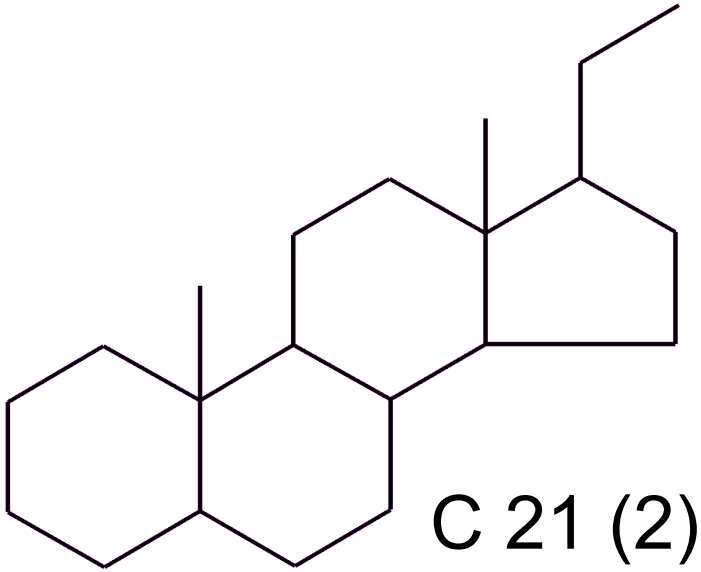
Classification of steroids



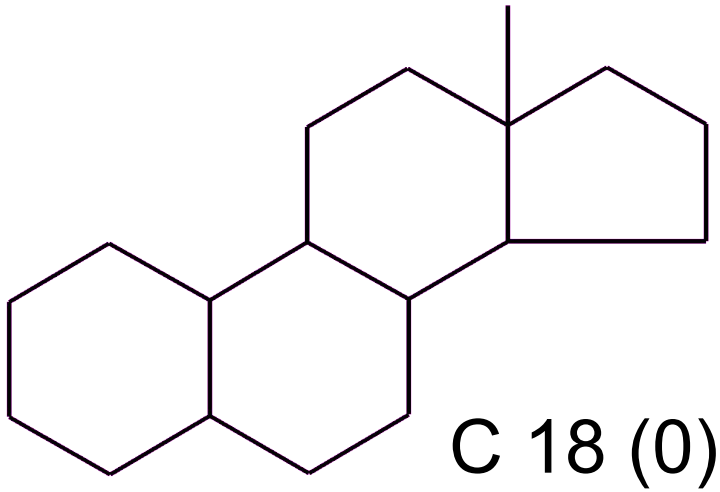
C 27 (8)



C 24 (5)

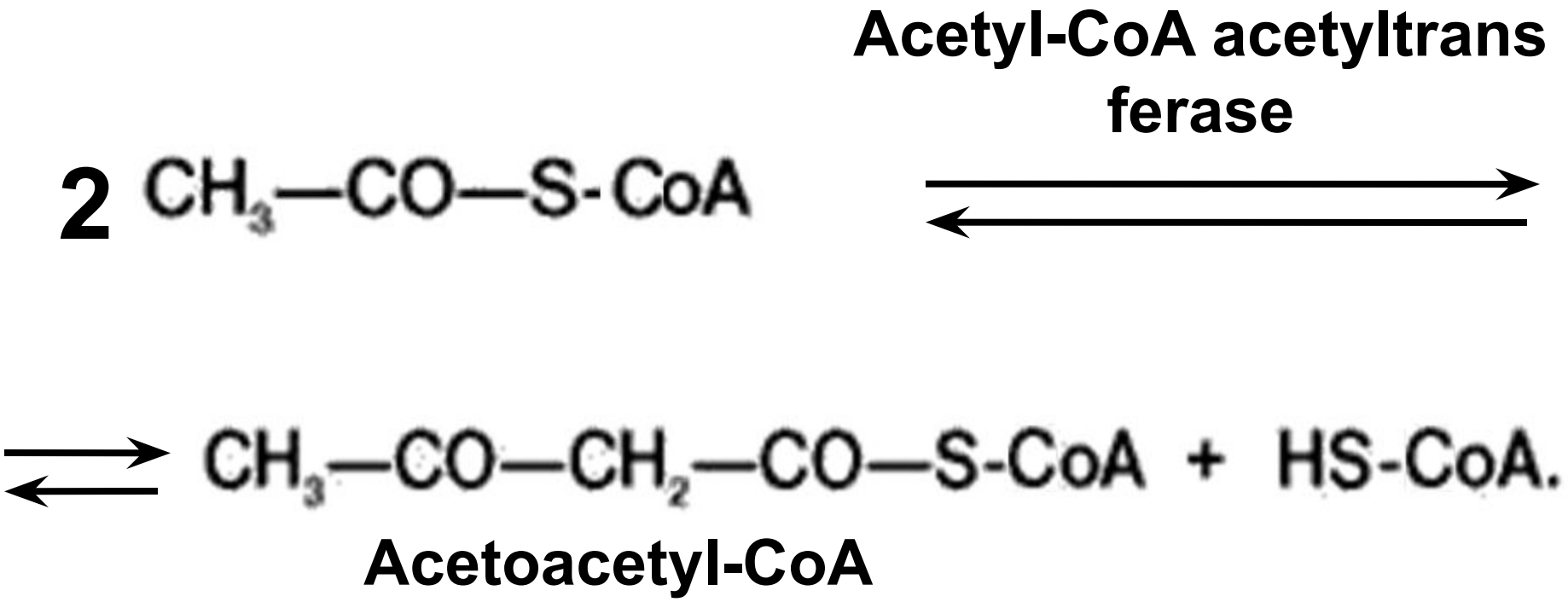


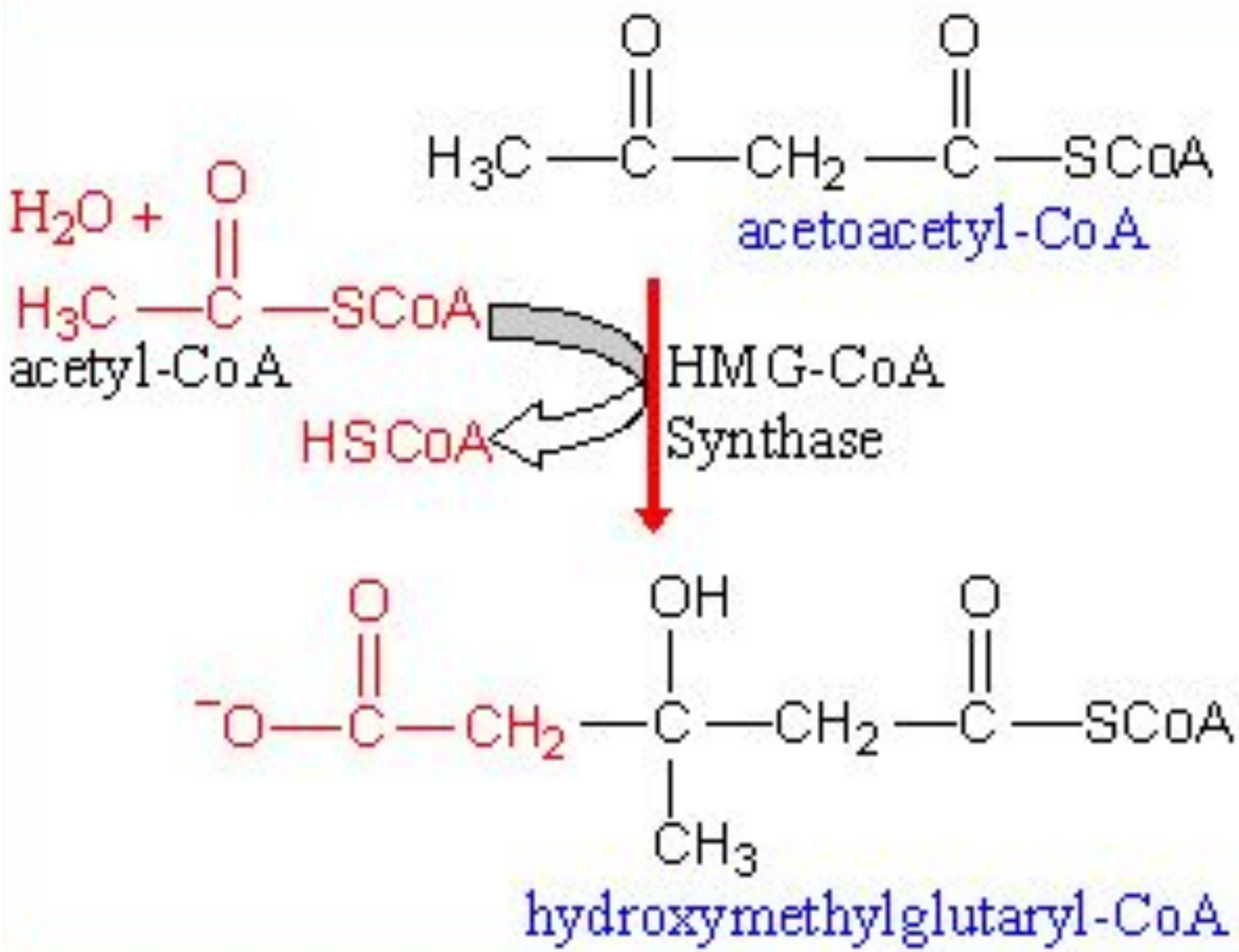
C 21 (2)

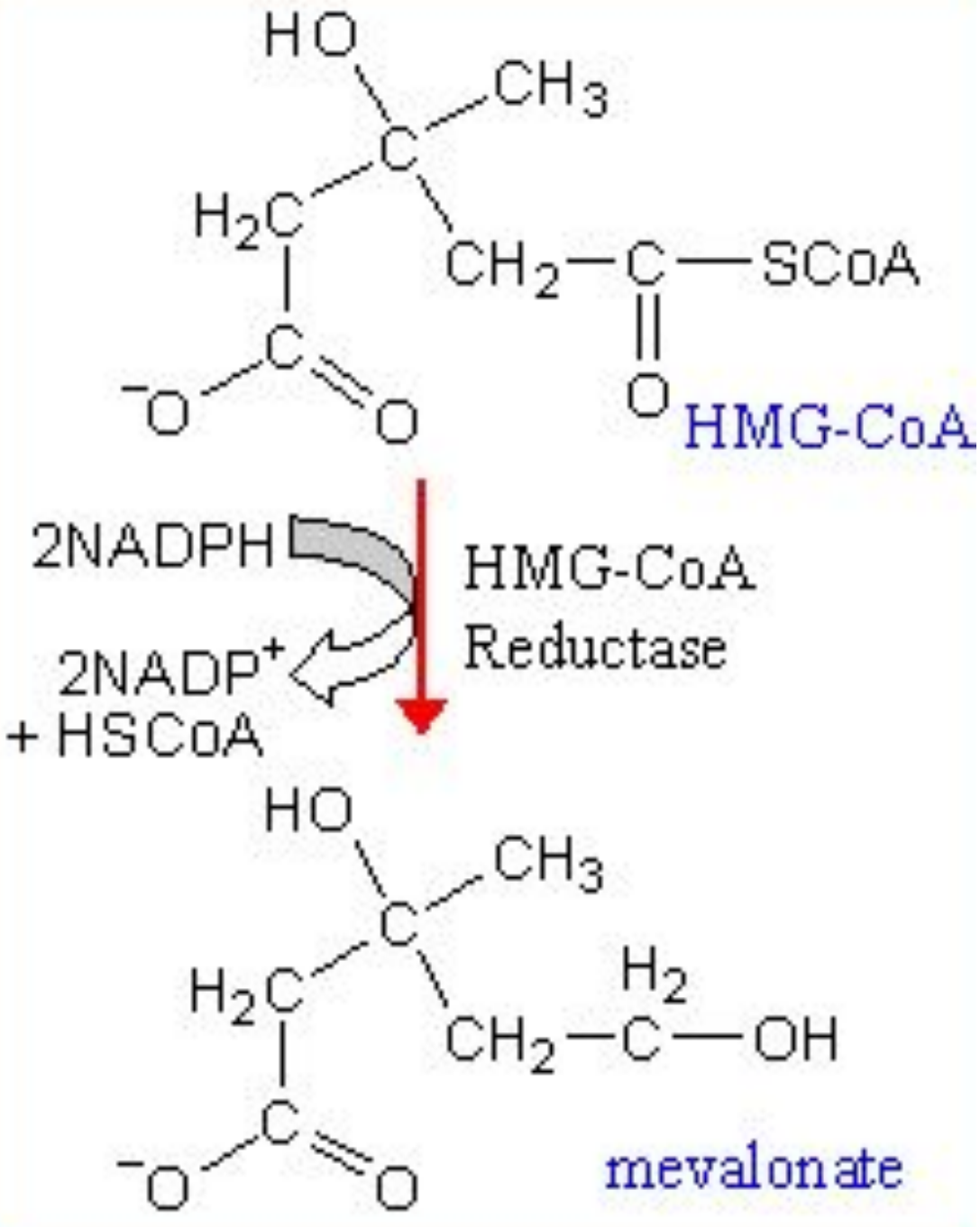


C 18 (0)

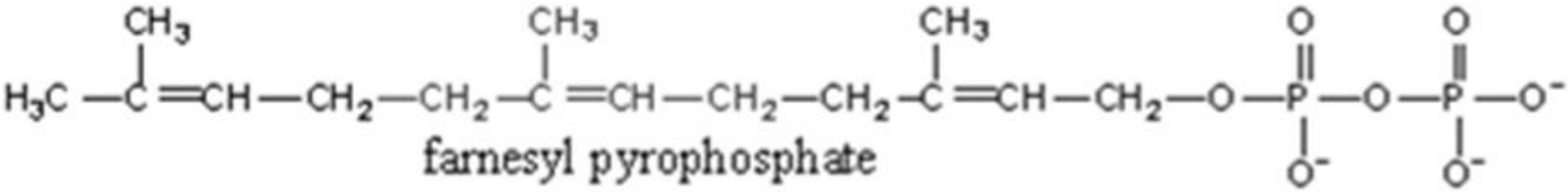
Cholesterol synthesis



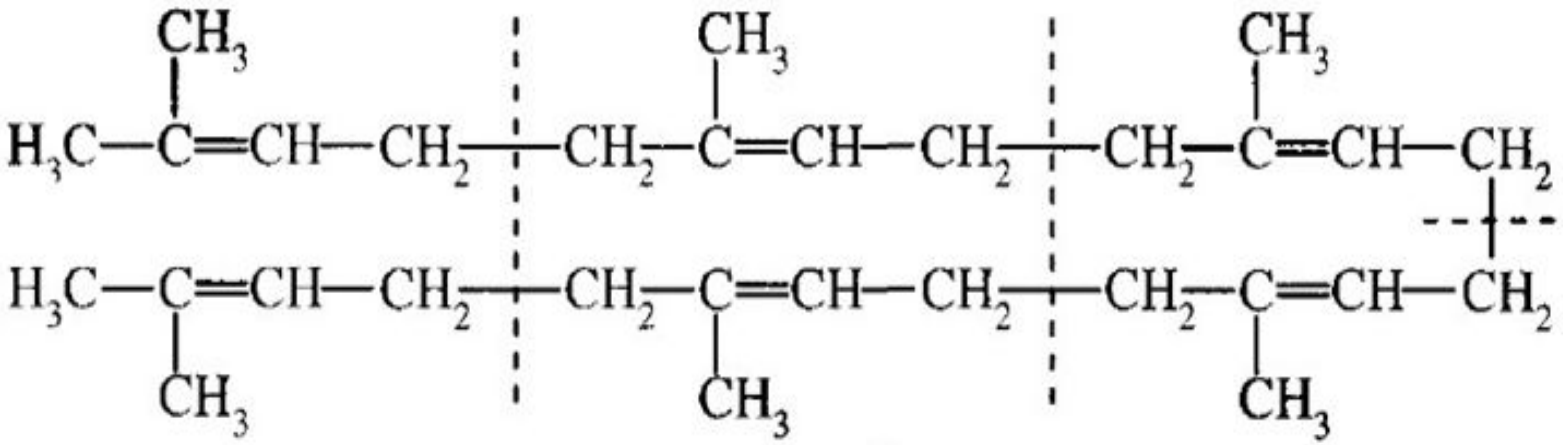

acetoacetyl-CoA
H2O +
acetyl-CoA
HMG-CoA
Synthase
HSCoA
hydroxymethylglutaryl-CoA

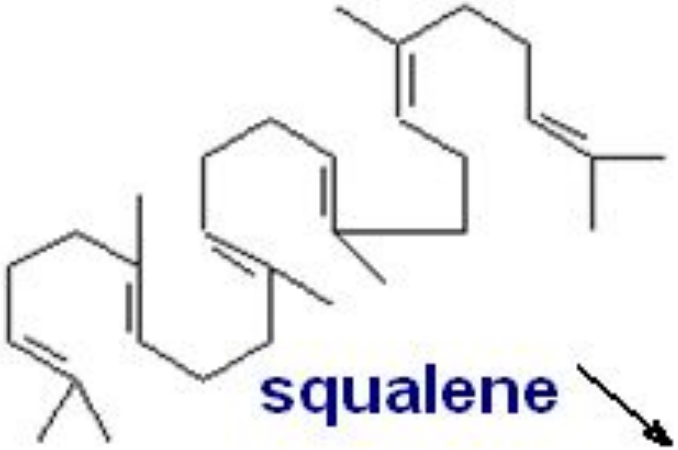

HO
CH3
C
H2C
CH2—C—SCoA
O
C
O
O
HMG-CoA
2NADPH
HMG-CoA
Reductase
2NADP+
+ HSCoA
HO
CH3
C
H2C
H2
CH2—C—OH
C
O
O
mevalonate

mevalonate $\xrightarrow{ATP}$ farnesyl pyrophosphate (C_{15})

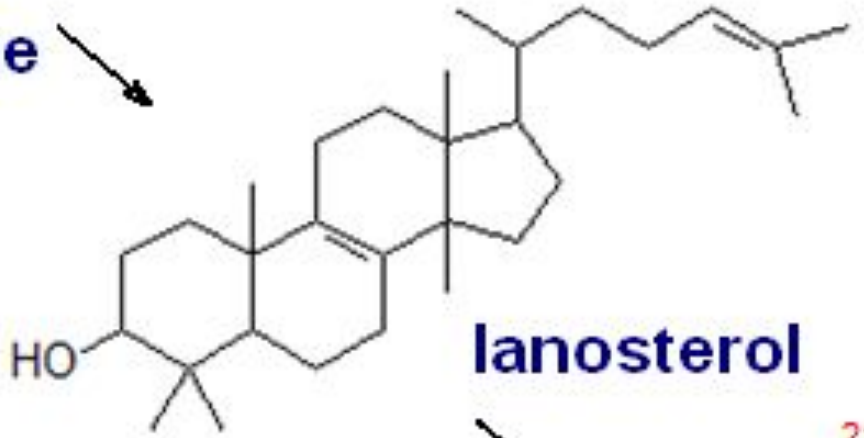


farnesyl pyrophosphate (C_{15}) $\xrightarrow{NADPH+H^+}$ squalene (C_{30})

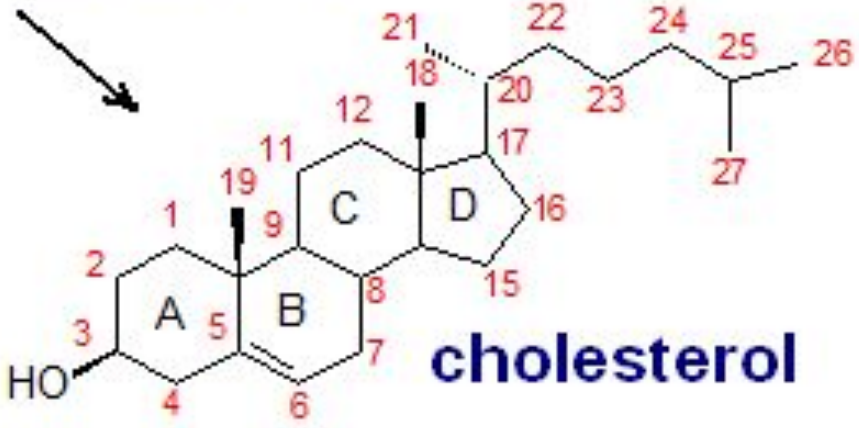




squalene

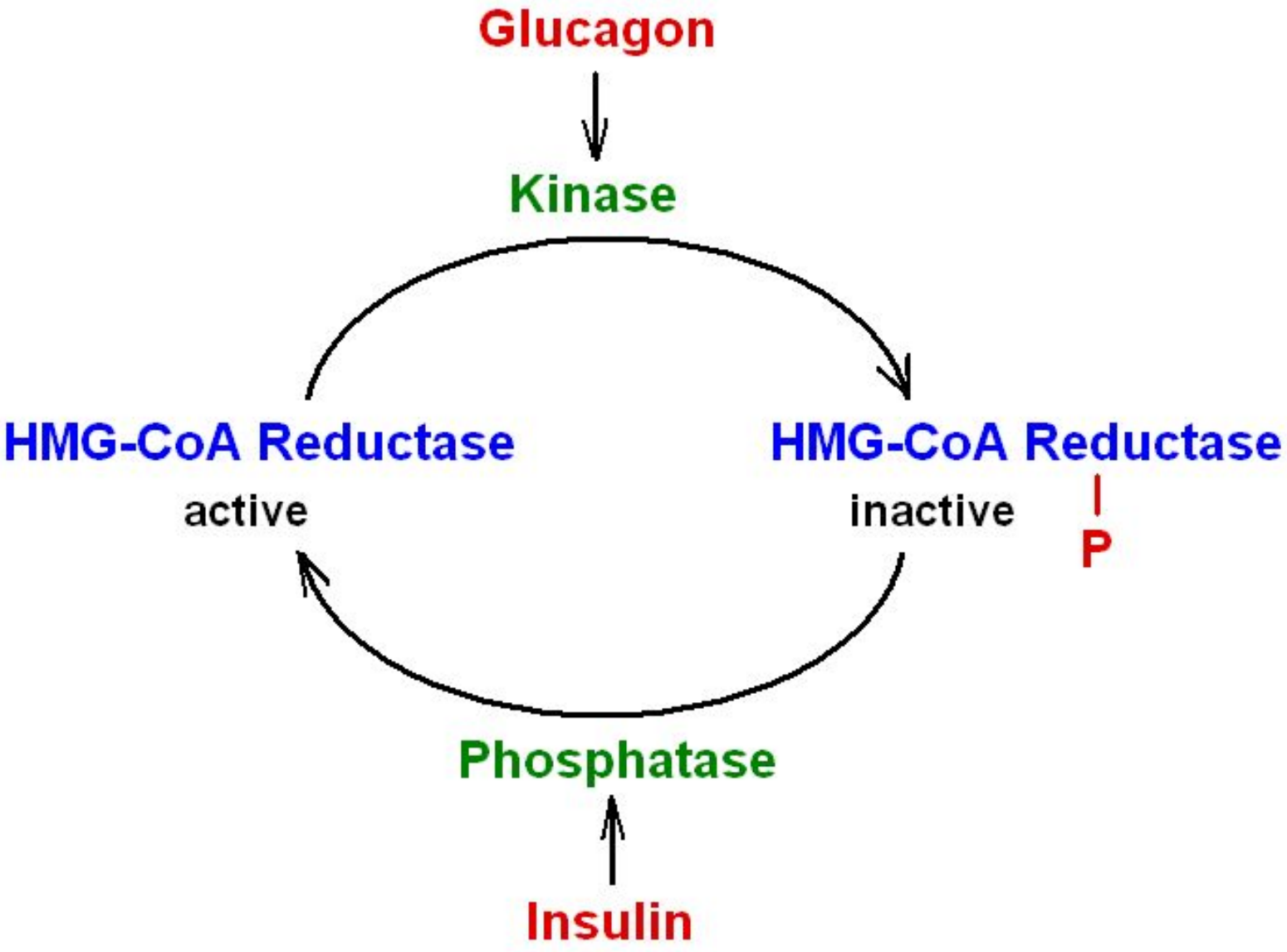


lanosterol

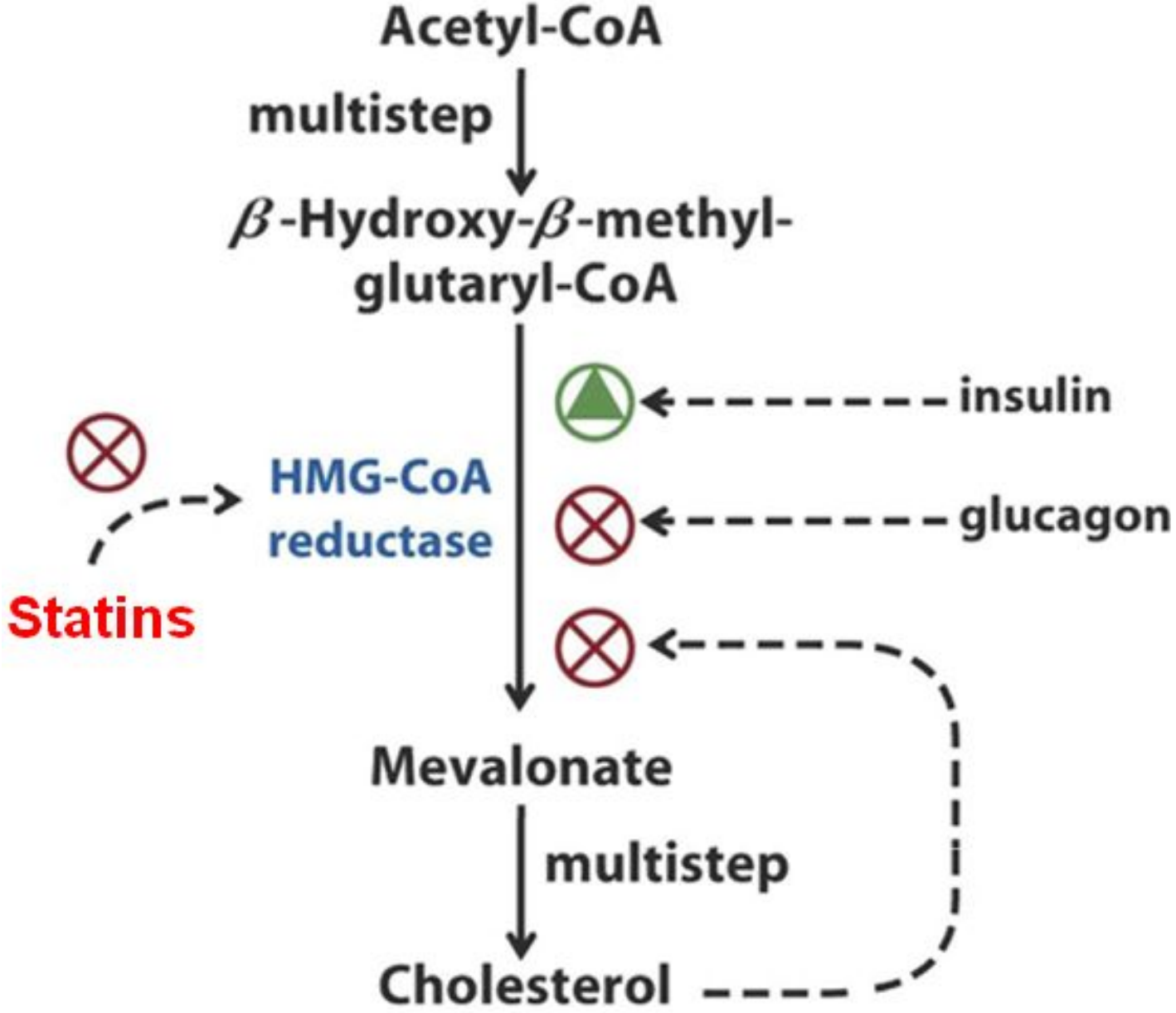


cholesterol

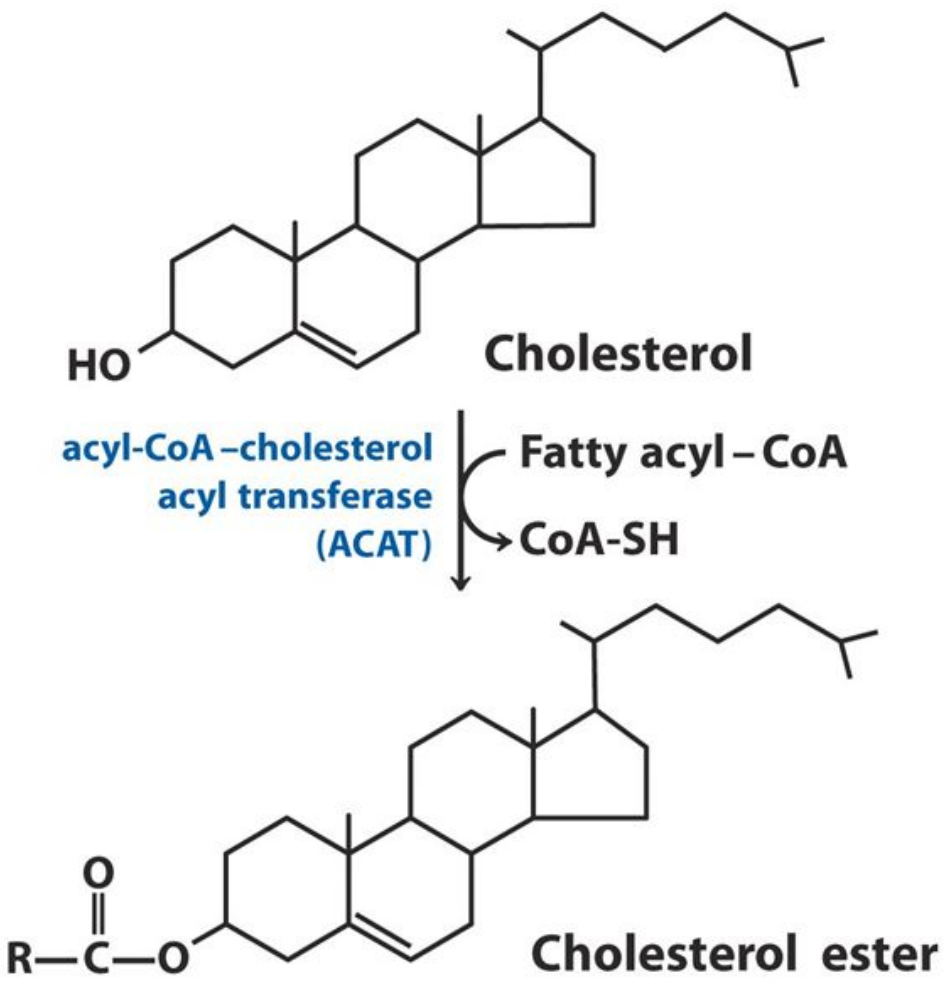
Regulation of cholesterol synthesis



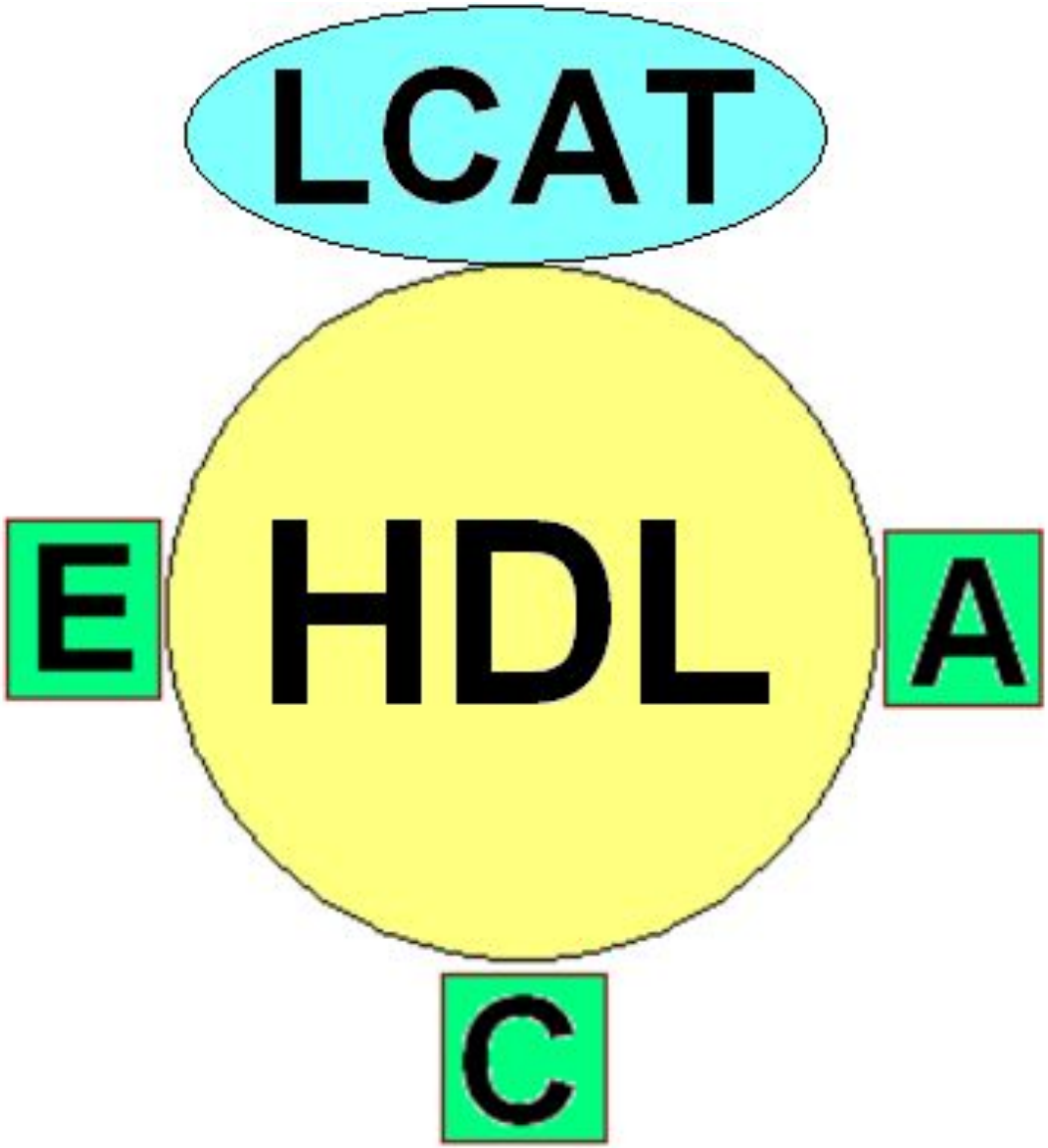
Regulation of cholesterol synthesis

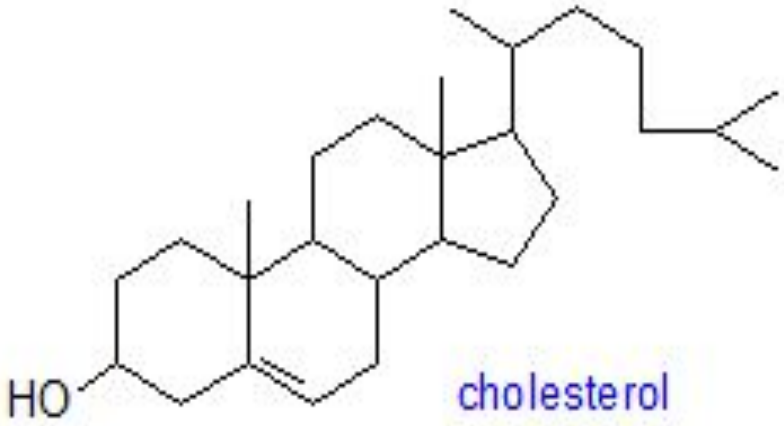


Cholesterol ester metabolism



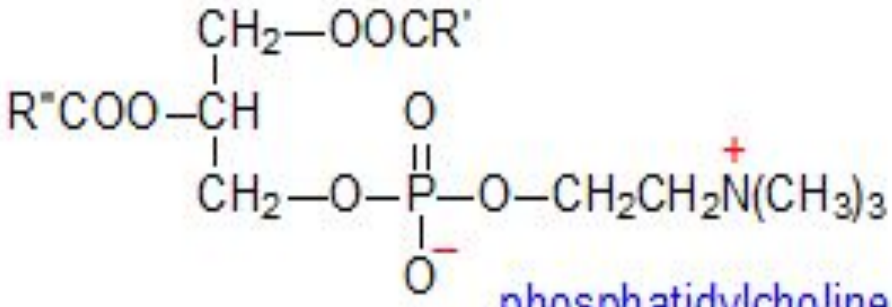
Acylcholesterol + $H_2O \rightarrow$ Fatty acid + Cholesterol


LCAT
E
HDL
A
C



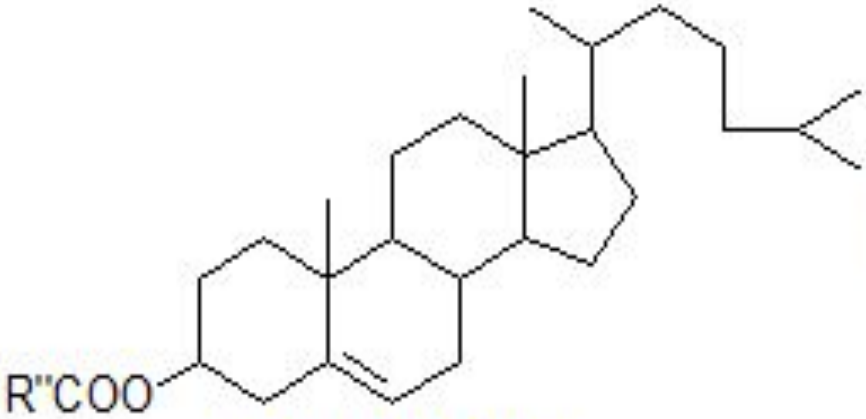
cholesterol

+



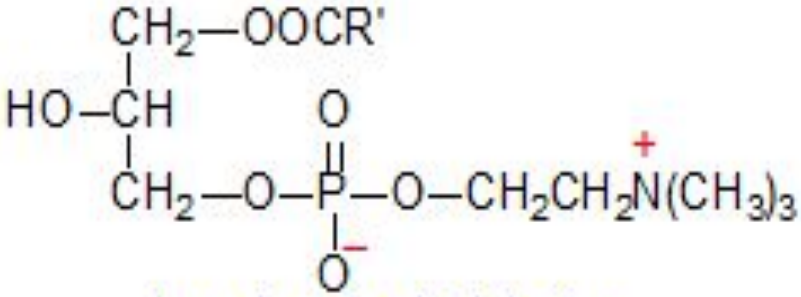
phosphatidylcholine

lecithin:cholesterol acyltransferase (LCAT)



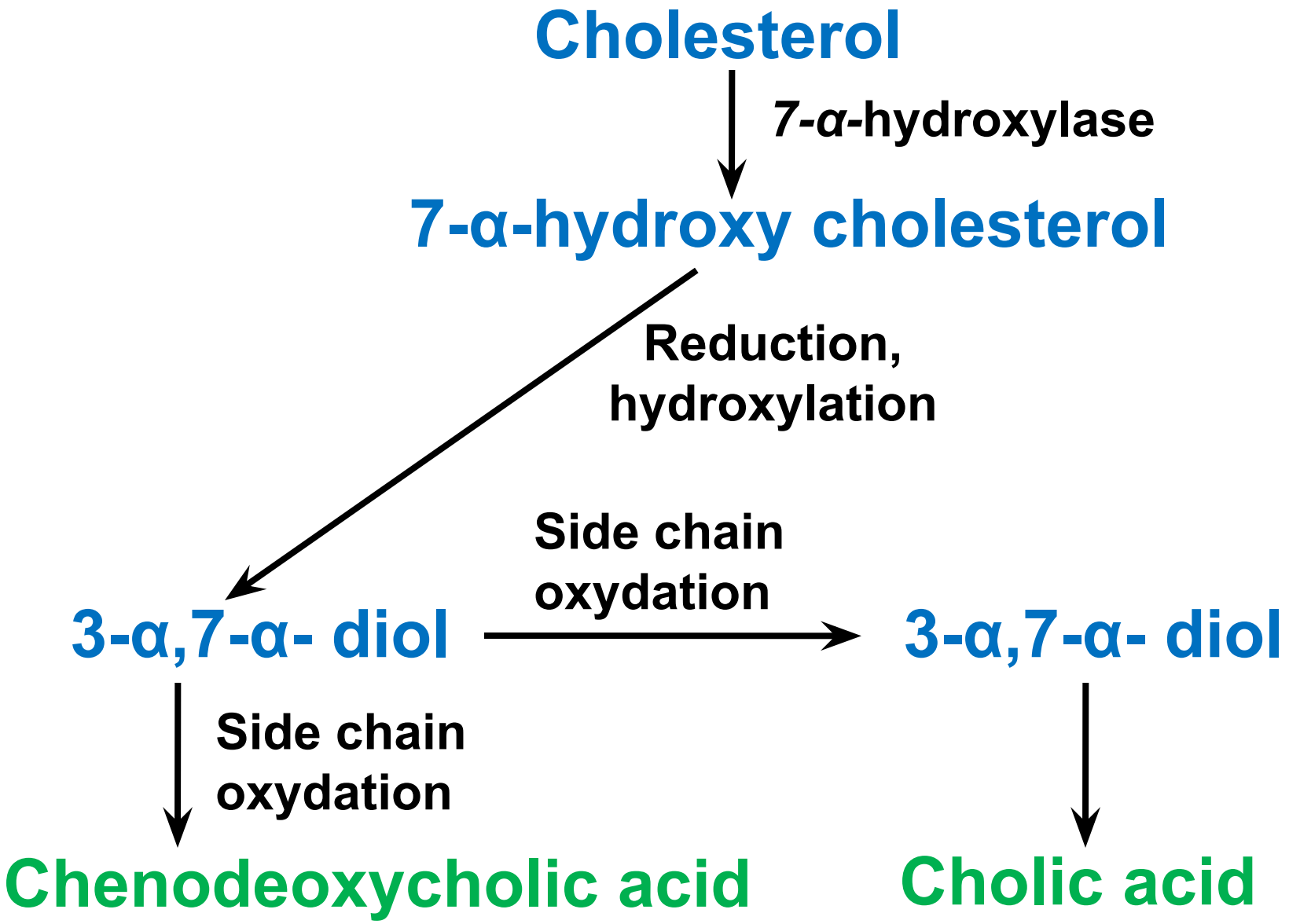
cholesterol ester

+

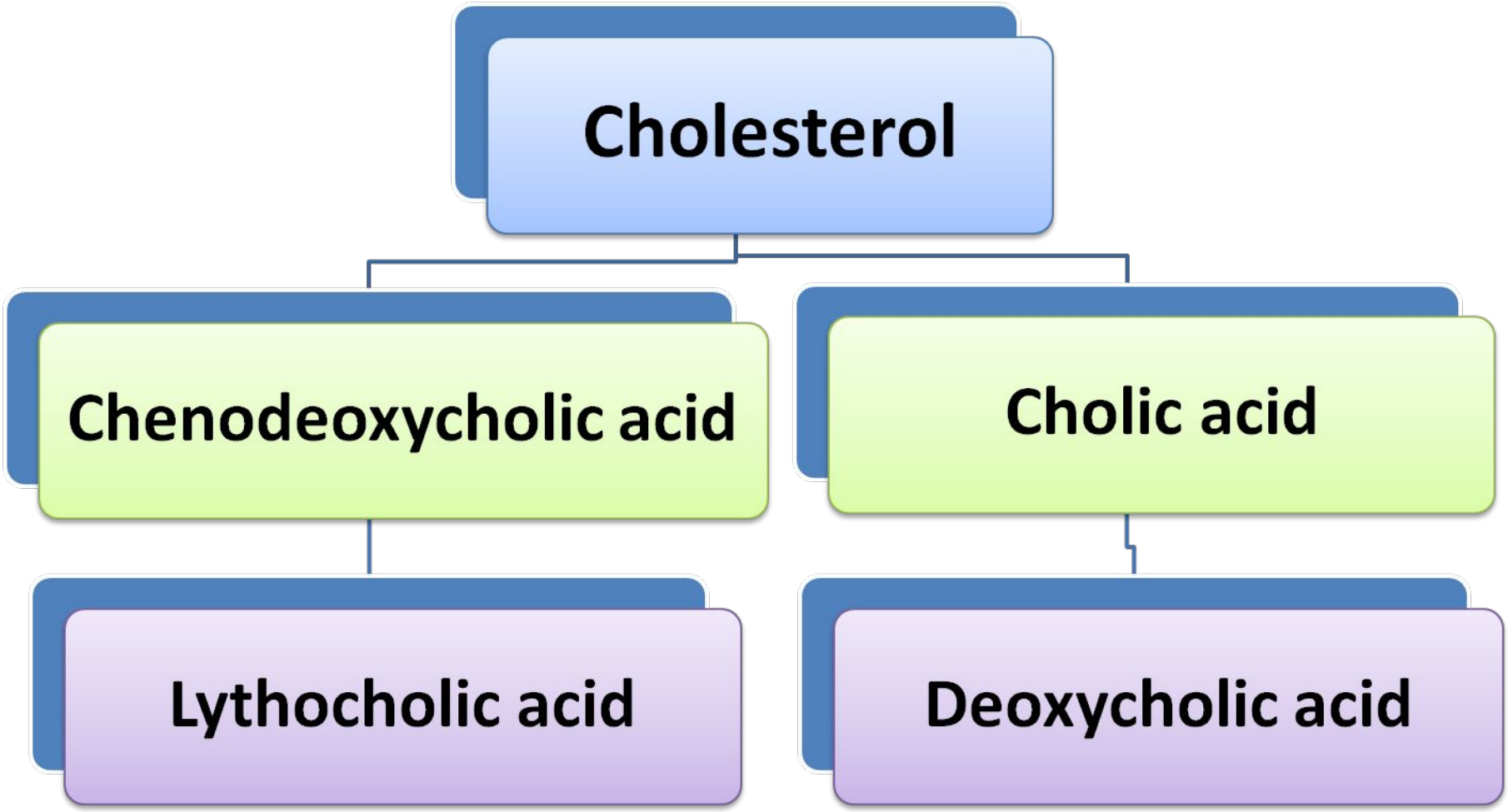


lysophosphatidylcholine

Bile acid synthesis



Bile acid synthesis

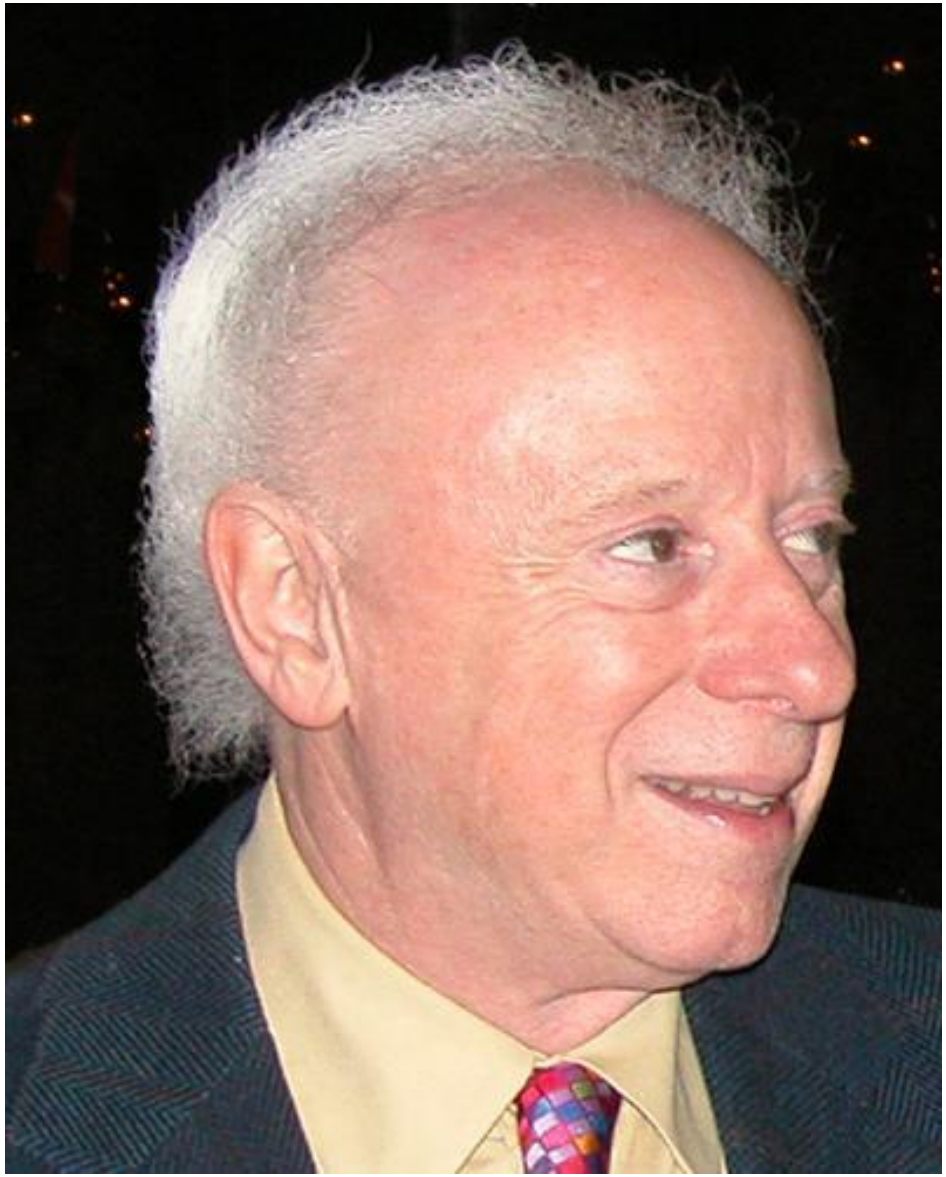


Stationary state

$$(\text{Cholesterol}_{endog} + \text{Cholesterol}_{exog}) =$$

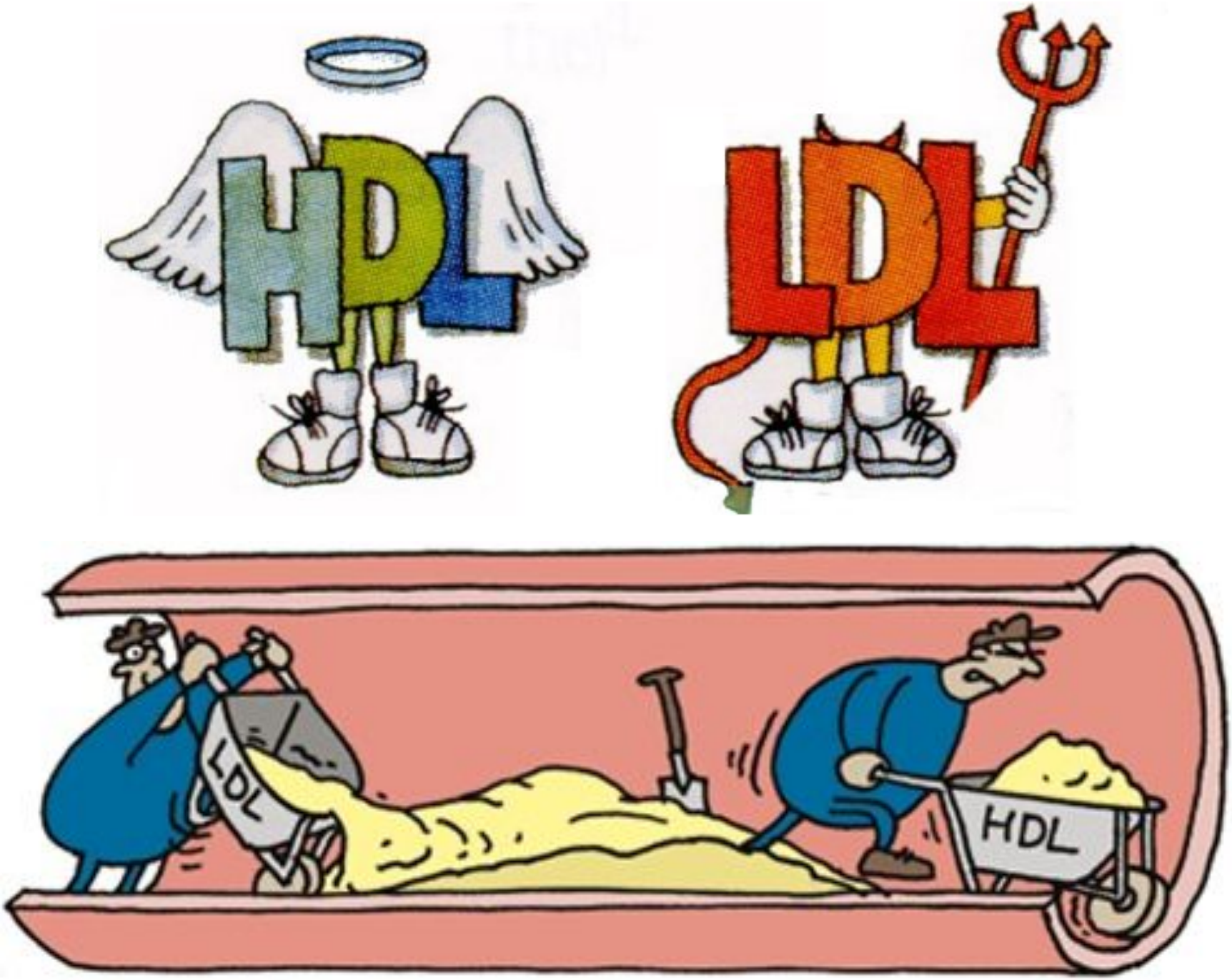
$$= (\text{Cholesterol}_{excr} + \text{Bile acids}_{excr})$$

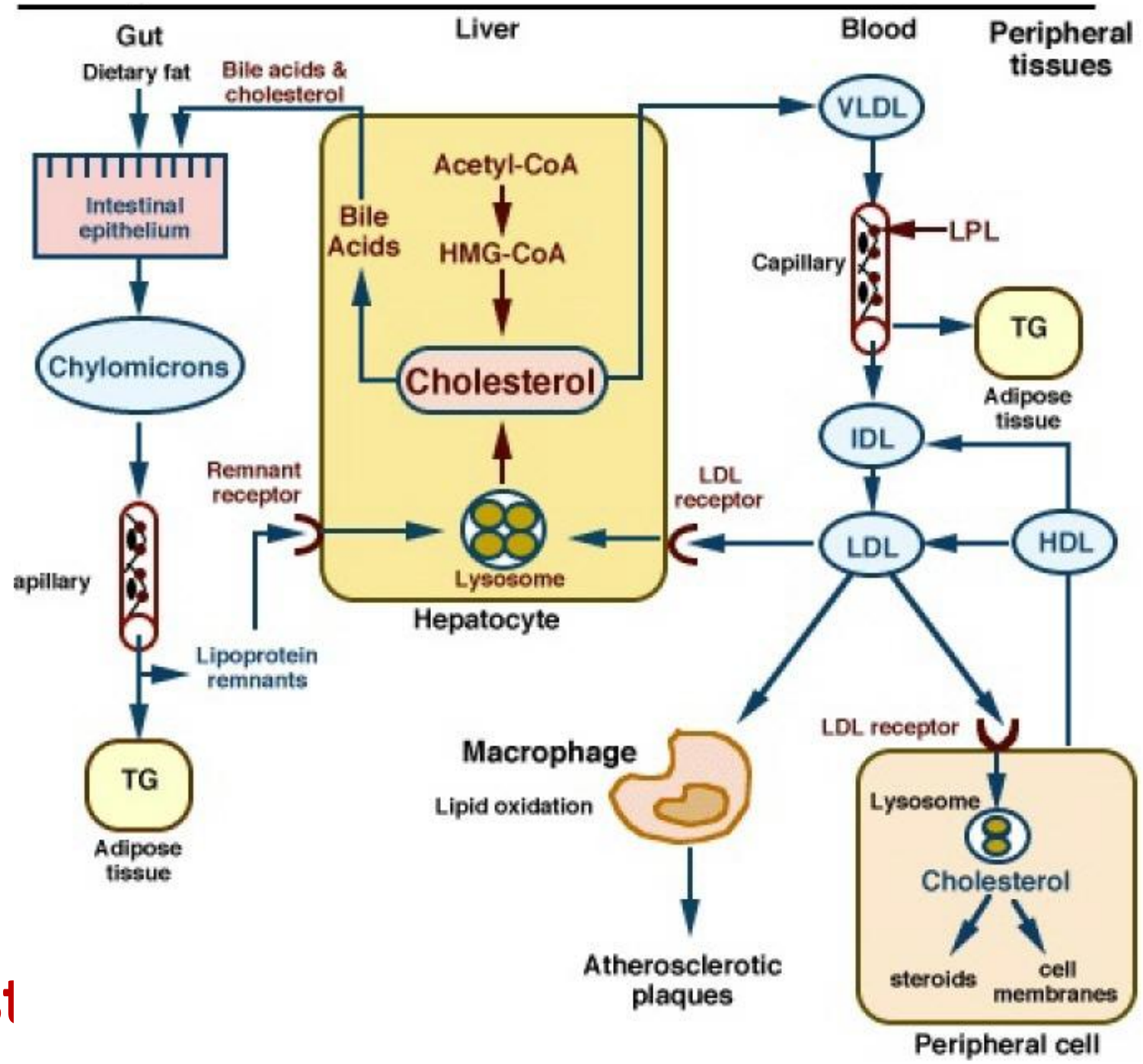
Joseph L. Goldstein



Hyperlipidemia classification

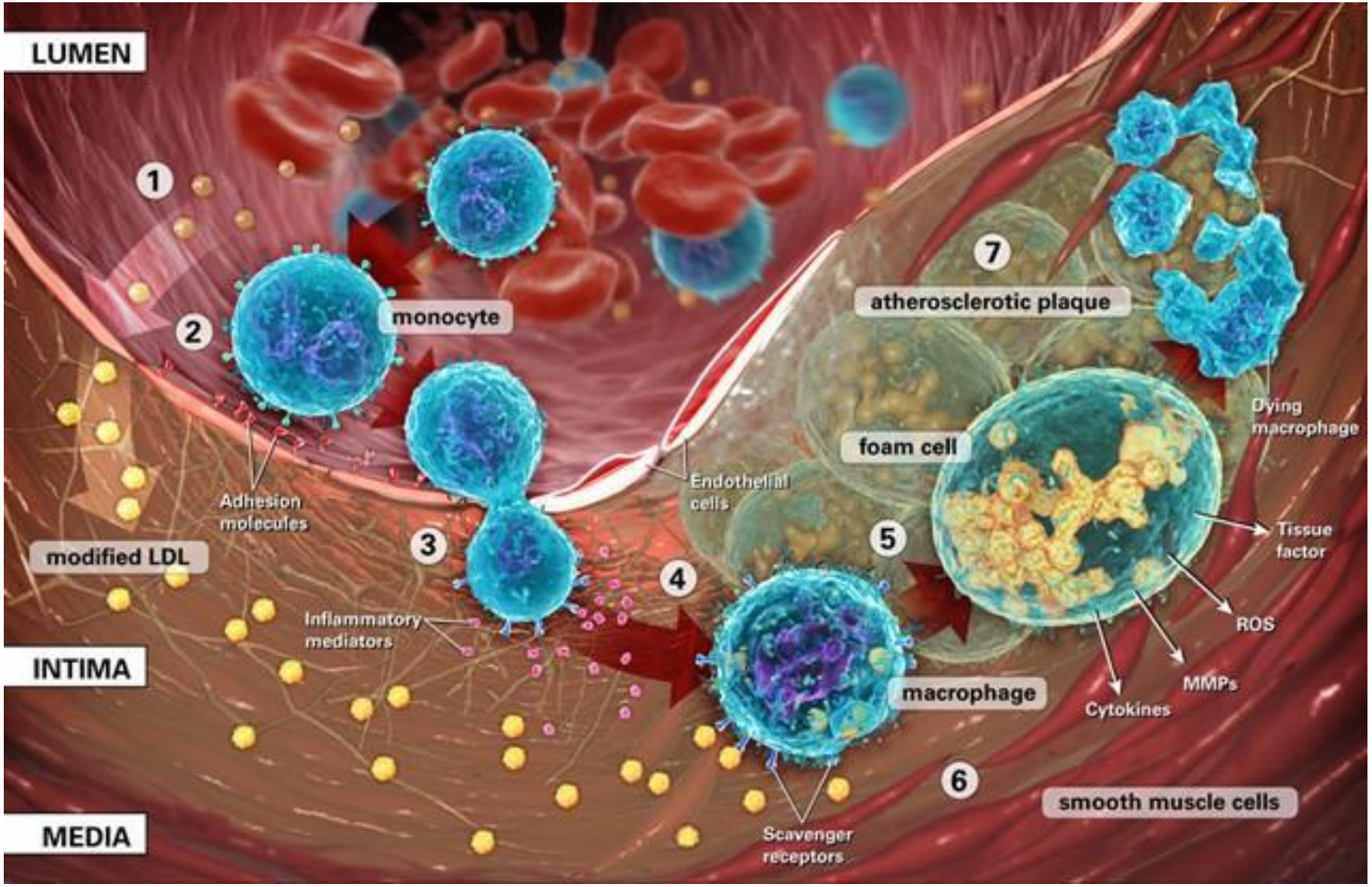
DISEASE	LIPID PROFILE	ETIOLOGY	
Type I Familial hyper-chylomicronemia	↑Chylomicrons	Deficiency in LPL or apoCII	
Type IIA Familial hyper-cholesterolemia	↑LDL	Decreased or no functional LDL receptor expression	*
Type IIB Familial combined hyperlipidemia	↑ LDL ↑ VLDL	Overproduction of VLDL by liver	*
Type III Familial dysbeta-lipoproteinemia	↑ IDL	Abnormal apoE	*
Type IV Familial hyper-triglyceridemia	↑ VLDL	Overproduction and/or impaired catabolism of VLDL	*
Type V Familial mixed hyper-triglyceridemia	↑Chylomicrons ↑VLDL	Increased production or decreased clearance of VLDL & chylomicrons.	


HDL
LDL
LDL
HDL

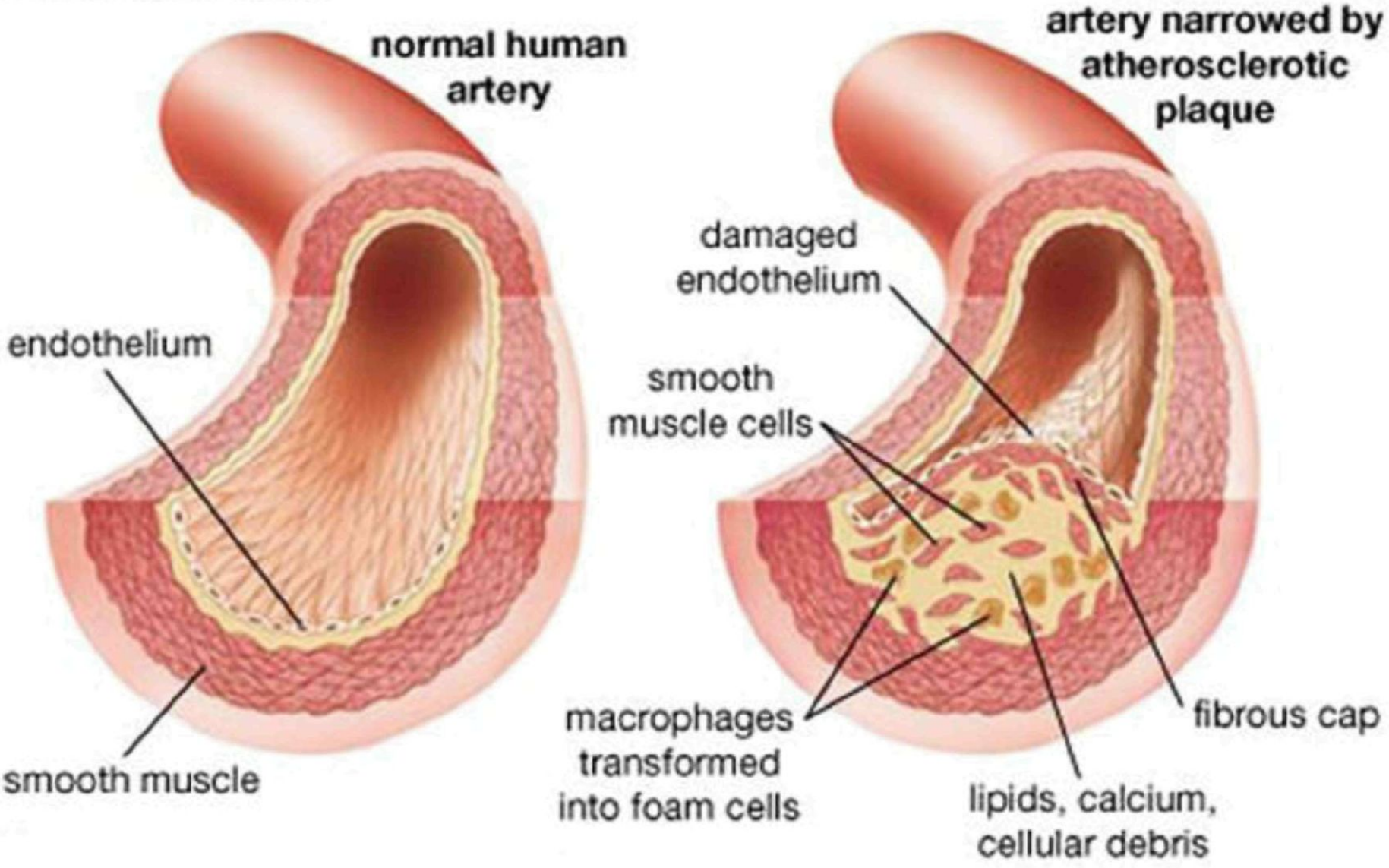

Gut
Liver
Blood
Peripheral tissues
Dietary fat
Bile acids & cholesterol
Intestinal epithelium
Chylomicrons
Acetyl-CoA
HMG-CoA
Bile Acids
Cholesterol
VLDL
Capillary
LPL
TG
Adipose tissue
IDL
LDL
HDL
Remnant receptor
LDL receptor
Lysosome
Hepatocyte
apillary
Lipoprotein remnants
TG
Adipose tissue
Macrophage
Lipid oxidation
Atherosclerotic plaques
LDL receptor
Lysosome
Cholesterol
steroids
cell membranes
Peripheral cell

Cholest

Atherosclerosis

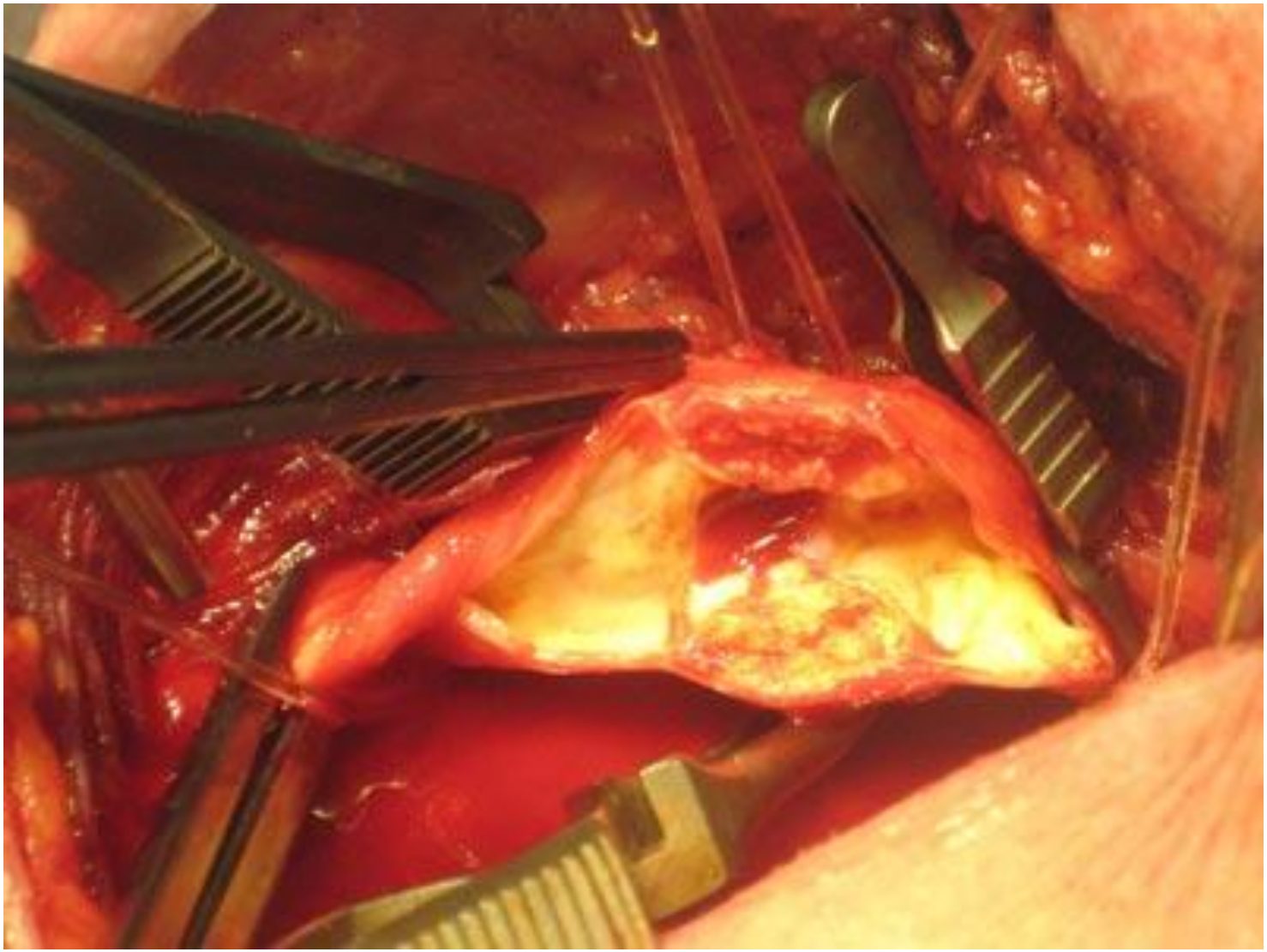


Atherosclerosis



Atherosclerotic plaque

Atherosclerotic plaque is surgically scraped from artery



Cholelithiasis

Xanthomatosis