
بسم الله الرحمن الرحيم

Pathophysiology of Lipid profile in clinical laboratory Exogenous and endogenous Lipids

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1401

Outlines

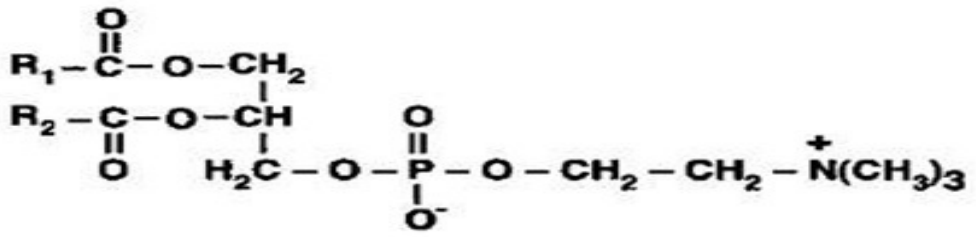
1) Biomedical importance
2) Daily needs & dietary lipids
3) Exogenous fat or fat-diet
4) Endogenous fat
5) Starve-feed cycle
6) Fasting & non-fasting lipid profile

1) Biomedical Importance

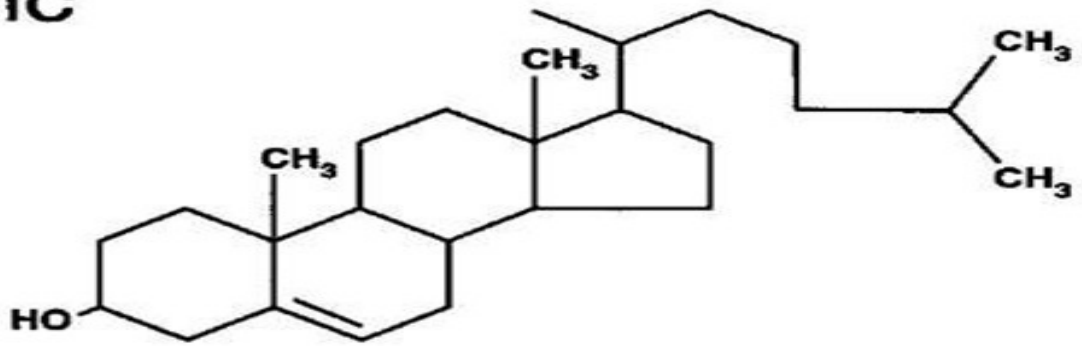
1-1) Major lipids & lipoproteins
1-2) Plasma lipoproteins
1-3) Atherosclerosis (CE)
1-4) Obesity (TAG or TG)
1-5) Fatty liver disease or FLD (TAG)
1-6) Diabetes mellitus or DM (TG & TC)
1-7) Gene expression (FC, FFA, …)
1-8) Signal transduction (DAG, IP3,…)
1-9) Exogenous lipids (TAG_{exo} or TG_{exo})
1-10) Endogenous lipids (FC_{endo}, CE_{endo}, PLs, …) and …

1-1) Major Lipids

Amphipathic

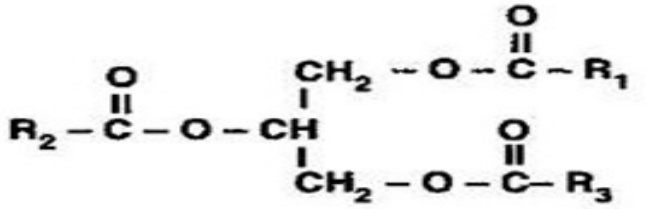


Phosphatidylcholine

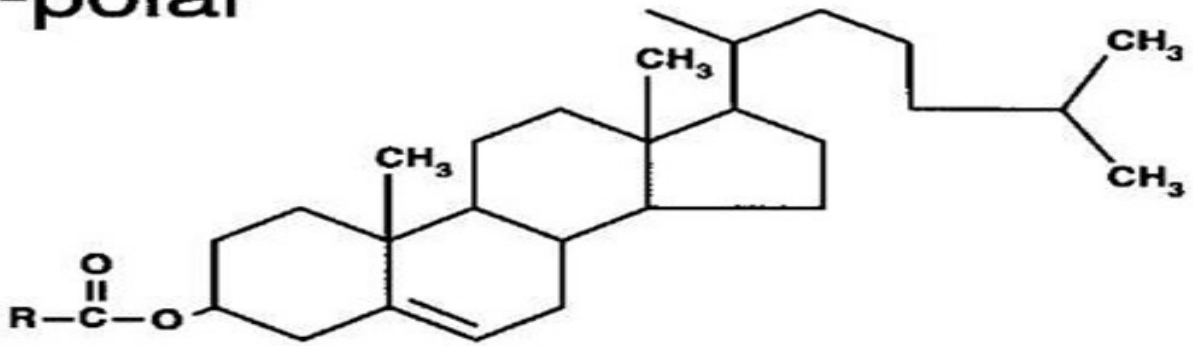


Free Cholesterol (FC)

Non-polar

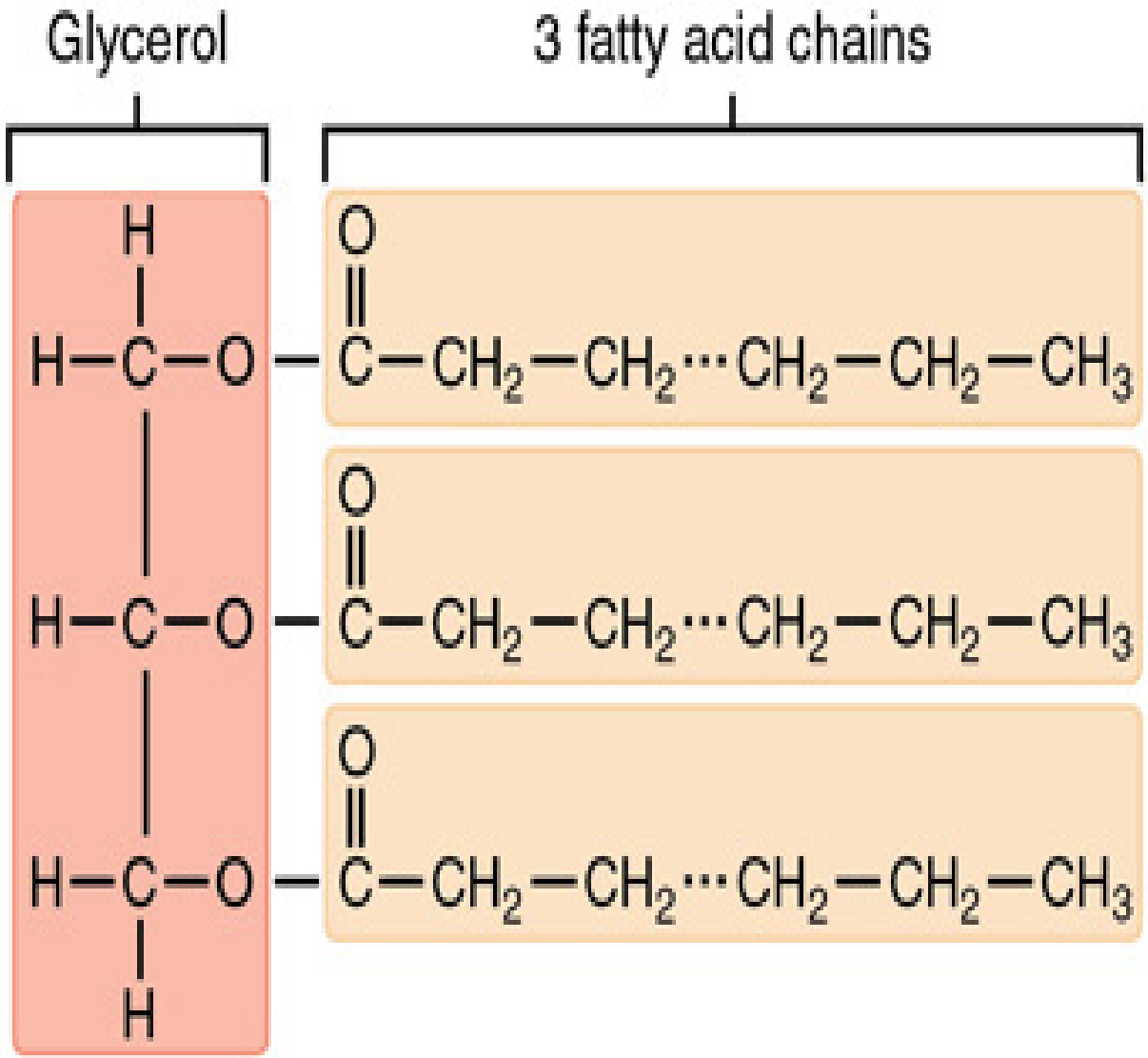


Triglyceride (TG) or
Triacylglycerol (TAG)

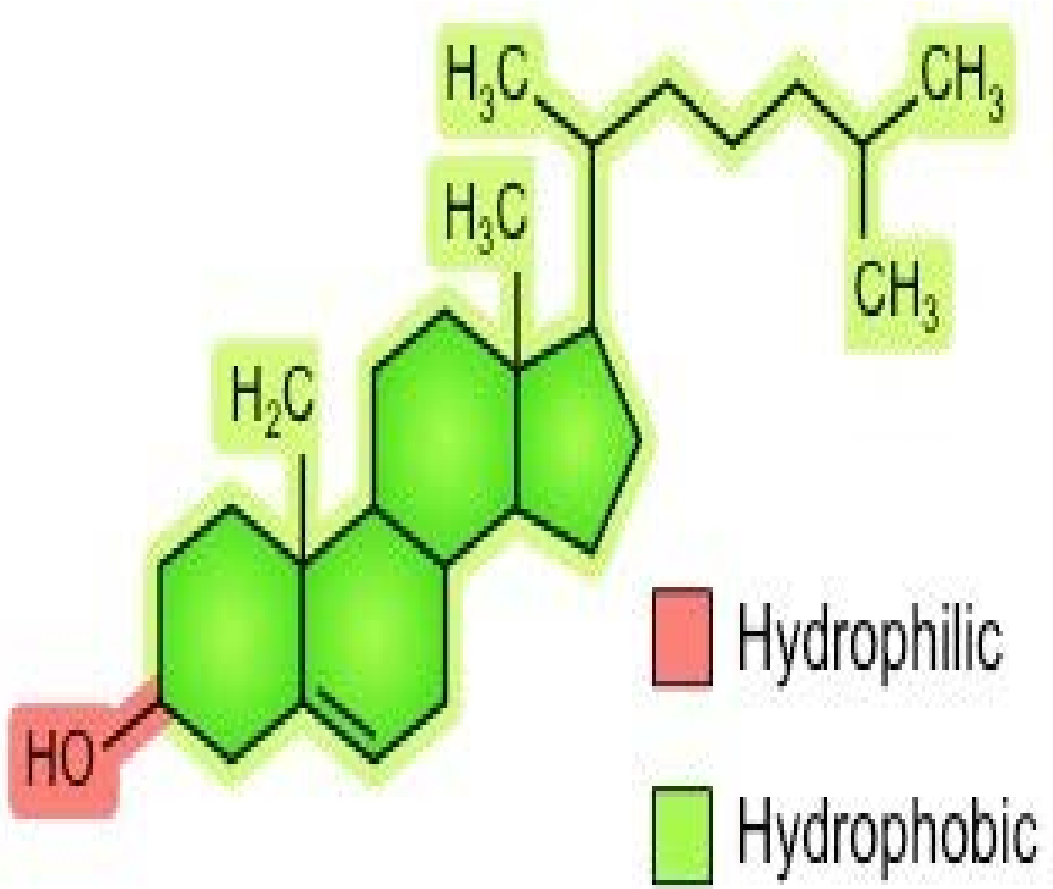


Cholesteryl Ester (CE)

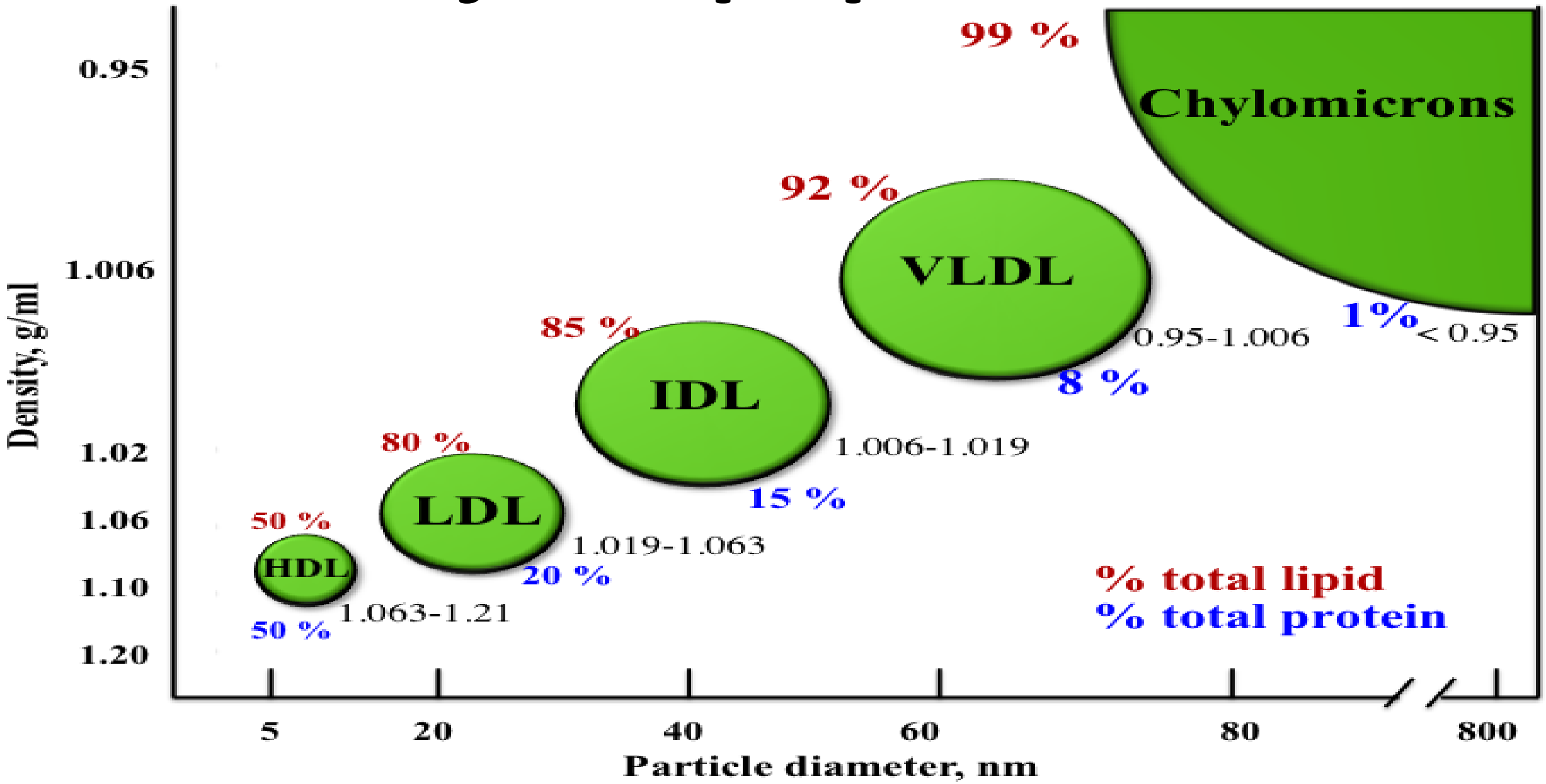
Triglyceride (TG)



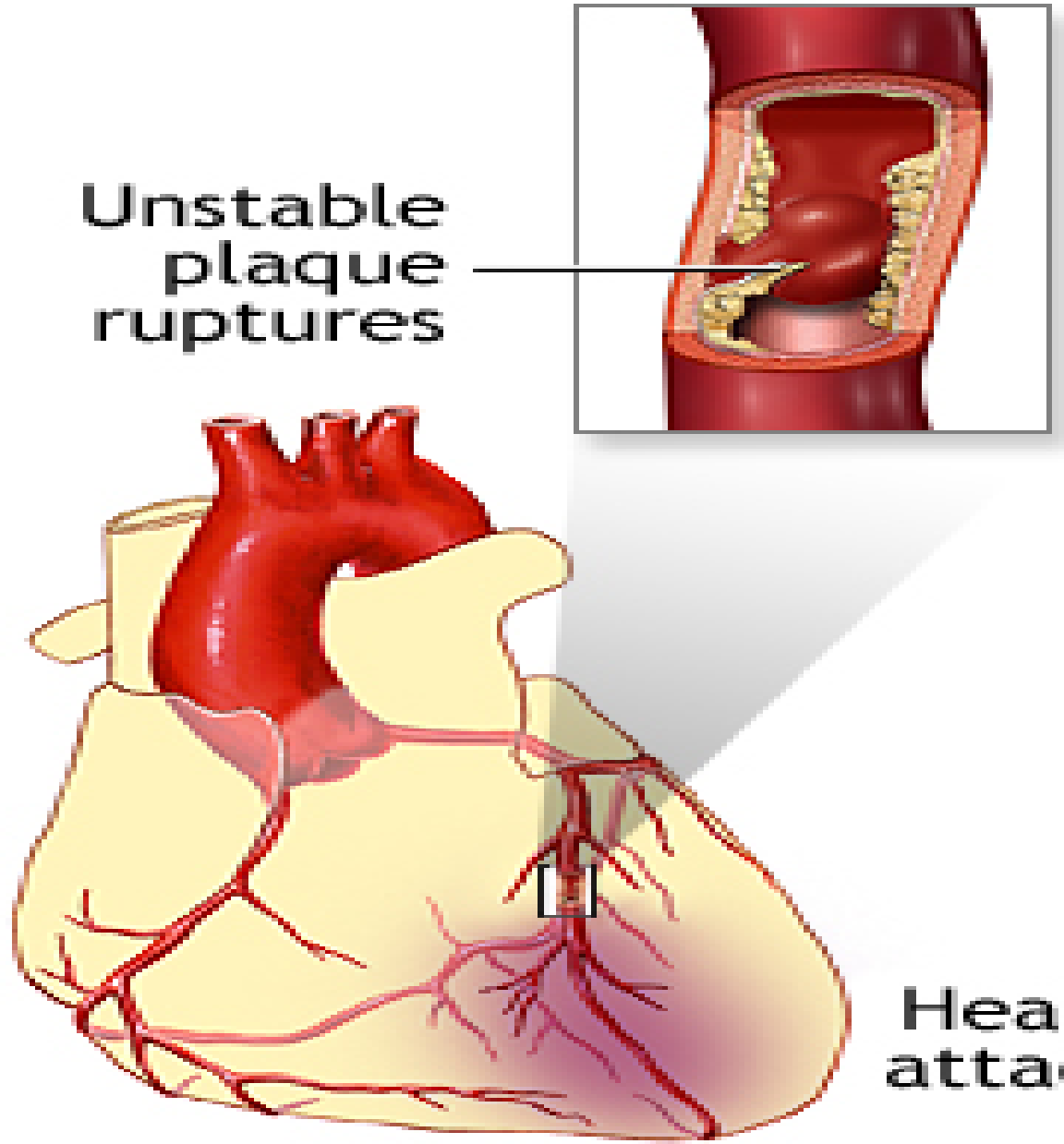
Free Cholesterol (FC)

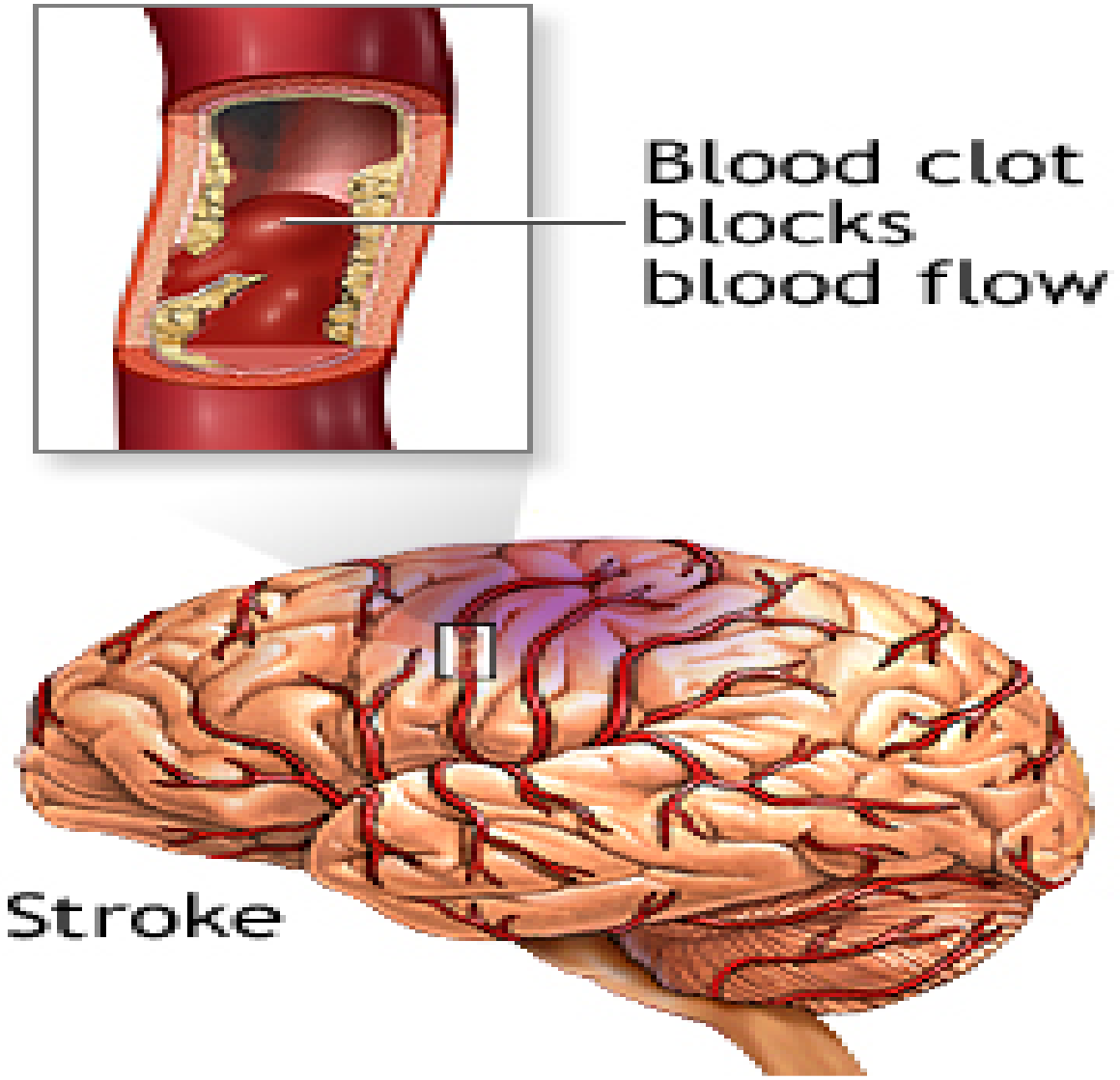


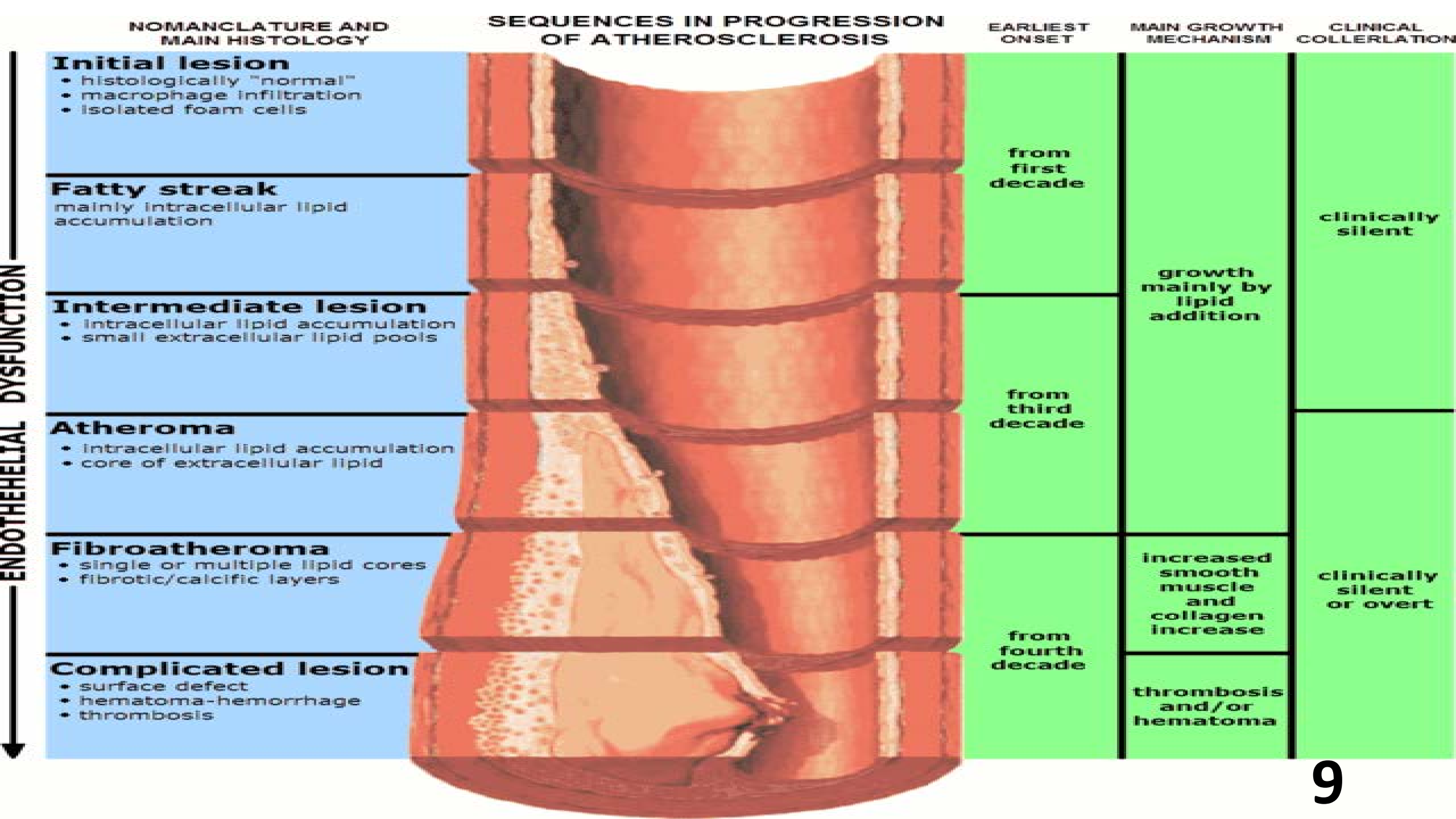
Major Lipoproteins



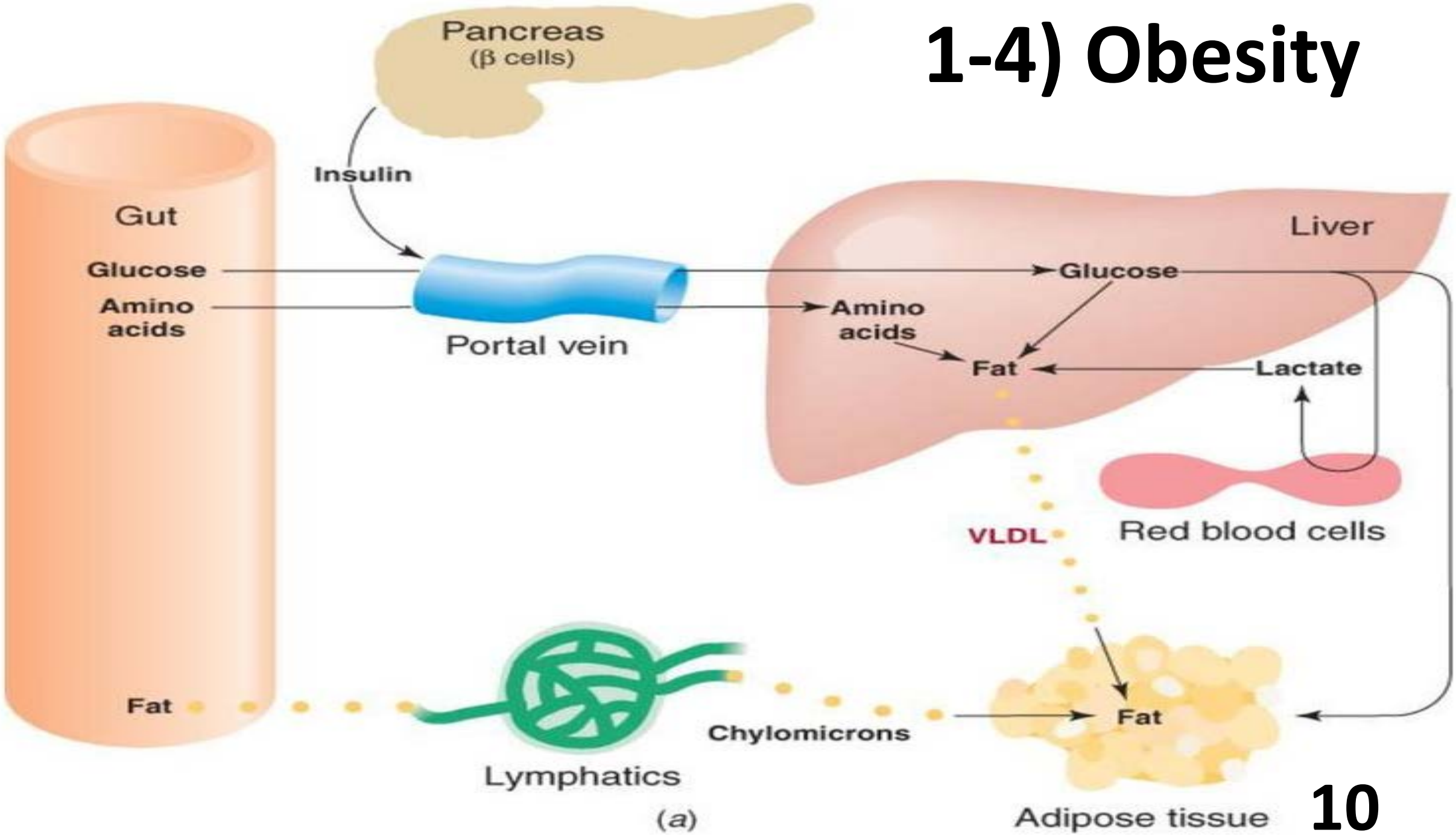
1-3) Atherosclerosis



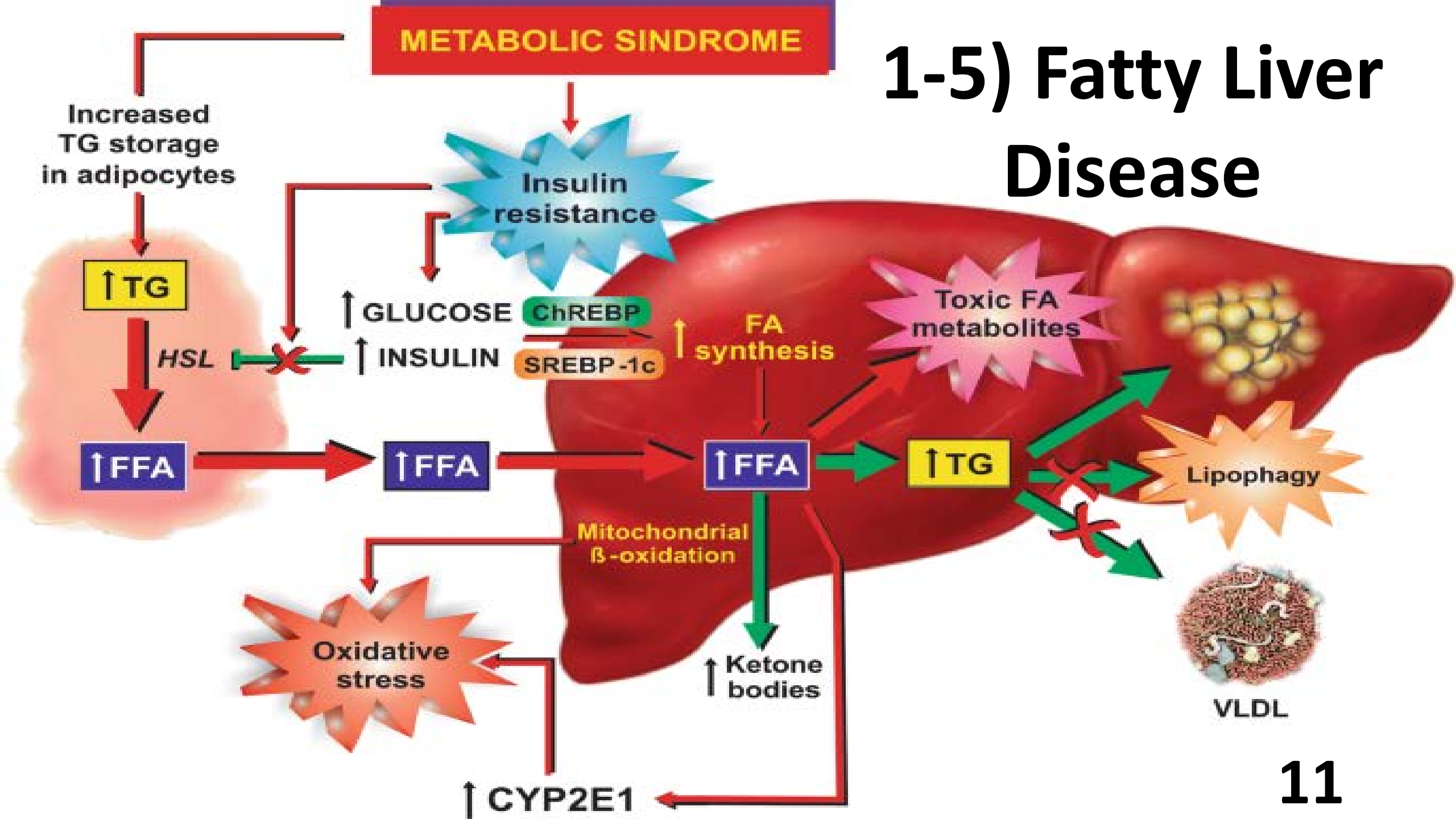



NOMANCLATURE AND MAIN HISTOLOGY
SEQUENCES IN PROGRESSION OF ATHEROSCLEROSIS
EARLIEST ONSET
MAIN GROWTH MECHANISM
CLINICAL COLLERLATION
ENDOTHEHELIAL DYSFUNCTION
Initial lesion
• histologically "normal"
• macrophage infiltration
• isolated foam cells
Fatty streak
mainly intracellular lipid accumulation
Intermediate lesion
• intracellular lipid accumulation
• small extracellular lipid pools
Atheroma
• intracellular lipid accumulation
• core of extracellular lipid
Fibroatheroma
• single or multiple lipid cores
• fibrotic/calcific layers
Complicated lesion
• surface defect
• hematoma-hemorrhage
• thrombosis
from first decade
from third decade
from fourth decade
growth mainly by lipid addition
increased smooth muscle and collagen increase
thrombosis and/or hematoma
clinically silent
clinically silent or overt

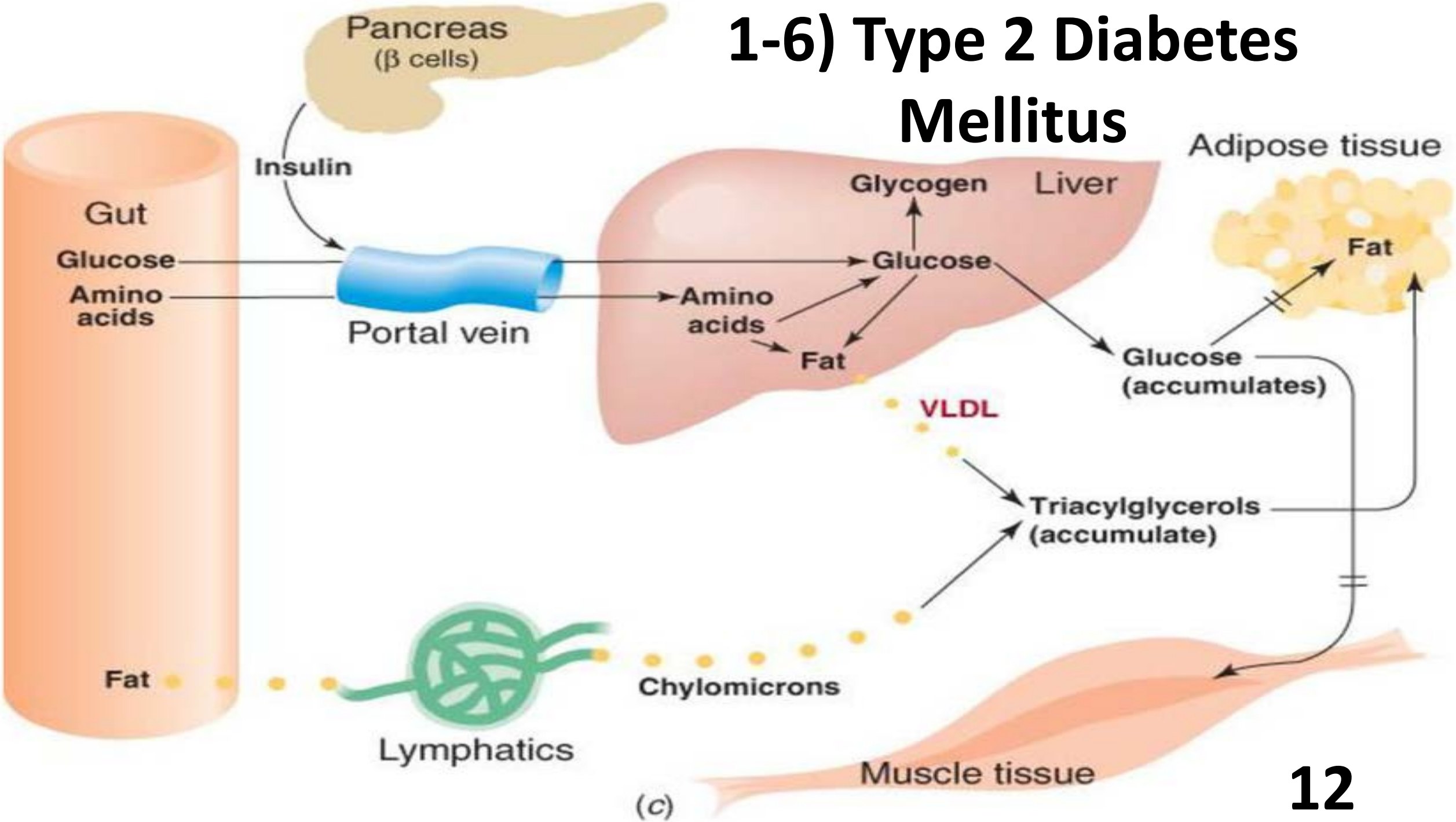
1-4) Obesity


Pancreas
(β cells)
Insulin
Gut
Glucose
Amino acids
Portal vein
Liver
Glucose
Amino acids
Fat
Lactate
VLDL
Red blood cells
Fat
Chylomicrons
Fat
Lymphatics
(a)
Adipose tissue

1-5) Fatty Liver Disease



1-6) Type 2 Diabetes Mellitus



2) Daily Needs & Dietary Lipids

- 1g/ 1kg/1day
- Energy reserves of human (70kg)

  12-15 kg in adipose tissue
- >95% TAG_{exo} (SFA*, PUFA**)
- <5% TC_{exo} ,PLs_{exo}

*SFA: Saturated Fatty Acid

**PUFA: Poly Unsaturated Fatty Acid

3) Exogenous Fat or Fat-diet or Dietary Lipids

Digestion & Absorption of Dietary Lipids in GIT

1- Oral phase: 2 min, 37°C, pH 7

2- Gastric phase: 2 h, 37°C, pH 3

3- Intestinal phase: 2h, 37°C, pH 7

Lipid Digestion: Sites and Enzymes

Sites:

1. **The stomach**
2. **The small intestine**

Enzymes:

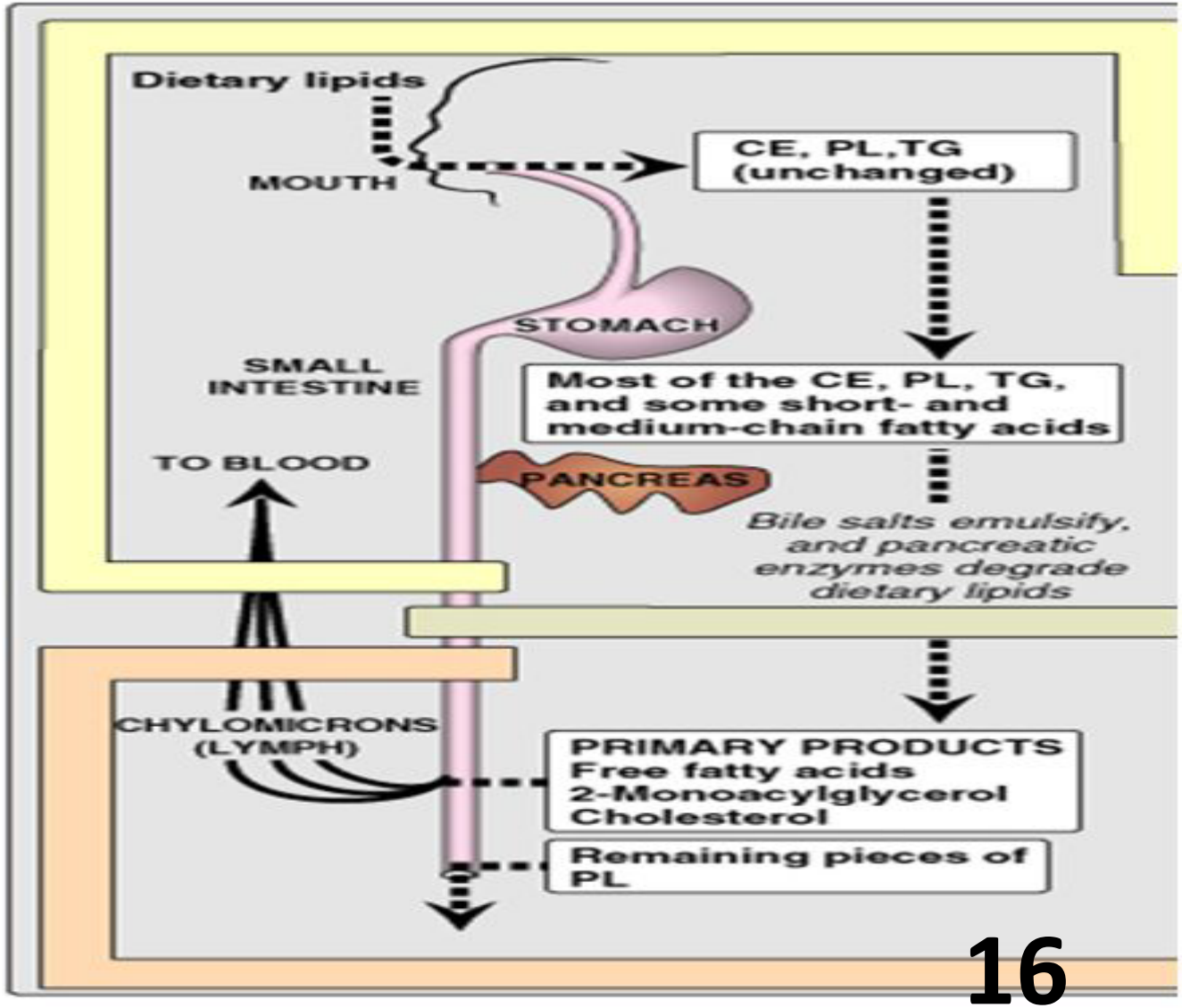
1. Act in stomach:

Mouth: Lingual lipase
Stomach: Gastric lipase

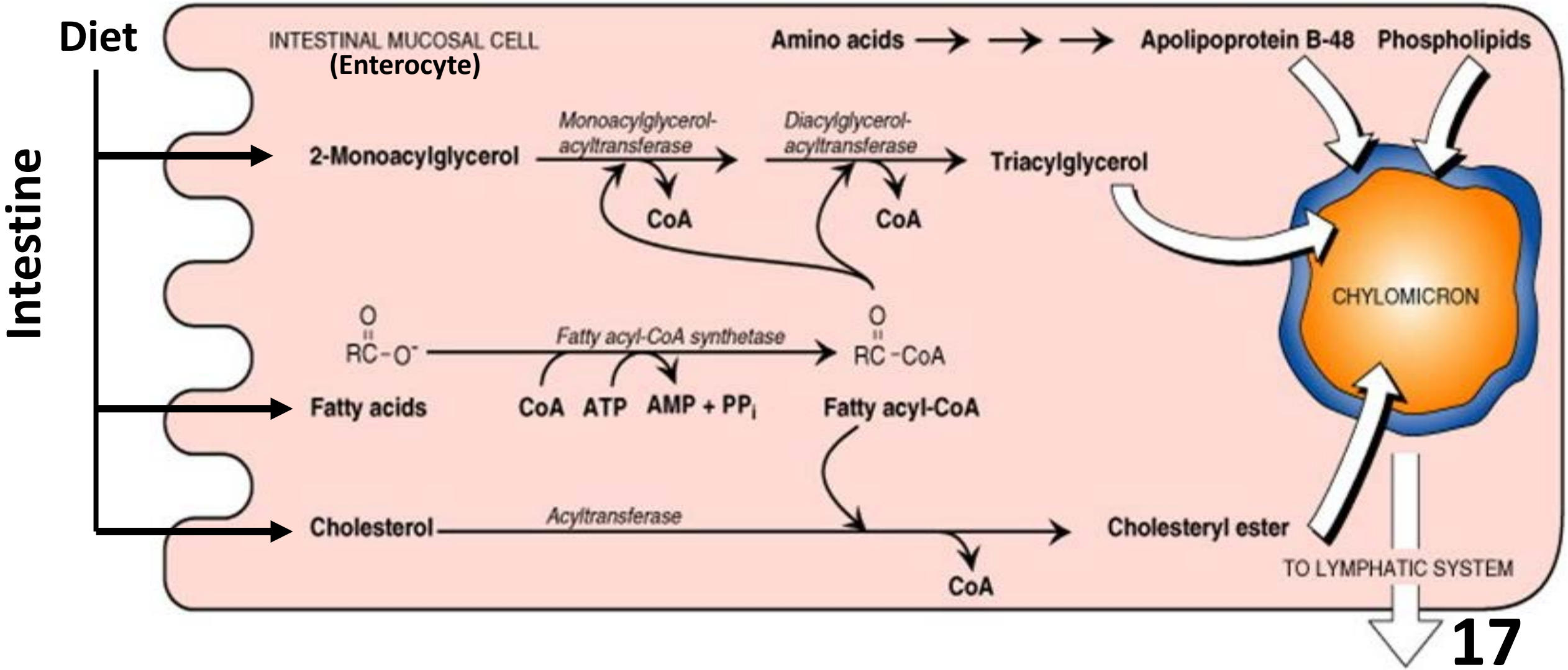
2. Act in small intestine

Pancreatic enzymes

Lipase and co-lipase
Cholesterol esterase
Phospholipase A2
Lysophospholipase



Resynthesis of Lipids & Assembly of Chylomicrons by Intestinal Mucosal Cells



Lipoprotein Lipase (LPL)

- **Extracellular** enzyme anchored by **heparan sulphate** to the capillary walls of **most tissues** especially those of adipose tissue, cardiac & skeletal muscles
- **BUT**: Adult liver does **not** have this enzyme
- It is synthesis & transfer to luminal surface of the capillary is **stimulated by insulin (in fed state)**
- **Activated** by ApoC-II
- Clearing factor (TAG→ FFA+Glycerol)

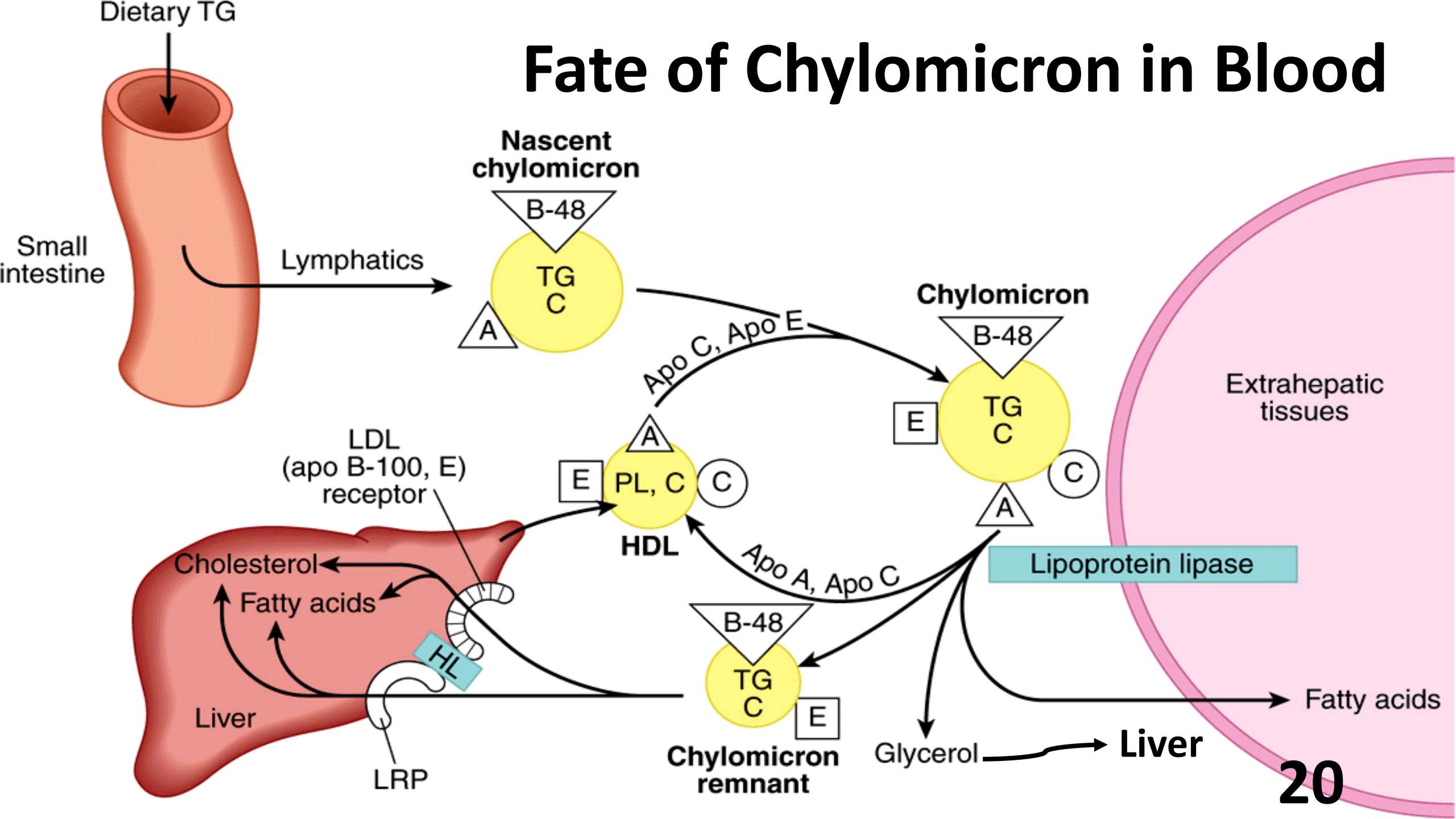
Function of LPL

- LPL hydrolyses circulating TG in CM to fatty acids & glycerol
- **Fatty acids** are stored (in adipose) or used for energy (in muscles)
- **Glycerol** is transferred to the liver (to be used for glycolysis, gluconeogenesis or lipid synthesis)

Deficiency of LPL (or ApoC-II)

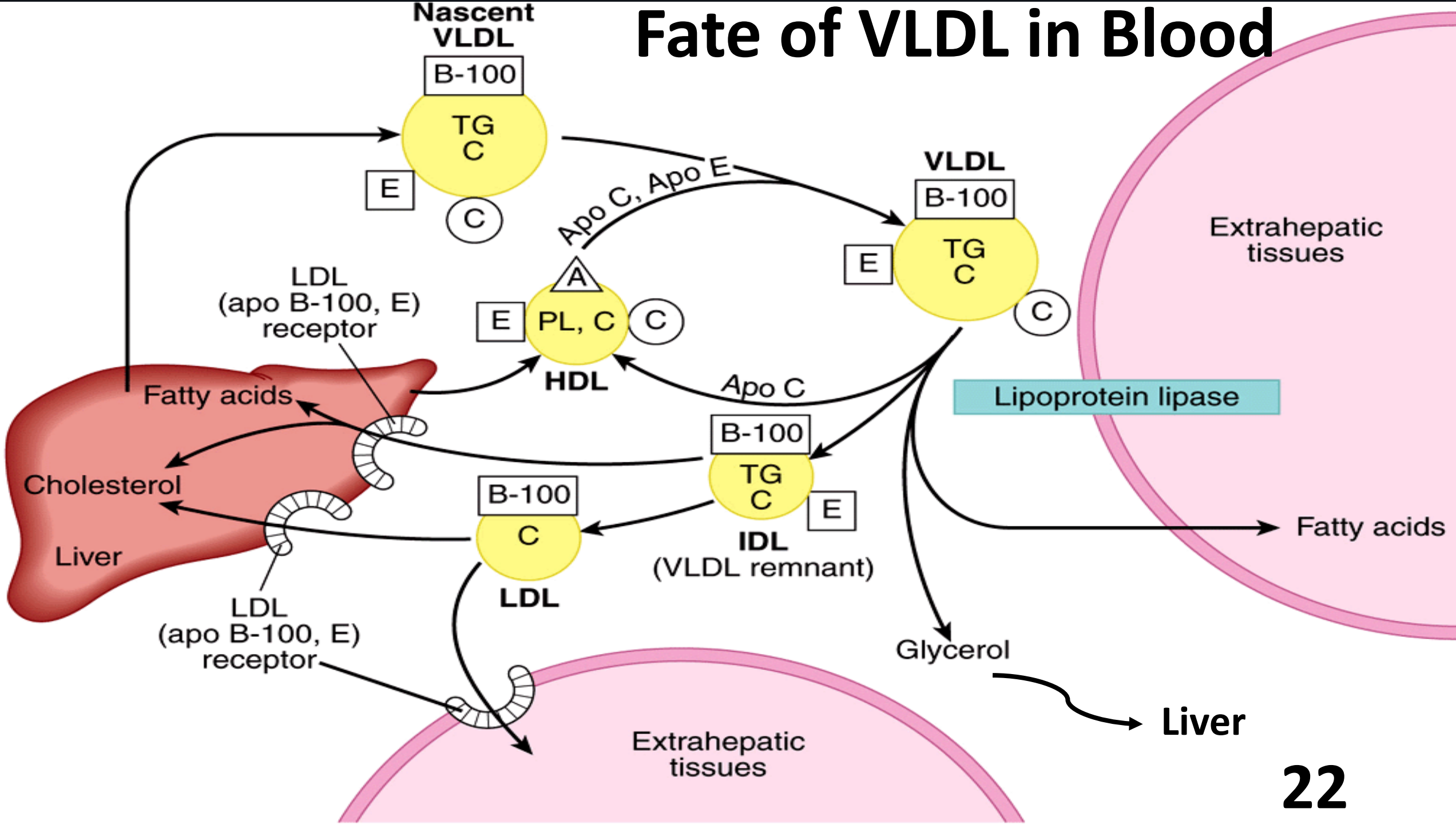
- Causes **type 1 hyperlipoproteinemia (familial lipoprotein lipase deficiency)**
- Accumulation of CM in plasma (**hypertriglyceridemia)**

Fate of Chylomicron in Blood

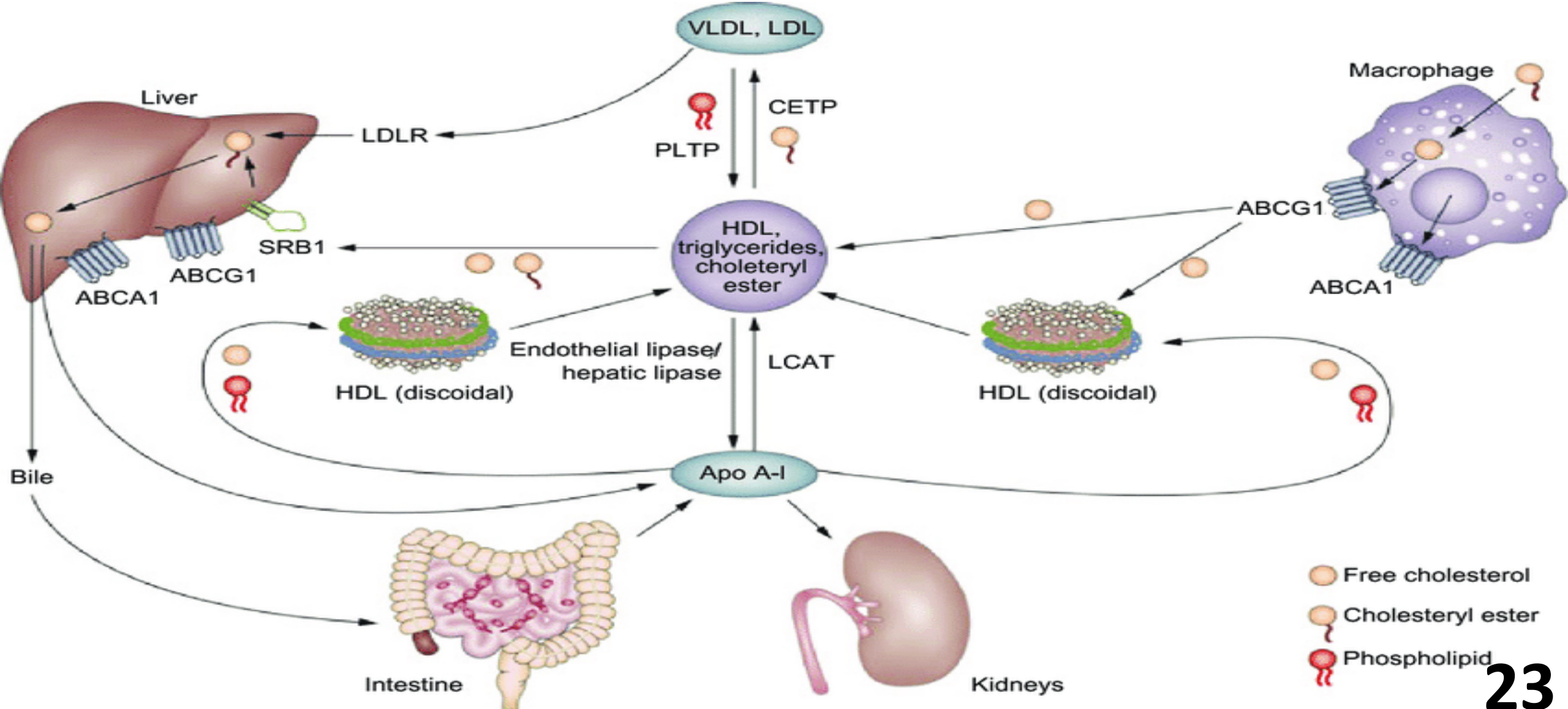


4) Endogenous fat

Fate of VLDL in Blood



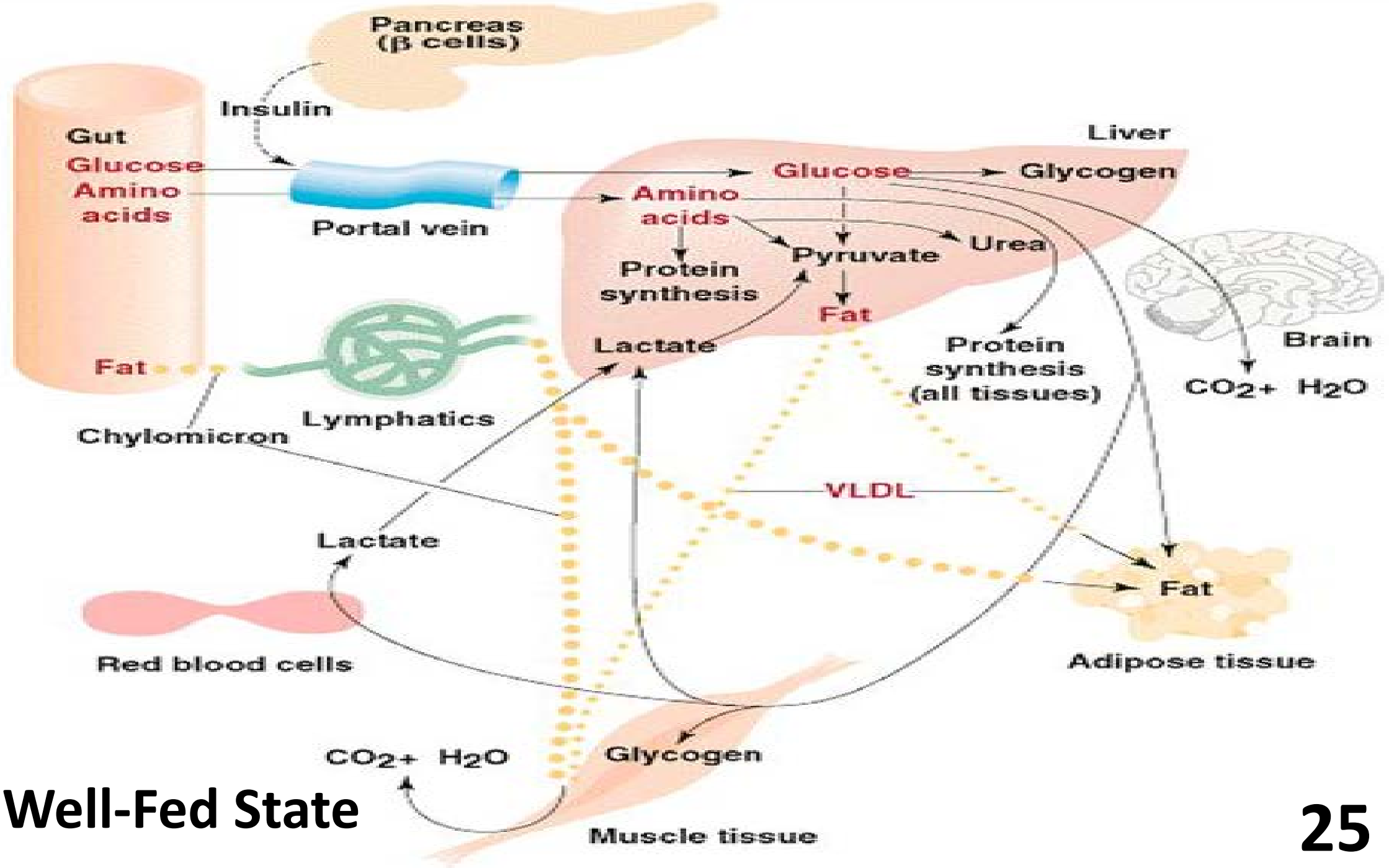
HDL Biosynthesis & Metabolism



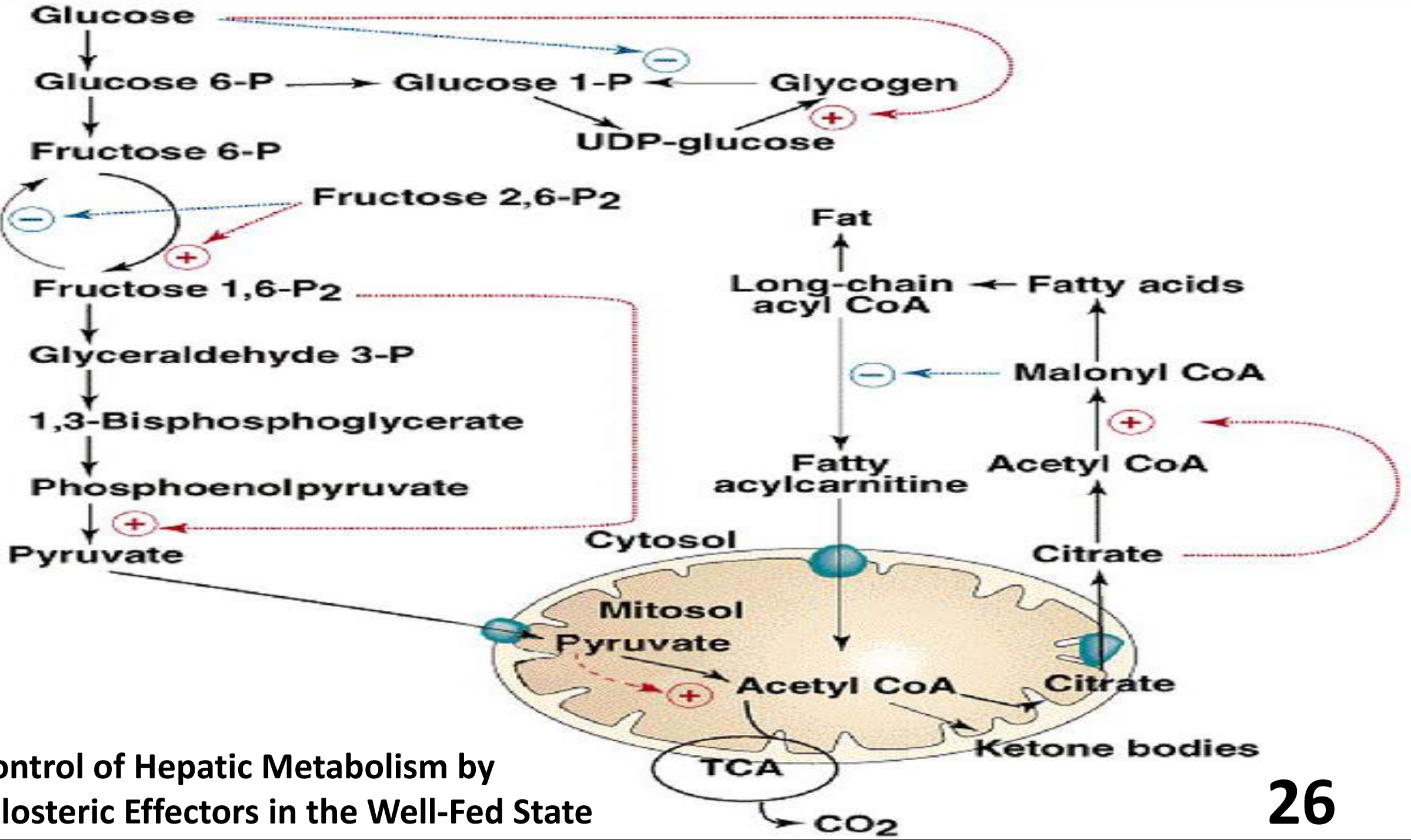
5) Starve-Feed Cycle

A) Well-Fed State

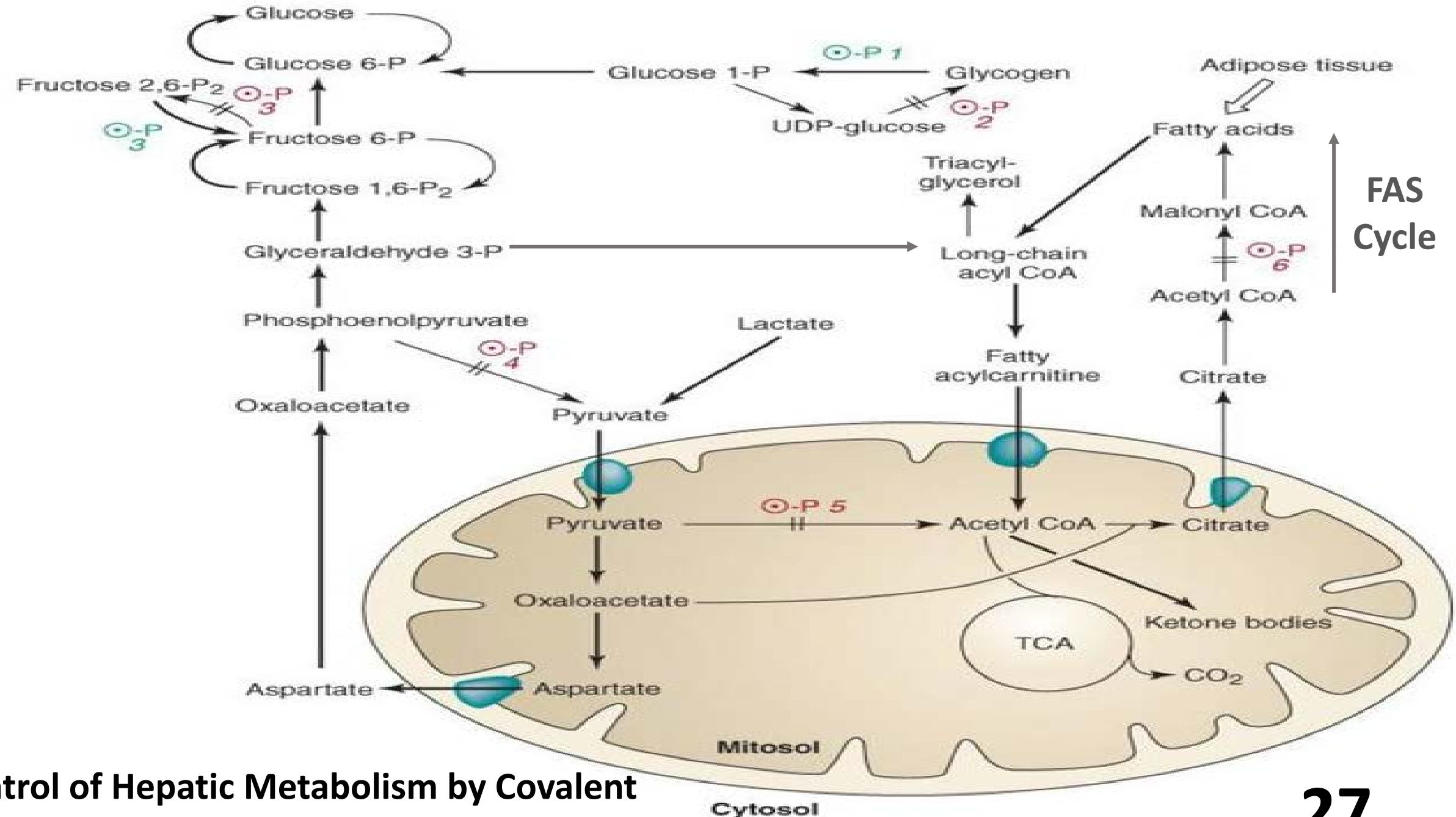
B) Fasting state



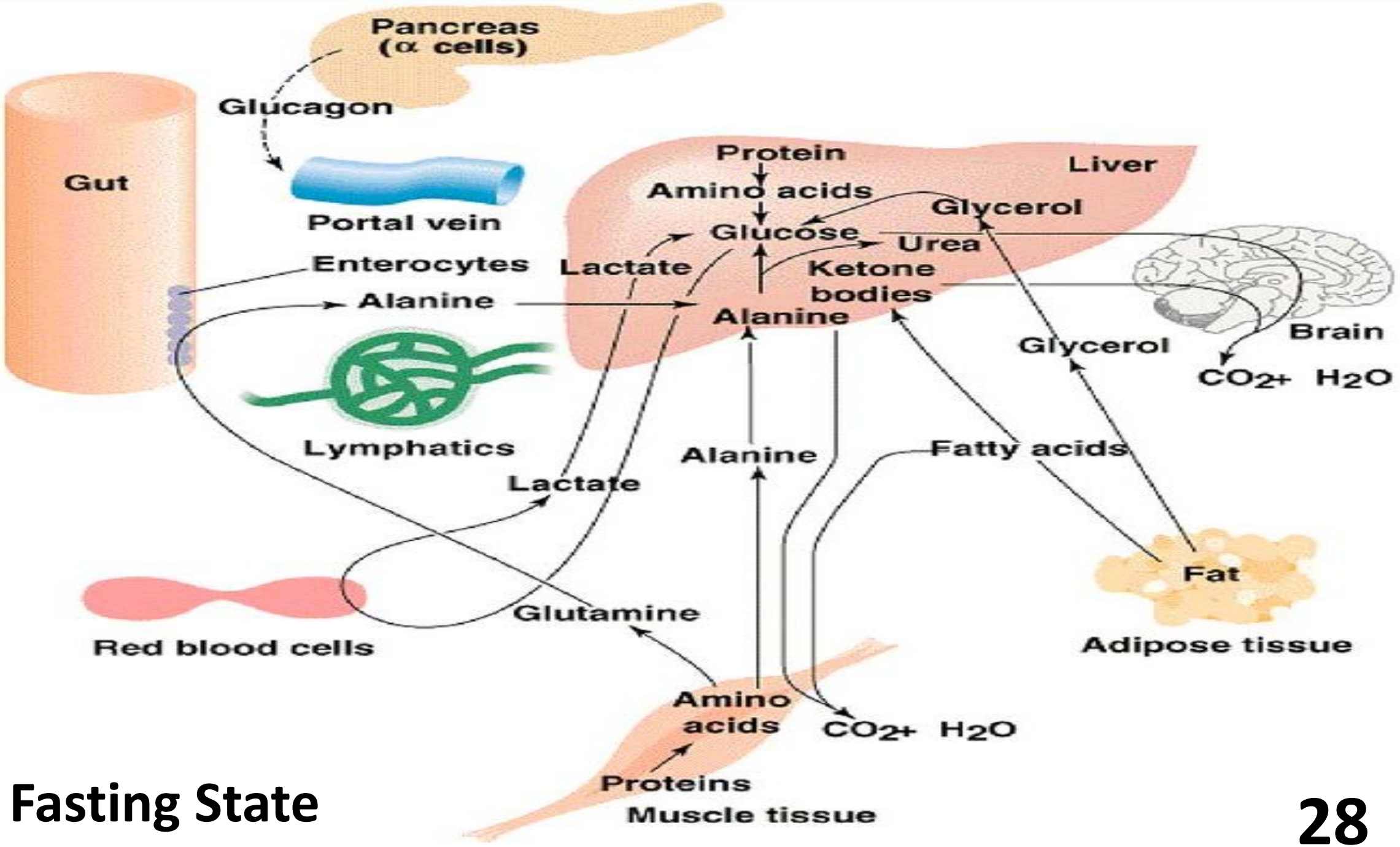
A) Well-Fed State



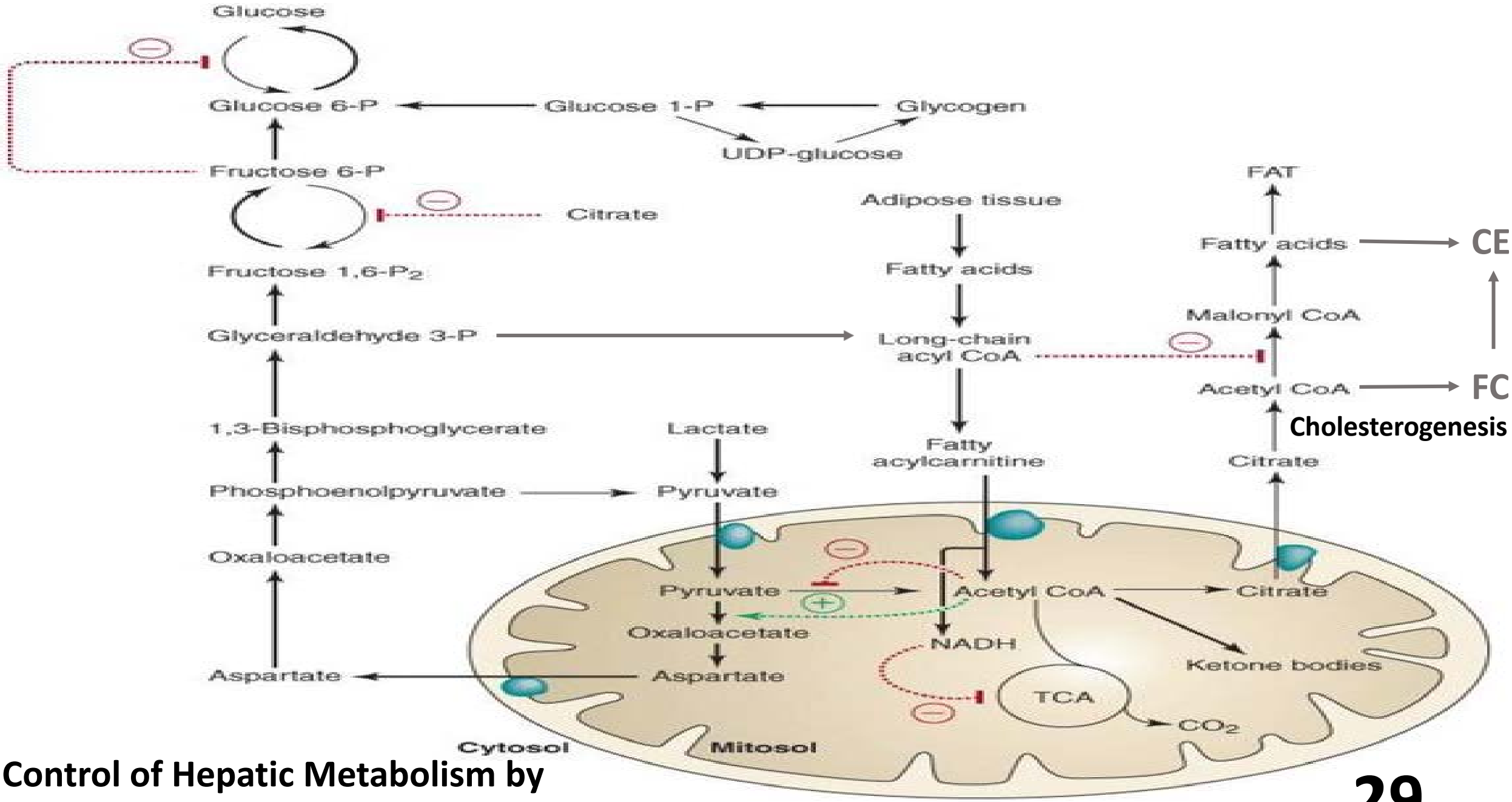
Control of Hepatic Metabolism by Allosteric Effectors in the Well-Fed State



Control of Hepatic Metabolism by Covalent Modification in the Well-Fed State

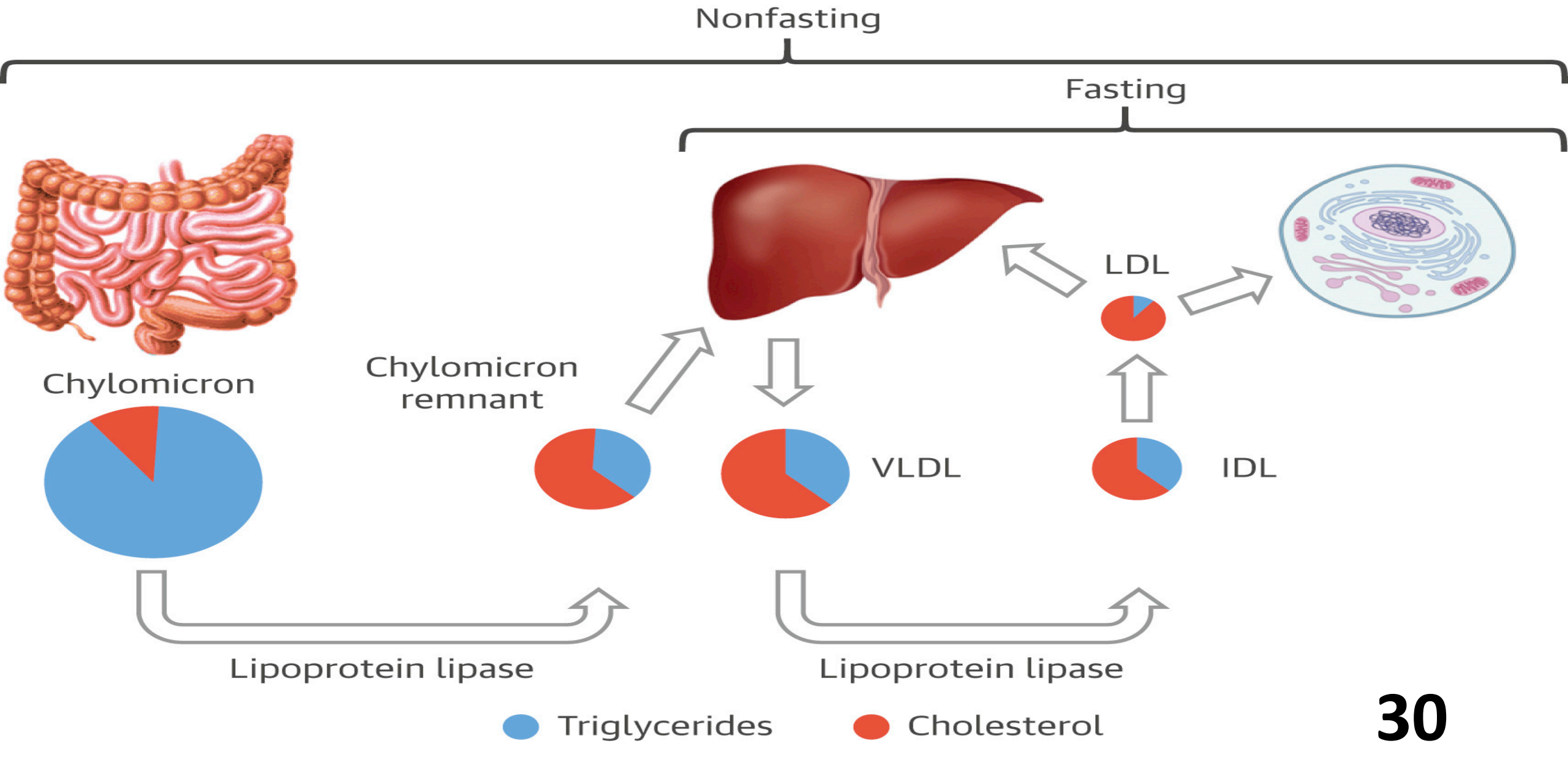


C) Fasting State

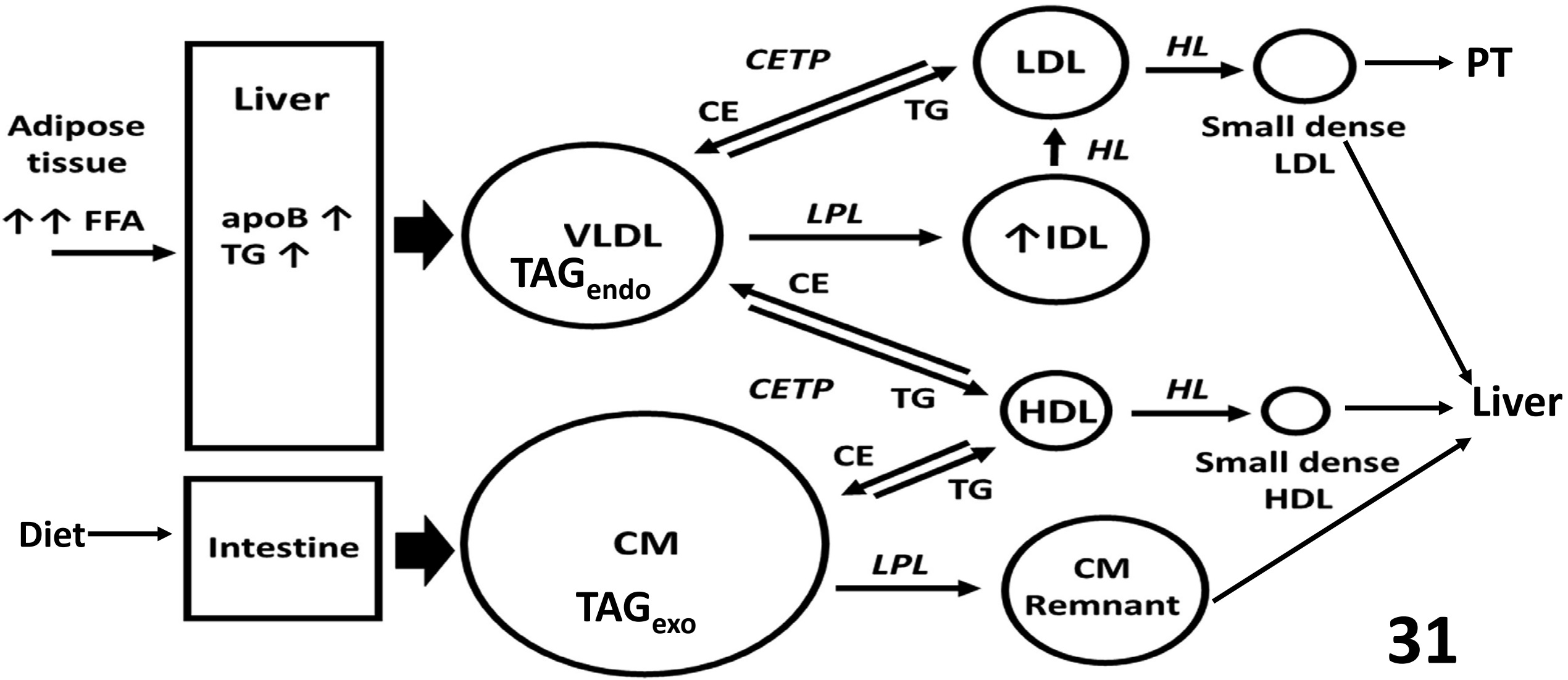


Control of Hepatic Metabolism by Allosteric Effectors in the fasting State

6) Fasting & Non-fasting Lipid Profile



6) Fasting & Non-fasting Lipid Profile



Key Points

- Large population studies have shown that **TC** & **HDL-C** do **not vary** but **LDL-C** & **TG** **vary slightly** after eating.
- Use of **non-HDL-C** in a non-fasting plasma sample captures the atherogenic effect of **remnant lipoproteins** and is a **better** indicator of cardiovascular risk **than LDL-C**.

درس معلم ار بود زمزمه محبتی
جمعه به مکتب آورد طفل گریزپای را

با تشکر از حسن توجه اساتید محترم
و حضار ارجمند

28 اردیبهشت 1401

Question Time