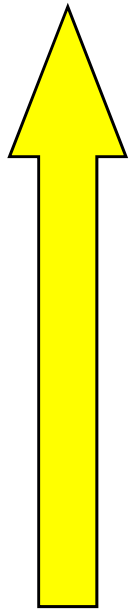
Lipoproteins

Seminar No. 3

A.1 - Lipids of Blood Plasma

Lipid	Plasma concentration
Cholesterol (C+CE)*	3-5 mmol/l
Phospholipids	~ 3 mmol/l
Triacylglycerols	~ 1.5 mmol/l
Free fatty acids (FFA)	~ 0.5 mmol/l



* C = free cholesterol, CE = cholesteryl-esters

Q.2

A.2 - FFA transport

- **FFA are non-polar species**, insoluble in water
- they always need transport systems
- In blood plasma - bound to albumin
- In cytoplasm – Z protein
- Across cell membrane – protein transporter, cotransport with Na^+
- Across mitochondrial membrane – ester with carnitine

Q.3

A.3

FFA come predominantly from adipose tissues

Q.4

A.4

a) Fasting state – action of glucagon – FFA are released from adipose tissues – 0.8 mmol/l

b) Postprandial state – 0.4 mmol/l

Q. 5

A.5 - Lipoprotein particle

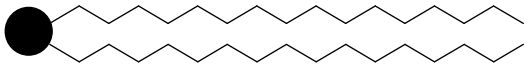
- **Polar surface monolayer**

  contact with polar aqueous environment

- **Non-polar core**

  completely separated from aqueous environment

Components of Surface Layer

Pictogram	Name
	?
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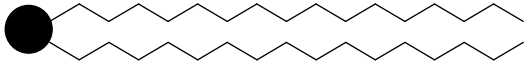
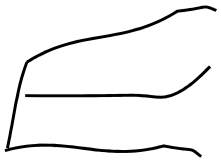
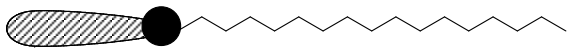
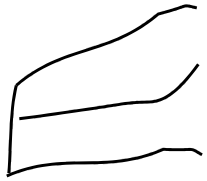
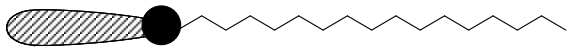
Components of Surface Layer

Pictogram	Name
	phospholipid (PL)
	free cholesterol (C)
	(apo)protein

Non-polar core of lipoprotein

Pictogram	Name
	?
	?

Non-polar core of lipoprotein

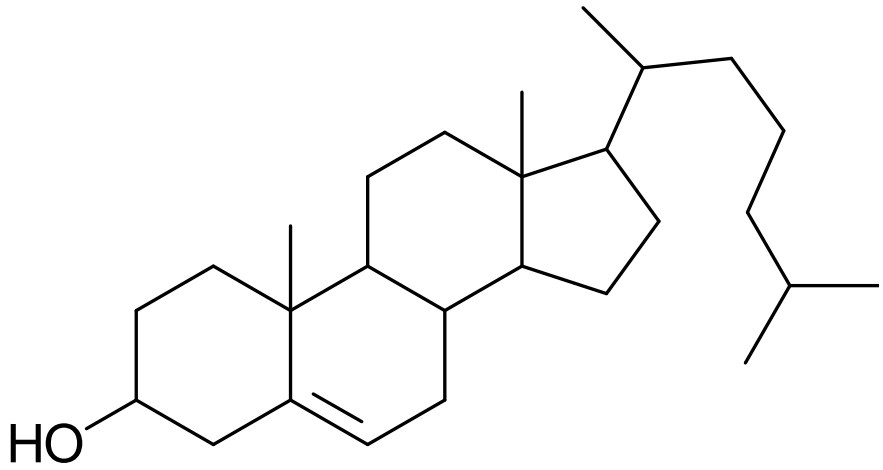
Pictogram	Name
	triacylglycerol (TG)
	cholesteryl ester (CE)

Q. 8

Draw formula of cholesterol

Describe the structure

Structure of cholesterol



27 carbon atoms

1 hydroxyl (C3)

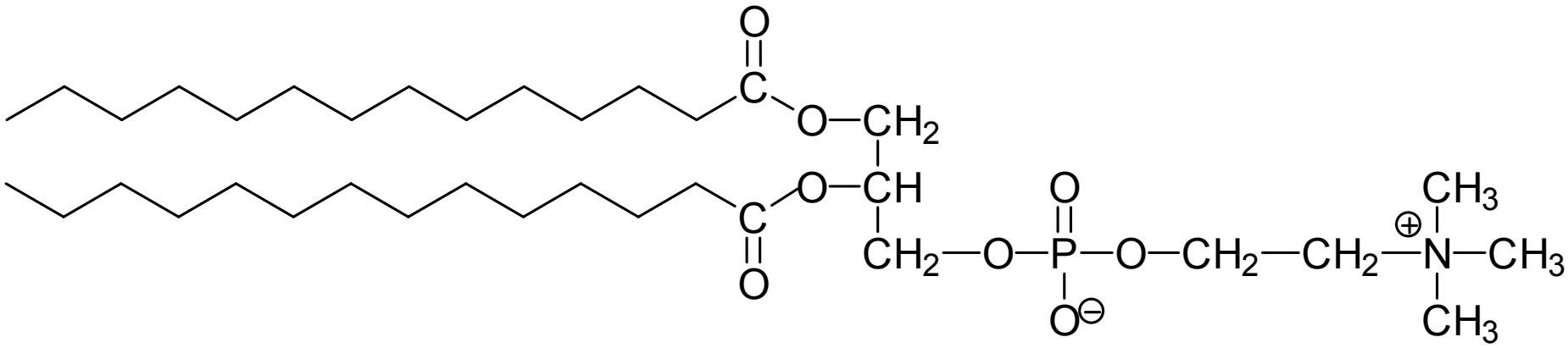
1 double bond (C5)

The only polar group

Chemical name: cholest-5-en-3β-ol

Draw formula of lecithin

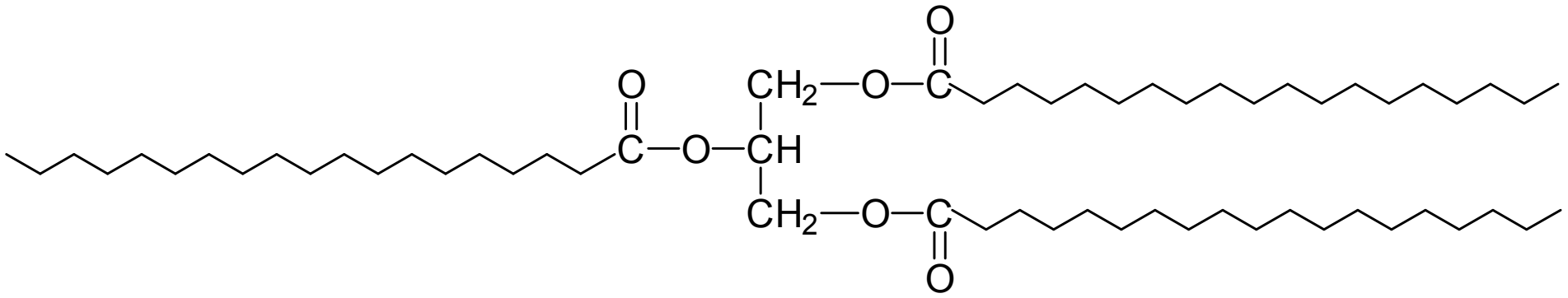
Structure of lecithin



phosphatidylcholine (lecithine)

Draw formula of triacylglycerol

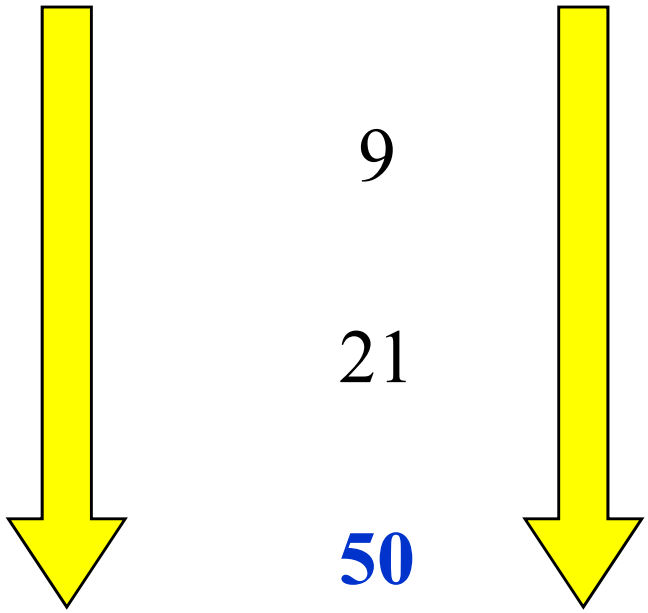
Triacylglycerol (TG)



Q.9 + Q.12

A.9,12 - Lipoproteins: Density *vs.* Composition

Class	Density (g/ml)	Proteins (%)	TAG (%)
CM	**0.90**	2	**84**
VLDL	0.95	9	54
LDL	1.05	21	11
HDL*	**1.20**	**50**	4



* HDL_2 < HDL_3

Q. 10

A. 10

CM contain predominantly TAG = **neutral** molecules

(without charge) $\Rightarrow$ they do not move in electric field

Q. 11

A. 11 - The Composition of Lipoproteins

Features to remember

Lipoprotein	Principal component
Chylomicrons	~ 85 % TAG
VLDL	~ 50 % TAG
LDL	~ 50 % cholesterol (mainly CE)
HDL	~ 50 % proteins

Apoproteins

Complete the table

Functions of apoproteins
the completion of the table

A-I LCAT activator

B-100 structure of VLDL, ligand for LDL receptor

B-48 structure of CM

C-II LPL activator

Transport functions of lipoproteins

Class	Origin	Transport
CM	enterocyte	exogenous TAG from GIT to peripheral tissues
VLDL	liver	endogenous TAG from liver to periph. tissues
LDL	plasma	cholesteryl esters to peripheral tissues
HDL	liver	free cholesterol from tissues to liver

Q.14

A.14

Liver receptors have **greater affinity to IDL**

to remove them from circulation because of apo E receptors

Q.15

A.15

LDL because:

- **Long half-life (2-4 days) !!**
- They are **stationary** (no remodelling in contrast to HDL)
- Contain a big portion of CE with PUFA

Enzymes in lipoprotein metabolism

Enzyme	Substrates	Reaction	Location
LPL	TAG of CM, VLDL	hydrolysis	capillaries
HL	TAG of IDL, HDL	hydrolysis	liver
LCAT	cholesterol + lecithin	esterification	HDL

LPL = lipoprotein lipase

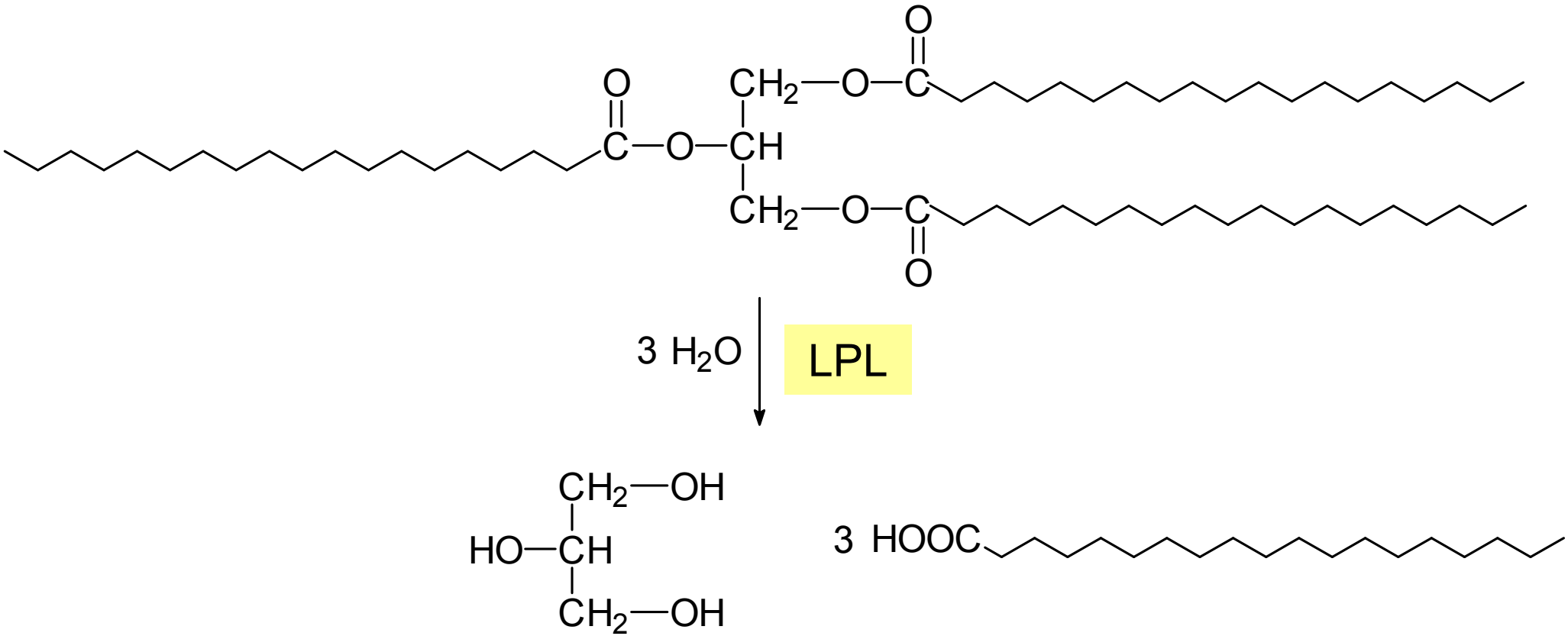
HL = hepatic lipase

LCAT = lecithin cholesterol acyltransferase

Q.17

Write the equation of reaction catalyzed by LPL

LPL reaction



TAG + 3 H_2O → glycerol + 3 FFA

Q. 16

A. 16

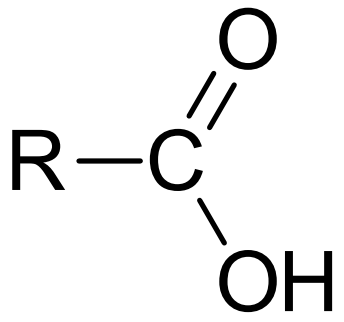
- Elevated CM and VLDL in serum – chylous serum

How can you detect chylomicrons in serum sample?

Q. 17 Write the equation of reaction catalyzed by LCAT (lecithin cholesterol **acyl**transferase)

What is acyl?

Acyl



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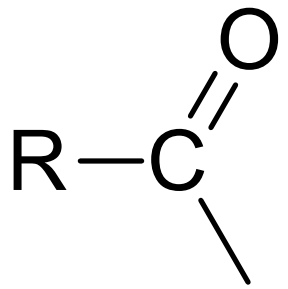
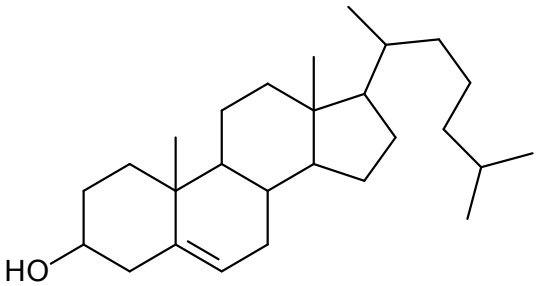


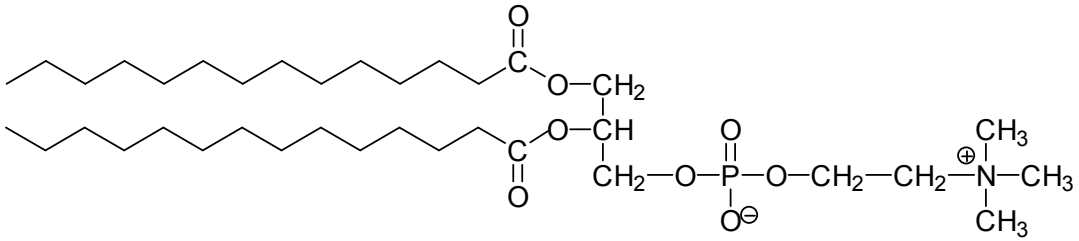
a

LCAT reaction

cholesterol + lecithin $\rightarrow$

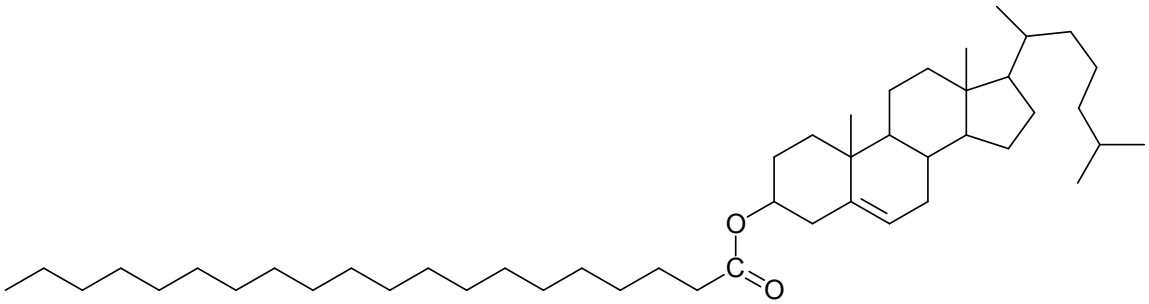


cholesterol

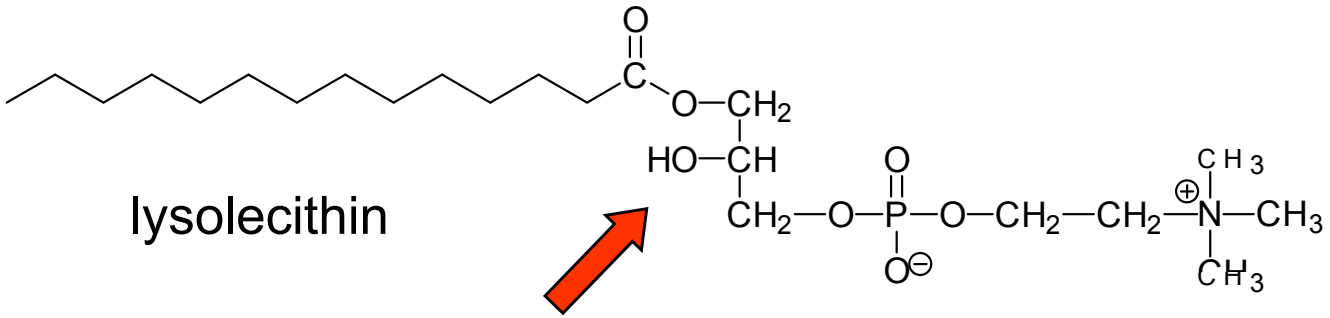


lecithin

LCAT



cholesteryl ester



lysolecithin

lyso = 2-deacyl

Metabolism of chymomicrons (CM)

- CM are produced in enterocytes, apo B-48
- They carry dietary TAG and CE to periph. tissues
- In plasma, CM receive apo E and apo C-II from HDL
- **Apo C-II activates lipoprotein lipase (LPL)**
- LPL is attached to capillary surface in adipose, cardiac and muscle tissues
- TAG are hydrolysed, apo C-II is returned to HDL
- CM particles begin to shrink – **remnants**
- Remnants bind to apo E receptors in liver, where they are hydrolytically degraded in lysosomes

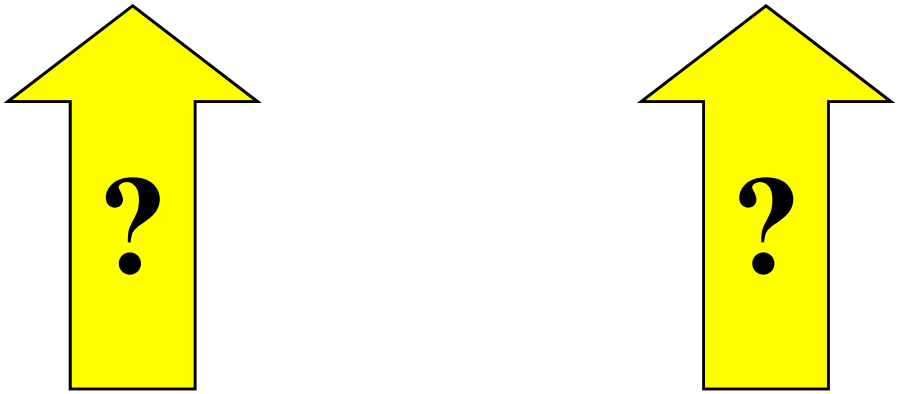
Q. 20

What is the result of deficient synthesis of apo B-48?

A. 20

No CM will be produced, dietary fat remains in stool (steatorrhoea)

Lipophilic vitamins and **essential FA** will be deficient.



Q. 21

A. 21

Feature	LPL	HSL
Substrate	TAG in circulation	TAG in stores
TAG stores are	increased	decreased
Stimulated by	insulin (inducer)	glucagon + adrenalin

Metabolism of VLDL

- VLDL are made in liver, they transport endogenous TAG to periph. tissues
- In plasma they take apo C-II from HDL (LPL activ.)
- TAG are removed by LPL action – VLDL become smaller and more densed = IDL
- IDL take some CE from circulating HDL
- **IDL are transformed into LDL by hepatic lipase**

Q. 24

A. 24

Food rich in lipids (fat) and saccharides (sugars)

Q. 27

Three pathways of LDL

1. LDL provide cholesterol to peripheral tissues *via* LDL receptors
2. The rest of LDL is taken up by liver and degraded
3. Small amount of LDL (chemically modified by oxidative stress) enters to some cells (endothelial) by non-specific endocytosis and alters them to „foam cells“

Q. 28

A. 28

- Apo B-100 is structural protein of VLDL
- If absent, VLDL cannot be made in liver
- TAG remain and accumulate in liver
- Liver steatosis

Q. 30

A. 30 Metabolism of HDL

- HDL particles are made in liver
- Nascent HDL are **disc-shaped** (bilayer of PL + proteins)
- HDL take free cholesterol (C) from cell membranes
- Once C is taken up, it is esterified by LCAT
- After this process HDL becomes spherical
- Spherical HDL are taken up by liver and CE are degraded

Q. 32

A. 32

- Apo A-I
- ABC transporter A1
- LCAT
- CETP
- SR-B1
- HL

Q. 34

A. 34

- LCAT
- Made in liver
- Acts on HDL
- Activated by apo A-I

Q. 35

A. 35

- During digestion:
  Pancreatic lipase, LPL

- In fasting:
  HSL

Cellular uptake of LDL

- LDL receptors are in clathrin-coated pits
- After binding, LDL+receptor are internalized by endocytosis
- Vesicle loses its clathrin coat and becomes endosome
- Receptor is removed and recycled
- LDL is hydrolyzed after fusing with lysosome
- Free cholesterol is released to make **cholesterol pool**

Intracellular cholesterol

- Free cholesterol (C) is immediately esterified by ACAT* to make intracellular storage
- Small amounf of C is incorporated into cell membrane
- Some C is converted into hormones (in some tissues)
- Some C is converted into bile acids (in liver)

* acyl-CoA cholesterol acyltransferase

Intracellular cholesterol regulates three processes

1. Decreases activity of HMG-CoA reductase
   (= synthesis of cholesterol)
2. Decreases synthesis of new LDL receptors
   (to block intake of LDL)
3. Enhances activity of ACAT (to make storage)

Q. 37

A. 37

- They are not recognized by LDL receptors in tissues
- They are taken by scavenger receptors in macrophages – and make foam cells
- The aggregation of foam cells – atherogenic plaques

Q.45

The Balance of Cholesterol

Input into body	g/day	Output from body	g/day
food	0.5 g	coprostanol (stool)	0.8 g
biosynthesis in body	1.0 g	bile acids (stool)	0.5 g
		sebum/desquamated cells	0.2 g
Total:	**1.5 g**	**Total:**	**1.5 g**

Q.

Which food is the main source of cholesterol?

A.

only animal fats (including fish):

lard, butter, bacon, egg yolk, mayonnaise,
fat meat, fat cheese

plant oils and margarines are cholesterol free

The next seminar you will write the revision test (15 Q) from

- **Seminar chapters 1-3**
- **Practical chapters 1-2**