Biochemistry
Team 434

Lipoprotein metabolism.

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Lipid compounds: We don't have lipid on its own because of transportation in blood (lipid is hydrophobic) that's why it's is linked with protein

Relatively water insoluble.

Therefore, they are transported in plasma (aqueous) as Lipoproteins. So it would be of more hydrophilic medium

Lipoproteins and Related Clinical Problems:

- **Atherosclerosis and hypertension.** most impoertant
- **Coronary heart diseases.**
- **Lipoproteinemias (hypo- and hyper-), (congenital disease)**
- **Fatty liver(1).** (abnormal accumulation of triglyceride in the liver).

(1) : Abnormal deposit of triglycerides in liver (normally found in subcutaneous adipose tissue or visceral tissue) it is benign but can progress into liver failure

Lipoprotein Structure:

Protein part (coat): **Apoproteins or apolipoproteins.** (apoproteins are polypeptides that combines with a prosthetic group(vitamins , sugars , lipids) to form a holoprotein)

Abbreviations: Apo-A, B, C, D, E.

Functions:

-Structural and transport function.(mainly).

-Enzymatic function.(co enzyme)

-Ligands for receptors. The receptors recognize the apo- protien part.

Lipid part (core) :

- **According to the type of lipoproteins.** The different types are due to different lipid components in different variations
- **Different lipid components in various combinations.**

Spherical molecules of lipids and proteins (apoproteins):

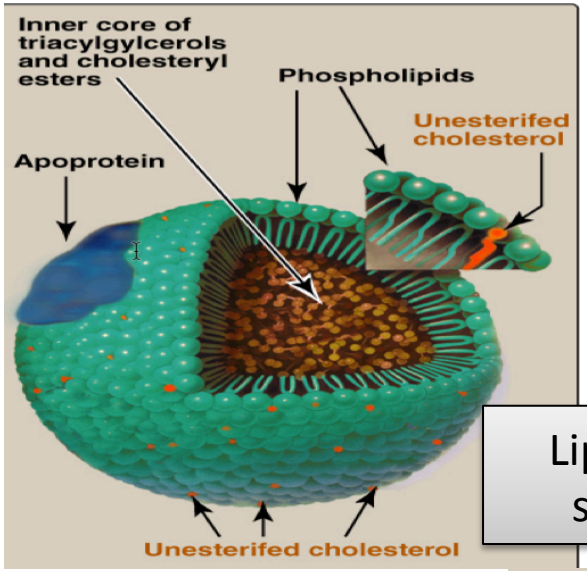
Outer coat: (hydrophilic)

Apoproteins Phospholipids Cholesterol.

Inner core: (hydrophopic)

TG.

Cholesterol ester. Esterified cholesterol (with fatty acid attatched at carbon 3) is more hydrophobic than free cholesterol so it is not found on the membranes.



	The major triglycerides transporters
	Major carriers of cholesterol
	The protein in HDL is the source of protein in the other molecules

Lipoprotein structure

Types of Lipoproteins:

-Chylomicrons Very very low density.

-Very Low density Lipoprotein (VLDL). (Free cholesterol)

-Low density Lipoprotein (LDL).

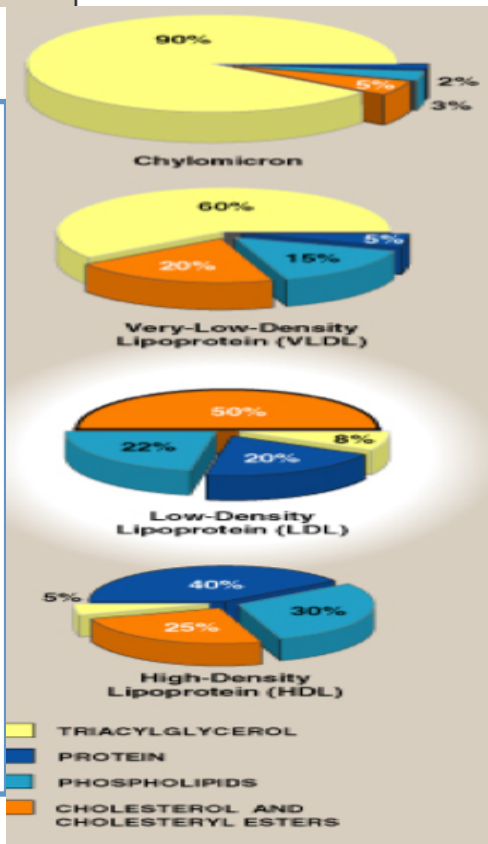
-High density Lipoprotein (HDL). (esterified cholesterol)

More proteins = more density = more hydrophobic.

- **Why do we have different types of lipoproteins?**

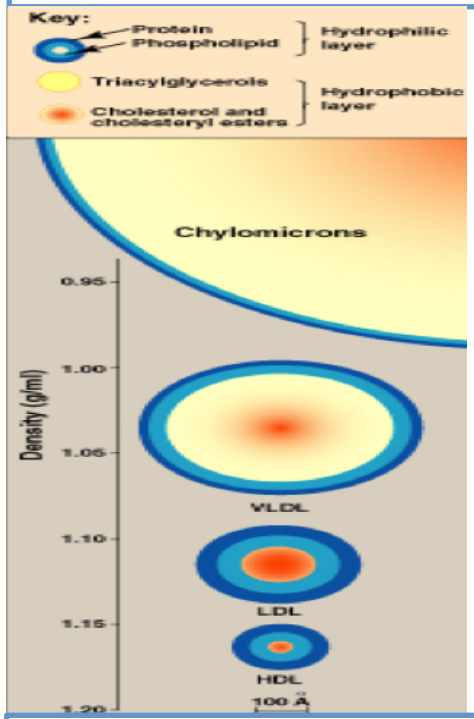
They differ in lipid and protein composition and therefore, they differ in:

1-Size and density 2-Electrophoretic mobility. (measurement of lipids mobility in an electric filed)

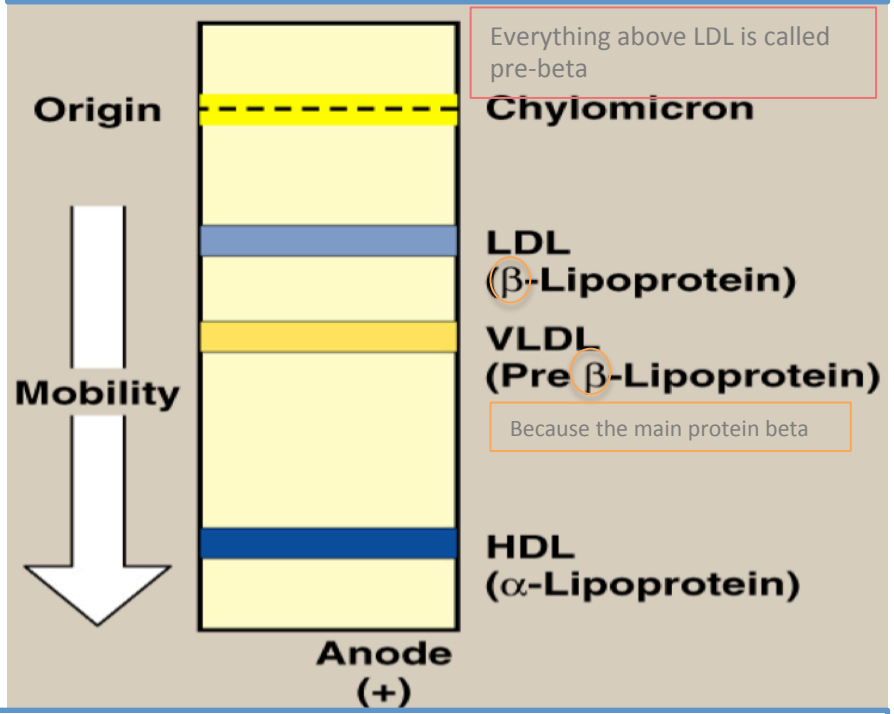


Ultracentrifugation of Lipoproteins

Separation of molecules in electric field



Lipoprotein electrophoresis: قدرة الجزيء على انه يتحرك في مجال كهربائي، من سالب لموجب او العكس، وهذا يعتمد على : الحجم



Plasma Lipoproteins:

For triacylglycerol transport (TG-rich):

Chylomicrons: TG of dietary origin.

VLDL: TG of endogenous (hepatic) synthesis.

For cholesterol transport (cholesterol-rich):

LDL: Mainly free cholesterol.

HDL: Mainly esterified cholesterol.

Chylomicrons

- Assembled in intestinal mucosal cells
- Lowest density
- Largest size (one micro)
- Highest % of lipids and lowest % proteins
- Highest triacylglycerol (dietary origin)
- Carry dietary lipids to peripheral tissues
- Responsible for physiological milky appearance of plasma (up to 2 hours after meal). (more than 2 hours it counts pathological)

Metabolism of VLDLs:

- Assembled and secreted by liver.
- Mature VLDLs in blood.
- Modifications of circulating VLDLs.
- End products: IDL(intermediate density lipoprotein)and LDL(degradation of TG in peripheral tissues will produce IDL from VLDL

* returning Apo-E and Apo-C2 (other name is Ascobic acid) to HDL will produce LDL from IDL) .

•Related diseases:

Hypolipoproteinemia:Abetalipoproteinemia

Hyperlipoproteinemias:

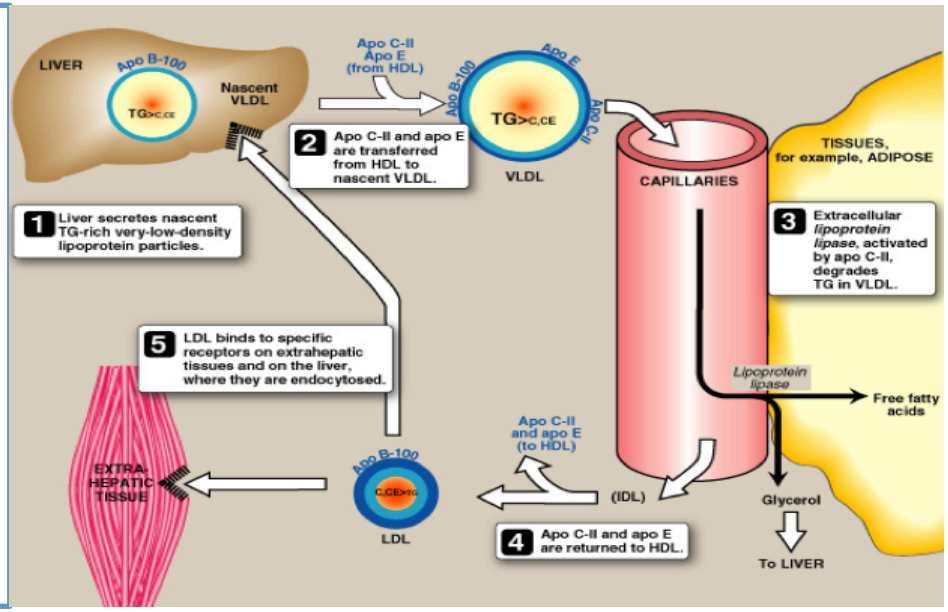
Type I hyperlipoproteinemia.

Familial type III hyperlipoproteinemia.

(Type II is associated with LDL receptors abnormalities)

Very Low Density Lipoproteins VLDLs:

- Assembled in liver.
- High triacylglycerol (hepatic origin).
- Carry lipids from liver to peripheral tissues.
- Nascent(immature) VLDL: contains Apo B-100 (type of protein).
- Mature VLDL:
  - Apo B-100 plus:
  - Apo C-II and Apo E (from HDL).



Metabolism of VLDLs: Mature VLDLs

- Assembled and secreted by liver directly into blood as nascent form
- Mature VLDLs: contain Apo B-100 plus Apo C-II and Apo E.
- ApoC-II is required for activation of lipoprotein lipase.
- Lipoprotein lipase is required to degrade TG into glycerol and fatty acids.

Lipoprotein lipase

- Extracellular enzyme, anchored by heparan sulfate(Complex CHO) to the capillary walls of most tissues
- Predominantly present in adipose tissue, cardiac & skeletal muscle
- Requires ApoC-II for activation
- Degrades TG into glycerol and free fatty acids
- Insulin stimulates its synthesis and transfer to the luminal surface of the capillary.
- If deficient (or if apo C-II is deficient)→type 1 hyperlipoproteinemia = familial lipoprotein lipase deficiency) (That's why diabetics are at risk of developing hyperlipoproteinemia)

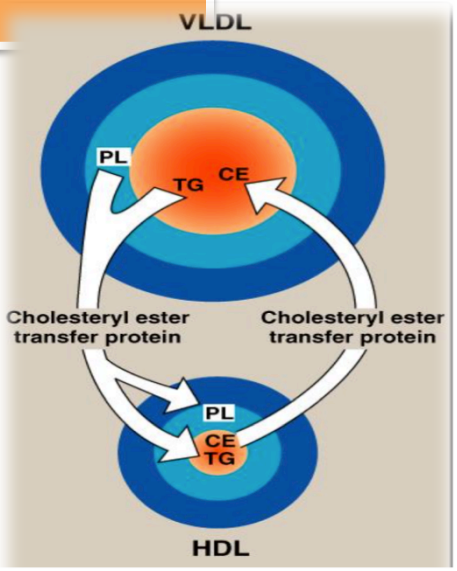
Modifications of Circulating VLDLs

1- Degradation of TG by lipoprotein lipase →, VLDLs become Smaller in size, More dense.

2- Apo C & Apo E return back to HDL

3- Some TG are transferred from VLDL to HDL in exchange with cholesterol ester (By cholesterol ester transfer protein) (Apo D)

VLDL → IDL (returns Apo E to HDL) → LDL



Lipid-Transfer Protein

VLDLs-Related Diseases

1- Hypolipoproteinemia

Abetalipoproteinemia

-Defect in TG-transfer protein.

-Apo B-100 cannot be loaded with lipid Accumulation of TG in liver.

إما التصنيع زاد عن قدرة الكبد على التصدير أو القدرة على التصدير قلت عن المعدل الملائم للتصنيع

2- Fatty Liver (hepatic steatosis)

-Imbalance between hepatic synthesis of TG and secretion of VLDLs.

-Accumulation of TG in liver

3- Hyperlipoproteinemia

- Type I Hyperlipoproteinemia

Familial Lipoprotein lipase deficiency.

-Due to deficiency of lipoprotein lipase or its cofactor (Apo C-II) (Deficiency in one or both).(That are important for the degradation of TG carried by lipoprotein)

-Shows a dramatic accumulation (≥1000 mg/dl) of chylomicrons in plasma.

-Usually associated with acute abdomen due to acute pancreatitis.

-↑ plasma TG even in the fasted state.

- Type III Hyperlipoproteinemia

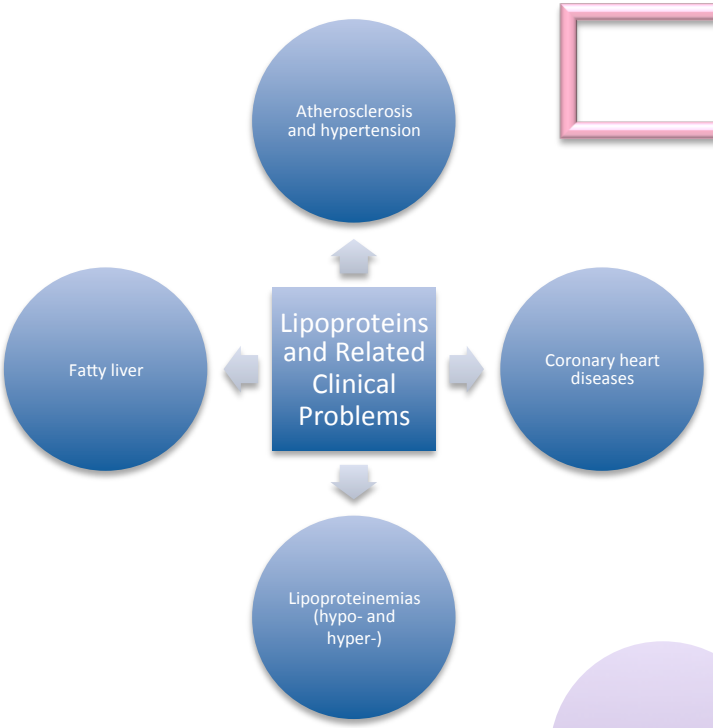
- (Familial dysbetalipoproteinemia)

-due to Apo E deficiency

- Associated with hypercholesterolemia & premature Atherosclerosis. (abnormal HDL which is important for transferring cholesterol to liver to be excreted)

All these diseases are congenital except fatty liver it can be either congenital or acquired

Summary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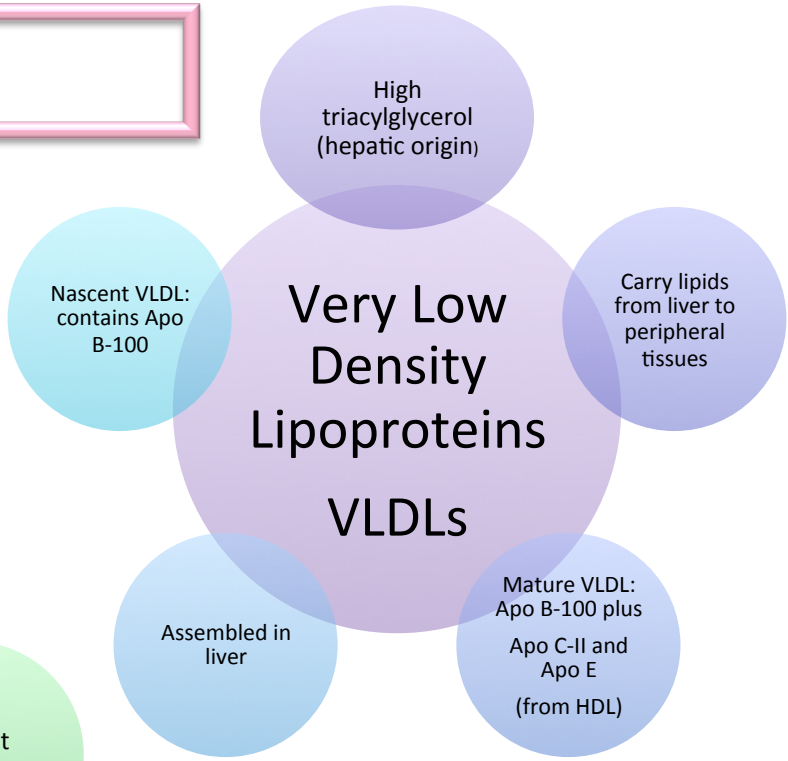
High triacylglycerol (hepatic origin)
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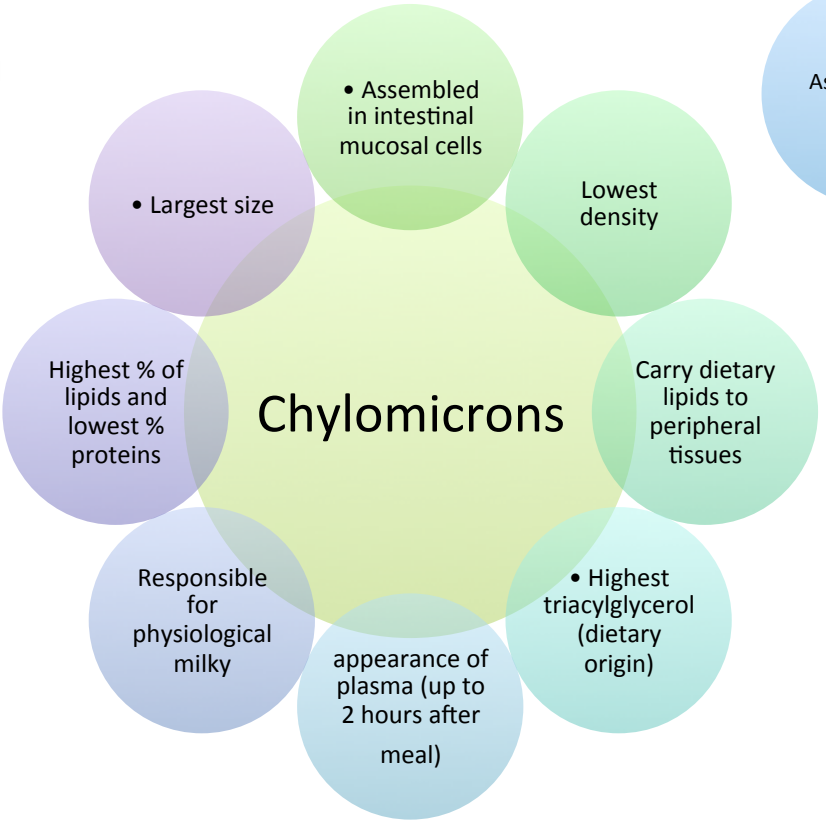
VLDLs
Carry lipids from liver to peripheral tissues
Assembled in liver
Mature VLDL: Apo B-100 plus
Apo C-II and Apo E
(from HDL)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appearance of plasma (up to 2 hours after meal)

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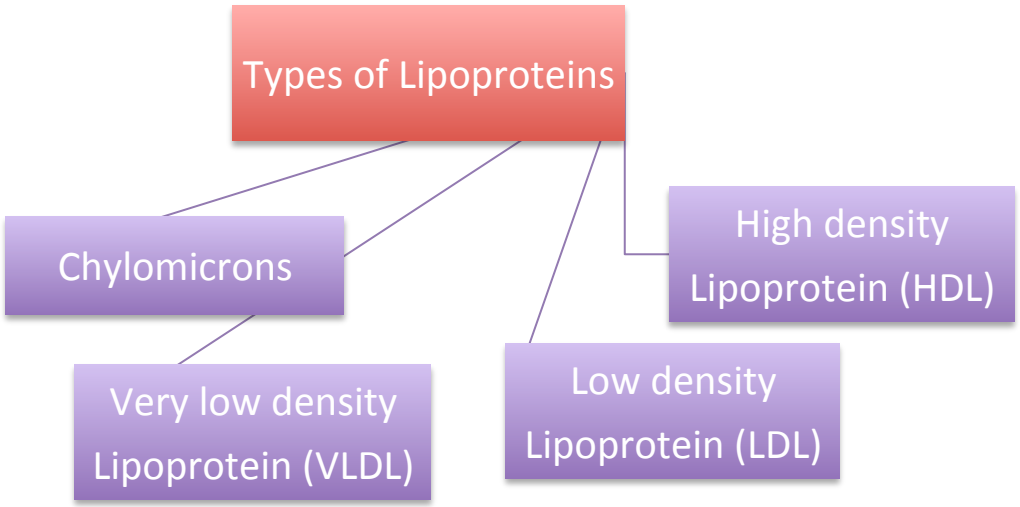


MCQ

1\Lipid compounds they are transported in plasma (aqueous) as ?
A\Lipoproteins
B\Apoproteins
C\Apolipoproteins

2\ Which one of the following has the Lowest density?
A\Very low density Lipoprotein (VLDL)
B\Low density Lipoprotein (LDL)
C\High density Lipoprotein (HDL)
D\Chylomicrons

3\ Which one of the following has the Largest size?
A\Very low density Lipoprotein (VLDL)
B\Low density Lipoprotein (LDL)
C\High density Lipoprotein (HDL)
D\Chylomicrons

4\which one of the following is Assembled and secreted by the liver?
A\Very low density Lipoprotein (VLDL)
B\Low density Lipoprotein (LDL)
C\High density Lipoprotein (HDL)
D\Chylomicrons

5\Which one of the following Requires ApoC-II for activation?
A\Lipoproteins
B\Lipoprotein lipase
C\Very Low Density Lipoproteins VLDLs

Videos

https://www.youtube.com/watch?v=Yanklj65zjs

Answers:

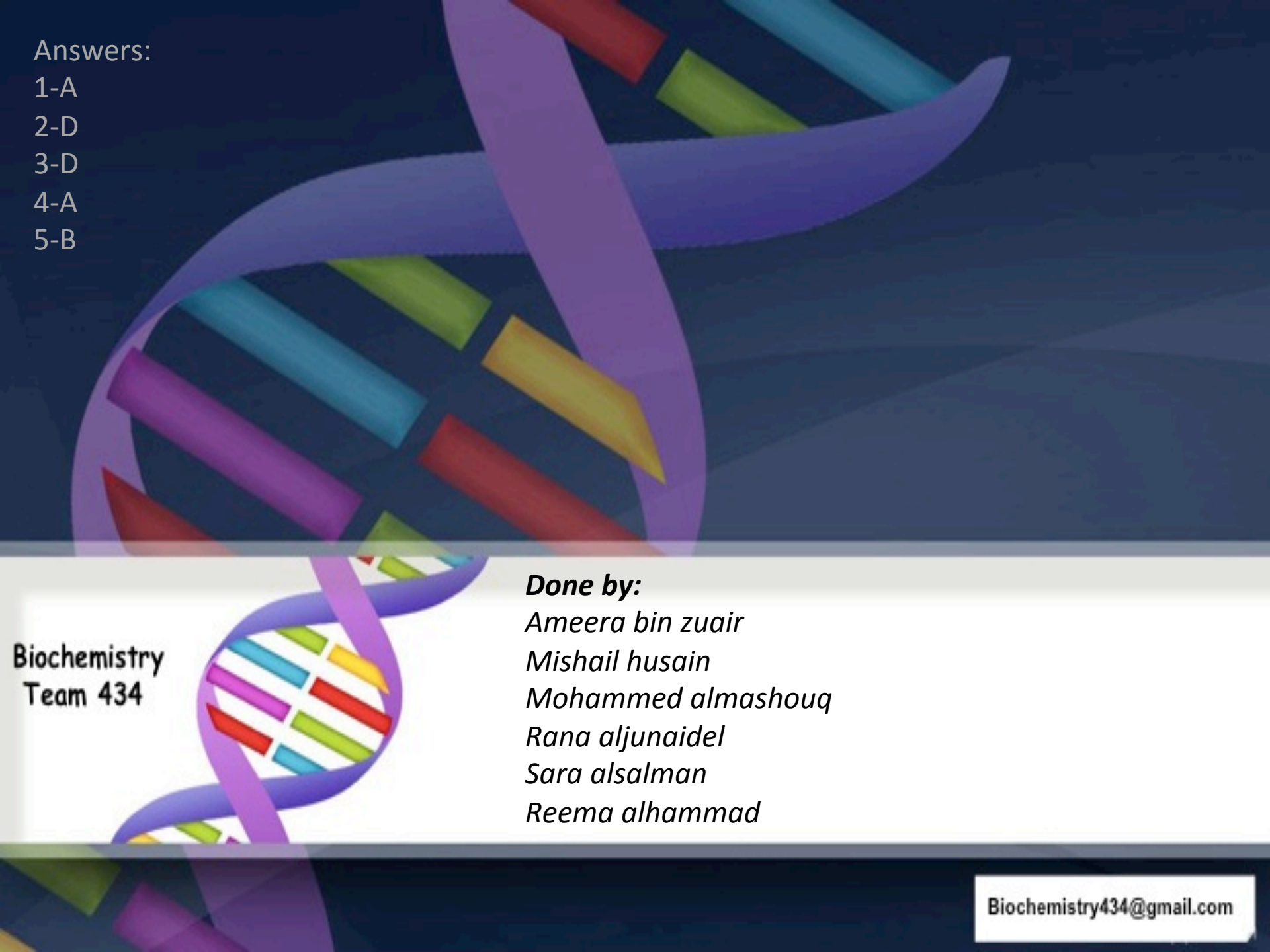
1-A

2-D

3-D

4-A

5-B



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