2014 2020
Medical Committee
The University Of Jordan

Biochemistry 2

◉ Sheet ○ Slides

Number: 16

Done by: Mohammed Karajeh

Corrected by: Jawad Al Masarweh

Subject: Slides 5

Doctor: Dr.Fasial

14/6/2015

in the last lecture we talked about regulation of fatty acid synthesis and oxidation and we said the oxidation is regulated by :

1) **the availability of fatty acid** when the blood glucose is low , the glucagon is high and stimulate the hydrolysis of TAG in the adipose tissue , thus fatty acid(FA) concentration in plasma increase and so on.

2) **The availability of NADH** if NADH levels are high this indicate high energy level in the cell so this will inhibit the oxidation because one of the step require NAD+

3) **the malonyl CoA** which is produced during fatty acid synthesis and indicate that fatty acid synthesis is active so it inhibit the entrance of fatty acyl CoA into mitochondria by joining it to carnitine (thus without entrance they will be no fatty acid oxidation)

Note: malonyl co is produced from acetyl CoA by ACC (acetyl CoA Carboxylase)

So if we want to increase FA (Fatty Acid) oxidation we should inhibit ACC, thus no more malonyl CoA will be produced so not more inhibition of oxidation at carnitine level →More FA oxidation. This inhibitor will be useful as anti-obesity drug (such drug doesn't not exists yet).

Elongation of fatty acid

Fatty acid is synthesized up to 16 carbons by fatty acid synthase(in the mitochondria) .

Elongation of FA More than 16 carbons is done only in ER. Using similar reactions but different enzymes.

The sequence of the reaction is as usual →acetyl CoA + malonyl CoA together in ER produce acyl CoA by several steps include using of 2NADPH , the purpose is to produce fatty acid longer than 16 carbons

Note: the fate of short chains of FA(about 6-8 Carbons , they are obtained from milk ,dairy products , butter..) is either <u>get used</u> or <u>elongation.</u>

In the mitochondria similar reaction to the oxidation but it in the reverse direction except for the step that use FAD (FA acyl dehydrogenase).

Note: elongation requires NADPH as electrons donor

Introduction of double bonds

A) Synthesis of monounsaturated fatty acid (e.g. oleic acid and palmitoleic acid)

Occurs In ER, but note that humans can't introduce a Double bond beyond carbon 9(usually the double bond is at carbon 9)

Take stearic acid (18 carbon saturated) can be converted into oleic acid (must be active→bound to acetyl CoA).

Two oxgyen atoms (O2) are needed .since 2 H+ will be removed only one oxgyen will be used to make H2O leaving us with a reactive oxgyen specie→ so a NAPDH will be used to donate 2 more H+ that will be accepted by that oxgyen atom giving another H2O.

These enzyme called delta 9 desaturase:cytochrome b 5 , the cytochrome is involve in the transfer electron from NADPH to oxygen .

Δ 9 desaturase can introduce double bond at carbon 9

formation and modification of polyunsaturated fatty acid

by elongation and desaturation

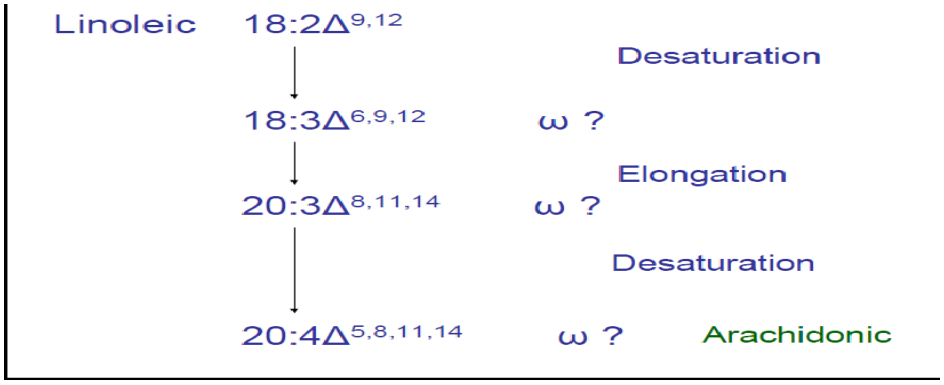
additional double bonds can be introduced by :

-delta 4 deasaturase

-delta 5 desaturase

-delta 6 desaturase

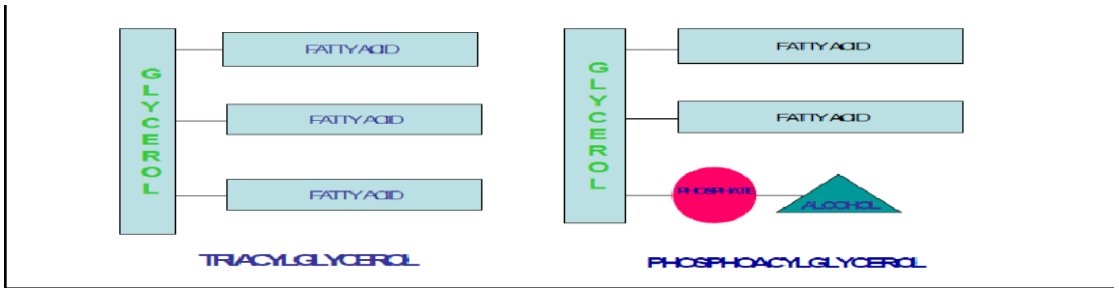
Note that between each double bond and another there should be CH2 thus if there is a double bond at carbon 9 , we can introduce another one at Carbon 6



As in the previous example we deduce that its an essential FA since body cant form a double bond at C12 also we note that addition of double bonds doesn't affect omega naming (all of them are omega6).

Arachidonic Acid is very important for inflammation ,it can be synthised from an essential FA thus its semi-essent

Biosynthesis of TAG and phosphoacylglycerol



-synthised at Liver and adipocytes to deal with excess carbs , note that they are only stored in adipocytes .

TriAcylGlycerol are made of 3FA and glycerol while Phosphoacylglycerol is made of 2FA, actived alcohol(phosphate+alcohol) and glycerol

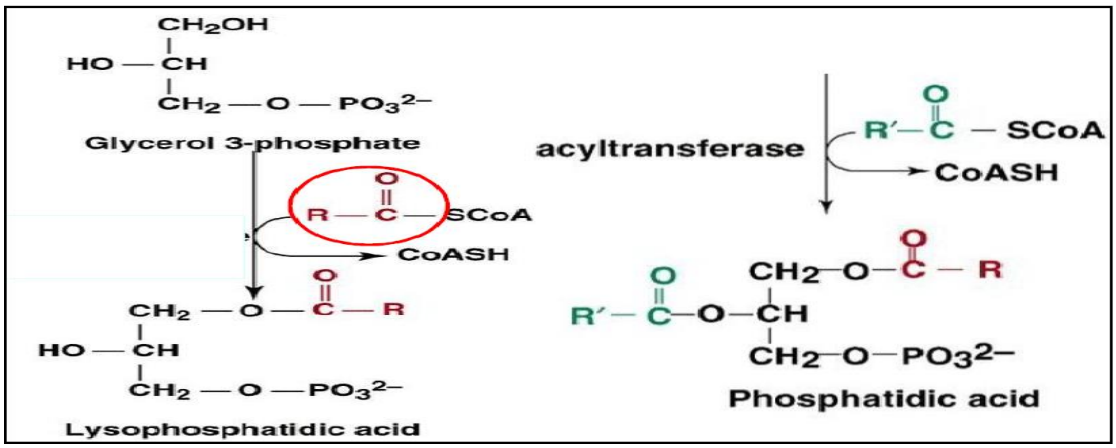
phosphotadic acid is common intermediate in synthesis of TAG and phosphpacylglycerol , its made of 2FA,phosphate and glvcerol

biosynthesis of TAG require :

1) FA Acyl CoA (active form of FA)
2) Glycerol 3 phosphate

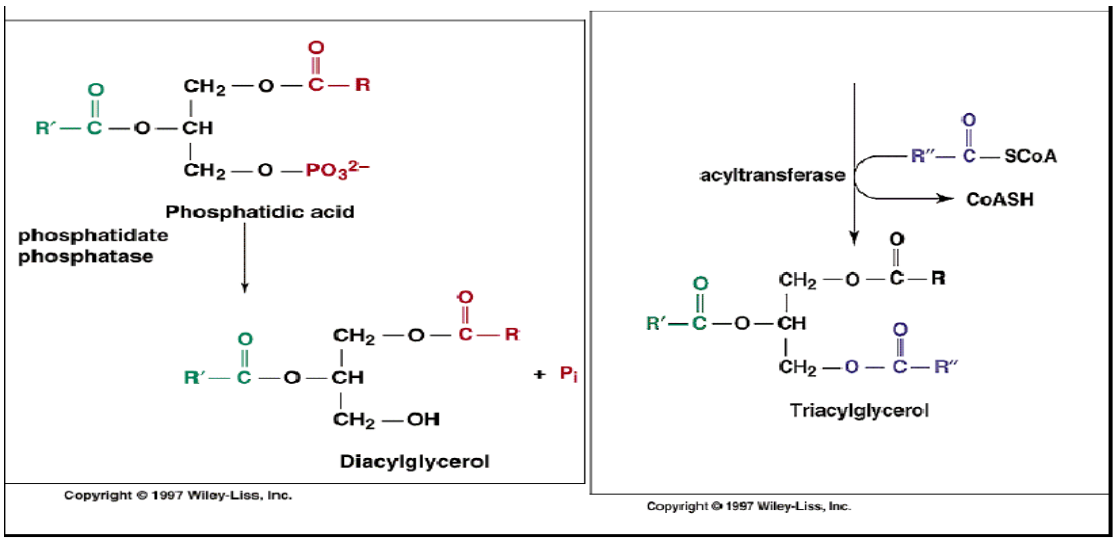
Notice that the reaction : TAG +H2O → DAG + FA have delta G is negative since hydrolysis reactions are Always exergonic.

The reverse reaction : DAG + FA→ TAG have postive delta G so must be coupled to acyl CoA to become negative(overall) .



The FA acyl CoA will be added by Acyltransferase at C1 forming lysophosphatidic acid.

Then using acyltransferase another acyl group will be transferred to carbon 2 forming phosphatidic acid.



The next step is removing phosphate group by phosphatidate phosphatase . Forming DAG(DiacylGlycerol) .and eventually another acyl transferase will change it into TAG.

Glycerol 3phosphate can be obtained by:

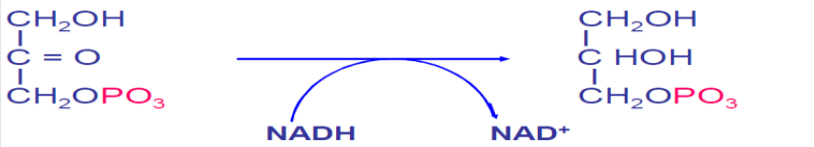
1) Glycerol kinase enzyme that is found only at the liver
2) DHAP(dihydroxyacetone phosphate) will be changed to glycerol 3 phosphate by DHAP dehydrogenase(this require NADH as H donor)→ occur at BOTH liver and adipocyte.

Production of Glycerol Phosphate

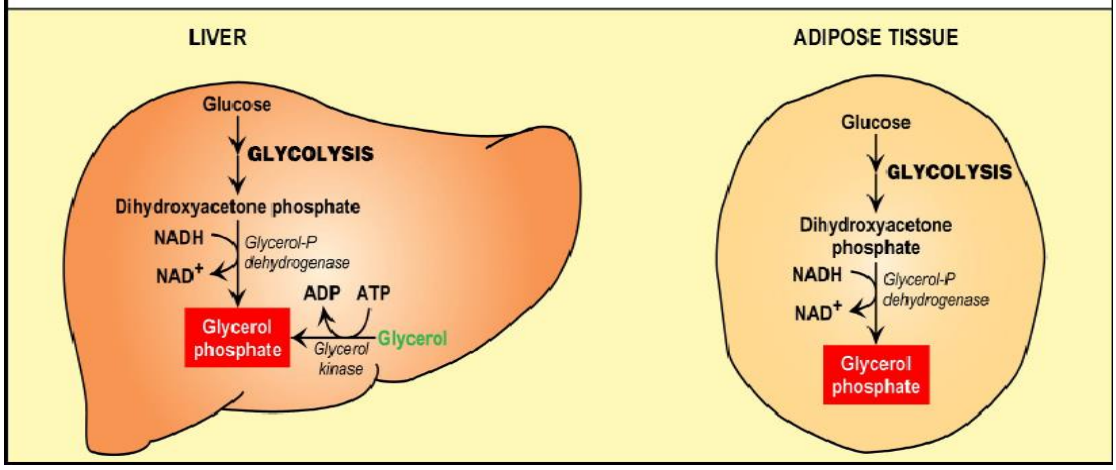
- Glycerol + ATP ----→ Glycerol 3 Phosphate

Enz: Glycerol Kinase

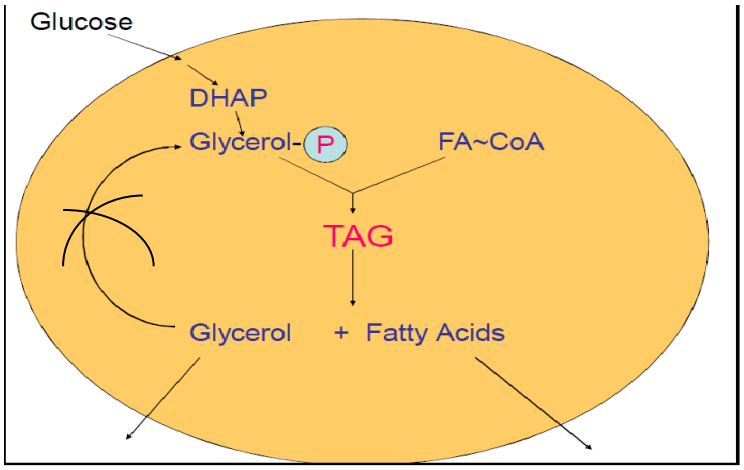
Not in Adipose tissue



Production of Glycerol Phosphate



Note that DHAP is intermediate in glycolysis .



90% of the volume of adipocyte is TAG droplets

When fatty acid is required by the action of glucagon and epinephrine , TAG is hydrolyzed to fatty acid and glycerol , and they are transported to the blood to reach different cells (for energy production)

The Synthesis on the other hand, it require glycerol phosphate and FA acyl CoA, if the glycerol kinase present in the adipocyte it will

phosphorlyte the produced glycerol (the synthesis and degradation in this case will proceed at the same time→ futile cycle) this process will require 1 ATP and activation of 3 FA will require 6 ATP thus we lose 7 ATP. That why glycerol kinase is not found in adipocytes, to prevent this wasted cycle.

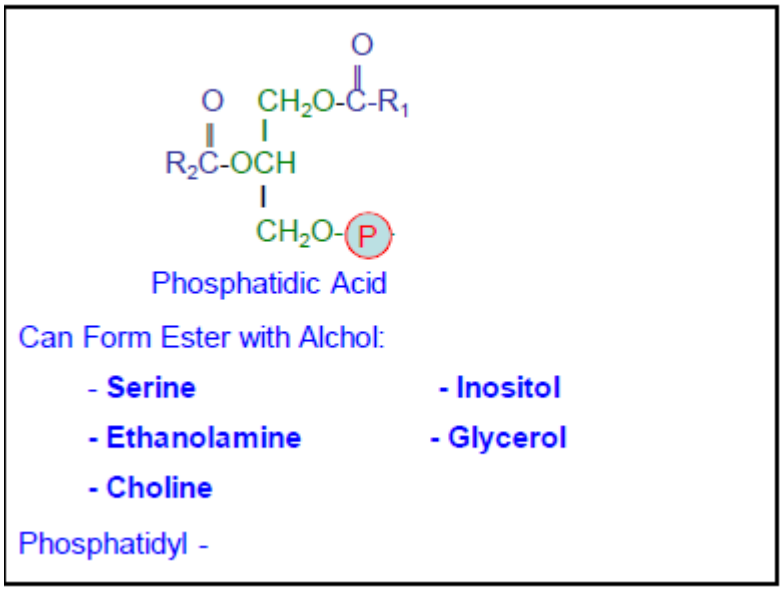
Remember that DHAP is obtained from glucose (by glucolysis) . this glucose enter Adipocyte through GLUT4(insulin dependent) so more insulin leads to more GLUT4 induction thus more glucose get in so more TAG synthesis.

The person who has a diabetes(low insulin) will complain loss of weight because the synthesis of TAG is impaired due to decrease in insulin level so the degradation occur but the synthesis don't.

The synthesis of phosphoacylglycerol (CH.17)

Also known as phosphoglyceride or glycerophospholipid

We already mentioned that the common compound in the synthesis is phosphatidic acid

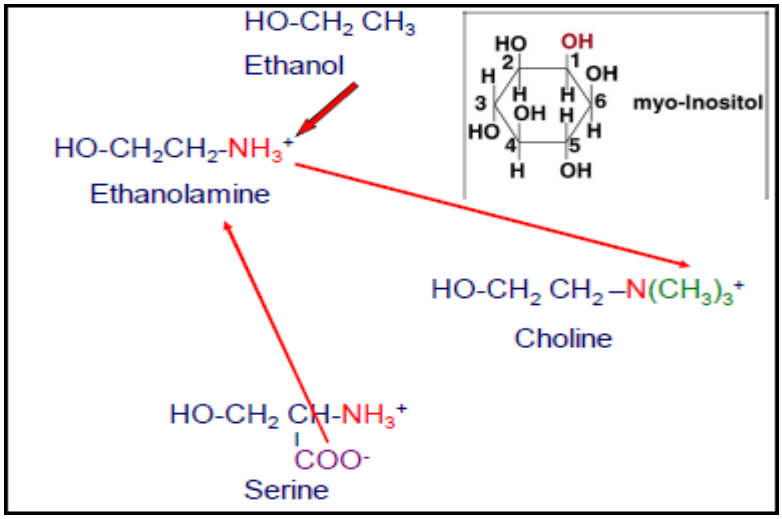


phosphatidic acid can form ester with alcohol like serine , ethanolamine ,choline and inositol /glycerol

note that:serine ,ethanolamine and choline are <u>amino alcohol</u>

the phosphatidic will form phosphatidyl-alcohol when linked to alcohol

you should know the structure of these alcohol :



The arrows show the relationships only <u>not</u> how they are synthesized.

Choline is quaternary amine

The amines always contain positive charge (basic group).

Inositol is look like the sugar but it is not a sugar, it contain 6 carbons with 6 alcohol groups (6 hydroxyl groups).

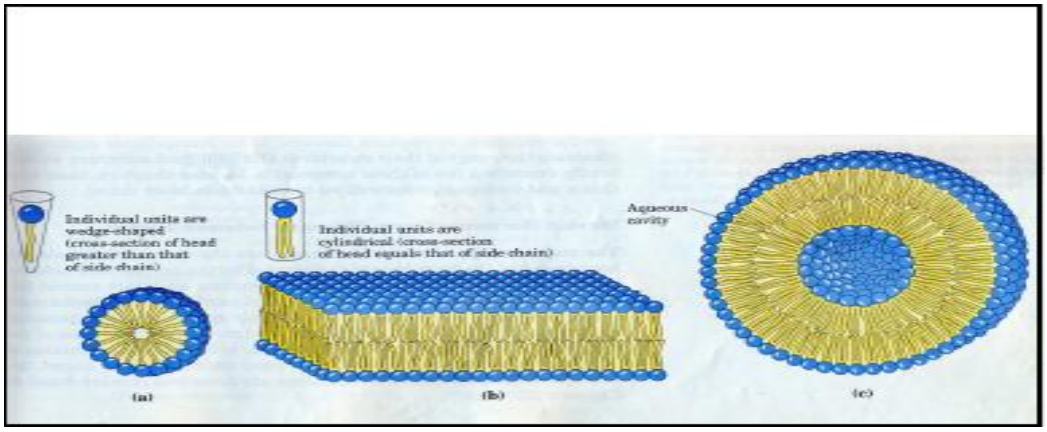
the phosphatidyl choline

Commonly known as <u>lecithin</u>

It has long hydrocarbon chain (FA→ R1, R2) with negatively charge phosphate and positively charge quaternary amine so this molecule is amphipathic (has hydrophobic and hydrophilic part)

The hydrophilic part comes from the charges on both (P- and N+) and the hydrophobic part by long FA

Note that it can form A micelle .



The micelle has hydrophilic surface and hydrophobic tails (the internal environment).

If you add phosphatidyl choline to a mixture of water and oil and you shake them very well , the oil will set into the micelles (hydrophobic environment) so the oil will be mixed with water ,this process called solubilization to solubilize oil or to form emulsion, aslo called emulsifying agent

phosphatidyl choline is found in milk powder and in chocolate bar in order to facilitate fat and water mixing .