Chapter 16 :

**Lipids** are group of substances, the common feature between them is that they are insoluble in water and soluble in organic solvents.

**Triacylgycerol :** Three fatty acids (called acyl groups) attached by **ester bond** to glycerol .

**Fatty acids** : long hydrocarbon chain which ends with “COOH” and that’s why they **are poorly soluble** **in water** (no groups are available to interact with water)

**Pka** is the Ph where 50% of the molecules are dissociated .

Pka for carboxyl group “COOH” is 4.8 , **If Ph is above Pka the acid will be in the anionic form “COO-“** so at Ph 7 fatty acids will be in the anionic form .

**Anionic form is**:

A little bit **more soluble** than the protonated form .

**For counting carbon atoms** in the fatty acid I usually **begin from the “COOH” group and give this C number 1**

**Another way :**

By using Greek letters.

 **“alpha” carbon** is the first carbon in **the hydro carbon** chain “its number is 2”

The next one is called **“beta”** “it is number 3”

 The last carbon regardless the number of carbon atoms in the hydrocarbon chain is known as **“omega”** (because it is the last letter in Greek letters ).

**To locate the place of the double bond** “If present” we should use the number of the **first** carbon that contributes to this double bond (example : double bond between carbon 9 and 10 … I only mention number 9) .

linoleic acid can be called “omega 6 fatty acid” (because the first double bond is number six **from the end of the chain**.)
 linoleic acid

Bonds in fatty acids are **non-conjugated** (separated by CH2 “mythel group” )

**Conjugated double bond** : Double-single-double-single and so on .

Note : You should memorize the marked fatty acids in the slides ☺

-The common name of fatty acids comes from the **sources which they have been isolated from
Butaric acid** : from butter
**Oleic acid** : from olives
**Palmatic acid** : from palm tree
**Linoleic and linolenic acids** : are taken from linen
**Arachidonic acid** : from peanuts

**Triacylglycerol** is the **major** energy reserve in the body in the form of fat .

**Its more efficient to store energy in the form of triacyglycerol rather than carbohydrates**
Why ?
 1-Fat is more reduced “no oxygen in the chain” so:
 when fat is oxidized it can generate more energy (9 kilocalorie / gram ) where as carbohydrates only produce 4 kilocalorie/ gram.

Note: you should memorize the previous numbers ☺

2- Fat is hydrophobic and will not absorb water if present inside the cell (60% of the cell is water)
whereas **every gram of carbohydrate will absorb 2 grams of water** .

-Adult’s body has 10 kilograms of fat so it can produce 90000 kilocalorie
 we need 2000 kilocalories per day (so we can stay 45 days using energy stored in our body)

To have the same amount of energy “90000 kilocalorie” but from carbohydrates we need 22.5 kilograms
to produce this amount of energy (and 45 kilo grams of water -since each 1 gram of carbohydrates absorb 2 grams of water- )
so I need **67 kilograms of carbohydrate and water to store the same amount of energy that fat does with 10 kilograms**
-Fat is the **major fuel used by tissues** (whereas the major circulating fuel is glucose)
“In 12 hours 540 kilocalories of fatty acids are used by our tissues ,,,but fatty acids in blood only give 3 kilocalories so:

 **fatty acids must be regenerated continuously in the blood throughout the 12 hours “high turnover rate”**

When compared to glucose in 12 hours our body consume 280 kilocalories from glucose
whereas glucose present in blood only gives 80 kilocalories so it also regenerate throughout the 12 hours but the **turnover rate is low “lower than fat**”

So we use fat continuously “**not only when needed”** and it is not a static reserve.

Adipose tissue stores the fat for other tissues to use it and there should be **a hormonal signal** to tell the adipose tissue that there are tissues in the body need fat /energy.

 Triacylglycerol can’t leave the cell as it is it must be **hydrolyzed** and it gives 3 fatty acids and glycerol
**“this reaction needs lipase enzyme”**

when lipase is activated by hormones like “glucagon , epinephrine , norepinerhrine , ACTH” **we call them hormone sensitive lipase “stimulated by lipase**”.

**Glucagon** is secreted when there is hypoglycemia so the body will use fat instead of glucose.
**Epinephrine and norepinephrine and ACTH** are secreted when there is stress .

Hormones don’t enter the cell they bind to a cell surface receptor on the membrane then adenylyl cyclase is stimulated which convert ATP to cAMP which activates protein kinase which **add phosohate** **group to hormone sensitive lipase which** **converts to its active form**.
Then active lipase will act on triacylglycerol and convert it to diacylglycerol then other or the same enzymes act on diacylglycerol to convert it to monoacylglycerol , then glycerol **“which is very hydrophilic-very soluble in water”** is carried to the liver then in liver

 A phosphate group is added on glycerol by **“glycerol kinase”**
then oxidation of glycerol phosphate “on the middle carbon” gives dihydroxyacetone phosphate
“which is intermediate in glycolysis and gluconeogenesis” but it will go in gluconeogenesis pathway because there is hypoglycemia (High levels of glucagon) .

Fatty acids are transported by **albumin** because they’re insoluble in water ,then degraded by oxidation at beta carbon “on carbon number 3” “beta oxidation” , then cleavage of two carbon units.

**Beta oxidation** :

**1- activation of fatty acid :** joining a fatty acid with coenzyme A then acyl coA will be formed (high energy bond will be formed-thioester bond-), so we need ATP (cleavage happens between phosphate number 1 and 2).

 The reaction is reversible because one high energy bond will be degraded and one high energy bond will be formed .

but we need it to be irreversible so there is an enzyme which degrade the remaining bond between the two phosphate groups “so overall I cleave two high energy bonds and synthesize one so the reaction will be irreversible” and the final product of ATP is AMP + two phosphate groups .
Then AMP will react with ATP to give two ADP molecules .

In general if you continuously remove products from the reaction this means that you’re making it irreversible

**So if the doctor asked how many ATP molecules are consumed in this step the answer is 2 (but how many ATP molecules did the enzyme catalyze the answer is 1)**

Short and medium fatty acid chains can be activated within mitochondrial matrix because they can penetrate the membrane “like butyric acid”.

**2- transport of long chains of fatty acids across mitochondrial membrane: (14<)**
inner mitochondrial membrane is impermeable for acyl coA ,so **carrier is required (carnitine shuttle**) :

fatty acyl coA easily penetrates the outer mitochondrial membrane , after penetrating, acyl group will be transferred from coA to carnitine and form acylcarnitine **via transferase enzyme CPT**
acylcarnitine then can be transported via proteins across the inner membrane then it reconverts to acyl coA using **transferase** “different from the previous enzyme” …. The resultant carnitine goes back to the inter mitochondrial space.

**3- Then for fatty acid oxidation:** two hydrogen atoms are removed from the fatty acid (by **dehydrogenase**) to FAD to produce FADH2 .. a double bond is introduced … water will be added to the compound “enol coA” (by **hydratase** enzyme) and the compound will be converted to alcohol on carbon number three **“markovnikov's rule is not applied because an enzyme will lead the reaction and it’s specific to add the OH group to carbon 3” beta hydroxyacyl coA will result”.**

Oxidation hydroxyl group into ketone group (by **dehydrogenase enzyme** ) “ketoacyl coA will result” NAD+ is converted to NADH in this reaction .

The first reaction **FAD was used** because the two hydrogen atoms **are adjacent to each other** , whereas NAD+ was used in the second reaction . **“redox potential has an effect on these reactions”**

If the cleavage happens **by water** the coA will detach and the fatty acid will be inactive again **“by enzyme hydrolase”** .
but since cleavage doesn’t happen by water the fatty acid is already activated “ **by enzyme thiolase**”

**\*\*The first activation is done once and 2 ATP are consumed once .**

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