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Subject: Final Exam - Chapter Twenty One

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Lipid Metabolism

☒ Introduction

- Lipids are broken down to **acetyl-CoA** and then enter the citric acid cycle, to be broken down to CO_2. The NADH and $FADH_2$ that were released are then used to produce ATP through the Electron Transport Chain **(ETC)**. This is called the **catabolism of lipids** and it **releases** large quantities of **energy**.
- In **lipid anabolism**, lipid synthesis begins when acetyl-CoA molecules join to form a long fatty acid chain. It represents an efficient way of **storing chemical energy**.
- **If** both anabolism and catabolism were to operate at the same place and through the same mechanism in the cell, then there would be **no net gain or loss of lipids**.
- The cell controls lipid synthesis and breakdown through different pathways, the following are the **main differences** between lipid synthesis and breakdown:

1. **Synthesis** takes place in the **cytosol,** whereas **catabolism** takes place in the **mitochondrion**.

مستمرون بالعطاء

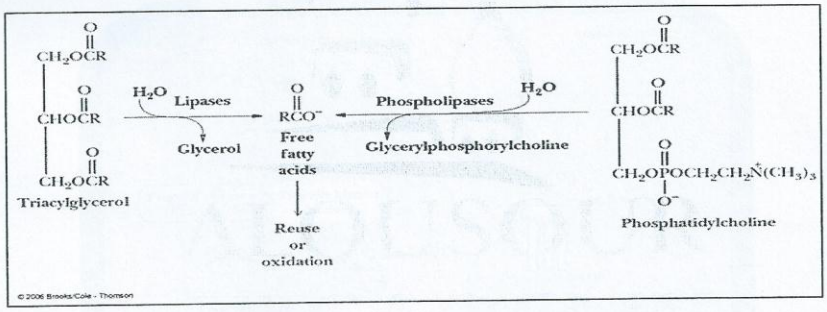
2. **NADPH** is the reducing agent in **lipid synthesis**, whereas **FAD** and **NAD^+** are the oxidizing agents in lipid **catabolism**.

3. Different activating ligands are used (for example, **CoA** is used in **catabolism**, whereas the **acyl carrier protein** (ACP) is used in **anabolism**).

☒ Lipid Catabolism

- For lipids to be used as a source of energy it has to enter the citric acid cycle. Lipids enter the cycle in the form of acetyl-CoA. The process of converting long chain fatty acids to acetyl-CoA is called **β-oxidation**.

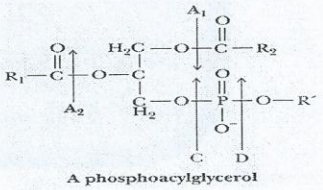
- In the human body lipid types that can be converted to acetyl-CoA (lipid types that can be used as energy sources) are **Triacylglycerols** and **Phosphoacylglycerols**. On the contrary, **sterols** [steroids that have a hydroxyl group as part of their structure] cannot be converted to acetyl-CoA and hence cannot be used to produce energy but are excreted.



- The first step for triacylglycerol and phospholipid to be converted to acetyl-CoA is to extract the fatty acids from the glycerol molecule, this is done by enzymes termed ***lipases*** for triacylglycerols and ***phospholipases*** for phospholipids.

- There are several types of phospholipases depending on the site at which they hydrolyze phospholipids. These enzymes are A1, A2, C, and D.

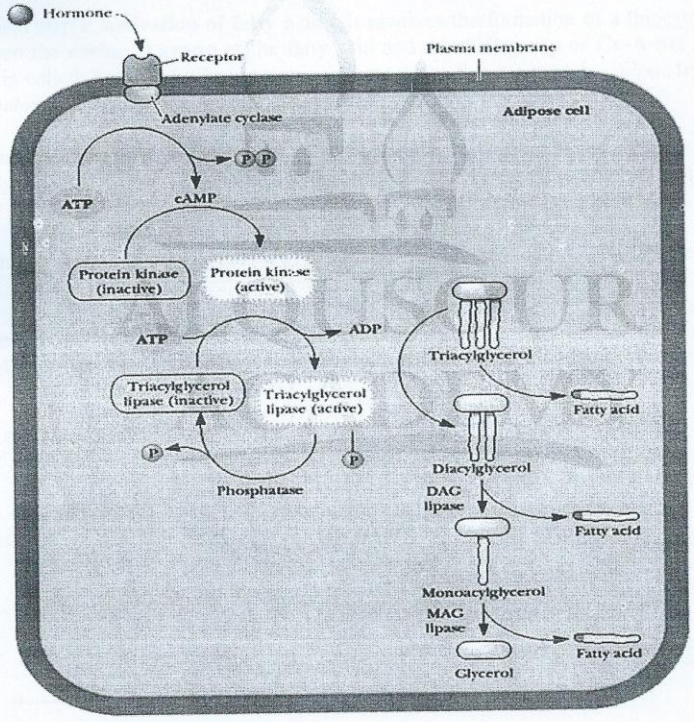
1. ***Phospholipase A_2***, this enzyme is widely distributed in nature; it mainly functions in the hydrolysis of phospholipids at the surface of the micelles. The site of action of phospholipase A2 is the B site.



2. ***Phospholipase D*** occurs in spider venoms and is responsible for the tissue damage that accompanies spider bites. Snake venoms also contain phospholipases, the lipid products of hydrolysis lyse RBCs preventing clot formation, so victims bleed to death in this situation.

- The phospholipases Conc. is relatively high in the venoms than the conc. of the toxin itself.

- The body controls the release of fatty acids from triacylglycerols in adipocytes through different hormones, these hormones bind to a receptor which activates **adenylate cyclase**, this leads to the production of **cAMP-dependent protein kinase (Protein Kinase A)**, and this kinase **phosphorylates triacylglycerols lipase** which cleaves the fatty acids from the glycerol backbone



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- The main hormone that has this effect is **epinephrine**, but **caffeine** can mimic epinephrine and activate this pathway.

Q: Why competitive runners often drink caffeine the morning of the race?

A: Because they want to burn fat more efficiently to spare their carbohydrate stores for later stages of the race.

☒ **Catabolism of lipids follows the following steps:**

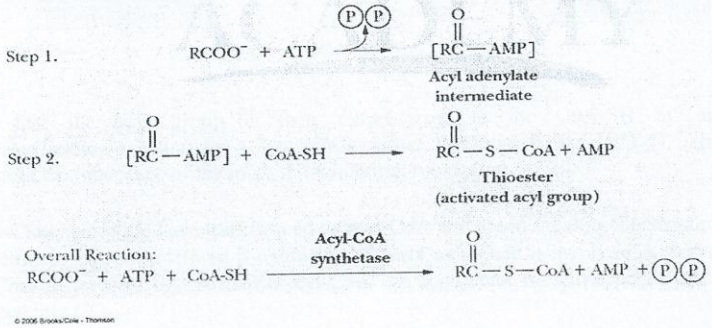
1. Fatty acids are released from triacylglycerols and phospholipids by the action of **lipases** and **phospholipases,** as described by the previously.

2. The next step is **activation of fatty acids**. It involves the formation of a thioester bond between the **carboxyl group** of the fatty acid and the thiol group of **Co-A-SH** to give what is called **Acyl-CoA**. The enzyme that catalyzes this reaction is called ***Acyl-CoA Synthetase***.

- This enzyme uses **ATP** as a source of energy to derive the reaction, in which case ATP is hydrolyzed to AMP and PP_i (Pyrophosphate) which is then cleaved to 2 P_i molecules. The energy released from the hydrolysis of ATP is then used to derive the reaction.

- This energy released (the conversion of ATP to AMP) is equivalent to 2 ATP molecules.

- This reaction occurs in the **cytosol**, whereas the remainder of the steps occurs in the **mitochondria**. This reaction is actually composed of 2 steps, and involves the formation of an **Acyl adenylate** intermediate, this is summarized by the following equations:



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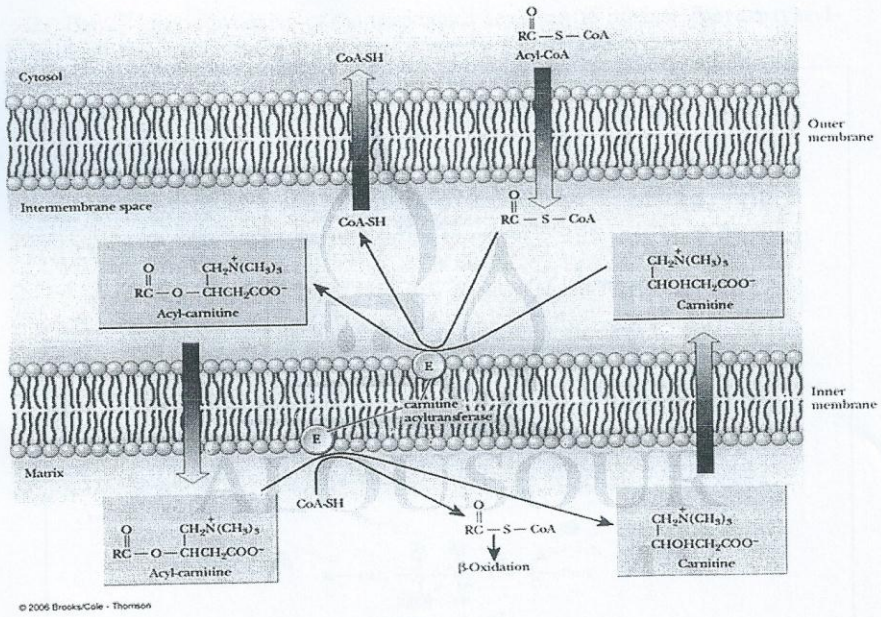
3. The 3rd step is transesterification. The acyl-CoA can cross the outer mitochondrial membrane but not the inner one, so an enzyme called **Carnitine Acyltransferase** located in the inner membrane (also called **Carnitine Palmitoyltransferase, CPT-I,** because of its specificity to acyl groups between 14 and 18 carbon atoms) transfers the acyl group from the acyl-CoA to **carnitine** to become **Acyl-carnitine** which then enters the inner membrane via a specific transporter called carnitine translocase.



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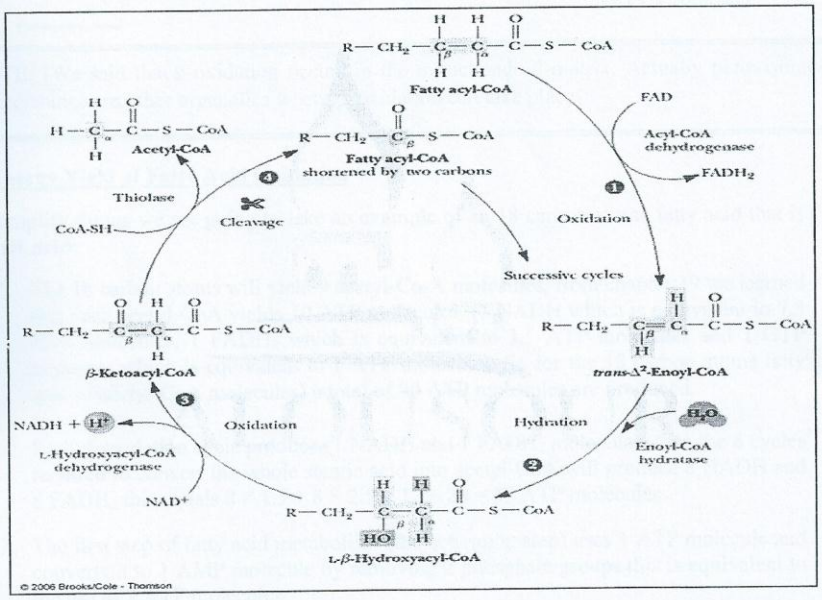
- After that the acyl group is then retransferred to the CoA-SH by another transesterification reaction by a second **Carnitine Acyltransferase CPT-II**, which is present in the inner face of the inner mitochondrial membrane.

- By now fatty acids are have transformed to acyl-CoA and are in the mitochondrial matrix, the following steps are termed **β-oxidation of fatty acids** and it involve the cleavage of acyl-CoA to Acetyl-CoA; so that acetyl-CoA can then enter the citric acid cycle to be oxidized into CO_2.

☒ Steps of β-oxidation:

1. The **Acyl-CoA** is oxidized to a **α, β unsaturated acyl-CoA** (also called β-enoyl-CoA); the product has the trans arrangement at the double bond. The reaction involves the reduction of FAD to $FADH_2$. The reaction is catalyzed by the enzyme **Acyl-CoA Dehydrogenase;** this is a FAD dependent enzyme.

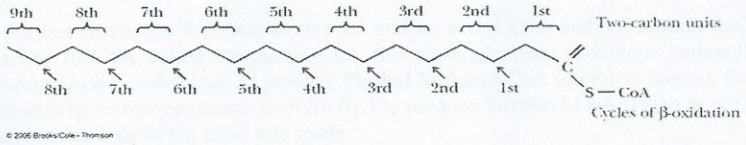
2. The 2nd step is hydration of the unsaturated acyl-CoA to produce **β-hydroxyacyl-CoA**; this is catalyzed by the enzyme ***Enoyl-CoA Hydratase***.



3. The 3rd step is a second oxidation reaction to produce **β-ketoacyl-CoA**, and the enzyme of this reaction is called **β-hydroxyacyl-CoA Dehydrogenase**. This enzyme uses NAD^+ as an oxidizing agent.

4. In the 4th step **β-ketoacyl-CoA** is cleaved into an **Acetyl-CoA** and an **Acyl-CoA** that is 2 carbon atoms shorter than the original molecule that entered the β-oxidation cycle. Here a molecule of CoA is required for the reaction to form the new thioester bond in the smaller acyl-CoA molecule. The enzyme that does this step is called ***Thiolase***.

- From the previous discussion one can calculate that a fatty acid composed of 18 carbon atoms will yield 9 acetyl-CoA molecules, also you should notice that the number of times the cycle should go for this fatty acid is 8 not 9 because the last cycle will yield the 2 acetyl-CoA molecules.



NOTE: [We said that β-oxidation occurs in the mitochondrial matrix. Actually peroxisomes and glyoxysomes are other organelles where β-oxidation can take place]

☒ Energy Yield of Fatty Acid Oxidation

To simplify things we are going to take an example of an 18 carbon atoms fatty acid that is **stearic acid**:

1. The 18 carbon atoms will yield 9 acetyl-Co-A molecules, from chapter 19 we learned that each acetyl-CoA yields 10 ATP molecules. (3 NADH which is equivalent to 7.5 ATP molecules, 1 $FADH_2$ which is equivalent to 1.5 ATP molecules and 1 GTP molecule which is equivalent to 1 ATP molecule). So for the 18 carbon atoms fatty acid (9 acetyl-CoA molecules) a total of 90 ATP molecules are produced.

2. Each β-oxidation cycle produces 1 NADH and 1 $FADH_2$ molecules, then the 8 cycles required to convert the whole stearic acid into acetyl-CoA will produce 8 NADH and 8 $FADH_2$ this equals $8 \times 1.5 + 8 \times 2.5 = 12 + 20 = 32$ ATP molecules.

3. The first step of fatty acid metabolism (the activation step) uses 1 ATP molecule and converts it to 1 AMP molecule by removing 2 phosphate groups this is equivalent to the use of 2 ATP molecules.

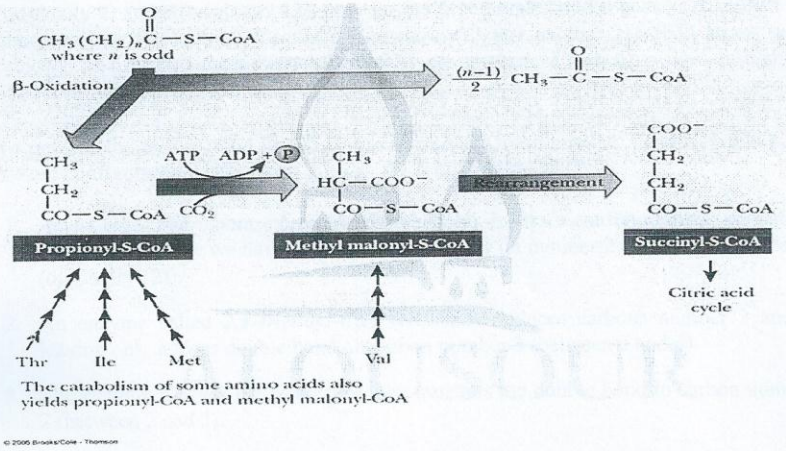
4. The overall energy yield is: $90 + 32 - 2 = 120$ ATP molecules from the 18 carbon atoms fatty acid.

NOTE: [The energy yield of the same number of carbon atoms from carbohydrates, that is 3 glucose molecules is $3 \times 32 = 96$ ATP molecules so the energy yield of lipid metabolism is higher].

NOTE: [Both carbohydrate and lipid catabolism involves the production of water through the citric acid cycle; this water is called metabolic water. This process can be a source of water to organism lives in desert such as Camel and Kangaroo rats].

☒ Catabolism of Odd-Carbon Fatty Acids:

- When a fatty acid containing an odd number of carbon atoms is to be oxidized it enters the β-oxidation cycle as regular, and then it proceeds as usual until the last round of the cycle.
- In the last reaction a 5 carbon is cleaved into an acetyl-CoA and a 3 carbon molecule attached to CoA called **Propionyl-CoA** this molecule then undergoes carboxylation (***propionyl-coA carboxlase***) to produce **Methyl Malonyl-CoA** (4 carbon atoms), this one then undergoes rearrangement (require B_{12}) to produce **Succinyl-CoA** which as we know is an intermediate of the citric acid cycle.



☒ Catabolism of Unsaturated Fatty Acids

- This can be divided into **monounsaturated** and **polyunsaturated** fatty acids. In **monounsaturated** fatty acids like oleic acid (oleoyl-CoA) which has a double bond at number 9 carbons. In this case the fatty acid enters the cycles of β-oxidation as usual and goes for 3 cycles, which cleaves 6 carbon atoms, leaving a 12 carbon acyl-CoA, on which the double bond is on carbon number 3 now (*cis*-Δ3-dodecenoyl-CoA).
- As you can recall that the first step of the β-oxidation cycle involves the formation of a *trans* double bond on carbon number 2 of the acyl-CoA.

- Because there is already a double bond on **carbon number 3**, then there is a need to change its position from carbon **#3** to carbon **#2**, and its configuration from *cis* to *trans*; (recall that most naturally occurring double bonds are in a *cis* configuration), this step is done by an enzyme called ***Enoyl-CoA isomeraze.*** After that the cycle continues as usual.

- In the case of **polyunsaturated fatty acids** the story is somewhat different. Let's take an example of linoleic acid which is composed of 18 carbon atoms and contains double bonds at both the 9^{th} and the 12^{th} carbon atoms, here again β-oxidation will start and continue till 3 cycles have passed (6 carbons have been removed).

- After that we have an acyl-CoA that contains 2 double bonds at carbon number 3 (originally 9) and 6 (originally 12), now for the first double bond it goes as described for oleic acid (by the enzyme ***Enoyl-CoA isomerase***). Here another 2 carbon atoms were removed and the last double bond (originally on number 12 then 6) is now on number 4and it is in a *cis* configuration.

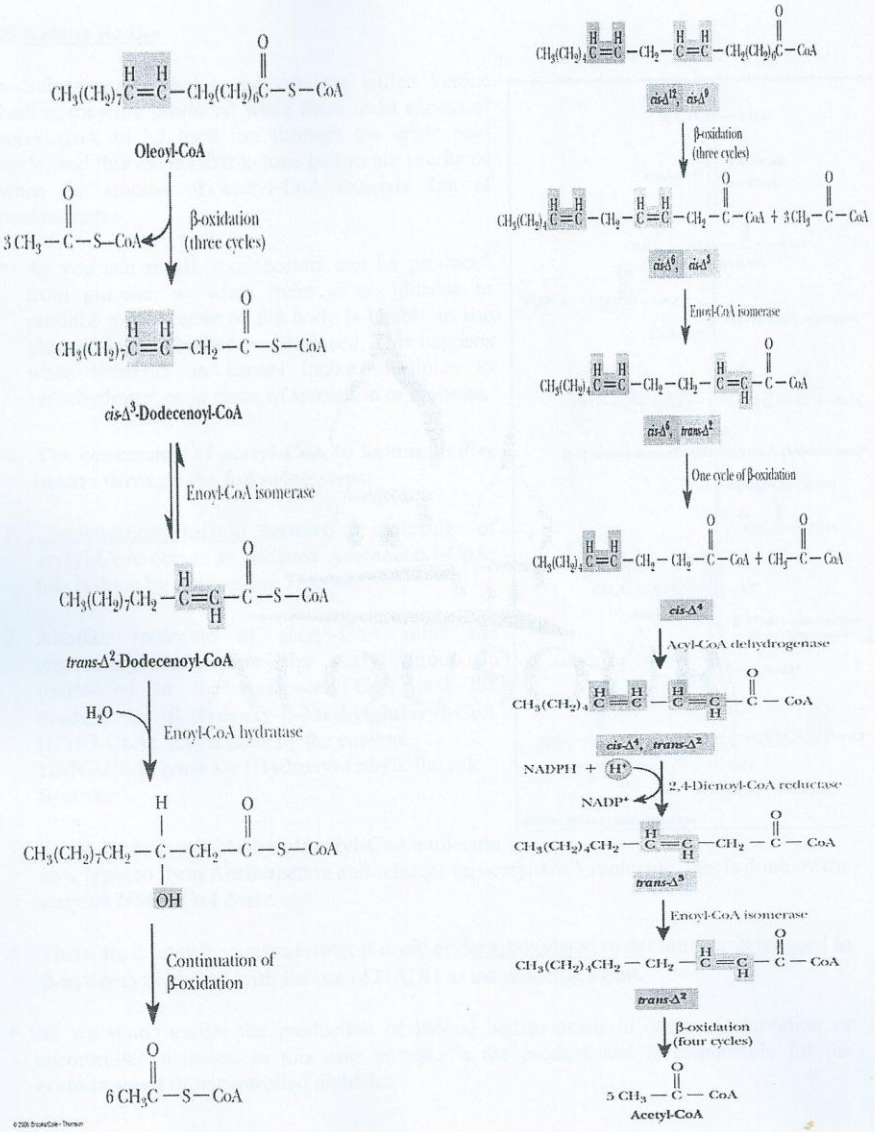
- To proceed the double bond should be transferred to carbon number 2 and it should be in a *trans* configuration, this is done through the following steps:

  1. ***Acyl-CoA dehydrogenase*** creates a double bond in a trans configurationon on carbon number 2, so now we have 2 double bonds (*trans* on number 2, and *cis* on number 4 (originally 12)).
  2. An enzyme called ***2,4-Dienoyl-CoA Reductase*** reduces carbons number 2 and 5 leaving only a *trans* double bond on carbon number 3 (between 3 and 4).
  3. The enzyme ***Enoyl-CoA isomerase*** then transfers the double bond to carbon number 2 (between 2 and 3).
  4. The oxidation process then proceeds as usual.

NOTE: [the acyl-CoA with 2 double bonds close together is a poor substrate for the enzyme Enoyl-CoA Hydratase, and hence the other double bond has to be removed to that the reaction can continue].

NOTE: [the oxidation of unsaturated fatty acids doesn't generate as many ATPs as it would for saturated fatty acid with the same number of carbons]. **WHY?!**

Answer: this is because the presence of a double bond means that the acyl-CoA dehydrogenase step will be skipped, thus fewer FADH2 will be produced.



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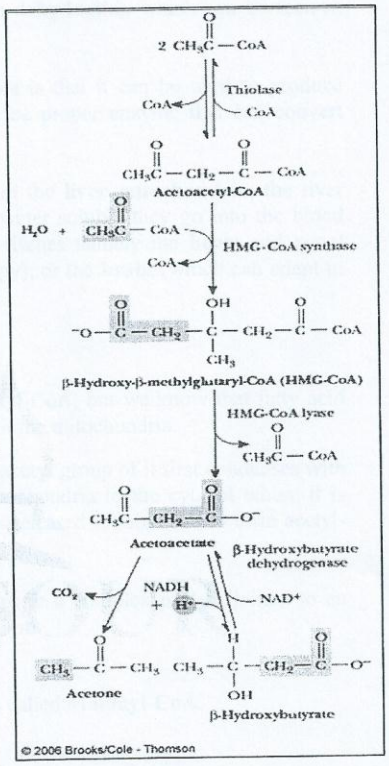
☒ Ketone Bodies

- Substances related to acetone are called ketone bodies, they are produced when there is an excess of acetyl-CoA to be used out through the citric acid cycle, and this means that ketone bodies are produced when the amount of acetyl-CoA exceeds that of oxaloacetate.

- As you can recall, oxaloacetate can be produced from glucose, so when there is no glucose to produce oxaloacetate or the body is unable to use glucose, ketone bodies are produced. This happens when there is an excess intake of lipids to carbohydrates, or in cases of starvation or diabetes.



☺ **The conversion of acetyl-CoA to ketone bodies occurs through the following steps:**

1. Condensation reaction between 2 molecules of acetyl-CoA occurs to produce **Acetoacetyl-CoA**; this is done by the enzyme ***Thiolase***.

2. Another molecule of acetyl-CoA joins the Acetoacetyl-CoA, here the acetyl group is transferred to the Acetoacetyl-CoA and the product is **β-Hydroxy-β-Methylglutaryl-CoA** (HMG-CoA), this is done by the enzyme **HMG-CoA Synthase** (HydroxyMethylGlutaryl Synthase).

3. The **β-Hydroxy-β-Methylglutaryl-CoA** molecule now lyses to form **Acetoacetate** and releases an acetyl-CoA molecule, this is done by the enzyme ***HMG-CoA lyase***.

4. There are 2 fates for **acetoacetate**, it is either decarboxylated to **acetone**, or is reduced to **β-hydroxybutyrate**, with the use of NADH as the reducing agent.

- As we stated earlier the production of ketone bodies occur in cases of starvation or uncontrolled diabetes, in this case acetone is the product and is responsible for the **acetone smell** of uncontrolled diabetics.

- In addition ketone bodies are acidic, that's why they can **lower the blood pH** (ketoacidosis) which causes the kidney to excrete H^+ in the urine, this occurs along with the release of Na^+ and K^+ and water, this results in **dehydration** which can be seen in uncontrolled diabetics.

- The final point we have to say about ketone bodies is that it can be used to produce **energy**, by entering the citric acid cycle, through the proper enzyme that can convert acetoacetate to acetyl-CoA.

- Although the production of ketone bodies occurs in the **liver mitochondria**, the liver cannot use them as a source of energy, but being water soluble they go into the blood stream to be used as a source of energy in other tissues namely the **heart** and **renal cortex** (where they are the preferred source of energy), or the **brain** (which can adapt to use ketone bodies as a source of energy).

☒ Fatty Acid Biosynthesis

- We know that fatty acids are synthesized from acetyl-CoA, but we know that fatty acid synthesis occurs in the cytosol, so, acetyl-CoA must exit the mitochondria.

- Since acetyl-CoA cannot exit the mitochondria, the acetyl group of it first condenses with oxaloacetate to form citrate, which then exits the mitochondria to the cytosol where it is converted again to oxaloacetate and the acetyl group is released to join CoA to form acetyl-CoA.

- Fatty acids are synthesized by adding acetyl groups to a complex protein joined to an acetyl group. So to produce fatty acids, the cell has to form:

1. **Primer** (an acetyl group joined to a protein).
2. **Substrate** to add acetyl groups, this substrate is called **Malonyl-CoA**.

☒ Steps of fatty acid synthesis:

1. The **formation of Malonyl-CoA**; after the acetyl group condenses with the CoA in the cytosol and the acetyl-CoA forms, then, acetyl-CoA is converted to Malonyl-CoA through an enzyme complex called ***Acetyl-CoA Carboxylase***; this complex is composed of 3 enzymes, ***Biotin Carboxylase***, ***Biotin Carrier Protein*** and ***Carboxyl Transferase***. It uses **Mn^{+2}**, **biotin** and **ATP** for activity.

In this step the biotin carrier protein is covalently attached to biotin through a lysine residue, the biotin Carboxylase transfers the carboxyl group (derived from HCO_3^-) to biotin, then carboxyl transferase, transfers the carboxyl group from biotin to acetyl-CoA to produce Malonyl-CoA.

NOTE: [Malonyl-CoA also inhibits the carnitine acyl transferase I; so that acyl-CoA doesn't enter the mitochondrion to undergo β-oxidation, in other words, synthesis and breakdown of fatty acids doesn't occur simultaneously]

2. The next step is a **priming step** in which, the acetyl group is transferred from acetyl-CoA to a protein called **Acyl Carrier Protein (ACP)**, and this is done by the enzyme ***Acyl Transferase***, which is part of the complex ***Fatty-Acid Synthase***, which is an enzyme complex responsible for the whole process of fatty acid synthesis.

NOTE: [the acetyl group was attached by a thioester bond to CoA, and is then transferred to ACP on a group called phosphopantithine by again a thioester bond].

3. The acetyl group is then retransferred from ACP to another protein called ***β-Ketoacyl-S-ACP-Synthase*** **(HS-KSase)**, the acetyl group attaches through a thioester bond to a cysteine residue on the HS-KSase.

NOTE: [By now Malonyl-CoA is ready to be added to the primer acetyl-KSase, the following steps are repeated successively as each group of 2 carbon atoms is added to the primer].

4. Before 2 carbon atoms are added to the primer, the Malonyl group of Malonyl-CoA is transferred to an ACP molecule to form **Malonyl-S-ACP**.

5. A condensation reaction occurs between **Malonyl-S-ACP** and **Acetyl-S-KSase**, in which Malonyl looses a CO_2 molecule and releases **acetyl-S-ACP** and the acetyl group of **acetyl-S-KSase** is transferred to the **acetyl-S-ACP** to produce **Acetoacetyl-ACP**.

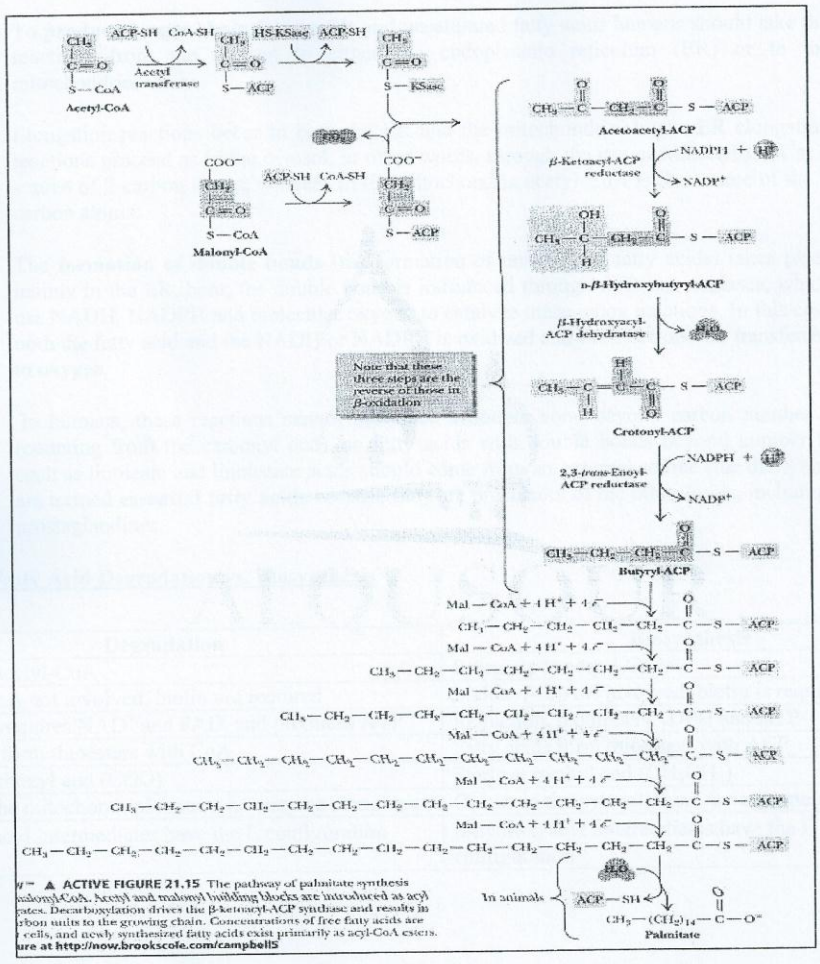
6. **Acetoacetyl-ACP** is then reduced to **β-hydroxybutryl-ACP** by the enzyme ***β-Ketoacyl-ACP Reductase*** which uses **NADPH** as a reducing agent.

7. **β-hydroxybutryl-ACP** is dehydrated to **Crotonyl-ACP** by the enzyme ***β-hydroxyacyl-ACP Dehydratase***.

8. **Crotonyl-ACP** is then reduced to **Butyryl-ACP** by the enzyme ***2,3-trans-Enoyl-ACP Reductase*** which uses **NADPH** as a reducing agent.

9. The cycle is repeated by adding an acetyl group from Malonyl-CoA each time, and this goes through the same mechanism until palmitate (16 Carbon atoms) is produced.

NOTE: In humans the enzyme fatty-acid Synthase stops at 16 carbons, however, longer chain fatty acids are produced by modifications to palmitoyl-ACP after that.



▲ **ACTIVE FIGURE 21.15** The pathway of palmitate synthesis malonylCoAs. Acetyl and malonyl building blocks are introduced as acyl ates. Decarboxylation drives the β-ketoacyl-ACP synthase and results in rbon units to the growing chain. Concentrations of free fatty acids are cells, and newly synthesized fatty acids exist primarily as acyl-CoA esters. ure at http://now.brookscole.com/campbell5

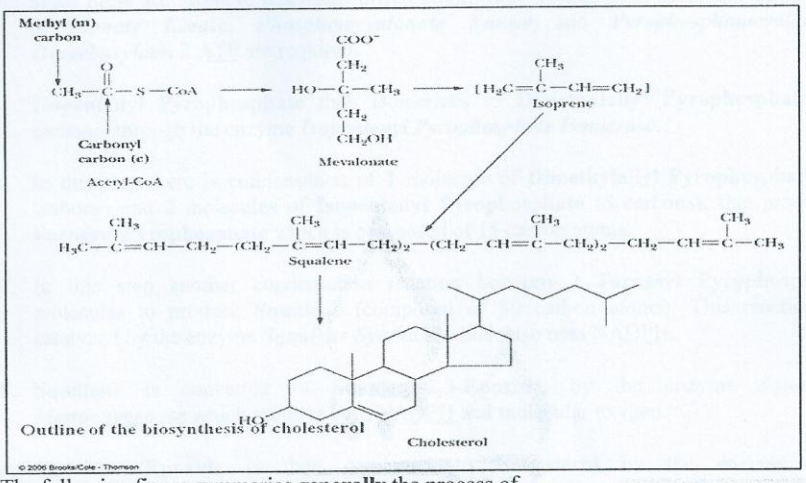
☒ Modifications to Palmitoyl-ACP

- To **produce longer chain fatty acids** and unsaturated fatty acids humans should take the reactions from the cytosol to either the endoplasmic reticulum (ER) or to the mitochondria.
- Elongation reactions occur in both the ER and the mitochondria. In the ER elongation reactions proceed as in the cytosol, in other words, through the use of Malonyl-CoA as a source of 2 carbon atoms, whereas in the mitochondria acetyl-CoA is the source of the 2 carbon atoms.
- The **formation of double bonds** (the formation of unsaturated fatty acids) takes place mainly in the ER, here; the double bond is introduced through different oxidases, which use NADH, NADPH and molecular oxygen to catalyze these redox reactions. In this case both the fatty acid and the NADH or NADPH is oxidized and the electrons are transferred to oxygen.
- In humans, these reactions cannot introduce a double bond beyond carbon number 9 (counting from the carboxyl end), so fatty acids with double bonds beyond number 9, such as linoleate and linolenate acids should come from an external source (the diet), and are termed **essential fatty acids** because they are precursors of the other lipids, including prostaglandines.

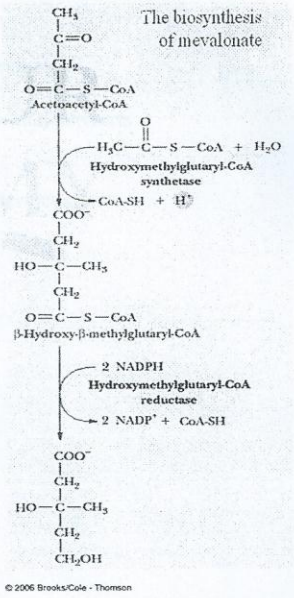
Fatty Acid Degradation vs. Biosynthesis

Degradation	Biosynthesis
Product is acetyl-CoA	Precursor is acetyl-CoA
Malonyl-CoA not involved, biotin not required	Malonyl-CoA is involved, biotin is required
Oxidation, requires NAD^+ and FAD, and produces ATP	Reduction, requires NADPH and ATP
Fatty acids form thioesters with CoA	Fatty acids form thioesters with ACP
Starts at carboxyl end (COO)	Starts at methyl end (CH_3CH_2)
Occurs in the mitochondrial matrix, no enzyme complexes	Occurs in the cytosol, there are enzyme complexes
β-hydroxyacyl intermediates have the L configuration	β-hydroxyacyl intermediates have the D configuration

Cholesterol Production



The following figure summaries **generally** the process of cholesterol synthesis:



Cholesterol is produced from acetyl-CoA through the following steps:

1. Condensation of 2 **acetyl-CoA** molecules by the enzyme ***Thiolase*** (as in the first step of ketone bodies production), **Acetoacetyl-CoA** is produced.

2. Condensation of **Acetoacetyl-CoA** by another **acetyl-CoA** molecule to produce **β-Hydroxy-β-methylglutaryl-CoA**, the enzyme that catalyzes this reaction is called ***Hydroxymethylglutaryl-CoA Synthetase***.

3. **β-Hydroxy-β-methylglutaryl-CoA** is reduced and hydrolyzed to **mevalonate** and CoA is released, the reducing agent is 2 NADPH. The enzyme that catalyzes this reaction is called ***Hydroxymethylglutaryl-CoA Reductase***. This is the major control point in cholesterol synthesis.

4. **Mevalonate** then undergoes phosphorylation, decarboxylation and then dephosphorylation reactions and produces **Isopentenyl Pyrophosphate** (5 carbons), since these are multiple reactions, different enzymes do the work here, and these are, ***Mevalonate Kinase***, ***Phosphomevalonate Kinase*** and ***Pyrophosphomevalonate Decarboxylase.*** 3 ATP are required.

5. **Isopentenyl Pyrophosphate** then isomerizes to **Dimethylallyl Pyrophosphate** (5 carbons) through the enzyme ***Isopentenyl Pyrophosphate Isomerase***.

6. In this step there is condensation of 1 molecule of **Dimethylallyl Pyrophosphate** (5 carbons) and 2 molecules of **Isopentenyl Pyrophosphate** (5 carbons), this produces **Farnesyl Pyrophosphate** which is composed of 15 carbon atoms.

7. In this step another condensation reaction between 2 **Farnesyl Pyrophosphate** molecules to produce **Squalene** (composed of 30 carbon atoms). This reaction is catalyzed by the enzyme ***Squalene Synthase*** which also uses NADPH.

8. **Squalene** is converted to **Squalene-2,3-Epoxide**, by the enzyme ***Squalene Monooxygenase*** which requires both NADPH and molecular oxygen.

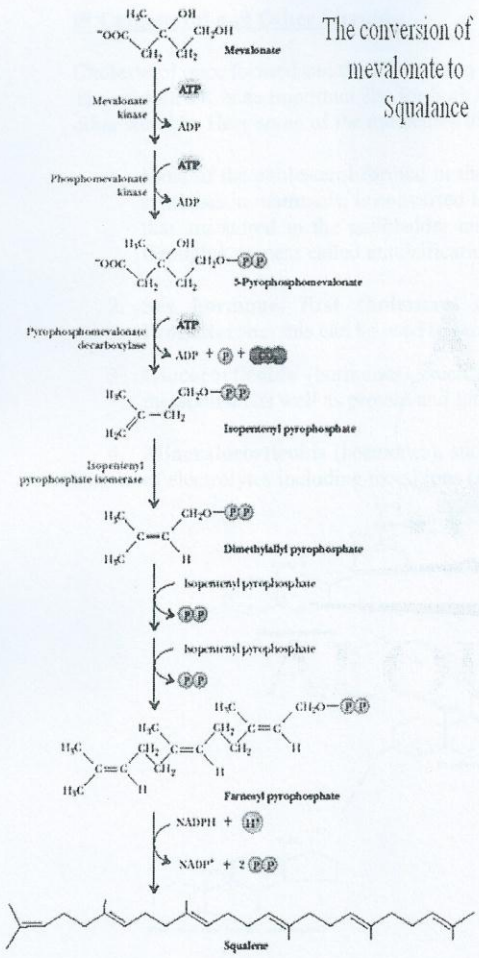
9. **Squalene Epoxide** is then converted to **Lanosterol** by the enzyme ***2,3-Oxidosquaiene:Lanosterol Cyclase***.

10. Many reactions then take place to convert **Lanoesterol** to **Cholesterol**:

- The primary route from lanosterol involves 20 steps, the last of which converts 7-dehydrocholesterol to cholesterol.

- An alternative route produces desmosterol as the penultimate intermediate.

The conversion of mevalonate to Squalance



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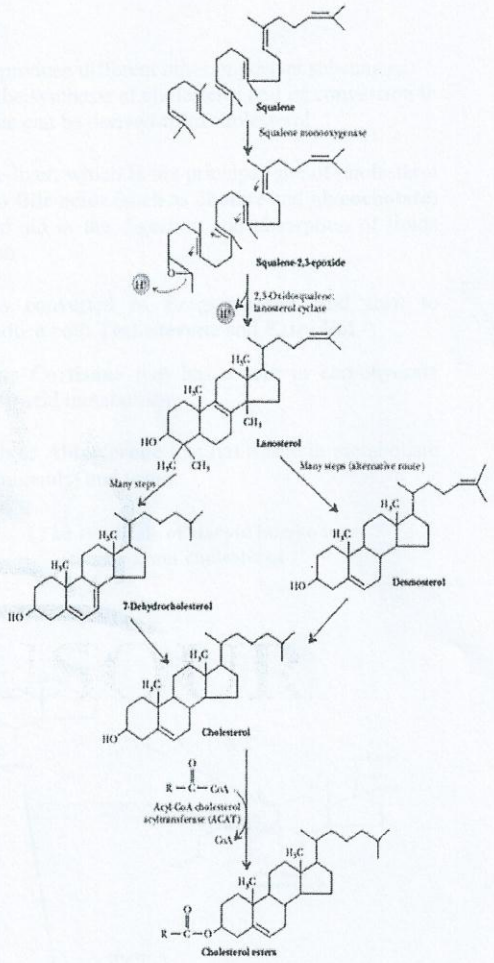

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☒ Cholesterol and Other Steroids:

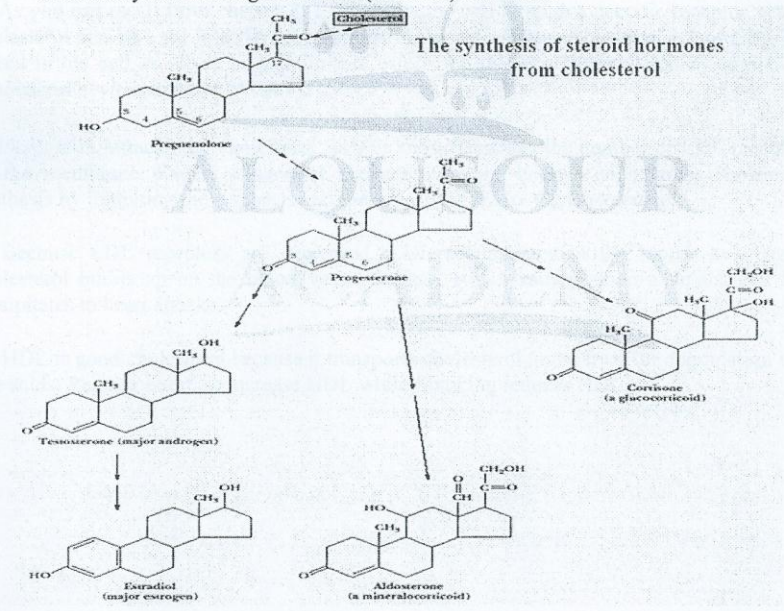
Cholesterol once formed can then be used to produce different other important substances. The smooth ER is an important site for both the synthesis of cholesterol and its conversion to other steroids. Here some of the molecules that can be derived from cholesterol:

1. Most of the cholesterol formed in the liver, which is the principal site of cholesterol synthesis in mammals, is converted to **Bile acids** (such as **cholate** and **glycocholate**) that are stored in the gallbladder and aid in the digestion and absorption of lipids through a process called emulsification.

2. **Sex hormone, first cholesterol is** converted to **Pregnenolone**, and then to **Progesterone**, this can be used to produce both **Testosterone** and **Estradiol**.

3. **Glucocorticoids** (hormones), such as **Cortisone** that has a role in carbohydrate metabolism as well as protein and fatty acid metabolism.

4. **Mineralocorticoids** (hormones), such as **Aldosterone** that has a role in metabolism of electrolytes including metal ions (minerals) and water.



The synthesis of steroid hormones from cholesterol

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☒ Cholesterol and Heart Disease

Cholesterol must be packaged for transport in the blood stream. Several classes of lipoproteins are involved in transport of lipids in blood; these can be summarized as follows:

1. Chylomicrons are involved in the transport of dietary lipid.
2. Very Low Density Lipoproteins (VLDL).
3. Intermediate Density Lipoprotein (IDL).
4. Low Density Lipoproteins (LDL).
5. High Density Lipoproteins (HDL).

- **The difference in the densities is a result of the difference in the protein content. The density increases as the protein content increases.**

- In the LDL molecule the inner portion is composed of cholesteryl esters (cholesterol esterified to an unsaturated fatty acid), on the surface of the LDL molecule, proteins such as apoprotein B-100, phospholipids, and unesterified cholesterol are present.

- As you can recall from chapter 8, LDL enters the cell through a specific receptor, where cholesterol can be used in different reactions in the cell. When cholesterol is not used it is stored in the cell as oleate or palmitoleate esters and this can be cattalized by ***acyl-CoA: cholesterol acyltransferase*** **(ACAT).**

- Increase in intracellular cholesterol, as you know decreases the number of LDL receptors on the membrane. Excess exogenous cholesterol intake inhibits endogenous cholesterol synthesis by inhibiting the synthesis and the activity of ***HMG-CoA reductase.***

- Because LDL receptors are decreased, LDL accumulates in the blood, as a result cholesterol builds up on the blood vessel surface, which causes atherosclerosis, and this precipitates to heart attacks.

- HDL is good cholesterol because it transports cholesterol to the liver for degradation into bile acids. Regular Exercise increase HDL while Smoking reduces HDL.

Questions:

1. In the oxidation of fatty acid, how many carbons removed at a time?

A. 1 carbon atom B. 2 carbon atom C. 3 carbon atom
D. 4 carbon atom E. 6 carbon atom

2. The end product of fatty acid oxidation is:

A. Lactate B. Pyruvate C. Acetone
D. Acetoacetic acid E. Acetyl CoA

3. All of the following are necessary for the synthesis of fatty acids <u>EXCEPT:</u>

A. Acetyl CoA B. CO_2 C.NADPH
D. $FADH_2$ E. ATP

4. Overproduction of acetyl CoA results in the formation of:

A. Glucose B. Saturated fatty acids
C. Esterified cholesterol D. Unsaturated fatty acids
E. Ketone bodies

5. In oxidation of fatty acid the cofactor serving as electron acceptors is/are:

A. NADP only B. NAD only C. NADP and FAD
D. NAD and FAD E. FAD

6. Which one of the following lipoprotein carries cholesterol from the peripheral tissue to the liver?

A. Chilomicrons B. LDL
C. HDL D. IDL

7. Ketone bodies is/are elevated in blood and urine during:

A. Diabetes mellitus
B. In starvation
C. Inadequate carbohydrate intake
D. Both A and B are correct
E. All A,B, and C are correct

SOLUTION

Question #	Answer
1-	B-2 carbon atom
2-	E-acetyl CoA
3-	D-$FADH_2$
4-	E-Ketone bodies
5-	D-NAD and FAD
6-	C-HDL
7-	E-all A,B, and C are correct

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