WEEK NO. 9

# METABOLISM

## DOCTOR 2019 | MEDICINE | JU


**DONE BY :**

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# -lippincott Question:

**1-Which one of the following statements about the digestion of lipids is correct?**

**A. Large lipid droplets are emulsified (have their surface area increased) in the mouth through the act of chewing (mastication).**

**B. The enzyme colipase facilitates the binding of bile salts to mixed micelles, maximizing the activity of pancreatic lipase.**

**C. The peptide hormone secretin causes the gallbladder to contract and release bile.**

**D. Patients with cystic fibrosis have difficulties with digestion because their thickened pancreatic secretions are less able to reach the small intestine, the primary site of lipid digestion.**

**E. Formation of triacylglycerol-rich chylomicrons is independent of protein synthesis in the intestinal mucosa.**

**2-Which one of the following statements about the absorption of lipids from the intestine is correct?**

**A. Dietary triacylglycerol must be completely hydrolyzed to free fatty acids and glycerol before absorption.**

**B. The triacylglycerol carried by chylomicrons is degraded by lipoprotein lipase to fatty acids that are taken up by muscle and adipose tissues and glycerol that is taken up by the liver.**

**C. Fatty acids that contain fewer than 12 carbon atoms are absorbed and enter the circulation primarily via the lymphatic system.**

**D. Deficiencies in the ability to absorb fat result in excessive amounts of chylomicrons in the blood.**

**3-Mice were genetically engineered to contain hydroxymethylglutaryl coenzyme A reductase in which serine 871, a phosphorylation site, was replaced by alanine.**

**Which of the following statements concerning the modified form of the enzyme is most likely to be correct?**

**A. The enzyme is nonresponsive to adenosine triphosphate depletion.**

B. The enzyme is nonresponsive to statin drugs.
C. The enzyme is nonresponsive to the sterol response element–sterol response element–binding protein system.
D. The enzyme is unable to be degraded by the ubiquitin–proteasome system

4-Calculate the amount of cholesterol in the low-density lipoproteins in an individual whose fasting blood gave the following lipid-panel test results: total cholesterol = 300 mg/dl, high-density lipoprotein cholesterol = 25 mg/dl, triglycerides = 150 mg/dl.
A. 55 mg/dl
B. 95 mg/dl
C. 125 mg/dl
D. 245 mg/dl

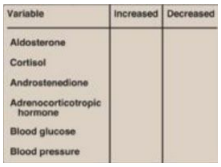
For Questions 5 and 6:
A young girl with a history of severe abdominal pain was taken to her local hospital at 5 a.m. in severe distress. Blood was drawn, and the plasma appeared milky, with the triacylglycerol level in excess of 2,000 mg/dl (normal = 4–150 mg/dl). The patient was placed on a diet extremely limited in fat but supplemented with medium-chain triglycerides.

5-Which of the following lipoprotein particles are most likely responsible for the appearance of the patient's plasma?
A. Chylomicrons
B. High-density lipoproteins
C. Intermediate-density lipoproteins
D. Low-density lipoproteins
E. Very-low-density lipoproteins

6-Which one of the following proteins is most likely to be deficient in this patient?
A. Apo A-I
B. Apo B-48
C. Apo C-II

**D. Cholesteryl ester transfer protein**
**E. Microsomal triglyceride transfer protein**

**7-Complete the table below for an individual with classic 21-α-hydroxylase deficiency relative to a normal individual.**



| Variable | Increased | Decreased |
|---|---|---|
| Aldosterone | | |
| Cortisol | | |
| Androstenedione | | |
| Adrenocorticotropic hormone | | |
| Blood glucose | | |
| Blood pressure | | |

**How might the results be changed if this individual were deficient in 17-α□hydroxylase, rather than 21-α-hydroxylase?**

# Answers:

**1-D.**

**Patients with cystic fibrosis, a genetic disease due to a deficiency of a functional chloride transporter, have thickened secretions that impede the flow of pancreatic enzymes into the duodenum. Emulsification occurs through peristalsis, which provides mechanical mixing, and bile salts that function as detergents. Colipase restores activity to pancreatic lipase in the presence of inhibitory bile salts that bind the micelles. Cholecystokinin is the hormone that causes contraction of the gallbladder and release of stored bile, and secretin causes release of bicarbonate. Chylomicron formation requires synthesis of apolipoprotein B-48**

**2-B.**

**The triacylglycerols (TAGs) in chylomicrons are degraded to fatty acids and glycerol by lipoprotein lipase on the endothelial surface of capillaries in muscle and adipose, thus providing a source of fatty acids to these tissues for degradation or storage and providing glycerol for hepatic metabolism. In the duodenum, TAG are degraded to one 2-monoacyl-glycerol + two free fatty acids that get**

**absorbed. Medium- and short-chain fatty acids enter directly into blood (not lymph), and they neither require micelles nor get packaged into chylomicrons. Because chylomicrons contain dietary lipids that were digested and absorbed, a defect in fat absorption would result in decreased production of chylomicrons.**

**3-A.**

**The reductase is regulated by covalent phosphorylation and dephosphorylation. Depletion of adenosine triphosphate results in a rise in adenosine monophosphate (AMP),**
**which activates AMP kinase (AMPK), thereby phosphorylating and inactivating the enzyme. In the absence of the serine, a common phosphorylation site, the enzyme cannot be phosphorylated by AMPK. The enzyme is also regulated physiologically through changes in transcription and degradation and pharmacologically by statin drugs**
**(competitive inhibitors), but none of these depends on serine phosphorylation.**

**4-D.**

**The total cholesterol in the blood of a fasted individual is equal to the sum of the cholesterol in low-density**
**lipoproteins plus the cholesterol in high-density lipoproteins plus the cholesterol in very-low-density lipoproteins (VLDLs). This last term is calculated by dividing the triacylglycerol value by 5 because cholesterol accounts for about 1/5 of the volume of VLDL in fasted blood.**

**5-A.**

**The milky appearance of her blood was a result of triacylglycerol-rich chylomicrons. Because 5 a.m. is presumably several hours after her evening meal, the patient must have difficulty degrading these lipoprotein particles. Intermediate-, low-, and high□density lipoproteins contain primarily cholesteryl esters, and, if one or more of these particles was elevated, it would cause hypercholesterolemia. Very-low-density lipoproteins do not cause the described “milky appearance” in plasma.**

**6-C.**

**The triacylglycerol (TAG) in chylomicrons is degraded by endothelial lipoprotein lipase, which requires apo C-II as a coenzyme. Deficiency of the enzyme or coenzyme results in decreased ability to degrade chylomicrons to their remnants, which get cleared by the liver. Apo A-I is the coenzyme for lecithin:cholesterol acyltransferase; apo B-48 is the ligand for the hepatic receptor that binds chylomicron remnants; cholesteryl ester transfer protein catalyzes the cholesteryl ester–TAG exchange between high-density and very□low-density lipoproteins (VLDLs); and microsomal triglyceride transfer protein is involved in the formation, not degradation, of chylomicrons (and VLDLs).**

**7-**

**21-α-Hydroxylase deficiency causes mineralocorticoids (aldosterone) and glucocorticoids (cortisol) to be virtually absent. Because aldosterone increases blood pressure, and cortisol increases blood glucose, their deficiencies result in a decrease in blood pressure and blood glucose, respectively. Cortisol normally feeds back to inhibit adrenocorticotropic hormone (ACTH) release by the pituitary, and, so, its absence results in an elevation in ACTH. The loss of 21-α□hydroxylase pushes progesterone and pregnenolone to androgen synthesis, therefore, causes androstenedione levels to rise. With 17-α-hydroxylase deficiency, sex hormone synthesis would be inhibited. Mineralocorticoid production would be increased, leading to hypertension.**

# -Past Papers:

**1-Which one of the following protein activates lipoprotein lipase?**

**a. Apolipoprotein A-I**

**b. Apolipoprotein B-48**

**c. Apolipoprotein C-II**

**d. Cholesteryl ester transfer protein**

**2- Needed to synthesize sphingomyelin from ceramide?**
**a. Phosphocholine**
**b. UDP-choline**
**c. Phosphatidylinositol**
**d. lecithin**

**3- What is used to catalyze degradation of sphingomyline into ceramide and phosphocholine?**
**a. Sphingomyelinase**
**b.Ceramidase**
**c.neuraminidase**
**d.hexoaminidase**

**5-Which of the following can be used to lose weight?**
**a. Inhibition of pancreatic lipases**
**b. Activation of pyruvate dehydrogenase**
**c. Inhibition of HMG-CoA reductase**
**d. Increasing absorption of fat**

**6-Glycerol after TAG hydrolysis:**
**a. is used in the liver and muscle for glycolysis**
**b. used to resynthesize fat in the liver**
**c. is used in the liver for gluconeogenesis**
**d. is metabolized in the kidney and excreted in the urine**

**7-Tay sach's disease leads to the accumulation of:**
**a. Gangliosides**
**b. Lecithin**
**c. Sphingomyelin**
**d. Cerebrosides**

**8-Familial hypercholesterolemia involves a deficiency in:**
**a. HMG-CoA reductase**
**b. Uptake of HDL by the liver**
**c. Synthesis of cholesterol**
**d. LDL endocytosis**

**9-something true about fatty milk:**
**a- digestion begins in mouth**
**b- digestion begins in the stomach**
**c- long chain fatty acid**

**10-something true about lipoproteins:**
**a-chylomicron has the lowest apolipoprotein percentage**
**b- chylomicron has the lowest TAG**
**C- HDL has the lowest apolipoprotein percentage**

**11-in HDL cholesterol is esterified from :-**
**a- acetyl CoA**
**b- phosphatidyl choline/lecithin**
**c- phosphartidylethanolamine**

**13-amide group in ceramide comes from:**
**a- serine**
**b- phosphatidyl choline c-sphingomylein**
**d- glutamine**
**e- glutamate**

**14- phosphatidyl serine is produced from phosphatidylethanolamine by:**
**a- carboxylation**
**b- decarboxylation**
**c- methylation**
**d- polar head exchange**
**e- more than one of the above**

**16-statin drugs act on:**
**a- inhibits reabsorption**
**b- bind to bile acid**
**c-HMG CoA reductase**

**17-Fastest lipoprotein to reach anode: A-HDL**
**B-LDL**
**C-VLDL**

D-IDL

**19-Apo-B100 is found only in:**
A-LDL
B-HDL
C-IDL
D-chylomicrons

**20-The excess dietary carbohydrates are converted to TAGs and transported to cells by?**
A-VLDL
B-HDL
C-Chylomicrons
D-IDL

**21-Regarding cholic acid synthesis:**
A-The first step is hydroxylation at carbon 7
B-this process occurr in the liver
C-cholic acid act as inhibitor for the hydroxylase
D-All of the above

**22-Phosphatidylcholine is formed from?**
A- phosphatidylethanolamine+ 3 SAM.
B- CDP-DAG + cholin
C- CMP+ phosphocholin

**23-The common intermediate for triacylglycerol and phospholipids synthesis is:**
A-phosphatidic acid.
B-cholic acid
C-lysophosphotidic acid
D-archadionic acid

**What is true about macrophages?**
they are sensitive to modified LDL

# Answers:

**1-C**
**2-D**
**3-A**
**5-A**
**6-C**
**7-A**
**8-D**
**9-B**
**10-A**
**11-B**
**13-A**
**14-D**
**16-C**
**17-A**
**19-A**
**20-A**
**21-D**
**22-A**
**23-A**

# -BRS QUESTIONS:

**1-A premature infant, when born, had low Apgar scores and was having difficulty breathing. The NICU physician injected a small amount of a lipid mixture into the child's lungs, which greatly reduced the respiratory distress the child was experiencing. In addition to proteins, a key component of the mixture was which one of the following?**
**(A) Sphingomyelin**
**(B) A mixture of gangliosides**
**(C) Triacylglycerol**
**(D) Phosphatidylcholine**
**(E) Prostaglandins E and F**

**2-An 8-month-old baby girl had normal growth and development for the first few months, but then progressively deteriorated with deafness, blindness, atrophied muscle, inability to swallow, and**

**seizures. Early on in the diagnosis of the child, it was noticed that a cherry red macula was present in both eyes. Considering the child in the above case, measurement of which one of the following would enable one to determine whether the mutation were in the hex A or hex B gene?**

**(A) GMl**
**(B) GM2**
**(C) Globoside**
**(D) Glucocerebroside**
**(E) Ceramide**

**3-A patient with high blood IDL-cholesterol levels was treated with lovastatin. This drug lowers blood cholesterol levels due primarily to which one of the following?**

**(A) Inhibition of absorption of dietary cholesterol**
**(B) Inhibition of LPL in adipose tissue**
**(C) Inhibition of citrate lyase in the liver**
**(D) Induction of IDL receptors in the liver and peripheral tissues**
**(E) Inhibition ofHMG-CoA reductase in the liver and peripheral tissues**

**4-A 2-day-old infant born at 32 weeks' gestation has had breathing difficulties since birth and is currently on a respirator and 100% oxygen. These difficulties occur because of which one of the following?**

**(A) An inability of the lung to contract to exhale**
**(B) An inability of the lung to expand when taking in air**
**(C) An inability of the lung to respond to insulin**
**(D) An inability of the lung to respond to glucagon**
**(E) An inability of the lung to produce energy**

**5-A patient with a hyperlipoproteinemia would most likely benefit from a low-carbohydrate diet if the lipoproteins that are elevated in the blood belong to which class of lipoproteins? Choose the one best answer.**

**(A) Chylomicrons**
**(B) VLDL**

(C) LDL
(D) HDL
(E) Chylomicrons and VLDL
(F) VLDL and LDL
(G) LDL and HDL

**6-An individual has been determined to have hypertriglyceridemia, with a triglyceride level of350 mg/dL (normal is <150 mg/dL). The patient decides to reduce this level by keeping his caloric intake the same, but switching to a lowfat, low-protein, high-carbohydrate diet. Three months later, after sticking faithfully to his diet, his triglyceride level was 375 mg/dL. This increase in lipid content is being caused by which component of his new diet?**

(A) Phospholipids
(B) Triglycerides
(C) Amino acids
(D) Carbohydrates
(E) Cholesterol

**7-**

6. Which one of the following best represents fasting conditions?

| | Activity of Hormone-Sensitive Lipase | Fate of Glycerol | VLDL Production | Modification of Acetyl-CoA Carboxylase | Ketone Body Production |
|---|---|---|---|---|---|
| (A) | Inactive | Glycolysis | High | Dephosphorylated | No |
| (B) | Active | Glycolysis | High | Phosphorylated | Yes |
| (C) | Inactive | Glycolysis | High | Dephosphorylated | No |
| (D) | Active | Gluconeogenesis | Low | Phosphorylated | No |
| (E) | Inactive | Gluconeogenesis | Low | Dephosphorylated | Yes |
| (F) | Active | Gluconeogenesis | Low | Phosphorylated | Yes |

**8-Which one of the following sequences places the lipoproteins in the order of most dense to least dense?**

(A) HDL/VLDL/chylomicrons/LDL
(B) HDL/LDL/VLDL/chylomicrons
(C) LDL/chylomicrons/HDL/VLDL
(D) VLDL/chylomicrons/LDL/HDL
(E) LDL/chylomicrons/VLDL/HDL

**9-**

. Which one of the following best describes the synthesis of triglyceride in adipose tissue?

| | Source of Fatty Acids | Source of Backbone | Requires CoA | Requires LPL | Requires 2-Monoacylglycerol |
|---|---|---|---|---|---|
| (A) | VLDL | Glycerol | Yes | No | Yes |
| (B) | Chylomicrons | Glycerol | No | Yes | No |
| (C) | VLDL and chylomicrons | DHAP | Yes | No | Yes |
| (D) | VLDL and chylomicrons | DHAP | Yes | No | No |
| (E) | Chylomicrons | DHAP | No | Yes | Yes |
| (F) | VLDL | Glycerol | No | Yes | No |

**10-The synthesis of fatty acids from glucose in the liver is best described by which one or the following?**

**(A) The pathway occurs solely in the mitochondria.**

**(B) It requires a covalently bound derivative of pantothenic acid.**

**(C) It requires NADPH derived solely from the pentose phosphate pathway.**

**(D) The pathway is primarily regulated by isocitrate.**

**[E) The pathway does not utilize a carboxylation reaction**

**11-**

**2.** Choose the one best answer that most accurately describes some properties of acetyl-CoA carboxylase.

| | Required Cofactor | Intracellular Location | Allosteric Modifier | Enzyme That Catalyzes a Covalent Modification |
|---|---|---|---|---|
| (A) | Biotin | Mitochondrial | Citrate | PKA |
| (B) | Biotin | Cytoplasmic | Citrate | AMP-activated protein kinase |
| (C) | Thiamin | Mitochondrial | Acetyl-CoA | PKA |
| (D) | Thiamin | Cytoplasmic | Acetyl-CoA | AMP-activated protein kinase |
| (E) | None | Mitochondrial | Malonyl-CoA | PKA |
| (F) | None | Cytoplasmic | Malonyl-CoA | AMP-activated protein kinase |

# -ANSWERS:

**1-The answer is D.**

**The premature infant is experiencing respiratory distress syndrome, which is caused by a deficiency of lung surfactant The lung cells do not begin to produce surfactant until near birth, and premature infants frequently are not producing sufficient surfactant**

**to allow the lungs to expand and contract as needed. The surfactant is composed of a number of hydrophobic proteins and dipalmitoylphosphatidylcholine. Sphingomyelin, gangliosides, triglyceride, and prostaglandins are not the components of the surfactant. The phosphatidylcholine content of the surfactant is 85% of the total lipids associated with the complex**

**2-The answer is C.**
**The child is exhibiting the symptoms of either Tay-Sachs or Sandhoff disease, both of which are sphingolipidoses. The hex A gene codes for hexosaminidase A, whereas the hex B gene codes for hexosaminidase B. The hex A protein consists of one A and one B subunit and cleaves only GM2. The hex B protein is a B dimer and cleaves both GM2 and globoside. In Tay-Sachs disease, a loss of hex A activity, globoside degradation is normal because the hex B protein is normal. The loss of hex B activity affects both hex A (because one subunit is of the B variant) and hex B (dimer) activity, and globoside will accumulate in Sandhoff disease, but not in Tay-Sachs disease.**

**3-The answer is D.**
**The class of drugs known as the statins (e.g., lovastatin) lower blood cholesterol levels through the induction ofLDL receptor expression on the liver and peripheral tissue cell surface. Statins directly inhibit HMG-CoA reductase, a key regulatory enzyme in cholesterol biosynthesis, which reduces intracellular cholesterol levels. The reduction of intracellular cholesterol leads to the induction of LDL receptors because the cells now need to obtain their cholesterol from the circulation. Ezetimibe inhibits the intestinal absorption of cholesterol. Statins do not inhibit LPL or citrate lyase.**

**4-The answer is B.**
**The baby has respiratory distress syndrome, caused by an inability to produce surfactant, a hydrophobic molecule that is secreted by the type II cells in the lung and coats the airways, reducing surface tension during contraction and allowing relatively easy expansion**

**of the lung during inhalation. This is due to the lungs not yet producing surfactant, which contains a few proteins and a large amount of dipalmitoylphosphatidylcholine. Respiratory distress syndrome is not related to insulin or glucagon response by the lung, or the ability of the lung cells to generate energy.**

**5-The answer is B.**
**VLDL is produced mainly from dietary carbohydrate, LDL is produced from VLDL, and chylomicrons contain primarily dietary triacylglycerol. Elevated HDL levels are desirable and are not considered to be a lipid disorder. HDL also contains low levels of triglyceride. A low-carbohydrate diet would be expected to reduce the level of circulating VLDL because of reduced fatty acid and triglyceride synthesis in the liver.**

**6-The answer is D.**
**Dietary glucose is the major source of carbon for synthesizing fatty acids in humans. In a high-carbohydrate diet, excess carbohydrates are converted to fat (fatty acids and glycerol) in the liver, packaged as VIDL, and sent into the circulation for storage in the fat cells. The new diet has reduced dietary lipids, which lower chylomicron levels, but the excess carbohydrate in the diet is leading to increased VIDL synthesis and elevated triglyceride levels. Dietary amino acids are usually incorporated into proteins, particularly in a low-protein diet**

**7-The answer is F.**
**During fasting, the hormone sensitive lipase of adipose tissue is activated by a mechanism involving increased glucagon (and decreased.insulin), cAMP, and PKA. Phosphorylation of hormone-sensitive lipase activates the enzyme. Triacylglycerols are degraded, and fatty acids and glycerol are released into the blood. In the liver, glycerol is converted to glucose by gluconeogenesis, and fatty adds are oxidized to produce ketone bodies. These fuels are released into the blood and supply energy to various issues. During fasting, the liver does not produce significant quantities oCVLDL. Fatty acid synthesis Is reduced because of the**

**phosphorylation and inactivation of acetyl-CoA carbm:ylase by the AMP-activated protein kinase**

**8-. The answer is B.**
**Because chylomicrons contain the most triacylglycerol, they are the least dense of the blood lipoproteins. Because VLDL contains more protein than chylomicrons, it is denser than chylomicrons, but less dense than LDL. Because LDL is produced by the degradation of the triacylglycerols ofVLDL, LDL is denser than VLDL. HDL is the most dense of the blood lipoproteins. It has the most protein and the least triacylglycerol**

**9-The answer is D.**
**Fatty acids, cleaved from 1he triacylglycerols of chylomicrons and VLDL by the action of LPL, are taken up by adipose cells and react with CoA to form fatty acyl-CoA. The LPL is not required to synthesize triglyceride within the adipocyte. Glucose is converted via DHAP to glycerol-3-phosphate, which reacts with fatty acyl-CoA to form phosphatidic acid. Adipose tissue lacks glycerol kinase and cannot use glycerol to directly fonn glycerol-3-phosphate. After inorganic phosphate is released from phosphatidic add, the resultant DAG reacts with another fatty acyl-CoA to form a triacylglycerol, which is stored in the adipose cells. (2-Monoacylglycerol is an intermediate for triglyceride synthesis only in intestinal cells and is not produced in the adipocyte.)**

**10-The answer is B.**
**The synthesis of fatty acids from glucose occurs in the cytosol, except for the mitochondrial reactions in which pyruvate is converted to citrate (pyruvate to oxaloacetate, pyruvate to acetyl-CoA, and oxaloacetate and acetyl-CoA condense to form citrate}. Biotin is required for the conversion of pyruvate to oxaloacetate (a carboxylation reaction}, which combines with acetyl-CoA to form citrate. Biotin is also required by acetyl-CoA carboxylase. Citrate, not isocitrate, is a key regulatory compound for acetyl-CoA carboxylase. Pantothenic acid is covalently bound to the fatty acid synthase complex as part of a**

**phosphopantetheinyl residue. During the reduction reactions on the synthase complex, the growing fatty acid chain ls attached to this residue. NADPH, produced by the malic enzyme as well as by the pentose phosphate pathway, provides the reducing equivalents.**

**11-The answer is B.**
**Biotin ls required for the acetyl-CoA carboxylase reaction in which the substrate, acetyl-CoA, ls carboxylated by1he addition ofC02 to form malonyl-CoA. This reaction occurs in the cytosol Malonyl-CoA provides 1he C-2 units that add to the growing fatty acid chain on the fatty acid synthase complex. As the growing chain is elongated, malonyl-CoA is decarboxylated. Citrate is an allosteric activator of the enzyme, and the enzyme is inhibited by phosphorylation by the AMP-activated protein kinase**

لـيست مـهمـتكم شهـادة تـنـالـونها !! إنّمـا مـهمـتكم أمّـة تُحيـونها
يـاخـلفـــاء الله في أرضه 🌿🌸!