Review Test

**Directions:** Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the one lettered answer or completion that is best in each case.

1. The enzyme that interconverts UDP-galactose and UDP-glucose is called an epimerase. This name is appropriate because glucose and galactose are epimers, which means that they are
(A) mirror images of each other
(B) ketoses rather than aldolases
(C) hexoses of the L configuration
(D) monosaccharides that differ only in the position of one hydroxyl group
(E) disaccharides that contain a β-1,4-glycosidic bond

2. The sugar shown below

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\[
\text{Sucrose (Glucose-α(1→2)-fructose)}
\]
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(A) contains a β-1,4 glycosidic bond
(B) is cleaved by lactase
(C) undergoes mutarotation
(D) contains a pentose sugar
(E) is sucrose (table sugar)

3. Which of the following statements concerning glycosaminoglycans is TRUE?
(A) They contain repeating disaccharides
(B) They are usually positively charged
(C) They contain short oligosaccharide chains
(D) They rarely contain sulfate groups
(E) They contain branches of N-acetylgalactosaminic acid

4. Which of the following statements concerning glycoproteins is TRUE?
(A) They are usually positively charged
(B) They never contain branched oligosaccharide chains
(C) They contain oligosaccharides that are synthesized on dolichol phosphate and transferred to serine residues
(D) They are degraded by lysosomal enzymes
(E) They are all secreted into the blood

5. The mucopolysaccharidoses are caused by deficiencies of enzymes involved in the degradation of
(A) fructose
(B) galactose
(C) glycosaminoglycans
(D) glycoproteins
(E) glycogen

6. After digestion of a piece of cake that contains flour, milk, and sucrose as its primary ingredients, the major carbohydrate products entering the blood are
(A) glucose
(B) fructose and galactose
(C) galactose and glucose
(D) fructose and glucose
(E) glucose, fructose, and galactose

7. A patient has a genetic defect that causes intestinal epithelial cells to produce disaccharidases of much lower activity than normal. Compared with a normal person, after eating a bowl of milk and oatmeal sweetened with table sugar, this patient will have higher levels of
(A) maltose, sucrose, and lactose in the stool
(B) starch in the stool
(C) galactose and fructose in the blood
(D) glycogen in the muscles
(E) insulin in the blood
8. A young infant, who was nourished by a synthetic formula, had a sugar in the blood and urine. This compound gave a positive reducing sugar test but was negative when measured with glucose oxidase. Treatment of blood and urine with acid (which cleaves glycosidic bonds) did not increase the amount of reducing sugar measured. Which of the following compounds is most likely to be present in this infant’s blood and urine?

(A) glucose  
(B) fructose  
(C) sorbitol  
(D) maltose  
(E) lactose

9. The degradation of glycogen normally produces

(A) more glucose than glucose 1-phosphate  
(B) more glucose 1-phosphate than glucose  
(C) equal amounts of glucose and glucose 1-phosphate  
(D) neither glucose nor glucose 1-phosphate  
(E) only glucose 1-phosphate

10. Which of the following statements about liver phosphorylase kinase is TRUE?

(A) It is present in an inactive form when epinephrine is elevated  
(B) It phosphorylates phosphorylase to an inactive form  
(C) It catalyzes a reaction that requires ATP  
(D) It is phosphorylated in response to elevated insulin  
(E) It is not affected by cAMP

11. A patient had large deposits of liver glycogen, which, after an overnight fast, had shorter than normal branches. This abnormality could be caused by a defective

(A) glycogen phosphorylase  
(B) glucagon receptor  
(C) glycogenin  
(D) amylo-1,6-glucosidase (a-glucosidase)  
(E) amylo-4,6-transferase (4:6 transferase)

12. An adolescent patient with a deficiency of muscle phosphorylase was examined while exercising her forearm by squeezing a rubber ball. Compared with a normal person performing the same exercise, this patient

(A) could exercise for a longer period of time without fatigue  
(B) had increased glucose levels in blood drawn from her forearm  
(C) had decreased lactate levels in blood drawn from her forearm  
(D) had lower levels of glycogen in biopsies of her forearm muscle

13. In which compartment of the cell does glycolysis occur?

(A) Mitochondrion  
(B) Nucleus  
(C) Soluble cytoplasm (cytosol)  
(D) Rough endoplasmic reticulum  
(E) Smooth endoplasmic reticulum

14. What type of bond is formed between phosphate and carbon 1 of 1,3-bisphosphoglycerate?

(A) Anhydride  
(B) Ester  
(C) Phosphodiester  
(D) Amide  
(E) Ether

15. During glycolysis, the conversion of compound I to compound II

\[
\begin{align*}
\text{CH}_2\text{OPO}_3^{2-} & \quad \text{COO}^- \\
\text{C} & \quad \text{C}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

Compound I  Compound II

(A) requires a dehydrogenase  
(B) releases inorganic phosphate  
(C) produces one molecule of ATP per molecule of product  
(D) is catalyzed by a phosphatase  
(E) requires two molecules of NADH

16. Which of the following statements about glycolysis is TRUE?

(A) Glucokinase catalyzes the conversion of glucose to glucose 6-phosphate in the liver  
(B) Phosphofructokinase I catalyzes the conversion of fructose 1,6-bisphosphate to dihydroxyacetone phosphate  
(C) When one molecule of glucose is converted to pyruvate via glycolysis, one molecule of NAD\(^+\) is reduced  
(D) When one molecule of glucose is converted to pyruvate via glycolysis, one carbon is lost as CO\(_2\)  
(E) Hexokinase catalyzes the conversion of fructose 6-phosphate to fructose 1,6-bisphosphate
17. In an embryo with a complete deficiency of pyruvate kinase, how many net moles of ATP are generated in the conversion of one mole of glucose to one mole of pyruvate?
   (A) 0
   (B) 1
   (C) 2
   (D) 3
   (E) 4

18. A positive allosteric activator of phosphofructokinase 1 in the liver is
   (A) ADP
   (B) acetyl CoA
   (C) fructose 2,6-bisphosphate
   (D) ATP
   (E) citrate

19. Which of the following is a regulatory mechanism of glycolysis?
   (A) Inhibition of phosphofructokinase 1 by AMP
   (B) Inhibition of hexokinase by its product
   (C) Activation of pyruvate kinase when glucose levels are elevated
   (D) Inhibition of aldolase by fructose 1,6-bisphosphate
   (E) Inhibition of glucokinase by fructose 2,6-bisphosphate

20. An alcoholic went on a weekend binge. The metabolism of ethanol produces NADH, mainly in the liver. As a result of high NADH levels, pyruvate is converted to
   (A) oxaloacetate
   (B) acetyl CoA
   (C) phosphoenolpyruvate
   (D) lactate

21. Caffeine inhibits 3',5'-cAMP phosphodiesterase, which converts cAMP to AMP. Which of the following effects would be observed if cells were treated with caffeine?
   (A) Decreased activity of liver protein kinase A
   (B) Decreased activity of muscle protein kinase A
   (C) Increased activity of liver pyruvate kinase
   (D) Decreased activity of liver glycogen synthase

22. Which of the following glycolytic enzymes is used in gluconeogenesis?
   (A) Glucokinase
   (B) Phosphofructokinase 1
   (C) Pyruvate kinase
   (D) Aldolase B

23. In the conversion of pyruvate to glucose during gluconeogenesis,
   (A) biotin is required
   (B) CO\textsubscript{2}, added in one reaction, appears in the final product
   (C) energy is utilized only in the form of GTP
   (D) all of the reactions occur in the cytosol

24. In gluconeogenesis, both alanine and lactate are converted in a single step to
   (A) oxaloacetate
   (B) acetyl CoA
   (C) phosphoenolpyruvate
   (D) pyruvate
   (E) aspartate

25. A common intermediate in the conversion of glycerol and lactate to glucose is
   (A) pyruvate
   (B) oxaloacetate
   (C) malate
   (D) glucose 6-phosphate
   (E) phosphoenolpyruvate

26. In which of the following compounds do carbons derived from pyruvate leave the mitochondria for the synthesis of glucose during fasting?
   (A) Malate
   (B) Acetyl CoA
   (C) Oxaloacetate
   (D) Lactate
   (E) Glutamine

27. An alcoholic who went on a weekend binge without eating any food was found to have severe hypoglycemia. Hypoglycemia occurred because the metabolism of ethanol prevented the production of blood glucose from
   (A) glycogen
   (B) lactate
   (C) glycerol
   (D) alanine
   (E) lactate, glycerol, and alanine

28. Dietary fructose is phosphorylated in the liver and cleaved to form
   (A) two molecules of dihydroxyacetone phosphate
   (B) one molecule each of dihydroxyacetone phosphate and glyceraldehyde
   (C) one molecule each of dihydroxyacetone phosphate and glyceraldehyde 3-phosphate
   (D) one molecule each of dihydroxyacetone and glyceraldehyde 3-phosphate
   (E) two molecules of glyceraldehyde 3-phosphate
29. In fructose intolerance, aldolase B is defective in the liver. It is still active in glycolysis, but not in the metabolism of dietary fructose. Which of the following is most likely to be found in a patient with fructose intolerance when compared with a normal person on a similar diet that includes sucrose?

(A) decreased levels of fructose in the blood
(B) elevated levels of glyceraldehyde in liver cells
(C) high levels of sucrose in the stool
(D) elevated levels of fructose 1-phosphate in liver cells
(E) decreased levels of fructose in the urine

30. A patient was found to have elevated levels of galactose and galactitol in the blood, but low cellular levels of galactose 1-phosphate. Which of the following enzymes is most likely defective?

(A) galactokinase
(B) UDP-glucose epimerase
(C) phosphoglucomutase
(D) galactose 1-phosphate uridylyl transferase
(E) hexokinase

31. Which of the following statements concerning lactose synthesis is TRUE?

(A) The reactions occur in most tissues
(B) α-Lactalbumin acts as a modifier of galactosyl transferase
(C) UDP-glucose reacts with galactose
(D) UDP-galactose requires dietary galactose for its synthesis

32. A pregnant woman who has a lactase deficiency and cannot tolerate milk in her diet is concerned that she will not be able to produce milk of sufficient caloric value to nourish her baby. She should be advised that

(A) she must eat pure galactose in order to produce the galactose moiety of lactose
(B) she will not be able to breast-feed her baby because she cannot produce lactose
(C) the production of lactose by the mammary gland does not require the ingestion of milk or milk products
(D) she can produce lactose by degrading α-lactalbumin.

33. A mother with a deficiency of galactose 1-phosphate uridylyl transferase

(A) can convert galactose to UDP-galactose for lactose synthesis during lactation
(B) can form galactose 1-phosphate from galactose
(C) can convert galactose to blood glucose
(D) can convert galactose to liver glycogen
(E) will have lower than normal blood galactose levels after ingestion of milk

34. The pentose phosphate pathway generates

(A) NADH, which may be used for fatty acid synthesis
(B) ribose 5-phosphate, which may be used for the biosynthesis of ATP
(C) pyruvate and fructose 1,6-bisphosphate by the transaldolase and transketolase reactions
(D) xylulose 5-phosphate by one of the oxidative reactions
(E) glucose from ribose 5-phosphate and CO₂

35. In an alcoholic with a thiamine deficiency, which enzyme of the pentose phosphate pathway would be less active than normal?

(A) The epimerase
(B) Transaldolase
(C) The isomerase
(D) Transketolase
(E) Glucose 6-phosphate dehydrogenase

36. In patients with Type 1 or Type 2 diabetes mellitus, the transport of glucose across cell membranes is diminished in

(A) brain
(B) liver
(C) red blood cells
(D) skeletal muscle

37. In an individual at rest who has fasted for 12 hours,

(A) gluconeogenesis is the major process by which blood glucose is maintained
(B) adenylate cyclase is inactivated in liver
(C) liver glycogen stores are depleted
(D) phosphorylase, pyruvate kinase, and glycogen synthetase are phosphorylated in liver
38. In a glucose tolerance test, an individual in the basal metabolic state ingests a large amount of glucose. If the individual is normal, this ingestion results in
   (A) enhanced glycogen synthase activity in liver
   (B) an increased ratio of phosphorylase a to phosphorylase b in the liver
   (C) an increased rate of lactate formation by erythrocytes
   (D) inhibition of glycogen synthase phosphatase activity in the liver

39. An infant with an enlarged liver has a glucose 6-phosphatase deficiency. This infant
   (A) cannot maintain blood glucose levels either by glycogenolysis or by gluconeogenesis
   (B) can use liver glycogen to maintain blood glucose levels
   (C) can use muscle glycogen to maintain blood glucose levels
   (D) can convert both alanine and glycerol to glucose to maintain blood glucose levels

40. A 16-year-old patient with Type 1 diabetes mellitus was admitted to the hospital with a blood glucose level of 400 mg/dL. (The reference range for blood glucose is 80-100 mg/dL.) One hour after an insulin infusion was begun, her blood glucose level had decreased to 320 mg/dL. One hour later, it was 230 mg/dL. The patient’s glucose level decreased because insulin
   (A) stimulates the transport of glucose across the cell membranes of the liver and brain
   (B) stimulates the conversion of glucose to glycogen and triacylglycerol in the liver
   (C) inhibits the synthesis of ketone bodies from blood glucose
   (D) stimulates glycolysis in the liver
   (E) inhibits the conversion of muscle glycogen to blood glucose

Questions 41-43
A patient presented with a bacterial infection that produced an endotoxin that inhibits phosphoenolpyruvate carboxykinase.

41. In this patient, inhibition of phosphoenolpyruvate carboxykinase would cause inhibition of glucose production from
   (A) alanine
   (B) glycerol
   (C) even-chain fatty acids
   (D) phosphoenolpyruvate

42. Administration of a high dose of glucagon to this patient 2-3 hours after a high-carbohydrate meal would
   (A) result in a substantial increase in blood glucose levels
   (B) decrease blood glucose levels
   (C) have little effect on blood glucose levels

43. Administration of a high dose of glucagon to this patient 30 hours after a high-carbohydrate meal would
   (A) result in a substantial increase in blood glucose levels
   (B) decrease blood glucose levels
   (C) have little effect on blood glucose levels

44. Mary Smith, a patient with Type 1 diabetes mellitus, has a fasting blood glucose level of 160 mg/dL and a HbA1c of 10%. These tests indicate that her current glycemic control is
   (A) good, and has been good during the past 6 weeks
   (B) poor, and has been poor during the past 6 weeks
   (C) good, but has been poor during the past 6 weeks
   (D) poor, but has been good during the past 6 weeks

Directions: Each group of items in this section consists of lettered options followed by a set of numbered items. For each item, select the one lettered option that is most closely associated with it. Each lettered option may be selected once, more than once, or not at all.

Questions 45-48
(A) Protein kinase A
(B) Phosphorylase kinase
(C) Glucagon receptor
(D) Phosphodiesterase

Match each enzyme below with the protein that most directly alters its activity.
Questions 49–51

(A) Glucose 6-phosphate dehydrogenase
(B) 6-Phosphogluconate dehydrogenase
(C) Transaldolase
(D) Transketolase

Match the products below with the enzyme that catalyzes their formation.

49. NADPH and a lactone
50. CO₂
51. Glyceraldehyde 3-phosphate in a reaction requiring thiamine pyrophosphate

Questions 52–58

Phosphoenolpyruvate

A

Lactate

B

Pyruvate

C

Acetyl CoA

D

E

Alanine

Oxaloacetate

Match each description below with the most appropriate enzyme (A–E) indicated in the diagram above.

52. Inhibited by NADH and acetyl CoA
53. Requires thiamine pyrophosphate
54. Activated by acetyl CoA
55. Requires biotin
56. Requires pyridoxal phosphate
57. Phosphorylated and inactivated by protein kinase A
58. Forms product (as indicated by the arrow) when NADH levels are elevated

Questions 59–62

(A) Dietary glucose
(B) Glucose produced by glycogenolysis
(C) Glucose produced by gluconeogenesis

For each time period below, choose the major source of glucose that is being oxidized by cells.

59. 1 hour after a meal
60. 4 hours after a meal
61. 2 days after a meal
62. after 6 weeks of fasting

Questions 63–68

(A) Galactosemia
(B) A hemolytic anemia
(C) Fructose intolerance
(D) Lactose intolerance
(E) McArdle's disease

For each enzyme below, choose the condition above that would result from a deficiency of that enzyme.

63. Lactase
64. Glucose 6-phosphate dehydrogenase
65. Galactokinase
66. Aldolase B
67. Muscle glycogen phosphorylase
68. Uridyl transferase
1-D. Glucose and galactose are not mirror images (enantiomers). They differ only in that they contain hydroxyl groups on different sides of carbon 4 (i.e., they are epimers). They are aldoses, not ketoses. They are hexoses (containing six carbons) in the D configuration. They are monosaccharides.

2-E. This sugar is sucrose. It contains glucose and fructose (two hexoses) joined by their anomeric carbons, thus it is not a reducing sugar and does not mutarotate.

3-A. Glycosaminoglycans are long, linear carbohydrate chains that contain repeating disaccharide units, which usually contain a hexosamine and a uronic acid. They often contain sulfate groups. The uronic acid and sulfate residues cause them to be negatively charged. They are unbranched and do not contain N-acetylneuraminic acid.

4-D. Glycoproteins contain branched oligosaccharide chains. These chains may be synthesized by addition of sugars to serine or threonine residues of the protein, or they may be synthesized on dolichol phosphate and transferred to asparagine residues on the protein. They are not positively charged. They are synthesized in the RER and Golgi and may be secreted from cells, anchored in the cell membrane, or segregated into lysosomes. They are internalized by endocytosis and degraded by lysosomal enzymes.

5-C. Glycosaminoglycans (formerly called mucopolysaccharides) are the long, linear polysaccharide chains of proteoglycans. They are synthesized and secreted by cells. Ultimately, they are taken up by cells via endocytosis and degraded by lysosomal enzymes. A deficiency of any one of these lysosomal enzymes can result in a mucopolysaccharidosis (e.g., Hurler's, Hunter's).

6-E. The cake contains starch, lactose (milk sugar), and sucrose (table sugar). Digestion of starch produces glucose. Lactase cleaves lactose to galactose and glucose, and sucrase cleaves sucrose to fructose and glucose.

7-A. In this patient, starch will be digested by salivary and pancreatic α-amylases to small oligosaccharides and maltose, but a lower than normal amount of glucose will be produced because of the deficiency of the brush border disaccharidases, which have maltase, isomaltase, sucrase, and lactase activity. Sucrose and lactose will not be cleaved. There will be more maltose, sucrose, and lactose in the stool and less monosaccharides in the blood and tissues. Insulin levels will be lower than normal.

8-B. Fructose gives a positive result in a reducing sugar test and a negative result in a glucose oxidase test. It is a monosaccharide, and, so, is not cleaved by acid. Glucose gives a positive test result with the enzyme glucose oxidase. Sorbitol has no aldehyde or ketone group, and, thus, cannot be oxidized in the reducing sugar test. Maltose and lactose are disaccharides that undergo acid hydrolysis, which doubles the amount of reducing sugar. This infant probably has benign fructosuria or the more dangerous condition, fructose intolerance. A galactose oxidase test would rule out the possibility that the sugar was galactose.

9-B. Phosphorylase produces glucose 1-phosphate from glucose residues linked α-1,4. Free glucose is produced from α-1,6-linked residues at branch points by an α-1,6-glucosidase. Degradation of glycogen produces glucose 1-phosphate and glucose in about a 10:1 ratio.

10-C. Glucagon in the liver and epinephrine in both the liver and muscle cause cAMP levels to rise, activating protein kinase A. Protein kinase A phosphorylates and activates phosphorylase kinase, which in turn phosphorylates and activates phosphorylase. These phosphorylation reactions require ATP.
11-D. If, after fasting, the branches were shorter than normal, phosphorylase must be functional and capable of being activated by glucagon. The branching enzyme (the 4:6 transferase) must be normal because branches are present. The protein glycogenin must be present in order for large amounts of glycogen to be synthesized and deposited. The defect has to be in the debranching enzyme (which contains an α-1,6-glucosidase). If the debrancher is defective, phosphorylase would break the glycogen down to the branch points, but complete degradation would not occur. Therefore, short branches would be present in the glycogen. If the short branches contain only one glucose unit, the defect is in the α-1,6-glucosidase activity of the debrancher. If they contained four glucose units, the defect would be in the 4:4 transferase activity of the debrancher.

12-C. This patient has McArdle's disease, a glycogen storage disease caused by a deficiency of muscle glycogen phosphorylase. Because she cannot degrade glycogen to produce energy for muscle contraction, she becomes fatigued more readily than a normal person, the glycogen levels in her muscle will be higher than normal, and her blood lactate levels will be lower. She will use more blood glucose, thus her blood glucose levels will be decreased.

13-C. All of the reactions of glycolysis occur in the cytosol.

14-A. The carboxylic acid (carbon 1) reacts with phosphoric acid, splitting out H₂O and forming an anhydride. Cleavage of this bond in the next step of glycolysis generates enough energy to produce one ATP from ADP and P₃.

15-A. Dihydroxyacetone phosphate (compound I) is isomerized to glyceraldehyde 3-phosphate and converted in a series of steps to pyruvate (compound II). One of the reactions requires glyceraldehyde 3-phosphate dehydrogenase, which uses one molecule of inorganic phosphate for each molecule of NADH it produces. In the conversion of one molecule of 1,3-bisphosphoglycerate to one molecule of pyruvate, two molecules of ATP are produced. A phosphatase is not required.

16-A. Glucokinase, a liver enzyme, converts glucose to glucose 6-phosphate. Phosphofructokinase 1 converts fructose 6-phosphate to fructose 1,6-bisphosphate. In glycolysis, one molecule of glucose is converted to two molecules of pyruvate and two molecules of NADH are produced. No carbons are lost as CO₂.

17-A. Normally, one mole of ATP is used to convert one mole of glucose to one mole of glucose 6-phosphate and a second to convert one mole of fructose 6-phosphate to the bisphosphate. Two triose phosphates are produced by cleavage of fructose 1,6-bisphosphate. As the two triose phosphates are converted to pyruvate, four ATPs are generated; two by phosphoglycerate kinase and two by pyruvate kinase. Net, two ATPs are produced. If pyruvate kinase is completely deficient, two less ATPs will be produced, thus net ATP production will be zero. It is unlikely that the embryo would survive with a complete deficiency of this enzyme.

18-C. Phosphofructokinase 1 is activated by AMP and fructose 2,6-bisphosphate. It is inhibited by ATP and citrate and not directly affected by acetyl CoA or ADP. In the liver, fructose 2,6-bisphosphate is the major activator.

19-B. Hexokinase is inhibited by its product, glucose 6-phosphate. PFK1 is activated by AMP and fructose 2,6-bisphosphate (F-2,6-P). F-2,6-P does not inhibit glucokinase. Aldolase is not inhibited by its substrate, fructose-1,6-P. Pyruvate kinase is inactivated by glucagon-mediated phosphorylation.

20-D. All of these compounds can be produced from pyruvate, but when NADH levels are elevated (and, thus, NAD⁺ levels are low), pyruvate is converted to lactate by lactate dehydrogenase. The bingeing alcoholic could develop a lactic acidosis.

21-D. If the phosphodiesterase that degrades cAMP were inhibited, cAMP levels would be elevated. Protein kinase A would become more active in the liver and muscle; pyruvate kinase would become less active; and glycogen synthase activity would be decreased.

22-D. During gluconeogenesis, glucokinase, phosphofructokinase 1, and pyruvate kinase are not active, and, thus, futile cycles do not occur. Aldolase B, the liver isozyme, is used both in glycolysis and gluconeogenesis.
Carbohydrate Metabolism

23-A. In the mitochondria, CO₂ is added to pyruvate to form oxaloacetate (OAA). The enzyme is pyruvate carboxylase, which requires biotin and ATP. OAA leaves the mitochondrion as malate or aspartate and is regenerated in the cytosol. OAA is converted to phosphoenolpyruvate by a reaction that utilizes GTP and releases the same CO₂ that was added in the mitochondrion. The remainder of the reactions occur in the cytosol.

24-D. Alanine is transaminated and lactate is oxidized by NAD⁺ to form pyruvate. The other compounds are not produced in a single step from alanine or lactate.

25-D. The only intermediate included on the list that glyceral has in common with lactate is glucose 6-phosphate. Glyceral enters gluconeogenesis as dihydroxyacetone phosphate. Therefore, it bypasses the other compounds.

26-A. Pyruvate is converted in the mitochondria to malate, which can cross the mitochondrial membrane. Oxaloacetate and acetyl CoA cannot. Lactate is produced from pyruvate in the cytosol. The reverse reaction is involved in gluconeogenesis. Glutamine is not derived from pyruvate during gluconeogenesis.

27-E. Ethanol metabolism (which produces high NADH levels) does not prevent glycogen degradation. In fact, glycogen stores would be rapidly depleted under these conditions because of decreased gluconeogenesis. Alanine is transaminated to pyruvate. The pyruvate/lactate equilibrium greatly favors lactate when NADH is high. Thus, alanine and lactate are prevented from producing glucose. Lactate levels are elevated, and a lactic acidosis can result. Glyceral normally enters gluconeogenesis by forming glyceral 3-P, which is oxidized to dihydroxyacetone phosphate. High NADH levels prevent this oxidation. Thus, the three major gluconeogenic precursors (alanine, glyceral, and lactate) do not form glucose because of the high NADH, and as glycogen stores are depleted, hypoglycemia results.

28-B. Fructose 1-phosphate is cleaved by aldolase B to dihydroxyacetone phosphate and glyceraldehyde.

29-D. Sucrose would still be cleaved by sucrase, thus it would not increase in the stool. Fructose would not be metabolized normally, therefore it would be elevated in the blood and urine. Aldolase B would not cleave fructose-1-P, thus its levels would be elevated and the product, glyceraldehyde, would not be produced.

30-A. Galactose is phosphorylated by galactokinase to galactose-1-P, which reacts with UDP-glucose in a reaction catalyzed by uridyl transferase to form UDP-galactose and glucose-1-P. An epimerase converts UDP-galactose to UDP-glucose. Phosphoglucomutase interconverts glucose-1-P and glucose-6-P. Hexokinase converts glucose to glucose-6-P. If galactose-1-P levels are low, but galactose (and galactitol) levels are elevated, the defect is in galactokinase.

31-B. UDP-galactose reacts with glucose to form lactose only in the mammary gland. α-Lactalbumin acts as a modifier of the enzyme galactosyl transferase, lowering its Kₘ for glucose. Glucose can be converted to UDP-glucose and epimerized to form the UDP-galactose used in lactose synthesis; therefore, dietary galactose is not required.

32-C. She will be able to breast-feed her baby because she can produce lactose. However, she does not have to eat pure galactose or even lactose. Glucose can be converted to UDP-galactose (Glucose → glucose 6-phosphate → glucose 1-phosphate → UDP-glucose → UDP-galactose). UDP-galactose reacts with glucose to form lactose. α-Lactalbumin is a protein that serves as the modifier of galactosyl transferase, which catalyzes this reaction.

33-B. A person with a uridyl transferase deficiency (classic galactosemia) can phosphorylate galactose but will not be able to react the galactose 1-phosphate with UDP-glucose to form UDP-galactose and glucose 1-phosphate. Therefore, she will not be able to convert galactose to UDP-galactose, liver glycogen, or blood glucose. Cellular galactose 1-phosphate and blood galactose levels will be elevated if she consumes galactose or lactose.
In the first three reactions of the pentose phosphate pathway, glucose is converted to ribulose 5-phosphate and CO₂, with the production of NADPH. These reactions are not reversible. Ribose 5-phosphate and xylulose 5-phosphate are formed from ribulose 5-phosphate by two of the non-oxidative reactions of the pathway. Ribose 5-phosphate is used for biosynthesis of nucleotides such as ATP. A series of reactions catalyzed by transketolase and transaldolase produce the glycolytic intermediates fructose 6-phosphate and glyceraldehyde 3-phosphate. Glucose is produced by gluconeogenesis in humans.

Transketolase would be less active because it requires thiamine pyrophosphate as a cofactor. Other enzymes do not require cofactors except for the two dehydrogenases, which require NADP⁺.

Insulin stimulates glucose transport into muscle and adipose cells. There is no significant stimulation in brain, liver, and red blood cells.

After 12 hours of fasting, liver glycogen stores are still substantial. Glycogenolysis is stimulated by glucagon, which activates adenylate cyclase. cAMP activates protein kinase A, which phosphorylates phosphorylase kinase, pyruvate kinase, and glycogen synthase. As a result, phosphorylase is activated, whereas glycogen synthase and pyruvate kinase are inactivated. Gluconeogenesis does not become the major process for maintaining blood glucose until 18–20 hours of fasting. After about 30 hours, liver glycogen is depleted.

Phosphorylase is decreased by a phosphatase. The ratio of phosphorylase a to phosphorylase b is decreased by a phosphatase, thus glycogen degradation decreases. Red blood cells continue to use glucose and form lactate at their normal rate.

Glucose 6-phosphatase deficiency results in a glycogen storage disease (von Gierke's disease) in which neither liver glycogen nor gluconeogenic precursors (e.g., alanine and glycerol) can be used to maintain normal blood glucose levels. The last step (conversion of glucose 6-phosphate to glucose) is deficient for both glycogenolysis and gluconeogenesis. Muscle glycogen cannot be used to maintain blood glucose because muscle does not contain glucose 6-phosphatase.

Blood glucose decreases because insulin stimulates the transport of glucose into muscle and adipose cells and stimulates the conversion of glucose to glycogen and triacylglycerols in the liver. Ketone bodies are not made from blood glucose. During fasting, when the liver is producing ketone bodies, it is also synthesizing glucose. Carbon for ketone body synthesis comes from fatty acids. Insulin stimulates glycogen synthesis, not glycogenolysis. Muscle glycogen is not converted to blood glucose.

Phosphoenolpyruvate carboxykinase converts oxaloacetate to phosphoenolpyruvate. It is a gluconeogenic enzyme required for the conversion of alanine and lactate (but not phosphoenolpyruvate or glycerol) to glucose. Acetyl CoA from oxidation of fatty acids is not converted to glucose.

By 2–3 hours after a high-carbohydrate meal, the patient's glycogen stores would be filled. Glucagon would stimulate glycogenolysis, and blood glucose levels would rise.

Thirty hours after a meal, liver glycogen is normally depleted, and blood glucose is maintained solely by gluconeogenesis after this time. However, in this case, a key gluconeogenic enzyme is inhibited by an endotoxin. Therefore, gluconeogenesis will not occur at a normal rate and glycogen stores will be depleted more rapidly than normal. Blood glucose levels will not change significantly if glucagon is administered after 30 hours of fasting.

Mary Smith's blood glucose is currently above the range for normal fasting blood glucose (80–100 mg/dL). Her HbA₁c is also above the normal 6%. Therefore, her glycemic control is poor at present and has been poor over the last 6 weeks.

Phosphorylase kinase phosphorylates phosphorylase b, converting it to the more active phosphorylase a, which releases glucose-1-P from glycogen.

Glycogen synthase is phosphorylated and inactivated by a cAMP-dependent protein kinase (protein kinase A).
Carbohydrate Metabolism

47-C. Glucagon combines with its membrane receptor, and the complex stimulates G proteins that activate adenylate cyclase in the cell membrane, causing the conversion of ATP to cAMP.

48-A. A cAMP-dependent protein kinase (protein kinase A) phosphorylates phosphorylase kinase, causing it to become active.

49-A. Both A and B produce NADPH, but only A produces 6-phosphogluconolactone.

50-B. 6-Phosphogluconate is decarboxylated to form ribulose 5-phosphate, NADPH, and CO₂.

51-D. Both transaldolase and transketolase produce glyceraldehyde 3-phosphate, but only transketolase requires thiamine pyrophosphate.

52-C. Pyruvate dehydrogenase is inhibited by NADH and acetyl CoA.

53-C. Pyruvate dehydrogenase requires thiamine pyrophosphate.

54-E. Pyruvate carboxylase is activated by acetyl CoA.

55-E. Pyruvate carboxylase requires biotin, CO₂, and ATP.

56-D. Alanine aminotransferase (transaminase) requires pyridoxal phosphate.

57-A. Pyruvate kinase is inactivated by protein kinase A. Pyruvate dehydrogenase is inactivated by a kinase that is a subunit of the enzyme complex.

58-B. Lactate dehydrogenase produces lactate from pyruvate when NADH levels are high.

59-A. Dietary glucose is the source of blood glucose for about 2 hours after a meal.

60-B. By 4 hours after a meal, digestion and absorption of carbohydrates have been completed, and liver glycogen is supplying glucose to the blood.

61-C. By 2 days after a meal, liver glycogen stores have been depleted, and gluconeogenesis is the only source of blood glucose.

62-C. After 6 weeks of fasting, gluconeogenesis is still the major process for production of blood glucose.

63-D. A lactase deficiency results in lactose intolerance, which is characterized by gas, bloating, and watery diarrhea following lactose ingestion.

64-B. A glucose 6-phosphate dehydrogenase deficiency results in a hemolytic anemia because adequate levels of NADPH are not produced by the pentose phosphate pathway. NADPH is required for the reduction of glutathione, which helps to prevent oxidative damage to cells.

65-A. Non-classical galactosemia is caused by a deficiency of galactokinase. Galactose accumulates and forms galactitol. Cataracts occur.

66-C. A deficiency of aldolase B results in fructose intolerance. Fructose 1-phosphate accumulates because it is not cleaved. Hypoglycemia results. The glycolytic reaction catalyzed by aldolase B is not affected.

67-E. In McArdle's disease, muscle glycogen phosphorylase is deficient. Strenuous exercise cannot be tolerated because muscle glycogen cannot be degraded.

68-A. In classical galactosemia, the uridyl transferase is deficient. Galactose, galactitol, and galactose 1-phosphate accumulate when galactose is ingested. Cataracts and hypoglycemia result.
nibus formation) initiates heart at-

ble, compromised in Fabry's disease.

ent of lung surfac-

infants do not stimulate respiratory

) from the unripe
hydrogenase of β-
compensate for the
hypoglycemia can
acetylglycerols are ex-

hydrogenase (MCAD)
levels. Hypoglycemia
are excreted in the

Review Test

Directions: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the one lettered answer or completion that is best in each case.

1. The process by which dietary lipids are digested and absorbed requires the

(A) production of very low density lipoprotein in the intestine
(B) synthesis of bile salts in the gallbladder
(C) hydrolysis of ester bonds in triacylglycerols
(D) presence of glycerol 3-phosphate in intestinal epithelial cells

2. A deficiency of pancreatic exocrine secretion can result in

(A) increased pH in the intestinal lumen
(B) increased absorption of fat-soluble vitamins
(C) decreased formation of bile salt micelles
(D) increased levels of blood chylomicrons
(E) decreased amounts of fat in the stool

3. Which one of the following statements about acetyl CoA carboxylase is correct?

(A) It requires thiamine for the carboxylation of acetyl CoA
(B) It utilizes citrate as a substrate
(C) It produces malonyl CoA, which is subsequently decarboxylated
(D) It is located mainly in the matrix of liver mitochondria

4. The synthesis of fatty acids from glucose in the liver

(A) occurs in mitochondria
(B) requires a covalently bound derivative of pantothenic acid
(C) utilizes NADPH derived solely from the pentose phosphate pathway
(D) is regulated mainly by isocitrate
(E) does not require biotin

5. The product of the fatty acid synthase complex in the liver can be

(A) elongated to stearic acid
(B) reduced to form oleic acid
(C) oxidized directly to palmitic acid
(D) converted to arachidonic acid
(E) converted into low-density lipoprotein and secreted into the blood

6. In the pathway for triacylglycerol synthesis in the liver,

(A) fatty acids directly react with glycerol 3-phosphate
(B) coenzyme A is not required
(C) phosphatidic acid is an intermediate
(D) a 2-monoylglycerol is an intermediate

7. For the synthesis of triacylglycerols in adipose tissue

(A) fatty acids are obtained from chylomicrons and very low density lipoprotein
(B) glycerol 3-phosphate is derived from blood glucose
(C) coenzyme A is not required
(D) a 2-monoylglycerol is an intermediate
(E) lipoprotein lipase catalyzes the formation of ester bonds

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. The conversion of HMG CoA to mevalonic acid

(A) requires NADH and H⁺
(B) is a key reaction in the synthesis of compounds that contain isoprene units
(C) is stimulated by cholesterol
(D) is a step in the synthesis of ketone bodies
(E) is inhibited by insulin

227
10. A patient with high blood cholesterol levels was treated with lovastatin. This drug lowers blood cholesterol levels because it inhibits
(A) absorption of dietary cholesterol
(B) lipoprotein lipase in adipose tissue
(C) citrate lyase in liver
(D) VLDL excretion by the liver
(E) HMG CoA reductase in liver and peripheral tissues

11. The compound shown below is

(A) a bile salt
(B) cholesterol
(C) a steroid hormone
(D) vitamin D₃
(E) a cholesterol ester

12. In the conversion of cholesterol to bile salts,
(A) carbon 8 is hydroxylated
(B) the side chain is oxidized and can be conjugated with serine or taurine
(C) the double bond is reduced
(D) the hydroxyl group on carbon 3 remains in the β-position

13. If intestinal pH decreases to 3 as a result of a deficiency of pancreatic exocrine secretion, which of the following will be most negatively charged?
(A) Glycocholic acid
(B) Taurocholic acid
(C) Palmitate
(D) Cholic acid
(E) Cholesterol

14. A person with an intestinal infection caused by a proliferation of bacteria in the gut would most likely have an increase in the
(A) synthesis of bile salts in the liver
(B) amount of conjugated bile salts in the intestine
(C) absorption of dietary lipid by intestinal cells
(D) body stores of fat-soluble vitamins

15. A person with a low-density lipoprotein (LDL) receptor deficiency was treated with lovastatin. As a consequence of the action of this drug, the person should have
(A) fewer LDL receptors in cell membranes
(B) increased de novo cholesterol synthesis
(C) increased ACAT activity
(D) lower blood cholesterol levels
(E) higher blood triacylglycerol levels

16. Which of the following is characteristic of high-density lipoprotein?
(A) It is digested by muscle lysosomes
(B) It carries cholesterol that is converted to cholesterol esters in the blood by the lecithin:cholesterol acyltransferase (LCAT) reaction
(C) It carries apoprotein E, an activator of lipoprotein lipase
(D) It is produced by the action of hormone-sensitive lipase on very low density lipoprotein (VLDL)

17. A patient with a hyperlipoproteinemia would be most likely to benefit from a low-carbohydrate diet if the lipoproteins that are elevated in the blood belong to the class of
(A) chylomicrons
(B) VLDL
(C) LDL
(D) HDL

18. A person with a type IIA hyperlipoproteinemia had a blood cholesterol level of 360 mg/dL (recommended level below 200 mg/dL) and blood triglyceride (triacylglycerol) levels of 140 mg/dL (recommended level below 160 mg/dL). This person most likely has
(A) a decreased ability for receptor-mediated endocytosis of LDL
(B) a decreased ability to degrade the triacylglycerols of chylomicrons
(C) an increased ability to produce VLDL
(D) an elevation of HDL in the blood
(E) a decreased ability to convert VLDL to IDL

19. The blood of a person who consumes large amounts of animal fat would most likely contain
(A) increased levels of chylomicrons
(B) increased levels of VLDL
(C) increased levels of HDL
(D) increased levels of LDL
(E) decreased levels of cholesterol
20. During fasting, which of the following statements about lipid metabolism is TRUE?
(A) Hormone-sensitive lipase is inhibited because the glucagon level in blood is increased and insulin is decreased
(B) Glycerol, released from adipose tissue, is utilized for glycogen synthesis in liver
(C) Liver is converting fatty acids, derived from adipose tissue, to ketone bodies
(D) Liver is actively synthesizing VLDL from carbohydrate

21. Which one of the following statements about fatty acids is TRUE?
(A) Fatty acids are very soluble in water and need no carrier in the blood
(B) When fatty acids are activated in the cytosol, ATP is converted to ADP
(C) Fatty acyl groups are covalently linked to carnitine by an enzyme inhibited by malonyl CoA
(D) Fatty acids can be oxidized to CO2 and H2O in the mitochondria of red blood cells

22. Which one of the following statements about β-oxidation is true?
(A) FAD is required to form a double bond in fatty acyl CoA
(B) Carbon 2 of the fatty acid is oxidized to form a β-hydroxy compound
(C) NAD+ removes water from the β-hydroxy fatty acyl CoA intermediate
(D) Thiolase removes one carbon from the β-keto intermediate
(E) Two acetyl CoA molecules are produced in each turn of the β-oxidation spiral

23. If 1 mole of the compound shown below is oxidized to CO2 and H2O in muscle mitochondria, what will be the approximate net number of moles of ATP produced?
\[
\text{CH}_3 - \text{(CH}_2)_3 - \text{CH} = \text{CH} - \text{CH}_2 - \text{COOH}
\]
(A) 95
(B) 97
(C) 110
(D) 114
(E) 119

24. Which one of the following statements about the conversion of fatty acids to ketone bodies is TRUE?
(A) Carnitine transports the fatty acid across the plasma membrane
(B) Activation of the fatty acid is driven by the conversion of ATP to ADP
(C) Thiolase cleaves HMG CoA
(D) Acetoacetate and acetyl CoA are produced by cleavage of HMG CoA
(E) The complete sequence of reactions occurs in all tissues of the body

25. The complete oxidation of
\[
\text{CH}_3 \quad \| \\
\text{C} - \text{CH}_2 - \text{COOH}
\]
to CO2 and H2O in muscle requires
(A) elevated insulin levels
(B) thiamine pyrophosphate
(C) HMG CoA synthetase
(D) biotin
(E) cytosolic ATP for activation of the molecule

26. Approximately how many net moles of ATP are generated when one mole of β-hydroxybutyrate is oxidized to carbon dioxide and water in skeletal muscle?
(A) 23
(B) 24
(C) 25
(D) 26
(E) 27

27. After an overnight fast, the blood levels of which of the following compounds will be higher in a person with a carnitine deficiency than in a normal person?
(A) Glucose
(B) Fatty acids
(C) Acetoacetate
(D) 3-Hydroxybutyrate

28. Newly synthesized fatty acids are not immediately degraded because
(A) tissues that synthesize fatty acids do not contain the enzymes that degrade fatty acids
(B) high NADPH levels inhibit β-oxidation
(C) transport of fatty acids into mitochondria is inhibited under conditions in which fatty acids are being synthesized
(D) in the presence of insulin, the key fatty acid degrading enzyme is not induced
(E) newly synthesized fatty acids cannot be converted to their CoA derivatives
29. Type 1 diabetes mellitus is caused by a decreased ability of the \( \beta \) cells of the pancreas to produce insulin. A person with Type 1 diabetes mellitus who has neglected to take insulin injections will have

(A) increased fatty acid synthesis from glucose in liver
(B) decreased conversion of fatty acids to ketone bodies
(C) increased stores of triacylglycerol in adipose tissue
(D) increased production of acetone

30. Which one of the following characteristics of phospholipids is TRUE?

(A) They always contain choline and glycerol
(B) They are an important source of energy during fasting
(C) They are a major component of membranes
(D) They are not charged in the body
(E) They are not soluble in water

31. A cytosine nucleotide is involved in the biosynthesis of a

(A) galactocerebroside
(B) ceramide
(C) phosphatidic acid
(D) phosphatidylcholine

32. Which one of the following is a characteristic of ceramide?

(A) It is not a precursor of gangliosides
(B) It is converted to sphingomyelin by reacting with a UDP-sugar
(C) It has palmitoyl CoA and serine as precursors
(D) It contains a glycerol moiety

33. The accumulation of the GM\(_2\) ganglioside in Tay-Sachs disease is caused by

(A) an increased synthesis of the ganglioside precursor, ceramide
(B) an increased concentration of the UDP-sugars required for ganglioside synthesis
(C) a genetic deficiency of phospholipase A\(_2\)
(D) a deficiency of a lysosomal enzyme that degrades gangliosides

34. Respiratory distress syndrome in premature newborns is caused by deficiency in the lungs of a

(A) sphingomyelin
(B) ganglioside
(C) triacylglycerol
(D) phosphatidylcholine
(E) prostaglandin

35. In the human, prostaglandins can be derived from

(A) glucose
(B) acetyl CoA
(C) arachidonic acid
(D) oleic acid
(E) leukotrienes

36. Which one of the following characteristics correctly describes prostaglandins?

(A) They are derived from fatty acids with 22 carbons
(B) They are linear compounds with no ring structures
(C) They do not contain keto or hydroxy groups
(D) They are synthesized from polyunsaturated fatty acids

37. A cyclooxygenase, which is inhibited by aspirin, is required for the production of

(A) thromboxanes from arachidonic acid
(B) leukotrienes from arachidonic acid
(C) phospholipids from arachidonic acid
(D) arachidonic acid from linoleic acid
Lipid Metabolism / 231

Directions: Each group of items in this section consists of lettered options followed by a set of numbered items. For each item, select the one lettered option that is most closely associated with it. Each lettered option may be selected once, more than once, or not at all.

Questions 38-41

(A) VLDL
(B) Chylomicron
(C) Fatty acid-albumin complex
(D) Bile salt micelle
(E) LDL

A molecule of palmitic acid, attached to carbon 1 of the glycerol moiety of a triacylglycerol, is ingested and digested. It passes into the blood, is stored in a fat cell, and ultimately is oxidized to CO₂ and H₂O in a muscle cell. Choose the molecular complex in the blood in which the palmitate residue is carried from the first site to the second.

38. From the lumen of the gut to the surface of
   the gut epithelial cell
39. From the gut epithelial cell to the blood
40. From the intestine through the blood to a
   fat cell
41. From a fat cell to a muscle cell

Questions 42-45

(A) Palmitate
(B) Acetoacetate
(C) Cholesterol
(D) Bile salts

Match the following descriptions with the appropriate lipid.

42. Oxidized by the brain during prolonged starvatin
43. Produced from acetyl CoA by most cells in the
   body
44. Efficiently recycled by the liver
45. Produced by the liver during fasting

Questions 46-52

(A) Lipoprotein lipase
(B) Pancreatic lipase
(C) Hormone-sensitive lipase
(D) Phospholipase A₂

Match the following descriptions with the appropriate enzyme.

46. Produces 2-monoacylglycerols
47. Degrades the triacylglycerols of chylomicrons in blood capillaries
48. Is activated by protein kinase A
49. Secretion is blocked in cystic fibrosis
50. A deficiency would be most likely to result in morbid obesity
51. Inhibited in an asthmatic patient who is treated with glucocorticoids
52. Less of the active enzyme is present in a patient with Type 1 diabetes mellitus who does not comply with treatment than in a normal person
1-C. Bile salts, synthesized in the liver and secreted by the gallbladder, emulsify dietary triacylglycerols, which contain ester bonds that are hydrolyzed by pancreatic lipase to produce fatty acids and 2-monoacylglycerols. These products are absorbed by intestinal epithelial cells, where they are reconverted to triacylglycerols (by a process that does not require glycerol 3-phosphate) and secreted into the lymph in chylomicrons. (VLDL are produced in the liver.)

2-C. The pancreas produces bicarbonate (which neutralizes stomach acid) and digestive enzymes (including the lipase that degrades dietary lipids). Decreased production of bicarbonate will lead to a decrease of intestinal pH. Lower levels of pancreatic lipase will result in decreased digestion of dietary triacylglycerols, which will lead to formation of fewer bile salt micelles. Intestinal cells will have less substrate for chylomicron formation, and less fat-soluble vitamins will be absorbed. More dietary fat will be excreted in the feces.

3-C. Biotin is required for the acetyl CoA carboxylase reaction in which the substrate, acetyl CoA, is carboxylated by the addition of CO₂ to form malonyl CoA. This reaction occurs in the cytosol. Malonyl CoA provides the 2-carbon 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.

4-B. The synthesis of fatty acids from glucose occurs in the cytosol, except for the mitochondrial reactions in which pyruvate is converted to citrate. Biotin is required for the conversion of pyruvate to oxaloacetate, 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 phosphopantethenyl residue. During the reduction reactions on the synthase complex, the growing fatty acid chain is attached to this residue. NADPH, produced by the malic enzyme as well as by the pentose phosphate pathway, provides the reducing equivalents.

5-A. The 16-carbon, fully saturated fatty acid, palmitate (16:0), is the product of the fatty acid synthase complex. It can be elongated by two carbons to form stearic acid (18:0), or it can be oxidized to form palmitoleic acid (16:1Δ9). Stearate can be oxidized to oleic acid (18:1Δ9). Arachidonic acid (20:4Δ5,8,11,14) can be synthesized from the essential fatty acid linoleate (18:2Δ6,9). It cannot be produced from palmitate. Fatty acids synthesized in the liver are converted to triacylglycerols, packaged in very low density lipoprotein, and secreted into the blood.

6-C. In the liver, 2 fatty acyl CoAs react with glyceral 3-phosphate to form phosphatidic acid, which releases inorganic phosphate to form a diacylglycerol. The diacylglycerol reacts with fatty acyl CoA to form a triacylglycerol.

7-A. Fatty acids, cleaved from the triacylglycerols of chylomicrons and VLDL by the action of lipoprotein lipase, are taken up by adipose cells and react with coenzyme A to form fatty acyl CoA. Glucose is converted via dihydroxyacetone phosphate to glyceral 3-phosphate, which reacts with fatty acyl CoA to form phosphatidic acid. (Adipose tissue lacks glyceral kinase and cannot use glyceral.) After inorganic phosphate is released from phosphatidic acid, the resultant diacylglycerol reacts with another fatty acyl CoA to form a triacylglycerol, which is stored in the adipose cells. (2-Monoacylglycerol is an intermediate only in intestinal cells.)

8-B. Because chylomicrons contain the most triacylglycerol, they are the least dense of the blood lipoproteins. Because VLDL contains more protein, it is more dense than chylomicrons. Because LDL is produced by degradation of the triacylglycerols of VLDL, LDL is more dense than VLDL. HDL is the most dense of the blood lipoproteins. It has the most protein and the least triacylglycerol.
8-B. In the synthesis of cholesterol, but not of ketone bodies, HMG CoA is reduced by NADPH + H+ to mevalonic acid (mevalonate). The enzyme, HMG CoA reductase, is highly regulated (it is inhibited by cholesterol and bile salts and induced by insulin). Mevalonic acid is converted to isopentenyl pyrophosphate, which provides isoprene units for the synthesis of cholesterol (and its derivatives), ubiquinone, dolichol, 1,25-dihydroxycholecalciferol, and compounds that contain geranyl or farnesy1 groups.

9-B. In the synthesis of cholesterol, bile acids, and fatty acids where they are absorbed. More digestive enzymes will lead to increased digestion of intestinal cells will be absorbed. More triacylglycerols, phosphatidic acid, and diacylglycerol accumulate in the cytosol. The mitochondrial enzyme that catalyzes this reaction is connected to fatty acid chain elongation by the pentose diphosphate pathway.

10-A. The class of drugs known as the statins (e.g., lovastatin) lower blood cholesterol levels by inhibiting HMG CoA reductase, a key regulatory enzyme in cholesterol biosynthesis.

11-A. This compound is the bile salt glycocholic acid. During its synthesis, the ring structure of cholesterol is hydroxylated and reduced, and the side chain is oxidized and conjugated with glycine. Although cholesterol can be converted to steroid hormones, this is not one of them. The cholesterol ring structure opens when vitamin D$_3$ is formed. When cholesterol is converted to a cholesterol ester, the hydroxy group at position 3 becomes esterified to a fatty acid.

12-C. During the conversion of cholesterol to bile salts, carbon 7 is hydroxylated. For cholic acid, carbon 12 is also hydroxylated. All hydroxyl groups, including the one on carbon 3, assume an $\alpha$ configuration. The double bond is reduced, and the side chain is oxidized and conjugated with glycine or taurine.

13-B. Taurocholic acid has the lowest pK ($pK = 2$) of these compounds. At pH 3, the ratio of negatively charged to uncharged taurocholate molecules would be approximately 10:1.

14-A. Bacteria in the intestine deconjugate and dehydroxylate bile salts, converting them to secondary bile salts. Therefore, the bile salts become less water-soluble and less effective as detergents, less readily absorbed, and more likely to be excreted in the feces than recycled by the liver. Fewer micelles would be produced, so less dietary lipid (including the fat-soluble vitamins) would be absorbed. Because fewer bile salts would return to the liver, more bile salts would be synthesized. Bile salts inhibit the $\Delta^7$-hydroxylase that is involved in their synthesis. In addition, the person's food intake might decrease which would augment some of the effects noted above.

15-D. HMG CoA reductase inhibitors cause cells to decrease the rate of cholesterol synthesis. Lower cellular levels of cholesterol cause decreased conversion of cholesterol to cholesterol esters (by the ACAT reaction) for storage and increased production of LDL receptors. An increased number of receptors will cause more LDL to be taken up by cells and degraded by lysosomes. Thus, blood cholesterol levels will decrease. Blood triacylglycerol levels will also decrease but not to a great extent because LDL contains only small amounts of triacylglycerol.

16-B. HDL is produced in the liver. It transfers apoprotein C$_\text{III}$, which activates lipoprotein lipase, to chylomicrons and VLDL. HDL picks up cholesterol from cell membranes. This cholesterol is converted to cholesterol esters by the ACAT reaction and transferred to other lipoproteins by the cholesterol ester transfer protein (CETP). Ultimately, these lipoproteins and HDL enter liver cells by endocytosis and are digested by lysosomal enzymes. Hormone-sensitive lipase degrades triacylglycerols stored in adipose cells.

17-B. VLDL is produced mainly from dietary carbohydrate, LDL from VLDL, and chylomicrons from dietary triacylglycerol. Elevated HDL levels are desirable and are not considered to be a lipid disorder.

18-A. Of the blood lipoproteins, LDL contains the highest concentration of cholesterol and lowest concentration of triacylglycerol. Elevated blood LDL levels (the result of decreased endocytosis of LDL) would result in high blood cholesterol levels and relatively normal triacylglycerol levels. A decreased ability to degrade the triacylglycerols of chylomicrons or to convert VLDL to LDL, as well as an increased ability to produce VLDL, would all result in elevated triacylglycerol levels. Because HDL helps to transfer cholesterol from peripheral cells to the liver, high levels are associated with low cholesterol.
19-A. Because chylomicrons are derived from dietary fat, they would be the lipid most likely to be elevated in the blood. VLDL levels would depend on other factors such as the amount of dietary carbohydrate and might or might not be elevated. LDL are derived from VLDL. It is unlikely that a high-fat diet would increase HDL levels. Because cholesterol is present in dietary fat of animal origin, cholesterol levels would most likely be increased.

20-C. During fasting, the hormone-sensitive lipase of adipose tissue is activated by a mechanism involving increased glucagon (and decreased insulin), cAMP, and protein kinase A. Triglycerides are degraded, and fatty acids and glycerol are released into the blood. In the liver, glycerol is converted to glucose and fatty acids to ketone bodies. These fuels are released into the blood and supply energy to various tissues. During fasting, the liver does not produce significant quantities of VLDL.

21-C. Fatty acids are very insoluble in water and are transported in the blood by serum albumin. They cross the plasma membrane and are converted to fatty acyl CoA by CoASH and ATP. In the process, ATP is converted to AMP, thus fatty acid activation utilizes the equivalent of 2 ATP. Fatty acids cross the mitochondrial membranes via a carnitine carrier system. A key enzyme in this process, carnitine acyl transferase I, is inhibited during fatty acid synthesis by malonyl CoA. In mitochondria, fatty acids are oxidized to CO2 and H2O. They cannot be oxidized in red blood cells, which lack mitochondria.

22-A. During fj-oxidation, a double bond is formed between the α and β carbons of a fatty acyl CoA, and FAD is reduced to FADH2. Then water adds across the double bond, and a β-hydroxy compound is formed. The hydroxyl group on carbon 3 (the β-carbon) is oxidized to a keto group by NAD+, which is converted to NADH + H+. Finally, a cleavage catalyzed by thiolase releases one acetyl CoA (which contains two carbons in the acetyl group).

23-C. This fatty acid contains 14 carbons. If it were fully saturated, it would undergo six spirals of fj-oxidation, which would produce 6 FADH2 and 6 NADH + H+, which would generate about 2 x 6 and 3 x 6 ATP, respectively, or a total of 30 ATP. Seven acetyl CoA would be produced, which would enter the TCA cycle and generate about 7 x 12, or 84 ATP. Therefore, for a fully saturated, 14-carbon fatty acid, approximately 114 ATP would be produced. However, 2 ATP are required to activate the fatty acid, reducing the ATP yield to 112. Because this fatty acid is unsaturated (it contains one double bond), one fewer FADH2 would be produced (two fewer ATP would be generated), and the net yield of ATP would be approximately 110.

24-D. Ketone bodies are synthesized in the liver from fatty acids derived from the blood. During the cytosolic activation of the fatty acid, ATP is converted to AMP. Carnitine is required to carry the fatty acyl group across the mitochondrial membrane. In the mitochondrion, the fatty acid is oxidized. Acetyl CoA and acetoacetyl CoA are produced and react to form HMG CoA, which is cleaved by HMG CoA lyase to form acetyl CoA and the ketone body acetoacetate.

25-B. This compound is acetoacetate, which is synthesized in the liver during fasting when blood insulin levels are low. HMG CoA synthetase is the key regulatory enzyme for synthesis, not oxidation. Acetoacetate is transported to tissues, such as muscle, where it is activated in the mitochondrion by succinyl CoA (not ATP), cleaved to 2 acetyl CoA, and oxidized via the tricarboxylic acid (TCA) cycle, which requires the vitamin thiamine as thiamine pyrophosphate, a cofactor for α-ketoglutarate dehydrogenase. Biotin is not required.

26-D. This reaction will produce 26 net moles of ATP, as follows: + 3 ATP produced from the NADH generated when β-hydroxybutyrate is oxidized to acetoacetate. - 1 ATP because, when succinyl CoA is converted to succinate via the thiotransferase reaction that converts acetoacetate to acetoacetyl CoA, no GTP is produced. + 24 ATP produced when 2 acetyl CoA are oxidized in the TCA cycle; therefore, + 26 ATP net.

27-B. After an overnight fast, fatty acids, released from adipose tissue, serve as fuel for other tissues. In the liver, β-oxidation supplies acetyl CoA for ketone body (acetoacetate and 3-hydroxybutyrate) synthesis. In a carnitine deficiency, blood levels of fatty acids will be elevated and ketone bodies will be low because carnitine is required to transport the fatty acids into mitochondria for β-oxidation and ketone body synthesis. Consequently, the body will use more glucose for energy, so glucose levels will decrease.
During fatty acid synthesis (which occurs in the cytosol), malonyl CoA is produced. Malonyl CoA inhibits carnitine acyltransferase I, an enzyme involved in the transport of fatty acids into mitochondria (where \( \beta \)-oxidation occurs).

Decreased insulin levels cause fatty acid synthesis to decrease and glucagon levels to increase. Adipose triacylglycerols are degraded, and fatty acids are released. They are converted to ketone bodies in liver, and a ketoacidosis can occur. Nonenzymatic decarboxylation of acetoacetate forms acetone, which causes the odor associated with diabetic ketoacidosis.

Phospholipids are important components of membrane but are also found in blood lipoproteins and in lung surfactant. They are amphipathic molecules that are not involved in storing energy but in interfacing between body lipids and their aqueous environment. They are soluble in water because they contain a phosphate residue that is negatively charged, and they often contain either choline, ethanolamine, or serine residues that have a positive charge at physiologic pH (A serine residue will contain both a negative charge and a positive charge.)

Cytosine nucleotides are not required for the synthesis of phosphatidic acid or ceramide.

Palmitoyl CoA and serine react to form a precursor that is converted to ceramide by formation of an amide with a fatty acyl CoA. Ceramide does not contain a glycerol moiety. Ceramide may be converted to sphingomyelin (by addition of a phosphocholine group), to a cerebroside (by a reaction with a UDP-sugar), and to a ganglioside (by reaction with UDP-sugars and CMP-NANA).

Accumulation of gangliosides is not caused by increased synthesis but rather by decreased degradation in lysosomes. Phospholipase A\(_2\) cleaves fatty acids from position 2 of phospholipids in cell membranes. It is not a lysosomal enzyme.

Respiratory distress syndrome is caused by a deficiency of lung surfactant, which is composed mainly of dipalmitoylphosphatidylcholine.

Prostaglandins can be synthesized from arachidonic acid (which requires the essential fatty acid, linoleate, for its synthesis). They cannot be synthesized from glucose, and they cannot be made from acetyl CoA or oleic acid. Although leukotrienes are derived from arachidonic acid, they are not precursors of prostaglandins.

Prostaglandins are synthesized from 20-carbon polyunsaturated fatty acids with three, four, or five double bonds. A cyclooxygenase converts the fatty acid to a compound that contains a 5-membered ring. In subsequent reactions, a series of prostaglandins is produced that contain various keto and hydroxy groups.

Arachidonic acid is produced from linoleic acid (an essential fatty acid) by a series of elongation and desaturation reactions. Arachidonic acid is stored in membrane phospholipids, released, and oxidized by a cyclooxygenase (which is inhibited by aspirin) in the first step in the synthesis of prostaglandins, prostacyclins, and thromboxanes. Leukotrienes require a lipoxygenase, rather than a cyclooxygenase, for their synthesis from arachidonic acid.

A palmitate residue attached to carbon 1 of a dietary triacylglycerol is released by pancreatic lipase and carried from the intestinal lumen to the gut epithelial cell in a bile salt micelle. Palmitate is absorbed into the intestinal cell and utilized to synthesize a triacylglycerol, which is packaged in a nascent chylomicron and secreted via the lymph into the blood. The chylomicron, containing the palmitate, matures in the blood by accepting proteins from HDL. It travels to a fat cell.

The chylomicron triacylglycerol is digested by lipoprotein lipase, and the palmitate enters a fat cell and is stored as triacylglycerol. It is released as free palmitate and carried, complexed with albumin, to a muscle cell, where it is oxidized.
42-B. Ketone bodies such as acetoacetate are oxidized by the brain during prolonged starvation.

43-C. Most cells produce cholesterol.

44-D. Ninety-five percent of the bile salts secreted by the liver are returned from the gut to the liver.

45-B. The liver produces ketone bodies such as acetoacetate during fasting.

46-B. Pancreatic lipase produces 2-monoacylglycerols.

47-A. Lipoprotein lipase, which is attached to cell membranes of blood capillary walls, degrades the triacylglycerols of chylomicrons and VLDL.

48-C. Hormone-sensitive lipase is phosphorylated and activated by protein kinase A in response to cAMP.

49-B. Cystic fibrosis, the result of a genetic defect in a chloride channel protein, is characterized by a decreased secretory activity. Pancreatic secretions are blocked. Therefore, food is not adequately digested.

50-C. Deficiencies in pancreatic lipase or lipoprotein lipase would result in decreased fat absorption from the gut and decreased deposition of fat in adipose tissue, respectively. Only a deficiency of hormone-sensitive lipase would result in increased fat stores because of a decreased ability to mobilize triacylglycerols from adipose tissue.

51-D. Glucocorticoids inhibit phospholipase A₂ and thus the release of arachidonic acid for eicosanoid synthesis. Certain leukotrienes cause bronchoconstriction. Inhibition of their synthesis aids asthma sufferers.

52-A. The synthesis of lipoprotein lipase (LPL) by adipose tissue and its secretion into capillaries is stimulated by insulin. In an untreated diabetic who does not produce enough insulin (Type 1 diabetes mellitus) or is resistant to its actions (Type 2 diabetes mellitus), the amount of LPL available to act on chylomicron and VLDL triacylglycerols would be low. Decreased insulin action causes the hormone-sensitive lipase of adipose cells to be active, releasing fatty acids and glycerol, which travel to the liver and form VLDL. Thus, diabetics tend to have high VLDL and chylomicron levels (hyperlipidemia).