1. Fill in the blank. The net yield in ATP production from β-oxidation of a C20:2(9,15) fatty acid is ____ in comparison with net yield in ATP production from β-oxidation of a C18:0 fatty acid

A. +1

B. +2

C. 0

D. -1

E. -2

2. Which of the following conditions produces increased levels of fatty acid synthesis in the cell?

A. glucagon-mediated phosphorylation of acetyl CoA carboxylase

B. activation of isocitrate dehydrogenase

C. fasting

D. high ATP / ADP ratio in the cell

E. all of the above

3. Metabolite that accumulates in Gaucher's disease.

A. ganglioside GM1

B. ganglioside GM2

C. sphingomyelin

D. glucocerebroside

E. galactocerebroside

Choose the single best answer for the following questions.

4. Which of the following enzymes does NOT participate in the utilization of triacylglycerol for energy?

A. enoyl CoA isomerase

B. ATP citrate lyase

C. pyrophosphatase

D. propionyl CoA carboxylase

E. β-hydroxybutyrate dehydrogenase

5. Given the standard reduction potentials for the two redox pairs shown:

$lipoate_{oxidized} + 2e + 2H^+ \rightarrow lipoate_{reduced}$ -0.29V

$NAD^+ + 2e + H^+ \rightarrow NADH$ -0.32V

what can be stated about ΔE for the standard state of the reaction below?

$NAD^+ + lipoate_{reduced} \rightarrow NADH + lipoate_{oxidized} + H^+$

A. ΔE = -0.03V

B. ΔE = -0.61V

C. ΔE = -0.29V

D. ΔE = +0.29V

E. correct answer not given

6. If the caloric equivalent of the Faraday, F, in the equation below is taken as 23 kcal per volt., what would be the free energy change associated with the movement of 4 mol of protons from the cytoplasm into the mitochondrial matrix, assuming that the total electrical and pH gradient across the inner membrane is equivalent to 200 millivolts (matrix negative with respect to the cytoplasm)?

$$\Delta G = -nF\Delta E$$

A. +92 kcal

B. +18.4 kcal

C. -4.6 kcal

D. -18.4 kcal

E. -184000 kcal

7. In carbon monoxide poisoning, CO can bind tightly to cytochrome oxidase and prevent it from binding to oxygen. How would this affect mitochondrial electron transfer?

A. NADH oxidase activity would not be impaired

B. electrons could still travel from succinate to oxygen to maintain respiration

C. CO would be reduced to HCOOH and released

D. all the respiratory chain carriers would be converted to their reduced forms

E. all the redox systems located between the flavoprotein associated with NADH dehydrogenase and cytochrome c oxidase would become fully oxidized

8. Suppose that a person has some sort of defect in skeletal muscle mitochondria so that the inner membrane of mitochondria is a poorer proton insulator than normal, i.e., protons tend to leak back into the matrix from the cytoplasm. You might logically expect to see all of the following EXCEPT

A. a lower than normal P/O ratio in mitochondria from a biopsy sample

B. higher than normal resting rates of respiration in mitochondria from a biopsy sample

C. muscle weakness

D. very low rates of respiration in the absence of ADP and phosphate

E. increased whole body heat production

9. One of the following statements is totally inconsistent with the chemiosmotic hypothesis proposed by P. Mitchell. Which is the inconsistent statement?

A. Adding ATP to intact mitochondria in the absence of an oxidizable substrate causes protons to be pumped from the matrix to the buffer in which the mitochondria are suspended

B. Introducing oxygen to mitochondria suspended in a buffer containing no dissolved oxygen causes a burst of respiration during which protons are pumped out of the matrix

C. Flat open sheets of inner mitochondrial membranes are capable of catalyzing oxidative phosphorylation when suspended in a buffer solution

D. Charged solutes such as pyruvate, phosphate, etc., do not simply diffuse through the inner membrane but require a carrier or porter system to get them across

E. The movement of a proton across the inner membrane can generate a gradient that consists of a ΔE and a ΔpH component

10. All of the following are suggested to be essential for the rotary mechanism proposed for oxidative phosphorylation EXCEPT

A. different conformations of the 3 β-subunits corresponding to an a) open site, b) a nucleotide loose-binding site, c) a nucleotide tight-binding site

B. the formation of an acyl phosphate from phosphate and enzyme which can transfer a phosphoryl group to ADP

C. asymmetric interactions between the γ subunit and the β-subunits

D. in principle, rotation of either the headpiece or the γ-subunit could be the rotator for ATP production

11. You are rounding with the demanding Dr. U. Hoptoitquick. The patient has chronic pancreatitis as a consequence of alcohol abuse. There is severe impairment of both pancreatic α– and β-cell function and evidence of diabetes mellitus. Dr. Hoptoitquick says that in such cases, 'oral hypoglycemic agents rarely help' and that 'insulin should be administered cautiously' Then he fixes YOU with a steely look and says, 'Luckily we have a year 1 medical student to explain the biochemical basis of these observations.' Your best response is

A. to say, 'Pass'

B. to say that the use of oral hypoglycemic agents is inappropriate for a patient with elevated blood glucose and insulin should always be administered with caution

C. to say that oral hypoglycemic agents such as sulfonyl ureas act by promoting the release of insulin and so may be ineffective if insulin synthesis by the β-cells is impaired

D. to say that glucagon and insulin regulate blood glucose by a push-pull mechanism and giving insulin to a patient with a glucagon insufficiency could cause severe hypoglycemia and possibly insulin coma

E. both C and D

12. An untreated patient with a prolonged very high fever might be expected to show any of the metabolic changes listed below (compared to a normal subject) EXCEPT

A. increased rate of gluconeogenesis

B. increased rate of ureagenesis

C. increased circulating levels of glucagon:insulin

D. increased breakdown of body proteins

E. decreased rate of respiration

13. If a normal individual eats a high carbohydrate meal after a 12 hour fast, blood glucose will be elevated and this elevation will be sensed by phosphorylase a, R-form in the liver. Suppose a person has a mutation that causes this form of phosphorylase to bind poorly to glucose, what sort of consequences might you expect to see?

A. the liver phosphorylase would still tend to be active even after a meal

B. the liver phosphorylase would remain in a form that binds to the sequestered protein phosphatase so that the latter would not be released

C. glycogen synthase would tend to remain in the inactive form after a meal because of the unavailability of the protein phosphatase to activate it

D. liver glycogen would be lower than normal even after a meal

E. all of the above

14. Suppose that mitochondria are isolated from the skeletal muscle of a patient with a mitochondrial myopathy. It is found that the mitochondria can oxidize succinate to fumarate at normal rates with a P/O ratio of 2. NADH-linked substrates are oxidized at 20% the normal rate with a P/O ratio of 3. The TCA cycle enzymes are all normal. Where is the most likely source of the metabolic defect?

A. complex 1

B. complex 2

C. complex 3

D. complex 4

E. ATP synthase

15. The pair of metabolites most commonly used to assess noninvasively the energy status of skeletal muscle by ^{31}P NMR is

A. creatinine and ATP

B. ATP and phosphate

C. ATP and AMP

D. phosphocreatine and phosphate

E. ATP and ADP

16. It has been reported that apparently healthy women carrying a mutant allele for ornithine transcarbamylase are at risk of developing hyperammonemia. What type of changes have been linked to hyperammonemia?

A. mood changes, e.g., depression, irritability

B. lethargy

C. nausea and vomiting

D. brain edema

E. all of the above

17. Compounds that have been administered to patients with urea cycle insufficiency arising from various causes include all of those listed EXCEPT

A. lactulose

B. benzoate

C. arginine

D. glycine

E. phenyl acetate

18. The transketolase enzyme requires which of the following for maximal activity?

A. thiamine pyrophosphate

B. biotin

C. CoA

D. dihydroxyacetone phosphate

E. Schiff base formation

19. Enzymes of the pentose phosphate pathway that are directly responsible for interconversions of 3-,4-,5-,6-, or 7-carbon sugars include

A. isomerase and transketolase

B. epimerase and transketolase

C. glucose 6-phosphate dehydrogenase

D. transketolase and transaldolase

E. isomerase and epimerase

20. The primary function of the pentose phosphate pathway is to produce

A. ATP and NAD^+

B. thiamine pyrophosphate and biotin

C. NADPH and ribose 5-phosphate

D. NADH and glyceraldehyde 3-phosphate

E. sedopheptulose 7-phosphate and fructose 6-phosphate

21. Under conditions of low blood glucose,

A. muscle glycogen is degraded to glucose to supply the blood with glucose

B. glucokinase becomes the main intercellular "glucose trapping" enzyme

C. liver glycogen is converted to pyruvate and lactate

D. liver glycogen is converted to blood glucose in reactions involving glucose 6-phosphatase

E. stored lactate is converted to glucose by muscle tissue

22. In a "fasting state",

A. the insulin / glucagon ratio is low

B. cAMP is formed in liver cells

C. hepatic protein phosphatase is inactivated

D. glycogen synthase is phosphorylated by protein kinase A

E. all of the above are correct

23. A patient presents with limited ability to sustain muscle activity. Your examination (including muscle biopsy, blood and urine analysis) shows elevated muscle glycogen levels, low blood lactate following exercise, hemolysis, and no evidence of hepatomegaly. The best explanation for your observations is an inherited deficiency of

A. glucose 6-phosphatase

B. debranching enzyme

C. muscle phosphorylase

D. lysosomal α-1,4-glycosidase

E. muscle phosphofructokinase

24. Glycoproteins contain complex carbohydrates which form a coat around the proteins. These carbohydrates are important in many biological recognition processes, such as

A. the cellular uptake of influenza virus

B. lymphocyte homing

C. egg / sperm recognition

D. regulation of protein life span

E. all above are correct

Choose the single best answer for the following questions.

25. Hunter's syndrome results from

A. β–glucuronidase deficiency

B. iduronate sulfatase deficiency

C. heparin sulfamidase deficiency

D. N-acetyltransferase deficiency

E. α-L-iduronidase deficiency

26. Lovastatin (or Pravachol) is prescribed for patients with hypercholesterolemia. This drug would be most effective when administered to patients

A. with high levels of hepatic cAMP

B. in a "fasting state"

C. with homozygous familial hypercholesterolemia

D. with a high insulin / glucagon ratio

E. all of the above

27. Excess cholesterol is most efficiently eliminated from the body as

A. chylomicrons

B. steroid hormones

C. bile acids

D. CO_2

E. 7-dehydrocholesterol

The following two questions are related

28. A female patient presents with abnormally high levels of urinary 17-ketosteroids and hypertension. This patient could be suffering from

A. Cushings Syndrome

B. Cushings Disease

C. an Adrenogenital Syndrome with 11β-hydroxylase deficiency

D. all the above

29. In an effort to better diagnose her condition you should order the analysis of

A. urinary 17-α-hydroxycorticosteroids

B. plasma 11-deoxycorticosterone

C. plasma ACTH

D. plasma aldosterone

E. all the above

30. The excessive synthesis of androgens in patients with the adrenogenital syndromes caused by deficiencies in the activity of 21-hydroxylase or 11β-hydroxylase in the adrenal cortex is created by

A. the feedback of cortisol on the anterior pituitary

B. high levels of plasma ACTH

C. increased levels of the side-chain splitting enzyme (17, 20-lyase)

D. the inability of the adrenal cortex to respond to ACTH

E. the stimulation of the adrenal cortex by FSH and LH

31. A patient in your clinic has presented with rickets (defective mineralization of bone). Suspecting a vitamin D_3 deficiency, 1α,25$(OH)_2$-vitamin D_3 was administered. There was no response to this treatment. A possible reason for the failure of 1α,25$(OH)_2$-vitamin D_3 to correct this anomaly could be

A. a deficiency in 1α-hydroxylase activity in the proximal kidney tubule

B. a deficiency in 25-hydroxylase activity in the liver

C. the patients lack of exposure to sun light (UV light)

D. a defective vitamin D receptor

E. hypophosphatemia

The following two questions are related.

32. Cells with G-protein mediated second messenger systems would be expected to have membrane receptors for

A. glucagon and epinephrine

B. insulin and epidermal growth factor

C. estrogen and progesterone

D. calmodulin and prostaglandins

E. parathyroid hormone and calmodulin

33. The G-protein is activated by the replacement of GDP by GTP and formation of GαGTP and Gβγ. An important component in the deactivation is the activity of GTPase and the re-formation of Gαβγ–GDP. When cells with deficient GTPase activity (mutated enzymes) are stimulated by the appropriate hormones (as in the previous question), they would contain persistently high levels of

A. protein kinase A and protein kinase C

B. diacylglycerol (DAG) and inositol triphosphate (IP3)

C. cAMP

D. adenylate cyclase and phospholipase C activities

E. all of above

34. In order for growth promoting peptide hormones to stimulate cellular proliferation via a second messenger system which culminates in the activation of nuclear processes, it is necessary that

A. tyrosine kinase directly activate mitogen activated protein kinase (MAP kinase)

B. the growth hormone bind to the nuclear membrane

C. tyrosine kinase first activate a serine / threonine kinase

D. the growth hormone is dephosphorylated

E. the G-protein is phosphorylated

35. Normally ovulation occurs in the mature follicle when plasma levels of estradiol rise rapidly. In certain infertile women ovulation may be promoted by administering only

A. a bolus injection of estradiol to women with a hypopituitary condition

B. a single injection of an antiestrogen to women with polycystic ovaries

C. a bolus injection of luteinizing hormones (LH) to women with hypopituitary condition

D. a single injection of progesterone to women with a hypopituitary condition

E. prostaglandin F2α

36. Luteinizing hormone (LH), follicle stimulating hormone (FSH) and adrenal corticotrophin hormone (ACTH) all bring about which of the following responses in their target tissues?

A. Stimulation of cholesterol esterase

B. Increased uptake of cholesterol into mitochondria

C. Stimulation of aromatase activity

D. Directly increase the activity of HMG-reduction

E. Stimulate the activity of membrane bound phospholipase A2

37. The major precursor of estradiol in the ovarian follicle is

A. dihydrotestosterone

B. 21-hydroxyprogesterone

C. estriol

D. androstenedione

E. cholic acid

38. An estrogen receptor has been cloned from a human breast tumor with a significant mutation in the E domain. From your knowledge of the mechanism of estrogen activity in target tissues, you would expect

A. this tumor to be hormone dependent (i.e. require estrogen for growth)

B. this receptor to bind DNA only after forming a complex with estradiol

C. this tumor to be hormone independent (i.e. does not require estrogen for growth)

D. that estradiol would bind DNA more efficiently

E. these tumor cells would not contain an estrogen response element

39. Certain steroid hormone target tissues have been shown to

A. metabolically form the active hormone in situ

B. metabolically deactivate the active hormone in situ

C. respond to the hormone by the induction of growth or differentiation

D. respond to the hormone by diminished growth or life span

E. all above are correct

40. Spironolactone, tamoxifen and RU486 are used clinically to prevent the activity of natural steroid hormones. All of these drugs function by

A. inhibiting the enzyme desmolase

B. blocking the CYT P450 enzymes

C. prohibiting the metabolic deactivation of steroid hormones in the liver and other tissues

D. forming an inactive complex with a specific gene regulatory protein

E. binding directly to hormone response elements

41. High levels of cholesterol block the synthesis of HMG-reductase and LDL receptor by

A. binding to the HMG-reductase and LDL receptor mRNAs

B. activating protein kinase C

C. decreasing the proteolytic formation of a peptide which binds to the sterol regulatory element

D. preventing the formation of GαGTP by binding to GTPase

E. binding to the sterol regulatory element

42. Which of the following is NOT a feature of biological membranes?

A. Asymmetric distribution of phospholipids on either face of the bilayer

B. Bilayer structure held together primarily by covalent interactions between proteins and lipids

C. Absence of flip-flop of molecules from one face of the bilayer to the other

D. Diffusion of molecules in two dimensions within the bilayer

E. Extrinsic proteins bound to membrane surface by ionic interactions

43. If the hydrophobic portion of a lipid bilayer is 35 Å wide, which of the following is the most likely number for how many amino acid residues it takes for a transmembrane-spanning region of an average intrinsic membrane protein to cross the bilayer?

A. 7

B. 14

C. 21

D. 28

E. 35

44. Which of the following forms channels in a bilayer membrane?

A. gramicidin

B. valinomycin

C. δ-aminolevulinate

D. tetrahydrofolate

E. phenylbutyrate

45. For every ATP hydrolyzed or synthesized, the F_1F_o ATPase transports 3 protons. The relationship between the free energy change (ΔG) and the protonmotive force (Δp) is $\Delta G = n \Delta p$, where n is the number of protons, in this case 3. If the $G^{0'}$ for ATP hydrolysis is 10 kcal / mole, and the transmembrane electrical gradient of protons across the mitochondrial membrane is 100 mV, interior negative, which of the following values is the minimum proton gradient ($[H^+]$ out / $[H^+]$ in) required to drive the synthesis of ATP? The value of 2.3RT is 1.36 kcal / mole. The value of F is 23,000 cal / volt-mole.

A. 1

B. 10

C. 100

D. 1000

E. 10000

F. 100000

46. Which of the following pairs of conditions will both result in decreased membrane fluidity?

A. increased saturation of fatty acids and decreased chain length

B. increased saturation of fatty acids and increased chain length

C. decreased saturation of fatty acids and decreased chain length

D. decreased saturation of fatty acids and increased chain length

E. increased temperature, regardless of fatty acid composition

Choose the single best answer for the following questions.

47. Which of the following is the biochemical target for digitoxigenin?

A. F_1F_o ATPase

B. Vacuolar ATPase

C. Ca^{2+}-ATPase

D. Na^+-K^+ ATPase

E. Na^+-Ca^{2+} antiporter

48. The enzyme complex defective in maple syrup urine disease (branched-chain ketoaciduria) most closely resembles which of the following in catalytic activities and cofactors?

A. pyruvate dehydrogenase

B. citrate synthase

C. malate dehydrogenase

D. citrate lyase

E. pyruvate carboxylase

49. Which of the following is pyridoxal phosphate NOT a cofactor for?

A. serine / threonine dehydratase

B. serine transhydroxymethylase

C. aspartate aminotransferase

D. methylmalonyl CoA mutase

50. Which of the following is an intermediate in the pathway of cysteine biosynthesis?

A. carbamyl phosphate

B. S-adenosyl methionine

C. succinyl CoA

D. pyridoxal phosphate

E. oxaloacetate

51. Which of the following molecules of the urea cycle is the immediate precursor of urea?

A. ornithine

B. citrulline

C. argininosuccinate

D. aspartate

E. arginine

F. carbamyl phosphate

52. Biliverdin is reduced to bilirubin, which is much less soluble than biliverdin, requiring additional steps to make bilirubin more soluble. What, then, is the advantage of converting biliverdin to bilirubin?

A. There is no obvious advantage

B. Bilirubin is glycosylated to increase its solubility

C. Bilirubin is a stronger reducing agent and anti-oxidant than biliverdin

D. Bilirubin represents a branch point in the pathway of heme degradation

E. Bilirubin moves through the plasma more easily than biliverdin

53. Which of the following is NOT a function of blood glutamine?

A. Recognized and excreted by kidney to remove excess nitrogen

B. pH regulation catalyzed by kidney glutaminase

C. Providing carbon skeletons for energy to the bowel

D. Movement of nitrogen from muscle to liver

54. Many enzymes involved in diabetes are subject to regulation by post translational phosphorylation / dephosphorylation. All of the following EXCEPT which one is active in the phosphorylated form.

A. hormone sensitive lipase

B. pyruvate kinase

C. glycogen phosphorylase

D. phosphorylase b kinase

E. PFK-2

55. An insulin effect in adipose tissue is to

A. increase glycolysis

B. increase lipolysis

C. increase proteolysis

D. decrease protein synthesis

E. decrease triglyceride synthesis

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

56. Intermediate common to the *de novo* biosynthesis of triacylglycerol, galactocerebroside, and sphingomyelin in human adipose tissue.

57. Metabolite generated by the action of phospholipase D on phosphatidylcholine.

58. Intermediate common in the catabolic metabolism of ganglioside GM_1, galactocerebroside, and sphingomyelin.

A. dihydroxyacetone phosphate

B. citrate

C. sialic acid

D. galactose

E. phosphoryl choline

F. ceramide

G. CDP-diacylglycerol

H. 1,2-diacylglycerol

I. phosphatidate

J. lysophosphatidate

K. glycerol 3-phosphate

59. Product of the FAD-linked oxidation reaction in β-oxidation of saturated fatty acids.

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

60. Product of the reaction catalyzed by the dehydratase activity of fatty acid synthase.

A. L-β-hydroxyacyl intermediate

B. D-β-hydroxyacyl intermediate

C. trans-Δ^2-enoyl intermediate

D. acetyl CoA

E. β-ketoacyl intermediate

61. A region of the sarcomere that consists primarily of myosin thick filaments

62. A region of the sarcomere that consists primarily of actin thin filaments

A. Z-line (or disk)

B. H-zone of the A band

C. M-line (or disk)

D. the myofibril

E. I-band

F. the outer (A1 zone) of the A band

63. In striated muscle the protein that binds to Ca^{2+} and initiates muscle contraction

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

64. In striated muscle the protein that binds to ATP, thereby breaking the cross bridges between thick and thin filaments

A. troponin-T

B. troponin-C

C. troponin-I

D. myosin

E. F-actin

F. G-actin

G. sarcoplasmic reticulum Ca^{2+} pump

65. The amount of this compound or protein in the urine is used as a measure of the extent of muscle proteolysis

66. The appearance of this compound or protein in the urine can be indicative of severe muscle damage that could lead to renal failureA. creatinine phosphate

B. lactate dehydrogenase

C. dystrophin

D. 3-methyl histidine

E. creatinine kinase

F. myoglobin

G. kinesin

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

67. A product of the phosphoenolpyruvate carboxykinase reaction

68. The enzyme involved in converting pyruvate to oxaloacetate

69. Low levels of this metabolite permit the formation of fructose 6-phosphate and its ultimate conversion to glucose

A. pyruvate dehydrogenase

B. phosphoenolpyruvate carboxykinase

C. pyruvate carboxylase

D. ATP

E. fructose-2,6-bisphosphate

F. CO_2

G. pyruvate

70. A patient with low serum calcium would be expected to show which of the following results from the analysis of body fluids relative to one with normal serum calcium levels?

71. A patient with low serum phosphate would be expected to show which of the following results from the analysis of body fluids relative to one with normal serum phosphate levels?

A. low urinary calcium

B. elevated plasma levels of parathyroid hormone

C. elevated levels of urinary phosphate

D. elevated plasma levels of $1\alpha,25(OH)_2$-vitamin D_3

E. all of the above

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

72. Protects kidney cells from the mineralocorticoid-like activity of cortisol

73. Used in clinical tests for the normal activity of the pituitary / adrenal axis

74. Increased by glucocorticoid activity in lymphocytes

A. metapyrone

B. aminotranferases (transaminases)

C. 4-hydroxyandrostenedione

D. I_kB

E. 11β-hydroxysteroid dehydrogenase

F. dexamethazone

G. 3β-hydroxydehydrogenase

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

75. Protein that is recognized and bound by receptor which is deficient in familial hypercholesterolemia

76. Removes cholesterol from peripheral cells

77. Active in the conversion of cholesterol to the bile acids

78. Bound by liver receptor in patients with homozygous familial hypercholesterolemia

79. Normally is composed of a high proportion of endogenously synthesized lipids

A. chylomicron

B. very low density lipoprotein (VLDL)

C. low density lipoprotein (LDL)

D. lecithin-cholesterol-acyl-transferase (LCAT)

E. lipoprotein lipase (LPase)

F. high density lipoprotein (HDL)

G. cholesterol 7α-hydroxylase

H. Apo B100

I. Apo A

J. remnant

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

Which of the listed amino acids becomes an essential amino acid in the following genetic diseases?

80. urea cycle disorder

81. phenylketonuria

82. defect in S-adenosyl methionine synthesis

A. ornithine

B. phenylalanine

C. methionine

D. arginine

E. tyrosine

F. cysteine