Chapter 14 Glycolysis, Gluconeogenesis, and the Pentose Phosphate Pathway

Multiple Choice Questions

1. **Glycolysis**
   Page: 522 Difficulty: 2 Ans: D
   Glycolysis is the name given to a metabolic pathway occurring in many different cell types. It consists of 11 enzymatic steps that convert glucose to lactic acid. Glycolysis is an example of:

   A) aerobic metabolism.
   B) anabolic metabolism.
   C) a net reductive process.
   D) fermentation.
   E) oxidative phosphorylation.

2. **Glycolysis**
   Page: 523 Difficulty: 1 Ans: C
   The anaerobic conversion of 1 mol of glucose to 2 mol of lactate by fermentation is accompanied by a net gain of:

   A) 1 mol of ATP.
   B) 1 mol of NADH.
   C) 2 mol of ATP.
   D) 2 mol of NADH.
   E) none of the above.

3. **Fates of pyruvate under anaerobic conditions: fermentation**
   Page: 523 Difficulty: 1 Ans: E
   During strenuous exercise, the NADH formed in the glyceraldehyde 3-phosphate dehydrogenase reaction in skeletal muscle must be reoxidized to NAD^+ if glycolysis is to continue. The most important reaction involved in the reoxidation of NADH is:

   A) dihydroxyacetone phosphate $\rightarrow$ glycerol 3-phosphate
   B) glucose 6-phosphate $\rightarrow$ fructose 6-phosphate
   C) isocitrate $\rightarrow$ α-ketoglutarate
   D) oxaloacetate $\rightarrow$ malate
   E) pyruvate $\rightarrow$ lactate

4. **Fates of pyruvate under anaerobic conditions: fermentation**
Page: 523 Difficulty: 2 Ans: C
If glucose labeled with ^{14}C in C-1 were fed to yeast carrying out the ethanol fermentation, where would the ^{14}C label be in the products?

A) In C-1 of ethanol and CO_2
B) In C-1 of ethanol only
C) In C-2 (methyl group) of ethanol only
D) In C-2 of ethanol and CO_2
E) In CO_2 only

5. **Glycolysis**
Page: 524 Difficulty: 2 Ans: E
The conversion of 1 mol of fructose 1,6-bisphosphate to 2 mol of pyruvate by the glycolytic pathway results in a net formation of:

A) 1 mol of NAD^+ and 2 mol of ATP.
B) 1 mol of NADH and 1 mol of ATP.
C) 2 mol of NAD^+ and 4 mol of ATP.
D) 2 mol of NADH and 2 mol of ATP.
E) 2 mol of NADH and 4 mol of ATP.

6. **Fates of pyruvate under anaerobic conditions: fermentation**
Page: 524 Difficulty: 3 Ans: C
In an anaerobic muscle preparation, lactate formed from glucose labeled in C-3 and C-4 would be labeled in:

A) all three carbon atoms.
B) only the carbon atom carrying the OH.
C) only the carboxyl carbon atom.
D) only the methyl carbon atom.
E) the methyl and carboxyl carbon atoms.

7. **Glycolysis**
Page: 525 Difficulty: 2 Ans: B
Which of the following statements is *not* true concerning glycolysis in anaerobic muscle?

A) Fructose 1,6-bisphosphatase is one of the enzymes of the pathway.
B) It is an endergonic process.
C) It results in net synthesis of ATP.
D) It results in synthesis of NADH.
E) Its rate is slowed by a high [ATP]/[ADP] ratio.

8. Glycolysis
Page: 525 Difficulty: 2 Ans: E
When a muscle is stimulated to contract aerobically, less lactic acid is formed than when it contracts anaerobically because:

A) glycolysis does not occur to significant extent under aerobic conditions.
B) muscle is metabolically less active under aerobic than anaerobic conditions.
C) the lactic acid generated is rapidly incorporated into lipids under aerobic conditions.
D) under aerobic conditions in muscle, the major energy-yielding pathway is the pentose phosphate pathway, which does not produce lactate.
E) under aerobic conditions most of the pyruvate generated as a result of glycolysis is oxidized by the citric acid cycle rather than reduced to lactate.

9. Glycolysis
Page: 525 Difficulty: 1 Ans: E
Glycolysis in the erythrocyte produces pyruvate that is further metabolized to:

A) CO_2.
B) ethanol.
C) glucose.
D) hemoglobin.
E) lactate.

10. Glycolysis
Page: 526 Difficulty: 2 Ans: A
When a mixture of glucose 6-phosphate and fructose 6-phosphate is incubated with the enzyme phosphohexose isomerase, the final mixture contains twice as much glucose 6-phosphate as fructose 6-phosphate. Which one of the following statements is most nearly correct, when applied to the reaction below (R = 8.315 J/mol·K and T = 298 K)?

Glucose 6-phosphate ↔ fructose 6-phosphate

A) $\Delta G'^{\circ}$ is +1.7 kJ/mol.
B) $\Delta G'^{\circ}$ is –1.7 kJ/mol.
C) $\Delta G'^{\circ}$ is incalculably large and negative.
D) $\Delta G'^{\circ}$ is incalculably large and positive.
E) $\Delta G'^{\circ}$ is zero.

11. Glycolysis
Page: 528 Difficulty: 2 Ans: D
In glycolysis, fructose 1,6-bisphosphate is converted to two products with a standard free-energy change ($\Delta G'^{\circ}$) of 23.8 kJ/mol. Under what conditions (encountered in a normal cell) will the free-energy change (ΔG) be negative, enabling the reaction to proceed to the right?

A) If the concentrations of the two products are high relative to that of fructose 1,6-bisphosphate.
B) The reaction will not go to the right spontaneously under any conditions because the $\Delta G'^{\circ}$ is positive.
C) Under standard conditions, enough energy is released to drive the reaction to the right.
D) When there is a high concentration of fructose 1,6-bisphosphate relative to the concentration of products.
E) When there is a high concentration of products relative to the concentration of fructose 1,6-bisphosphate.

12. Glycolysis
Page: 529 Difficulty: 3 Ans: E
Glucose labeled with ^{14}C in C-1 and C-6 gives rise in glycolysis to pyruvate labeled in:

A) A and C.
B) all three carbons.
C) its carbonyl carbon.
D) its carboxyl carbon.
E) its methyl carbon.

13. Glycolysis
Page: 529 Difficulty: 2 Ans: E
If glucose labeled with ^{14}C at C-1 (the aldehyde carbon) were metabolized in the liver, the first radioactive pyruvate formed would be labeled in:

A) all three carbons.
B) both A and C.
C) its carbonyl carbon.
D) its carboxyl carbon.
E) its methyl carbon.

14. Fates of pyruvate under anaerobic conditions: fermentation
Page: 529 Difficulty: 2 Ans: B
In an anaerobic muscle preparation, lactate formed from glucose labeled in C-2 would be labeled in:

A) all three carbon atoms.
B) only the carbon atom carrying the OH.
C) only the carboxyl carbon atom.
D) only the methyl carbon atom.
E) the methyl and carboxyl carbon atoms.

15. Fates of pyruvate under anaerobic conditions: fermentation
Page: 529 Difficulty: 2 Ans: C
If glucose labeled with ^{14}C in C-3 is metabolized to lactate via fermentation, the lactate will contain ^{14}C in:

A) all three carbon atoms.
B) only the carbon atom carrying the OH.
C) only the carboxyl carbon atom.
D) only the methyl carbon atom.
E) the methyl and carboxyl carbon atoms.

16. Fates of pyruvate under anaerobic conditions: fermentation
Page: 529 Difficulty: 2 Ans: E
Which of these cofactors participates directly in most of the oxidation-reduction reactions in the fermentation of glucose to lactate?

A) ADP
B) ATP
C) $FAD/FADH_2$
D) Glyceraldehyde 3-phosphate
E) $NAD^+/NADH$

17. Fates of pyruvate under anaerobic conditions: fermentation
Page: 529 Difficulty: 1 Ans: B
In comparison with the resting state, actively contracting human muscle tissue has a:

A) higher concentration of ATP.
B) higher rate of lactate formation.
C) lower consumption of glucose.
D) lower rate of consumption of oxygen
E) lower ratio of NADH to NAD^+.

18. Glycolysis
Pages: 529-531 Difficulty: 2 Ans: C
The steps of glycolysis between glyceraldehyde 3-phosphate and 3-phosphoglycerate involve all of the following *except:*

A) ATP synthesis.
B) catalysis by phosphoglycerate kinase.
C) oxidation of NADH to NAD^+.
D) the formation of 1,3-bisphosphoglycerate.
E) utilization of P_i.

19. **Glycolysis**
Page: 530 Difficulty: 2 Ans: A
The first reaction in glycolysis that results in the formation of an energy-rich compound (i.e., a compound whose hydrolysis has a highly negative $\Delta G'^\circ$) is catalyzed by:

A) glyceraldehyde 3-phosphate dehydrogenase.
B) hexokinase.
C) phosphofructokinase-1.
D) phosphoglycerate kinase.
E) triose phosphate isomerase.

20. **Glycolysis**
Page: 530 Difficulty: 1 Ans: D
Which of the following is a cofactor in the reaction catalyzed by glyceraldehyde 3-phosphate dehydrogenase?

A) ATP
B) Cu^{2+}
C) heme
D) NAD^+
E) $NADP^+$

21. **Glycolysis**
Page: 532 Difficulty: 2 Ans: A
Inorganic fluoride inhibits enolase. In an anaerobic system that is metabolizing glucose as a substrate, which of the following compounds would you expect to increase in concentration following the addition of fluoride?

A) 2-phosphoglycerate
B) Glucose
C) Glyoxylate
D) Phosphoenolpyruvate
E) Pyruvate

22. **Feeder pathways for glycolysis**
Page: 534 Difficulty: 1 Ans: C
Glycogen is converted to monosaccharide units by:

A) glucokinase.
B) glucose-6-phosphatase
C) glycogen phosphorylase.
D) glycogen synthase.
E) glycogenase.

23. Feeder pathways for glycolysis
Page: 537 Difficulty: 3 Ans: C
Galactosemia is a genetic error of metabolism associated with:

A) deficiency of galactokinase.
B) deficiency of UDP-glucose.
C) deficiency of UDP-glucose: galactose 1-phosphate uridylyltransferase.
D) excessive ingestion of galactose.
E) inability to digest lactose.

24. Fates of pyruvate under anaerobic conditions: fermentation
Page: 538 Difficulty: 2 Ans: E
Which of the following statements is *incorrect*?

A) Aerobically, oxidative decarboxylation of pyruvate forms acetate that enters the citric acid cycle.
B) In anaerobic muscle, pyruvate is converted to lactate.
C) In yeast growing anaerobically, pyruvate is converted to ethanol.
D) Reduction of pyruvate to lactate regenerates a cofactor essential for glycolysis.
E) Under anaerobic conditions pyruvate does not form because glycolysis does not occur.

25. Fates of pyruvate under anaerobic conditions: fermentation
Page: 538 Difficulty: 2 Ans: A
The ultimate electron acceptor in the fermentation of glucose to ethanol is:

A) acetaldehyde.
B) acetate.
C) ethanol.
D) NAD^+.
E) pyruvate.

26. Fates of pyruvate under anaerobic conditions: fermentation
Page: 538 Difficulty: 2 Ans: D
In the alcoholic fermentation of glucose by yeast, thiamine pyrophosphate is a coenzyme required by:

A) aldolase.
B) hexokinase.
C) lactate dehydrogenase.
D) pyruvate decarboxylase.
E) transaldolase.

27. Gluconeogenesis
Page: 543 Difficulty: 2 Ans: A
Which of the following compounds *cannot* serve as the starting material for the synthesis of glucose via gluconeogenesis?

A) acetate
B) glycerol
C) lactate
D) oxaloacetate
E) α-ketoglutarate

28. **Gluconeogenesis**
Page: 544 Difficulty: 2 Ans: A
An enzyme used in both glycolysis and gluconeogenesis is:

A) 3-phosphoglycerate kinase.
B) glucose 6-phosphatase.
C) hexokinase.
D) phosphofructokinase-1.
E) pyruvate kinase.

29. **Gluconeogenesis**
Page: 544 Difficulty: 2 Ans: B
Which one of the following statements about gluconeogenesis is *false*?

A) For starting materials, it can use carbon skeletons derived from certain amino acids.
B) It consists entirely of the reactions of glycolysis, operating in the reverse direction.
C) It employs the enzyme glucose 6-phosphatase.
D) It is one of the ways that mammals maintain normal blood glucose levels between meals.
E) It requires metabolic energy (ATP or GTP).

30. **Gluconeogenesis**
Page: 547 Difficulty: 2 Ans: D
All of the following enzymes involved in the flow of carbon from glucose to lactate (glycolysis) are also involved in the reversal of this flow (gluconeogenesis) *except:*

A) 3-phosphoglycerate kinase.
B) aldolase.
C) enolase.
D) phosphofructokinase-1.
E) phosphoglucoisomerase.

31. **Gluconeogenesis**
Page: 548 Difficulty: 2 Ans: A
In humans, gluconeogenesis:

A) can result in the conversion of protein into blood glucose.
B) helps to reduce blood glucose after a carbohydrate-rich meal.
C) is activated by the hormone insulin
D) is essential in the conversion of fatty acids to glucose.
E) requires the enzyme hexokinase.

32. **Gluconeogenesis**
Page: 548 Difficulty: 2 Ans: C
Which of the following substrates *cannot* contribute to net gluconeogenesis in mammalian liver?

A) alanine
B) glutamate
C) palmitate
D) pyruvate
E) α-ketoglutarate

33. The pentose phosphate pathway of glucose oxidation
Page: 549 Difficulty: 2 Ans: E
Which of the following statements about the pentose phosphate pathway is correct?

A) It generates 36 mol of ATP per mole of glucose consumed.
B) It generates 6 moles of CO_2 for each mole of glucose consumed
C) It is a reductive pathway; it consumes NADH.
D) It is present in plants, but not in animals.
E) It provides precursors for the synthesis of nucleotides.

34. The pentose phosphate pathway of glucose oxidation
Page: 549 Difficulty: 2 Ans: E
The main function of the pentose phosphate pathway is to:

A) give the cell an alternative pathway should glycolysis fail.
B) provide a mechanism for the utilization of the carbon skeletons of excess amino acids.
C) supply energy.
D) supply NADH.
E) supply pentoses and NADPH.

35. The pentose phosphate pathway of glucose oxidation
Page: 549 Difficulty: 2 Ans: B
The metabolic function of the pentose phosphate pathway is:

A) act as a source of ADP biosynthesis.
B) generate NADPH and pentoses for the biosynthesis of fatty acids and nucleic acids.
C) participate in oxidation-reduction reactions during the formation of H_2O.
D) provide intermediates for the citric acid cycle.
E) synthesize phosphorus pentoxide.

36. The pentose phosphate pathway of glucose oxidation
Page: 550 Difficulty: 2 Ans: E
Which of the following statements about the pentose phosphate pathway is *incorrect*?

A) It generates CO_2 from C-1 of glucose.
B) It involves the conversion of an aldohexose to an aldopentose.
C) It is prominant in lactating mammary gland.
D) It is principally directed toward the generation of NADPH.
E) It requires the participation of molecular oxygen.

37. The pentose phosphate pathway of glucose oxidation
Page: 550 Difficulty: 2 Ans: D
Glucose breakdown in certain mammalian and bacterial cells can occur by mechanisms other than classic glycolysis. In most of these, glucose 6-phosphate is oxidized to 6-phosphogluconate, which is then further metabolized by:

A) an aldolase-type split to form glyceric acid and glyceraldehyde 3-phosphate.
B) an aldolase-type split to form glycolic acid and erythrose 4-phosphate.
C) conversion to 1,6-bisphosphogluconate.
D) decarboxylation to produce keto- and aldopentoses.

E) oxidation to a six-carbon dicarboxylic acid.

38. **The pentose phosphate pathway of glucose oxidation**
Page: 550 Difficulty: 2 Ans: A
Which of the following enzymes acts in the pentose phosphate pathway?

A) 6-phosphogluconate dehydrogenase
B) Aldolase
C) Glycogen phosphorylase
D) Phosphofructokinase-1
E) Pyruvate kinase

39. **The pentose phosphate pathway of glucose oxidation**
Page: 550 Difficulty: 3 Ans: C
The oxidation of 3 mol of glucose by the pentose phosphate pathway may result in the production of:

A) 2 mol of pentose, 4 mol of NADPH, and 8 mol of CO_2.
B) 3 mol of pentose, 4 mol of NADPH, and 3 mol of CO_2.
C) 3 mol of pentose, 6 mol of NADPH, and 3 mol of CO_2.
D) 4 mol of pentose, 3 mol of NADPH, and 3 mol of CO_2.
E) 4 mol of pentose, 6 mol of NADPH, and 6 mol of CO_2.

40. **The pentose phosphate pathway of glucose oxidation**
Page: 550 Difficulty: 2 Ans: A
Glucose, labeled with ^{14}C in different carbon atoms, is added to a crude extract of a tissue rich in the enzymes of the pentose phosphate pathway. The most rapid production of $^{14}CO_2$ will occur when the glucose is labeled in:

A) C-1.
B) C-3.
C) C-4.
D) C-5.
E) C-6.

41. **The pentose phosphate pathway of glucose oxidation**
Page: 550 Difficulty: 2 Ans: A
In a tissue that metabolizes glucose via the pentose phosphate pathway, C-1 of glucose would be expected to end up principally in:

A) carbon dioxide.
B) glycogen.
C) phosphoglycerate.
D) pyruvate.
E) ribulose 5-phosphate.

Short Answer Questions

42. **Glycolysis**
Page: 521 Difficulty: 2 Ans: C
There are a variety of fairly common human genetic diseases in which enzymes required for the breakdown of fructose, lactose, or sucrose are defective. However, there are very few cases of people

having a genetic disease in which one of the enzymes of glycolysis is severely affected. Why do you suppose such mutations are seen so rarely?

Ans: The glycolytic pathway is so central to all of cellular metabolism that mutations in glycolytic enzymes are lethal; embryos with such mutations would not survive.

43. Glycolysis
Page: 522 Difficulty: 2 Ans: C
Define "fermentation" and explain, by describing relevant reactions, how it differs from glycolysis. Your explanation should include a discussion of the role of NADH in the reaction(s).

Ans: Fermentation is the operation of the glycolytic pathway under anaerobic conditions. Under aerobic conditions, the pyruvate produced by glycolysis is oxidized to acetyl-CoA, which passes through the citric acid cycle. NADH produced in the oxidations passes electrons to O_2, and is thus recycled to NAD^+ allowing the continuation of the glycolytic reactions. When no O_2 is available to reoxidize the NADH produced by the glyceraldehyde 3-phosphate dehydrogenase reaction, electrons from NADH must be passed to one of the products of glycolysis, such as pyruvate or acetaldehyde, forming lactate or ethanol.

44. Glycolysis
Page: 523 Difficulty: 1 Ans: C
In glycolysis there are two reactions that require one ATP each and two reactions that produce one ATP each. This being the case, how can fermentation of glucose to lactate lead to the net production of two ATP molecules per glucose?

Ans: The two reactions that produce ATP in glycolysis (those catalyzed by phosphoglycerate kinase and pyruvate kinase) involve three-carbon compounds, whereas the two reactions that consume ATP occur at the level of hexoses. In glycolysis, each hexose yields two trioses, each of which undergoes the reactions that yield ATP. The ATP yield for triose reactions therefore must be doubled for stoichiometric comparison with the ATPs consumed in hexose phosphorylation. Two ATP molecules are consumed and four are produced for each glucose that passes through the pathway, resulting in a net yield of two ATP per glucose.

45. Glycolysis
Page: 523 Difficulty: 2 Ans: C
Briefly describe the possible metabolic fates of pyruvate produced by glycolysis in humans, and explain the circumstances that favor each.

Ans: Under aerobic conditions, pyruvate is oxidized to acetyl-CoA and passes through the citric acid cycle. Under anaerobic conditions, pyruvate is reduced to lactate to recycle NADH to NAD^+, allowing the continuation of glycolysis.

46. Glycolysis
Page: 523 Difficulty: 2
Show how NADH is recycled to NAD^+ under aerobic conditions and under anaerobic conditions. Why is it important to recycle NADH produced during glycolysis to NAD^+?

Ans: Cells contain a limited supply of NAD^+ and NADH. The oxidation of glyceraldehyde 3-phosphate requires NAD^+ as as electron acceptor—it converts NAD^+ to NADH. Unless this NADH is recycled to NAD^+, oxidative metabolism in this cell will cease for lack of an electron acceptor. Under aerobic conditions, NADH passes electrons to O_2; under anaerobic conditions, NADH reduces pyruvate to lactate, and is thereby recycled to NAD^+.

47. Fates of pyruvate under anaerobic conditions: fermentation
Page: 523 Difficulty: 2
Explain with words, diagrams, or structures why lactate accumulates in the blood during bursts of very vigorous exercise (such as a 100-meter dash).

Ans: During vigorous exercise, the cardiovascular system cannot deliver O_2 to the muscle tissue fast enough to maintain aerobic conditions. As glycolysis proceeds under anaerobic conditions, NAD^+ is converted to NADH (during the glyceraldehyde 3-phosphate dehydrogenase reaction), but the muscle tissue has no O_2 to which NADH can pass electrons. To recycle NADH to NAD^+, which is essential for continuing glycolysis, electrons from NADH are used to reduce pyruvate to lactate.

48. Fates of pyruvate under anaerobic conditions: fermentation
Page: 523 Difficulty: 2
Describe the fate of pyruvate, formed by glycolysis in animal skeletal muscle, under two conditions: (a) at rest, and (b) during an all-out sprint. Show enough detail in your answer to explain *why* pyruvate metabolism is different in these two cases.

Ans: (a) At rest, plenty of O_2 is being delivered to the muscle, and pyruvate formed during glycolysis is oxidized to acetyl-CoA by the pyruvate dehydrogenase complex. Acetyl groups then enter the citric acid cycle and are oxidized to CO_2 (b) Under the conditions of all-out exertion, skeletal muscle cannot be supplied with enough O_2 to keep metabolism completely aerobic; under these conditions, muscle tissue must function anaerobically. Pyruvate is reduced to lactate to recycle NADH, formed by glycolysis, to NAD^+, so that glycolysis can continue.

49. Fates of pyruvate under anaerobic conditions: fermentation
Page: 523 Difficulty: 2
During strenuous activity, muscle tissue demands large quantities of ATP, compared with resting muscle. In white skeletal muscle (in contrast with red muscle), ATP is produced almost exclusively by fermentation of glucose to lactate. If a person had white muscle tissue devoid of the enzyme lactate dehydrogenase, how would this affect his or her metabolism at rest and during strenuous exercise?

Ans: Lactate dehydrogenase allows cells to pass electrons from NADH to pyruvate, thus regenerating NAD^+ for continued glycolysis under anaerobic conditions. The lack of this enzyme would cause no significant problems at rest because aerobic red muscle tissue would function well. During strenuous exercise, however, the absence of lactate dehydrogenase would severely reduce the ability of muscle to perform anaerobically.

50. Glycolysis
Page: 524 Difficulty: 2
There are two reactions in glycolysis in which an aldose is isomerized to a ketose. For one of these reactions draw the structures of the aldose and the ketose. For both reactions the $\Delta G'^{\circ}$ is positive. Briefly explain how the reactions are able to proceed without the input of additional energy.

Ans: The two reactions are those catalyzed by phosphohexose isomerase and triose phosphate isomerase:

glucose 6-phosphate → fructose 6-phosphate
(aldose) (ketose)

dihydroxyacetone phosphate → glyceraldehyde 3-phosphate
(ketose) (aldose)

Although both of these reactions have standard free-energy changes ($\Delta G'^{\circ}$) that are positive, they can occur within cells because the products are immediately removed by the next step in the pathway. The result is a very low steady-state concentration of the products, making the actual free-energy changes (ΔG) negative:

$\Delta G = \Delta G'^{\circ} + RT \ln ([\text{products}]/[\text{substrates}])$

(See also Chapter 14.)

51. Glycolysis
Page: 524 Difficulty: 3
Describe the part of the glycolytic pathway from fructose 6-phosphate to glyceraldehyde 3-phosphate. Show structures of intermediates, enzyme names, and indicate where any cofactors participate.

Ans: This part of the pathway involves the reactions catalyzed by phosphofructokinase-1, aldolase, and triose phosphate isomerase. (See the figures from pp. 533-534.)

52. Glycolysis
Page: 524 Difficulty: 2
Describe the glycolytic pathway from fructose 1,6-bisphosphate to 1,3-bisphospho-glycerate, showing structures of intermediates and names of enzymes. Indicate where any cofactors participate.

Ans: The answer should show the reactions catalyzed by aldolase, triose phosphate isomerase, and glyceraldehyde 3-phosphate dehydrogenase. (See figures from pp. 533-536.)

53. Feeder pathways for glycolysis
Page: 524 Difficulty: 3
Yeast can metabolize D-mannose to ethanol and CO_2. In addition to the glycolytic enzymes, the only other enzyme needed is phosphomannose isomerase, which converts mannose 6-phosphate to fructose 6-phosphate. If mannose is converted to ethanol and CO_2 by the most direct pathway, which of the compounds and cofactors in this list are involved?

A. Lactate
B. Acetaldehyde
C. Acetyl-CoA
D. FAD
E. Glucose 6-phosphate
F. Fructose 1-phosphate
G. Pyruvate
H. Lipoic acid
I. Thiamine pyrophosphate
J. Dihydroxyacetone phosphate

Ans: B, G, I, J

54. The pentose phosphate pathway of glucose oxidation
Page: 524 Difficulty: 2
Rat liver is able to metabolize glucose by both the glycolytic and the pentose phosphate pathways. Indicate in the blanks if the following are properties of glycolytic (G), pentose phosphate (P), both (G + P), or neither (0):

_____ NAD^+ is involved.
_____ CO_2 is liberated.
_____ Phosphate esters are intermediates.
_____ Glyceraldehyde 3-phosphate is an intermediate.
_____ Fructose 6-phosphate is an intermediate.

Ans: G; P; G + P; G; G

55. Glycolysis
Page: 526 Difficulty: 2
In the conversion of glucose to pyruvate via glycolysis, all of the following enzymes participate. Indicate the order in which they function by numbering them.
_1_ hexokinase
_4__ triose phosphate isomerase
_2__ phosphohexose isomerase
_6__ enolase
_5__ glyceraldehyde 3-phosphate dehydrogenase
_7__ pyruvate kinase
_3__ phosphofructokinase-1

Which of the enzymes represents a major regulation point in glycolysis?
Which catalyzes a reaction in which ATP is produced?
Which catalyzes a reaction in which NADH is produced?

Ans: 4; 2; 6; 5; 7; 3; phosphofructokinase-1; pyruvate kinase; glyceraldehyde 3-phosphate dehydrogenase

56. Glycolysis
Page: 526 Difficulty: 2 Ans: C
The conversion of glucose into glucose 6-phosphate, which must occur in the breakdown of glucose, is thermodynamically unfavorable (endergonic). How do cells overcome this problem?

Ans: Cells often drive a thermodynamically unfavorable reaction in the forward direction by coupling it to a highly exergonic reaction through a common intermediate. In this example, to make glucose 6-phosphate formation thermodynamically favorable, cells transfer phosphoryl groups from ATP to glucose. ATP "hydrolysis" is highly exergonic, making the overall reaction exergonic. (Numerical solution below not required.)

	Glucose + P_i →	glucose 6-phosphate + H_2O	$\Delta G'^\circ = +13.8$ kJ/mol
	ATP + H_2O →	ADP + P_i	$\Delta G'^\circ = -30.5$ kJ/mol
Sum:	ATP + glucose →	ADP + glucose 6-phosphate	$\Delta G'^\circ = -16.7$ kJ/mol

See p. 498; see also Chapter 14.

57. Glycolysis
Page: 528 Difficulty: 3
The conversion of glyceraldehyde 3-phosphate to dihydroxyacetone phosphate is catalyzed by triose phosphate isomerase. The standard free-energy change ($\Delta G'^\circ$) for this reaction is –7.5 kJ/mol. Draw the two structures. Define the equilibrium constant for the reaction and calculate it using only the data given here. Be sure to show your work. ($R = 8.315$ J/mol·K; $T = 298$ K)

Ans: See Fig. 15-4, p. 535.

$$K_{eq}' = \frac{[\text{glyceraldehyde 3-phosphate}]}{[\text{dihydroxyacetone phosphate}]}$$

$$\Delta G'^\circ = -RT \ln K_{eq}'$$

$$\ln K_{eq}' = \frac{\tilde{}\,\Delta G'^\circ}{RT}$$

$$\ln K_{eq}' = \frac{7{,}500 \text{ J/mol}}{(8.315 \text{ J/mol·K})(298 \text{ K})} = 3.027$$

$$K_{eq}' = 20.6$$

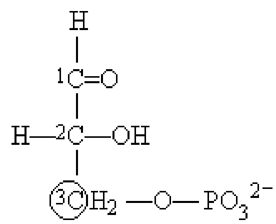
(See also Chapter 14.)

58. Glycolysis
Page: 529 Difficulty: 3
When glucose is oxidized via glycolysis, the carbon atom that bears the phosphate in the 3-phosphoglycerate formed may have originally been either C-1 or C-6 of the original glucose. Describe this pathway in just enough detail to explain this fact.

Ans: The 3-phosphoglycerate derived from glucose by glycolysis is formed from glyceraldehyde 3-phosphate. The action of aldolase on fructose 1,6-bisphosphate produces dihydroxyacetone phosphate (derived from C-1, C-2, and C-3 of glucose) and glyceraldehyde 3-phosphate (derived from C-4, C-5, and C-6 of glucose). When triose phosphate isomerase then converts dihydroxyacetone phosphate to glyceraldehyde 3-phosphate, C-3 of glyceraldehyde 3-phosphate will contain both C-1 and C-6 from glucose. (See Fig. 15-4, p. 535.)

59. Glycolysis
Page: 529 Difficulty: 3
When glucose labeled with a ^{14}C at C-1 (the aldehyde carbon) passes through glycolysis, the glyceraldehyde 3-phosphate that is produced from it still contains the radioactive carbon atom. Draw the structure of glyceraldehyde 3-phosphate, and circle the atom(s) that would be radioactive.

Ans: The labeled carbon is C-3.



60. Glycolysis
Page: 529 Difficulty: 3
At which point in glycolysis do C-3 and C-4 of glucose become chemically equivalent?

Ans: When dihydroxyacetone phosphate is converted into glyceraldehyde 3-phosphate by triose phosphate isomerase, C-3 and C-4 of glucose become equivalent; they are both C-1 of glyceraldehyde 3-phosphate. (See Fig. 15-4, p. 535.)

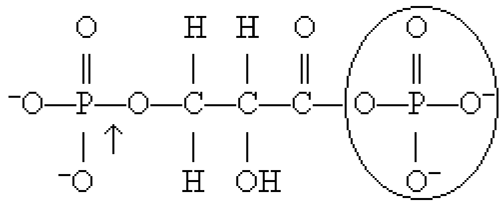
61. Glycolysis
Page: 529 Difficulty: 2
Explain why P_i (inorganic phosphate) is absolutely required for glycolysis to proceed.
Ans: Inorganic phosphate (P_i) is an essential substrate in the reaction catalyzed by glyceraldehyde 3-phosphate dehydrogenase.

62. Glycolysis
Page: 529 Difficulty: 2
If brewer's yeast is mixed with pure sugar (glucose) in the absence of phosphate (P_i), no ethanol is produced. With the addition of a little P_i, ethanol production soon begins. Explain this observation in 25 words or less.

Ans: The reaction catalyzed by glyceraldehyde 3-phosphate dehydrogenase requires P_i as a substrate. Without P_i, glycolysis ceases, and no ethanol is produced.

63. Glycolysis
Page: 530 Difficulty: 2
Draw the structure of 1,3-bisphosphoglycerate. Indicate with an arrow the phosphate ester, and circle the phosphate group for which the free energy of hydrolysis is very high.

Ans:



64. Glycolysis
Page: 531 Difficulty: 2
Two reactions in glycolysis produce ATP. For each of these, show the name and structure of reactant and product, indicate which cofactors participate and where, and name the enzymes.

Ans: The two reactions are those catalyzed by phosphoglycerate kinase and pyruvate kinase. (See reactions on pp. 537 [top] and 539 [bottom].)

65. Feeder pathways for glycolysis
Page: 534 Difficulty: 3
Explain why the phosphorolysis of glycogen is more efficient than the hydrolysis of glycogen in mobilizing glucose for the glycolytic pathway.

Ans: Phosphorolysis yields glucose 1-phosphate, which can be converted into glucose 6-phosphate without the investment of energy from ATP. Hydrolysis of glycogen yields free glucose, which must be converted into glucose 6-phosphate (at the expense of ATP) before it can enter glycolysis.

66. Feeder pathways for glycolysis
Page: 534 Difficulty: 3
Describe the process of glycogen breakdown in muscle. Include a description of the structure of glycogen, the nature of the breakdown reaction and the breakdown product, and the required enzyme(s).

Ans: Muscle glycogen consists of linear polymers of $\alpha(1 \rightarrow 4)$-linked D-glucose, with many branches formed by $\alpha(1 \rightarrow 6)$ glycosidic linkages to D-glucose. Glycogen phosphorylase in muscle catalyzes phosphorolytic cleavage of the terminal residue at the nonreducing ends, producing glucose 1-phosphate. When phosphorylase approaches $\alpha(1 \rightarrow 6)$ branch points, a second enzyme (the "debranching enzyme") removes the four glucose residues nearest the branch point and reattaches them in $\alpha(1 \rightarrow 4)$ linkage at a nonreducing end. Now phosphorylase can continue to degrade the molecule.

67. Feeder pathways for glycolysis
Pages: 535-536 Difficulty: 2
Explain the biochemical basis of the human metabolic disorder called lactose intolerance.

Ans: In lactose intolerance, the enzyme lactase, found in the surface of intestinal epithelial cells in children, has been lost in adulthood. Without this enzyme, the individual cannot hydrolyze lactose in the small intestine and take up the resulting monosaccharides; instead, lactose passes into the large intestine, where it is metabolized by bacteria, producing gastric distress.

68. Gluconeogenesis
Page: 543 Difficulty: 1
What is gluconeogenesis, and what useful purposes does it serve in people?

Ans: Gluconeogenesis is the biosynthesis of glucose from simpler, noncarbohydrate precursors such as oxaloacetate or pyruvate. During periods of fasting, when carbohydrate reserves have been exhausted, gluconeogenesis provides glucose for metabolism in tissues (brain, erythrocytes) that derive their energy primarily from glucose metabolism.

69. Gluconeogenesis
Pages: 544-545 Difficulty: 3
In gluconeogenesis, how do animals convert pyruvate to phosphoenolpyruvate? Show structures, enzymes, and cofactors.

Ans: Pyruvate is converted into phosphoenolpyruvate in two steps:
(1) Pyruvate + HCO_3^- + ATP $\longrightarrow$ oxaloacetate + ADP + P_i
(2) Oxaloacetate + GTP $\longrightarrow$ CO_2 + GDP + phosphoenolpyruvate
The first reaction is catalyzed by pyruvate carboxylase, which requires biotin as a cofactor; the second, by phosphoenolpyruvate carboxykinase. [See Fig. 20-3, p. 727].

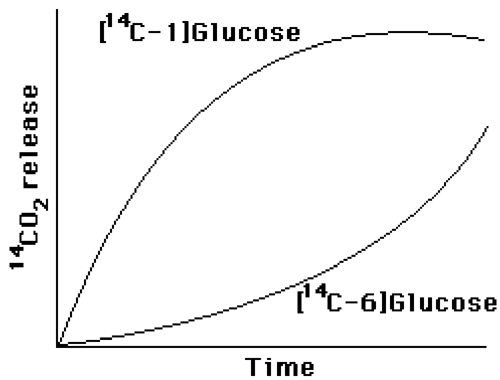
70. The pentose phosphate pathway of glucose oxidation
Page: 549 Difficulty: 2
The bacterium *E. coli* can grow in a medium in which the only carbon source is glucose. How does this organism obtain ribose 5-phosphate for the synthesis of ATP? (Do not describe ATP synthesis, just the origin of ribose 5-phosphate.) Show structures and indicate where cofactors participate.

Ans: Ribose 5-phosphate is produced from glucose by the reactions of the pentose phosphate pathway. (See Fig. 15-20, p. 558.)

71. The pentose phosphate pathway of glucose oxidation
Page: 549 Difficulty: 1
What are the biological functions of the pentose phosphate pathway?

Ans: The pentose phosphate pathway produces pentose phosphates (for nucleotide synthesis) and NADPH (reducing agent for biosynthetic processes).

72. The pentose phosphate pathway of glucose oxidation
Page: 550 Difficulty: 2
An extract of adipose (fat) tissue can metabolize glucose to CO_2. When glucose labeled with ^{14}C in either C-1 or C-6 was added to the extract, $^{14}CO_2$ was released with the time courses shown below. What is the major path of glucose oxidation in this extract? Explain how you reached this conclusion.



Ans: The tissue must be oxidizing glucose primarily by the pentose phosphate pathway, in which C-1 is released (as CO_2) earlier than C-6. During glycolysis, C-1 and C-6 become equivalent at the level of glyceraldehyde 3-phosphate, and C-1 and C-6 are thus released simultaneously (during passage of acetate through the citric acid cycle).