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Answers to In-Text Review Questions, Chapter 2, Energy Production

1. **Distinguish between anabolism and catabolism. Is cellular respiration anabolic or catabolic?**

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   Anabolism—energy transformation in which small molecules are combined to make a larger one resulting in the buildup of tissues; requires the utilization of ATP energy.

   Catabolism—energy transformation in which large molecules are broken down into smaller ones and energy is produced; the production of ATP from the breakdown of carbohydrate, fat, or protein.

2. **Name and briefly summarize the four steps of carbohydrate metabolism.**

   Pages 35–43, Figures 2.6, 2.8, 2.9, 2.10, and 2.12

   The four stages of carbohydrate metabolism are as follows:

   I. Glycolysis
   - Begins with glucose or glycogen
   - Consists of 10 (aerobic) or 11 (anaerobic) steps
   - Ends with pyruvic acid (aerobic) or lactic acid (anaerobic)
   - Produces two (glucose) or three (glycogen) ATP as net gain by substrate-level phosphorylation and two NADH + H^+

   II. Formation of acetyl CoA
   - Begins with pyruvic acid
   - Consists of two steps
   - Ends with acetyl CoA
   - Produces two NADH + H^+
   - No ATP produced directly

   III. Krebs cycle
   - Begins with acetyl CoA combining with oxaloacetate
   - Consists of eight steps
   - Ends with oxaloacetate

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- Produces two ATP directly by substrate-level phosphorylation, six NADH + H^+, and two $FADH_2$

IV. Electron transport and oxidative phosphorylation

- Begins with the release of the hydrogen ions (H^+) and electrons from NAD^+ and FAD.
- Proceeds as a series of chemical reactions that shuttles the electrons along the respiratory chain cytochromes. The final electron acceptor is oxygen. The H^+ are transported into the intermembrane space creating an electrochemical gradient and current. This electrical energy synthesizes ATP from ADP + P_i.
- 30 ATP (skeletal muscle) or 32 ATP (cardiac muscle) are produced by oxidative phosphorylation.

3. Explain how a count of 30 ATP is achieved by cellular respiration if the fuel substrate is glucose in skeletal muscle. Why is the count often 31, 32, and 33?

Pages 42-44, 55 Table 2.1

Tissue	Substrate	ATP Yield
Skeletal muscle	Glucose	30
	Glycogen	31
Cardiac muscle	Glucose	32
	Glycogen	33

- Glucose always produces 1 less ATP than glycogen because glycogen enters after step 1 where 1 ATP is used thereby, yielding a net gain of 3, not 2 ATP, for glycolysis. Skeletal muscle always produces 2 less ATP than cardiac muscle because the hydrogens are transferred from NAD^+ to FAD in the glycerol-phosphate shuttle (skeletal muscle) but continue to be carried by NAD^+ in the malate-aspartate shuttle (cardiac muscle) when the hydrogens from glycolysis cross the mitochondria membrane.

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When using the multiplier of 2.5 for NADH + H^+ and 1.5 for $FADH_2$, a count of 30 ATP is achieved if the fuel substrate is glucose in skeletal muscle by:

- 2 ATP from direct substrate-level phosphorylation; glycolysis
- 3 ATP from NADH + $H^+ \rightarrow FADH_2$; glycolysis
- 5 ATP from 2 NADH + H^+; stage II
- 2 ATP from substrate-level phosphorylation; Krebs cycle
- 18 ATP from $FADH_2$ + NADH + H^+; Krebs cycle; oxidative phosphorylation

- A total of 30 ATP molecules are produced if the fuel substrate is glucose and the muscle is skeletal. A total of 31 ATP are produced if the fuel substrate is glycogen and the muscle is skeletal. A total of 32 ATP are produced if the fuel substrate is glucose and the muscle is cardiac. A total of 33 ATP are produced if the fuel substrate is glycogen and the muscle is cardiac.

4. Why is beta-oxidation necessary before fat can be used as an energy substrate? Describe what occurs during beta-oxidation.

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Beta-oxidation is necessary to reduce the fat from a 14 to 24 carbon unit (that it typically is) to a 2 carbon unit. This 2 carbon unit can be converted to acetyl CoA, enter the Krebs cycle, and subsequently undergo electron transport and oxidative phosphorylation to resynthesize ATP.

In beta-oxidation, the fatty acid is first activated by the breakdown of ATP to AMP. Concurrently coenzyme A is added. Hydrogens are removed with one pair being picked up by FAD and the other by NAD^+. The bond is broken between the alpha carbon (C_2) and the beta carbon (C_3) resulting in the removal of two carbons (C_1 + C_2). These two carbons are then used to form acetyl coenzyme A. This process is repeated for all but except the last pair of carbons since the last pair form acetyl CoA itself.

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5. **State how the calculation is completed to determine the number of ATP produced from fatty acids. Complete an example using a fat having 24 carbons.**

   Pages 43-44

   a. n/2−1 = 24/2−1 = 11 times through beta-oxidation.
   b. Each cycle produces 1 $FADH_2$ and 1 NADH + H^+, which in turn produce 4 total ATP. 11 cycles × 4 = 44 ATP.
   c. Each time through beta-oxidation (11) plus the last step (1) produces acetyl CoA. Each acetyl CoA yields 1 ATP, 3 NADH, and 1 $FADH_2$ in the Krebs cycle for a net gain of 10 ATP for each acetyl CoA. 10 ATP × 12 acetyl CoA = 120 ATP.
   d. 120 ATP + 44 ATP = 164 ATP minus 2 ATP used in activation = 162 ATP from a 24 carbon fat.

6. **Name and describe the process that amino acids must undergo before being used as a fuel substrate. Why is this process necessary?**

   Pages 47–49

   Amino acids must undergo transamination or oxidative deamination before being used as a fuel. This is necessary because all amino acids contain an amino group (NH_2) that must be removed before it can enter the Krebs cycle. Transamination simply involves the transfer of the NH_2 amino group from an amino acid to a keto acid, resulting in a new amino acid and different keto acid. Deamination is the removal of the amino group that produces ammonia and a keto acid.

7. **Identify the locations in the metabolic pathways where amino acids may enter. How does the ATP count differ between these locations?**

   Pages 47, 56, Figure 2.2

   Amino acids can enter the metabolic pathways as pyruvic acid, as acetyl CoA, or in several locations in the Krebs cycle. The latter are converted to pyruvate before being used. If the amino acid is used as pyruvate, 12.5 ATP are produced; if the amino acid enters as acetyl CoA, 10 ATP are produced.

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8. **Why is acetyl CoA called the universal common intermediate?**

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   Acetyl CoA is called the universal common intermediate because all substrates whether they go through glycolysis, beta-oxidation, or transamination/oxidative deamination can and do form acetyl CoA before entering the Krebs cycle and ET/OP.

9. **Why might the breath of someone suffering from anorexia nervosa smell sweet?**

   Page 47

   When the supply of glucose is inadequate, oxaloacetate must be converted into glucose, and because it is no longer available to bind to acetyl CoA, the acetyl CoA from the fatty acid is converted into three forms of ketones (acetoacetic acid, beta-hydroxybutyric acid, and acetone). It is the acetone that gives the sweet fruity smell in anorexic individuals who typically have inadequate diets, hence insufficient glucose supplies.

   Ketosis is more likely to result from a purposeful low carbohydrate diet, an inadequate diet (as in anorexia nervosa), or diabetes than from prolonged exercise, since the muscles will use the ketones as fuel. During exercise, aerobically trained individuals can utilize ketones more effectively than can untrained individuals.

10. **Describe the role of enzymes in the metabolic pathways. Identify the rate-limiting enzymes in Stages I, III, and IV of carbohydrate metabolism. How are enzymes regulated?**

    Pages 35, 40, and 41, Figures 2.6, 2.9, and 2.10

    Enzymes catalyze each step in the metabolic pathways. That is, they speed up a chemical reaction that would take place anyway without themselves being changed.

    Rate-limiting enzymes:

    - Stage I Phosphofructokinase (PFK)

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- Stage III Isocitrate dehydrogenase (ICD)
- Stage IV Cytochrome oxidase

Enzymes are regulated by modulators. Positive modulators stimulate the production of ATP (positive feedback), and negative modulators inhibit the production of ATP (negative feedback)

Positive Modulators	**Negative Modulators**
ADP	ATP
AMP	CP
P_i	Citrate
Increase in pH	FFA
	Decrease in pH

11. What are the goals of metabolic regulation during exercise? How are these goals achieved by the interaction of the sympathetic nervous system and the hormonal system?

Pages 47–53, Figure 2.17, Table 2.3

The goals of metabolic regulation during exercise are:

a. To provide sufficient fuel for ATP production to meet the energy demands
b. To maintain blood glucose levels at near-resting values because the brain and nervous system must have glucose as a fuel

These goals are achieved by the coordinated actions of the sympathetic nervous system and the endocrine system. The catecholamines (epinephrine and norepinephrine) and glucagon are released in a matter of seconds to minutes and insulin is suppressed. The result is a decrease in glucose uptake by nonactive cells, a decrease in glycogenesis and lipogenesis, and an increase in glycogenolysis, gluconeogenesis, and lipolysis. If the exercise continues for a long period of time, growth hormone and cortisol increase (bringing about an increase in glycogen formation in a further attempt to conserve carbohydrate) and, in addition, make protein available as a fuel source. Thyroxine potentiates the effect of the other hormones.

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12. Compare the relative availability and use of carbohydrate, fat, and protein fuel substrates on the basis of the intensity and duration of exercise.

Pages 53, 54, Tables 2.4 and 2.5

The relative availability of the energy substrates is as follows:

- Fat—highest by far
- Protein—medium but not desirable to use muscle mass as fuel
- Carbohydrate—low

The relative use of the energy substrates is as follows:

	Exercise Continuum—Dynamic Rhythmic Exercise		
	Low intensity ⟷ High intensity Long duration ⟷ Short duration		
Fat CHO Protein	High Low/medium Low	Medium Medium	Low High Negligible

	Rest	Static and very intense dynamic exercise
Fat CHO Protein	 High/medium Low	Negligible High Negligible

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Worksheet Answers, Chapter 2, Energy Production

Exercise 1.

Diagram: Cellular Respiration Overview. Place the listed terms in the proper location in the following flow diagram. An asterisk (*) represents a process. See Figure 2.2 on page 31.

1. Polypeptides
2. Amino Acids
3. *Oxidative Deamination (Note: 3 and 4 may be reversed)
4. *Transamination
5. Keto Acids
6. Polysaccharides
7. Glucose
8. *Glycolysis
9. Pyruvic Acid
10. Acetyl CoA
11. *Krebs Cycle
12. *Electron Transport System
13. *Oxidative Phosphorylation
14. Triglycerides
15. Glycerol (Note: 15 and 16 may be reversed)
16. Free Fatty Acids
17. *Beta-Oxidation

Exercise 2. Diagram: Mitochondria

1. Outer membrane	Barrier but allows metabolic substrates/products to freely cross
2. Inner membrane	Impermeable to NADH + H^+; necessitates shuttle system (malate-aspartate = cardiac muscle; glycerol-phosphate = skeletal muscle);

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	permeable to water and oxygen; location for Stage IV, ETS/OP
3. Matrix	Location for Stages II and all but step 6 of Stage III
4. Intermembrane space	Area into which H^+ (removed from NAD^+ and FAD) are pumped during electron transport and from which they move into the matrix via ball-and-stalk apparatus during oxidative phosphorylation
5. Ball-and-stalk protein complexes (apparatus)	Location of ATP synthesis
6. DNA	Allows adaptation of self-replication when ATP demand increases

Exercise 3.

Matching.

A) Match the chemical formula from Column II with the corresponding name from Column I.

Column I	Column II
__***C***__ Pyruvic Acid	A. $C_6H_{12}O_6$
__***A***__ Glucose	B. $2C_3H_6O_3$
__***B***__ Lactic Acid	C. $2C_3H_4O_3$

B) Arrange the steps in their proper sequence to describe electron transport/oxidative phosphorylation.

__***E***__ Step 1	A. ATP moves into the intermembrane space through ATP-ADP antiporter protein.

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__***G***__ Step 2	B. Oxygen serves as the electron acceptor.
__***B***__ Step 3	C. ATP moves out of the mitochondria; ADP + P_i moves in.
__***D***__ Step 4	D. H^+ move from the intermembrane space into the mitochondrial matrix through the ball-and-stalk apparatus.
__***F***__ Step 5	E. Electrons are transferred from NADH + H^+ and $FADH_2$ at Complex I and II, respectively, while H^+ are deposited into the mitochondrial matrix.
__***A***__ Step 6	F. H^+ movement produces an electrical current that activates ATP synthetase that, in turn, phosphorylates ADP to ATP.
__***C***__ Step 7	G. Electrons shuttle from CoQ to cytochromes b, c_1, c, a, and a_3 and move across the width of the inner membrane.

C) Match the actual (not theoretical) ATP production from Column II with the fuel substrate in Column I.

Column I	Column II
__***D***__ Glucose—cardiac muscle	A. 31
__***A***__ Glycogen—skeletal muscle	B. 10
__***C***__ Fat—16 carbon palmitate	C. 106
__***B***__ Protein—converted to acetyl CoA	D. 32

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	E. 12.5
	F. 108
	G. 30
	H. 33

D) Match the predominant fuel source from Column II with the exercise intensity and duration given in Column I.

1. __***B***__	A. free fatty acids
2. __***C***__	B. muscle glycogen
3. __C_	C. muscle glycogen, liver glycogen, blood-borne glucose
4. __***A***__	D. amino acids
5. __***A***__	

E) Match the metabolic reaction in Column II with the correct name for the metabolic process in Column I

Column I: Metabolic Process	Column II: Metabolic Reaction
__***G***__ Beta-oxidation	A. ADP + P_i → ATP
__***L***__ Gluconeogenesis (Cori cycle)	B. Alanine → Glucose
__***B***__ Gluconeogenesis (Felig cycle)	C. Amino acid → Keto acid + NH_3
__***I***__ Glycogenesis	D. Amino acid (1) + Keto acid (1) → Amino acid (2) + Keto acid (2)
__***K***__ Glycogenolysis	E. ATP → ADP + P_i + E
__***H***__ Glycolysis	F. Fats → FFA + glycerol

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__***E***__ Hydrolysis	G. FFA → acetyl CoA
__***J***__ Lipogenesis	H. Glucose→ pyruvic acid/lactic acid
__***F***__ Lipolysis	I. Glucose + glucose →glycogen
__***C***__ Oxidative Deamination	J. Glycerol + FFA → Fats
__***A***__ Oxidative Phosphorylation	K. Glycogen → Glucose + glucose
__***D***__ Transamination	L. Pyruvate/lactate → glucose

F) Label each of the following substances as being either a positive modulator (stimulates a rate-limiting enzyme in a metabolic pathway) or a negative modulator (inhibits a rate-limiting enzyme in a metabolic pathway) in the intracellular regulation of cellular regulation.

__***A***__ ADP	A. Positive modulator
__***A***__ AMP	B. Negative modulator
__***B***__ ATP	
__***A***__ Calcium	
__***B***__ Citrate	
__***B***__ CP	
__***B***__ pH decrease	
__***A***__ pH increase	
__***A***__ P_i	

Exercise 4.

Table: Hormonal regulation of metabolism during exercise. Complete the following table indicating which hormone(s) is/are responsible for the indicated action in regulating metabolism during exercise.

Metabolic Action	Protein/Amino	Increased	Increased	Decreased

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	Acid Breakdown and Utilization	Mobilization and Utilization of FFA	Breakdown and Utilization of Glycogen; Gluconeogenesis	Uptake of Glucose into Nonworking Cells
Hormone(s)	Growth Hormone; Cortisol	Glucagon; Epinephrine; Norepinephrine; Growth Hormone; Cortisol	Glucagon; Epinephrine; Norepinephrine; Growth Hormone; Cortisol	Glucagon; Growth Hormone; Cortisol

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