

# Instructor's Answer Key

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## Chapter 19: Regulation of Metabolism

### Answers to Test Your Understanding of Concepts and Principles

1. Rising levels of blood glucose stimulate insulin secretion and inhibit glucagon secretion from the pancreas. During fasting, blood glucose levels fall causing the levels of insulin secretion to fall and the levels of glucagon secretion to rise. In uncontrolled type I diabetes, the insulin levels are also extremely low because the beta cells are destroyed; and the glucagon levels are very high, because without insulin, hyperglycemia is unable to inhibit glucagon secretion. The low insulin and high glucagon levels of both states promote increased fat breakdown and increased production of ketone bodies. In fasting, the blood glucose level is low, but in type I diabetes it is high as a result of continued eating of carbohydrates and because of the rapid breakdown of stored hepatic glycogen. [Note: This question is also answered in the Student Study Guide.]
2. Glucocorticoids stimulate the breakdown of protein in muscles, which provides a greater number of amino acids to the tissue cells. These hormones also stimulate the liver to increase its production of hepatic enzymes, including those involved in gluconeogenesis. Since most enzymes are proteins, this partly explains the increased production of proteins by the liver. As a result of these actions, the amino acids provided by the breakdown of muscle proteins can be converted to glucose by the liver or be used in the synthesis of new proteins. Glucocorticoids thus promote an increase in blood glucose levels by stimulating gluconeogenesis.
3. Thyroxine stimulates the utilization of ATP by almost all cells. Since ATP exerts a negative feedback inhibition on cell respiration, the effect of thyroxine on ATP results in an increase in cell respiration (metabolism) in almost all cells in the body. As a result, more calories are consumed for a given level of activity and therefore more weight is lost when thyroxine levels are higher. A hypothyroid person has a tendency to gain weight because the person's metabolic rate is slower than that of a person who has normal thyroid activity. Since heat is generated by metabolic activity, a person who is hypothyroid has less metabolic heat production and thus greater sensitivity to cold.
4. Thyroxine and growth hormone both stimulate protein synthesis (anabolism) and promote the utilization of fats (catabolism) for energy. However, thyroxine stimulates glucose uptake and utilization by tissues whereas growth hormone promotes the sparing of blood glucose for energy consumption by inhibiting glycolysis. Growth hormone thus acts to raise the blood glucose concentration, and for this reason is said to have a "diabetogenic" effect.

5. Vitamin D is produced by the skin and converted to more active forms by chemical changes in the kidneys and liver. It is thus a prehormone. If the skin does not produce sufficient vitamin D due to inadequate exposure to ultraviolet light, vitamin D must be ingested in the diet—and thus is also a vitamin. People with osteoporosis have excessive rates of calcium phosphate resorption from bone as compared to deposition, possibly as a result of inadequate absorption of calcium. Since vitamin D derivatives promote the absorption of calcium from the intestine and thus raise the blood calcium levels, taking vitamin D may help people with osteoporosis raise their blood calcium levels and promote the deposition of bone calcium.
6. Insulin resistance refers to abnormally low tissue sensitivity to the hormone, insulin. Insulin resistance is compounded by the decreased tissue sensitivity that accompanies obesity and inactivity. Diet (weight loss) and exercise can increase tissue sensitivity to insulin to help control type 2 (non-insulin-dependent) diabetes mellitus.
7. Insulin-like growth factors (IGF) are polypeptides produced by many tissues that are similar in structure to proinsulin that have insulin-like effects. They also serve as mediators of some of growth hormone's actions. The term *somatomedins* is often used to refer to two of these factors, designated IGF-1 and IGF-2. In response to growth hormone stimulation, the liver produces and secretes IGF-1, which stimulates cell division and growth. IGF-2 has more insulin-like actions.
8. (a) During periods of fasting, insulin secretion decreases and glucagon secretion increases. Less insulin slows cellular uptake of blood glucose. Glucagon stimulates glucose release from the liver by stimulating glycogenolysis, gluconeogenesis, lipolysis, and ketogenesis. These effects help maintain adequate levels of blood glucose for the brain and provide alternate energy sources for other organs. (b) During the intestinal absorption of a high carbohydrate-low protein meal, insulin secretion promotes the uptake of blood glucose into tissues cells. This lowers the blood glucose concentration and increases the energy reserves of glycogen, fat, and protein. (c) Meals that are high in protein and carbohydrates stimulate both the secretion of insulin and glucagon to maintain glucose homeostasis.
9. Inadequate intake of dietary calcium or vitamin D → decreased blood calcium levels → increased levels of parathyroid hormone and 1,25-dihydroxyvitamin D<sub>3</sub> → *increased bone resorption*. Adequate intake of dietary calcium or vitamin D → normal blood calcium levels → normal levels of parathyroid hormone and 1,25-dihydroxyvitamin D<sub>3</sub> → balance between bone resorption and *deposition*.
10. *Gigantism*—condition associated with excessive secretion of growth hormone in childhood, or before epiphyseal discs have sealed.  
*Acromegaly*—condition associated with excessive secretion of growth hormone in adulthood, or after epiphyseal discs have sealed.  
*Laron dwarfism*—condition associated with a genetic insensitivity to the effects of growth hormone; also associated with a reduction in the number of growth hormone receptors in target cells.  
*Kwashiorkor*—condition associated with protein malnutrition in children; symptoms include low growth rates and low levels of IGF-1 in the blood.

## Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. Your friend may be approaching her metabolic set point controlled by a regulatory system called an adipostat. With exercise and dieting she was able to lose her excess weight successfully but now is perhaps approaching her ideal body weight as established by a lower body mass index (BMI). If true, she has very little spare adipose tissue as fuel reserves and would have to exercise more and to restrict calorie intake even more to continue her weight loss.
2. Obesity in childhood is due to an increase in both the size and number of adipocytes. The increased adipocyte number in childhood is due to an increase in both mitotic division of the adipocytes and the conversion of preadipocytes (derived from fibroblasts) into new adipocytes. A high circulating level of fatty acids from a high-fat diet, particularly of saturated fatty acids, promotes this differentiation (specialization). Thus negative feedback works to increase the storage of excess fatty acid consumption in adipose tissue, causing obesity. The differentiation of adipocytes requires the action of PPAR $\gamma$ , a nuclear receptor protein and a specific type of prostaglandin as the ligand. Adipocytes also produce and secrete regulatory molecules such as leptin (an appetite suppressant) and tumor necrosis factor-alpha (TNF $\alpha$ ). When released from adipocytes, TNF $\alpha$  may act to reduce the sensitivity of cells (primarily skeletal muscle fibers) to insulin. This may contribute to the greater insulin resistance that is observed in obese people.
3. Insulin stimulates the insertion of GLUT4 channels via fusion of intracellular vesicles into the plasma membrane of its target cells. In this way, insulin stimulates glucose entry by facilitated diffusion through an increased number of GLUT4 channels into primarily skeletal and cardiac muscles, adipose tissue, and liver. The plasma glucose level is thus lowered while the synthesis of energy-storage molecules such as glycogen and fat is promoted. Exercise alone, like insulin, increases the number of membrane GLUT4 carriers fused into skeletal muscle cell fiber membranes. Thus, exercise also promotes glucose diffusion into skeletal muscle fibers, lowers plasma glucose levels, and helps to oppose the insulin resistance that develops with type 2 diabetes mellitus and obesity.
4. During exercise, muscle GLUT4 channels increase the uptake of glucose into skeletal muscle fibers. As blood glucose levels fall, the pancreas secretes glucagon, which stimulates glycogenolysis in the liver and thus helps to raise the blood glucose concentration. Glucagon also stimulates the production of enzymes in the liver that convert fatty acids into ketone bodies (ketogenesis). Since this is a race, the sympathoadrenal system is also activated. This results in the release of catecholamine hormones from the adrenal medulla and neurotransmitters from sympathetic neurons. The effects of epinephrine and norepinephrine are similar to those of glucagon. Furthermore, prolonged exercise stimulates the release of ACTH from the anterior pituitary that, in turn, stimulates the adrenal cortex to release hydrocortisone and other glucocorticoids. Like glucagon, hydrocortisone promotes lipolysis and ketogenesis; and it also stimulates gluconeogenesis (glucose synthesis from primarily amino acids).

5. The  $\beta_3$  adrenergic receptors are primarily located in brown adipose tissue with a few in the ordinary white fat of humans. Sympathetic nerves, acting through the release of norepinephrine can stimulate  $\beta_3$  adrenergic receptors on brown adipocytes to produce an “uncoupling” protein that uncouples oxidative phosphorylation in mitochondria by causing the leakage of protons ( $H^+$ ) from the intermembrane space. This decreases the production of ATP, which in turn stimulates a greater increase in cell respiration and consequent heat production. A hypothetical  $\beta_3$  adrenergic receptor agonist drug might help in the treatment of obesity by stimulating increased cell respiration in brown adipocytes and other target tissues, resulting in an increased consumption of metabolic fuel molecules with relatively little ATP production. The increased caloric expenditure of energy would lower circulating levels of fuel molecules more rapidly and deplete adipose stores sooner, leading to lower total body fat and weight loss.

6. In a person with type 1 diabetes mellitus, an overdose of insulin will produce an immediate, severe hypoglycemia (low blood sugar). The symptoms may progress from early tremor, hunger, weakness, blurred vision, and mental confusion to later unconsciousness and possibly, a coma. All symptoms are related to the sudden lack of glucose-driven ATP production. If she remains conscious the obvious treatment is to remove the excess insulin or to oppose/block the action of insulin on its target tissues. The more practical clinical treatment would be to oppose insulin effects by giving catecholamine hormones such as epinephrine (or norepinephrine). In addition to stimulating an increase in metabolism, the catecholamines act in ways that resemble the actions of glucagon. Epinephrine would cause glycogenolysis and the release of glucose from the liver as well as lipolysis and release of fatty acids from adipose tissue. These actions would oppose the hypoglycemia until the excess exogenous insulin could be metabolized and disposed.