

Scott K. Powers • Edward T. Howley

Exercise Physiology

Theory and Application to Fitness and Performance

SEVENTH EDITION

Chapter

5

Hormonal Responses to Exercise

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Objectives

- 1. Describe the concept of hormone-receptor interaction.**
- 2. Identify the four factors influencing the concentration of a hormone in the blood.**
- 3. Describe the mechanism by which steroid hormones act on cells.**
- 4. Describe the “second messenger” hypothesis of hormone action.**
- 5. Describe the role of hypothalamus-releasing factors in the control of hormone secretion from the anterior pituitary gland.**

Objectives

- 6. Describe the relationship of the hypothalamus to the secretion of hormones from the posterior pituitary gland.**
- 7. Identify the site of release, stimulus for release, and the predominant action of the following hormones: epinephrine, norepinephrine, glucagon, insulin, cortisol, aldosterone, thyroxine, growth hormone, estrogen, and testosterone.**
- 8. Discuss the use of testosterone (an anabolic steroid) and growth hormone on muscle growth and their potential side effects.**

Objectives

- 9. Contrast the role of plasma catecholamines with intracellular factors in the mobilization of muscle glycogen during exercise.**
- 10. Briefly discuss the following four mechanisms by which blood glucose homeostasis is maintained: mobilizing glucose from liver glycogen stores, mobilizing plasma free fatty acids from adipose tissue, synthesizing glucose from amino acids and glycerol in the liver, and blocking glucose entry into cells.**

Objectives

- 11. Describe the changes in the hormones insulin, glucagon, cortisol, growth hormone, epinephrine, and norepinephrine during graded and prolonged exercise and discuss how those changes influence the four mechanisms used to maintain the blood glucose concentration.**
- 12. Describe the effect of changing hormone and substrate levels in the blood on the mobilization of free fatty acids from adipose tissue.**

Outline

- **Neuroendocrinology**
 - Blood Hormone Concentration*
 - Hormone-Receptor Interaction*
- **Hormones: Regulation and Action**
 - Hypothalamus and the Pituitary Gland*
 - Thyroid Gland*
 - Parathyroid Gland*
 - Adrenal Gland*
 - Pancreas*
 - Ovaries and Testes*
- **Hormonal Control of Substrate Mobilization During Exercise**
 - Muscle-Glycogen Utilization*
 - Blood Glucose Homeostasis During Exercise*
 - Hormone-Substrate Interaction*

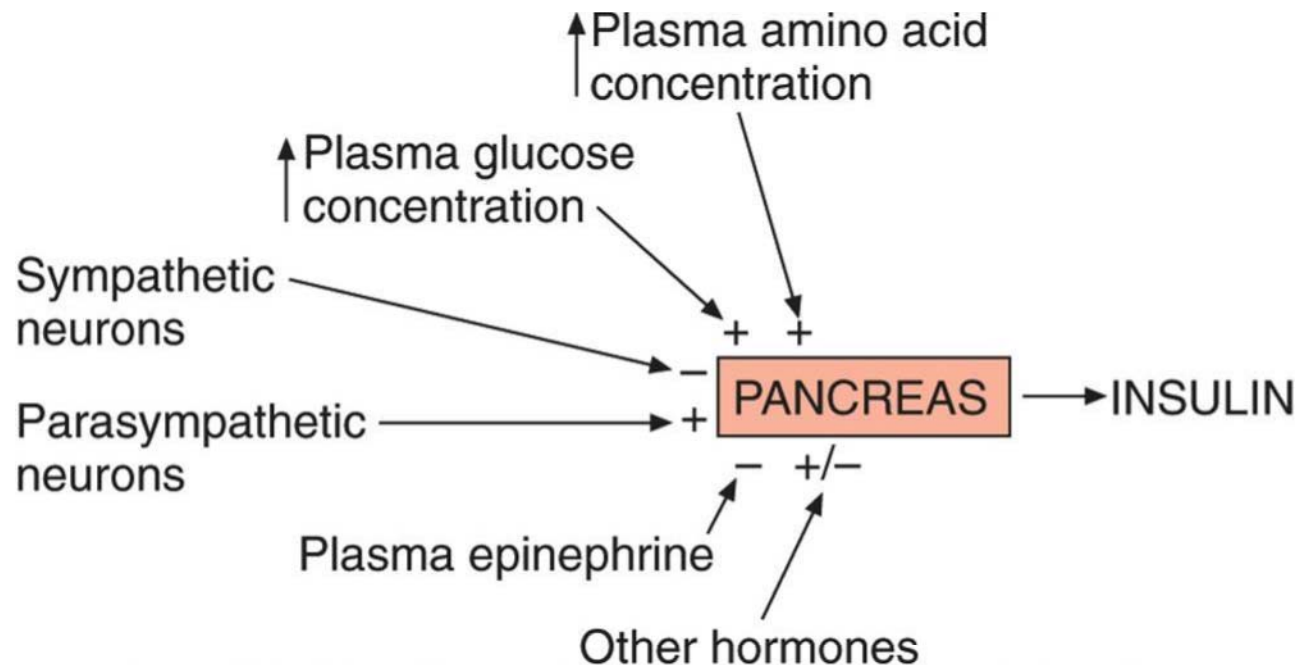
Neuroendocrinology

- **Neuroendocrine system**
 - Endocrine system releases hormones
 - Nervous system uses neurotransmitters
- **Endocrine glands**
 - Release hormones directly into the blood
- **Hormones**
 - Alter the activity of tissues that possess receptors to which the hormone can bind
 - Several classes based on chemical makeup
 - Amino acid derivatives
 - Peptides/protein
 - Steroids

Blood Hormone Concentration

- **The effect of a hormone on a tissue is determined by the plasma concentration**
- **Determined by:**
 - Rate of secretion of hormone from endocrine gland
 - Magnitude of input
 - Stimulatory versus inhibitory input
 - Rate of metabolism or excretion of hormone
 - At the receptor and by the liver and kidneys
 - Quantity of transport protein
 - Steroid hormones
 - Changes in plasma volume

Factors That Influence the Secretion of Hormones



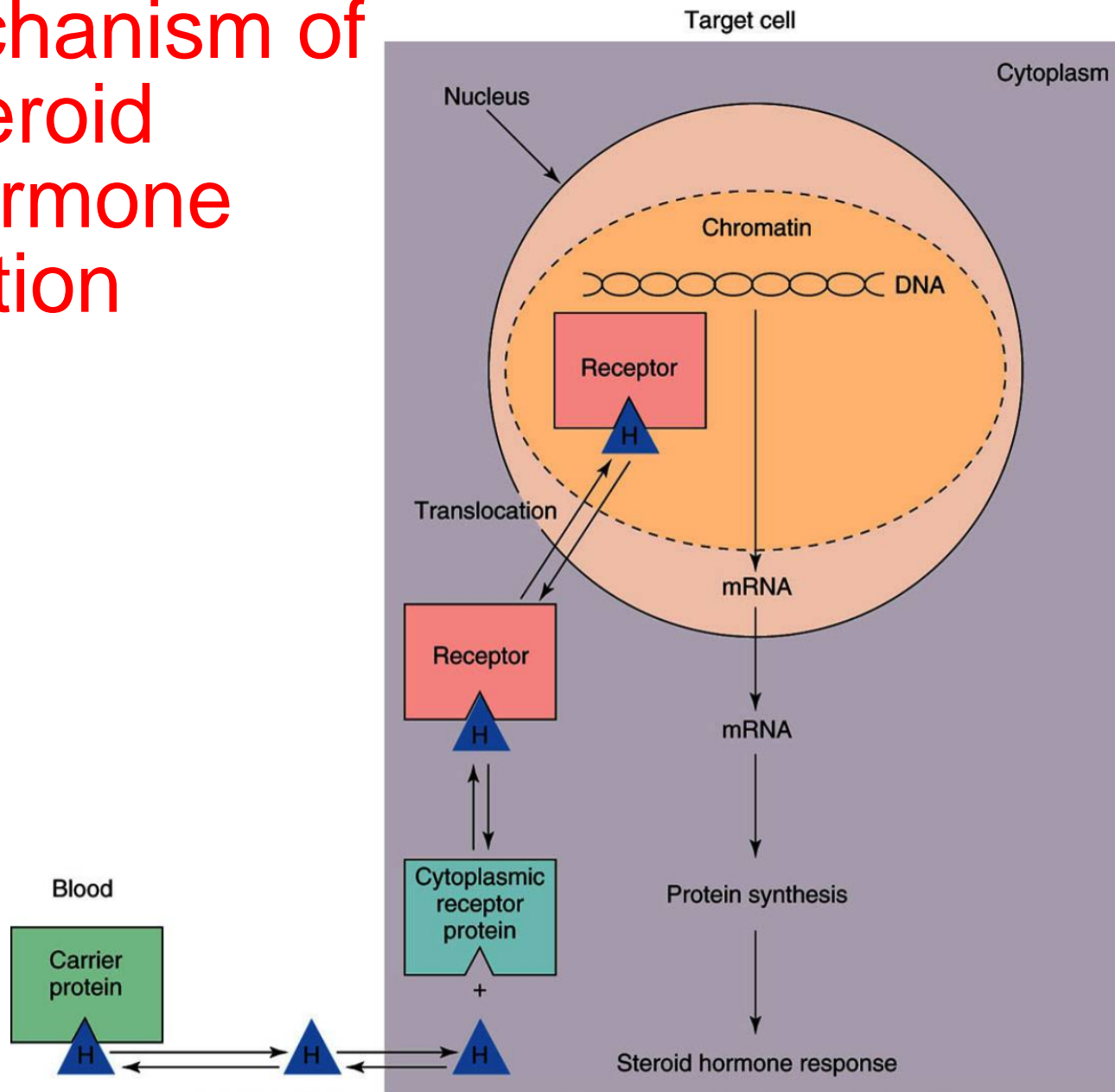
Hormone-Receptor Interactions

- **Hormones only affect tissue with specific receptors**
- **Magnitude of effect dependent on:**
 - Concentration of the hormone
 - Number of receptors on the cell
 - Affinity of the receptor for the hormone
- **Downregulation**
 - Decrease in receptor number in response to high concentration of hormone
- **Upregulation**
 - Increase in receptor number in response to low concentration of hormone

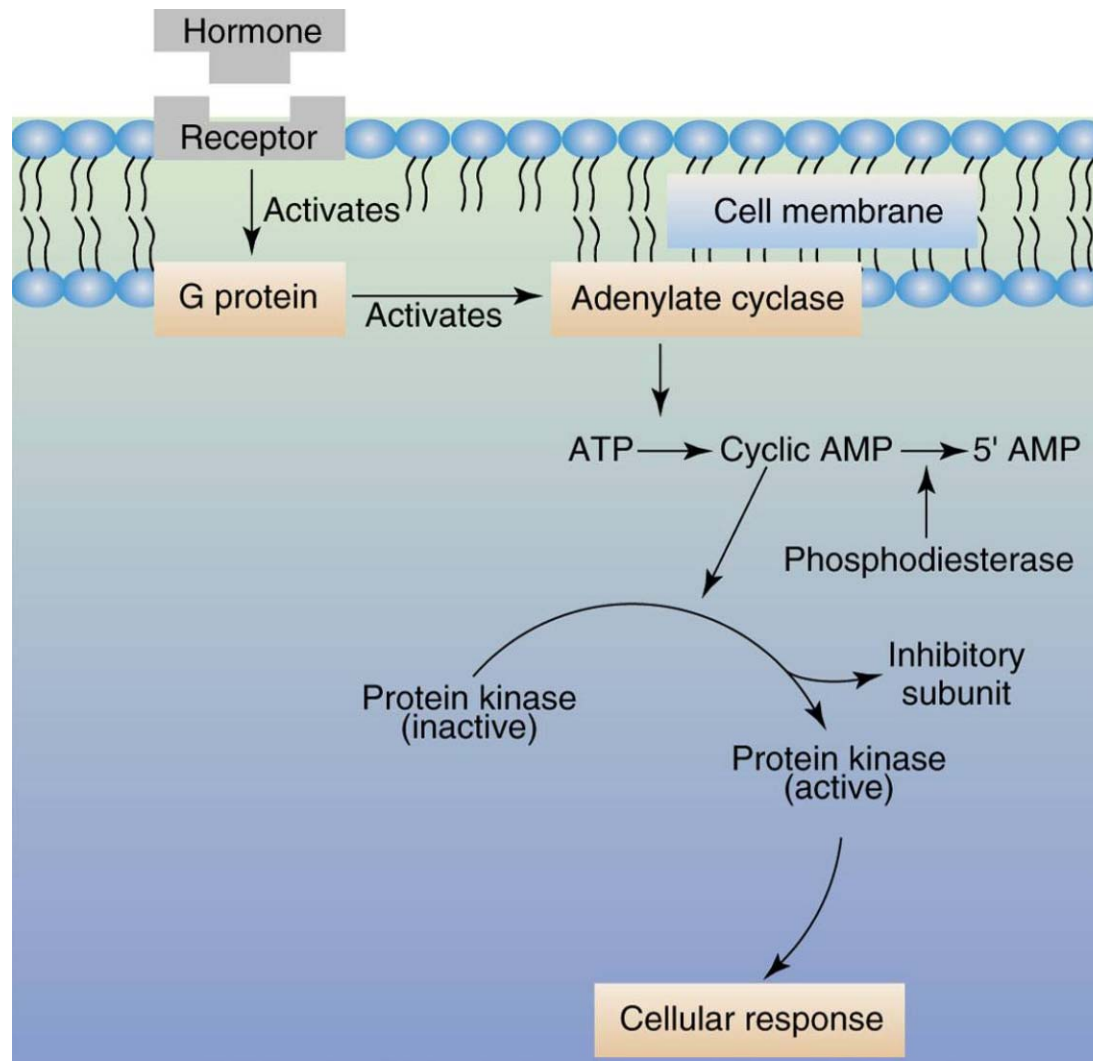
Mechanisms of Hormone Action

- **Altering membrane transport**
 - Insulin
- **Altering activity of DNA to modify protein synthesis**
 - Steroid hormones
- **Activating second messengers via G protein**
 - Cyclic AMP
 - Ca^{+2}
 - Inositol triphosphate
 - Diacylglycerol
- **Tyrosine Kinase**
 - Insulin and growth hormone

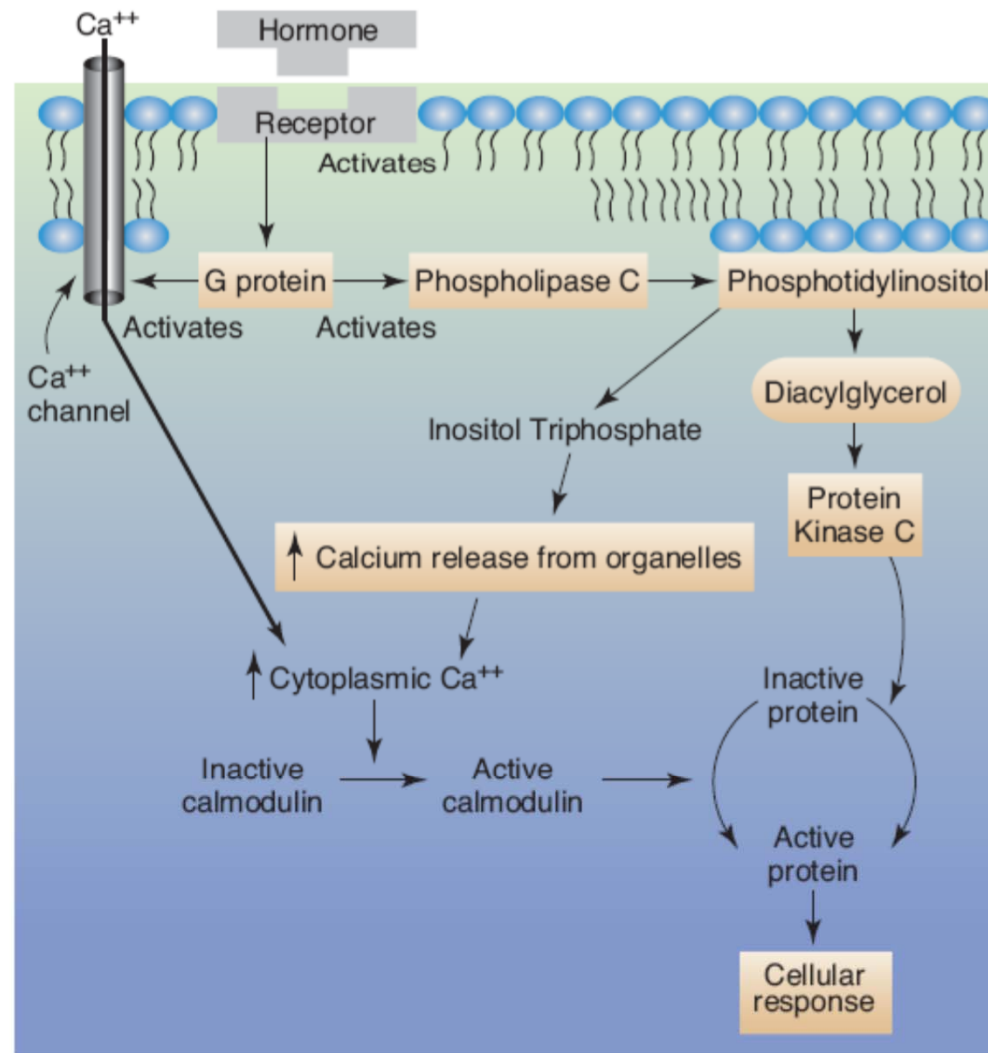
Mechanism of Steroid Hormone Action



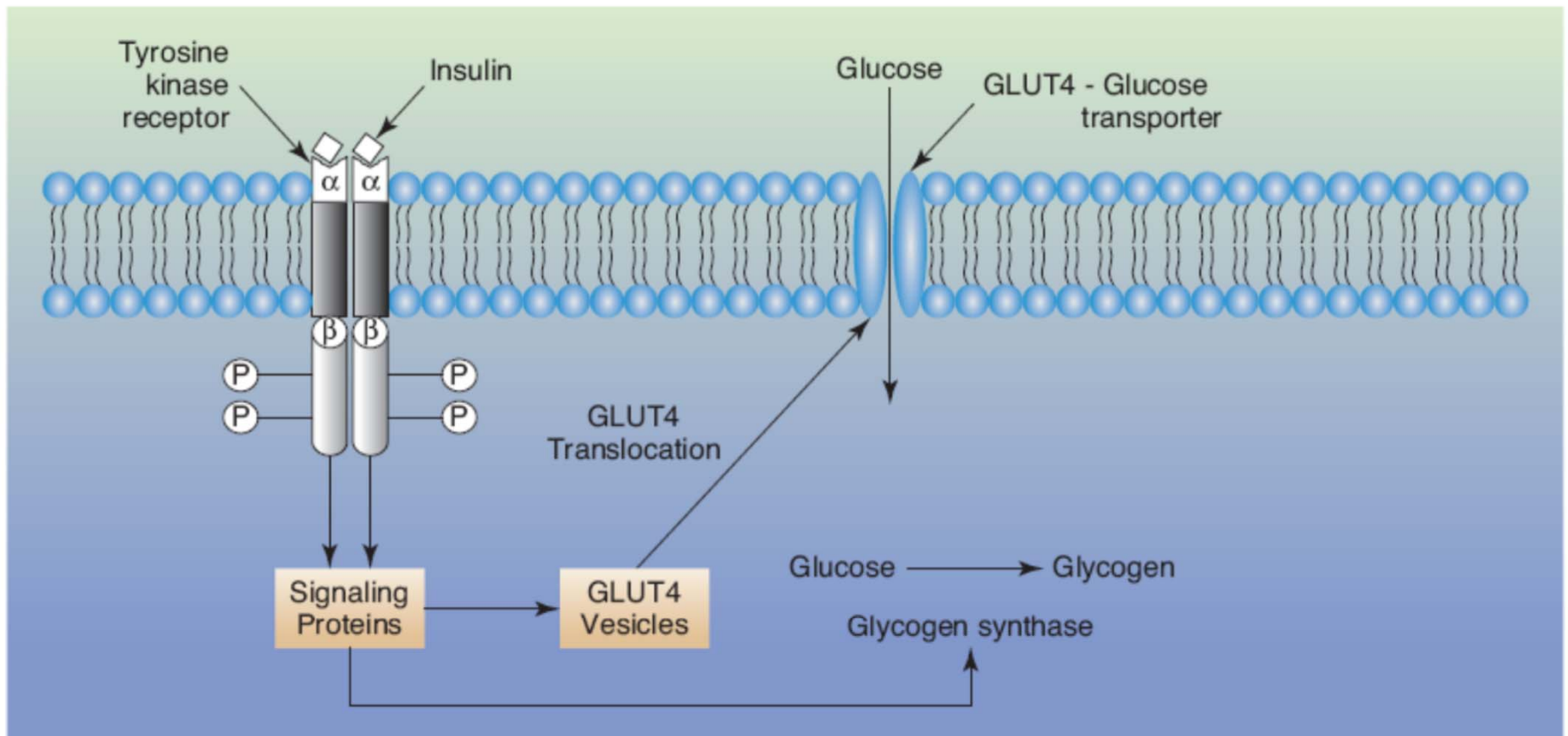
Cyclic AMP “Second Messenger” Mechanism



Calcium and Phospholipase C Second Messenger Mechanisms



Insulin Receptor

**Figure 5.5**

In Summary

- The hormone-receptor interaction triggers events at the cell; changing the concentration of the hormone, the number of receptors on the cell, or the affinity of the receptor for the hormone will all influence the magnitude of the effect.
- Hormones bring about their effects by modifying membrane transport, activating/suppressing genes to alter protein synthesis, and activating second messengers (cyclic AMP, Ca^{++} , inositol triphosphate, and diacylglycerol).

Hormones: Regulation and Action

- **Hormones are secreted from endocrine glands**
 - Hypothalamus and pituitary glands
 - Thyroid and parathyroid glands
 - Adrenal glands
 - Pancreas
 - Testes and ovaries

Hypothalamus and Pituitary Gland

- **Hypothalamus**
 - Controls secretions from pituitary gland
- **Anterior Pituitary Gland**
 - Adrenocorticotrophic hormone (ACTH)
 - Follicle-stimulating hormone (FSH)
 - Luteinizing hormone (LH)
 - Melanocyte-stimulating hormone (MSH)
 - Thyroid-stimulating hormone (TSH)
 - Growth hormone (GH)
 - Prolactin
- **Posterior Pituitary Gland**
 - Oxytocin
 - Antidiuretic hormone (ADH)

Hypothalamus

- **Stimulates release of hormones from anterior pituitary gland**
 - Releasing hormones or factors
- **Provides hormones for release from posterior pituitary gland**

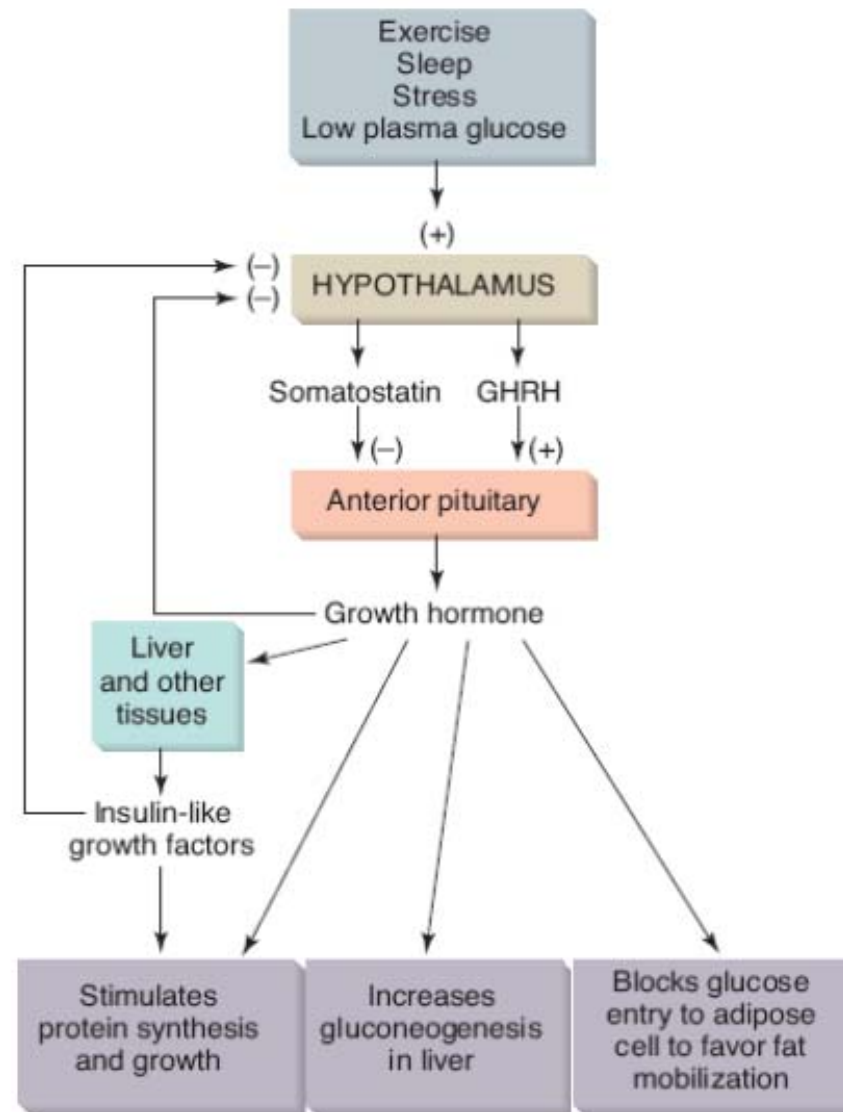
Anterior Pituitary Gland

- **Adrenocorticotrophic hormone (ACTH)**
 - Stimulates cortisol release from adrenal glands
- **Follicle-stimulating hormone (FSH)**
- **Luteinizing hormone (LH)**
 - Stimulates production of testosterone and estrogen
- **Melanocyte-stimulating hormone (MSH)**
- **Thyroid-stimulating hormone (TSH)**
 - Controls thyroid hormone release from thyroid gland
- **Prolactin**
- **Growth hormone (GH)**

Growth Hormone

- **Stimulates release of insulin-like growth factors (IGFs)**
 - IGF-1 in muscle responsible for muscle growth
- **Essential growth of all tissues**
 - Amino acid uptake and protein synthesis
 - Long bone growth
- **Spares plasma glucose**
 - Reduces the use of plasma glucose
 - Increases gluconeogenesis
 - Mobilizes fatty acids from adipose tissue

Influences on Growth Hormone Release

**Figure 5.6**

A Closer Look 5.1

Growth Hormone and Performance

- **GH increases protein synthesis in muscle and long bone growth**
 - Used to treat childhood dwarfism
 - Also used by athletes and elderly
- **More adverse effects than benefits**
- **No evidence that GH promotes strength gains**
 - Protein synthesis is collagen, not contractile protein
- **Difficult to detect usage by athletes**

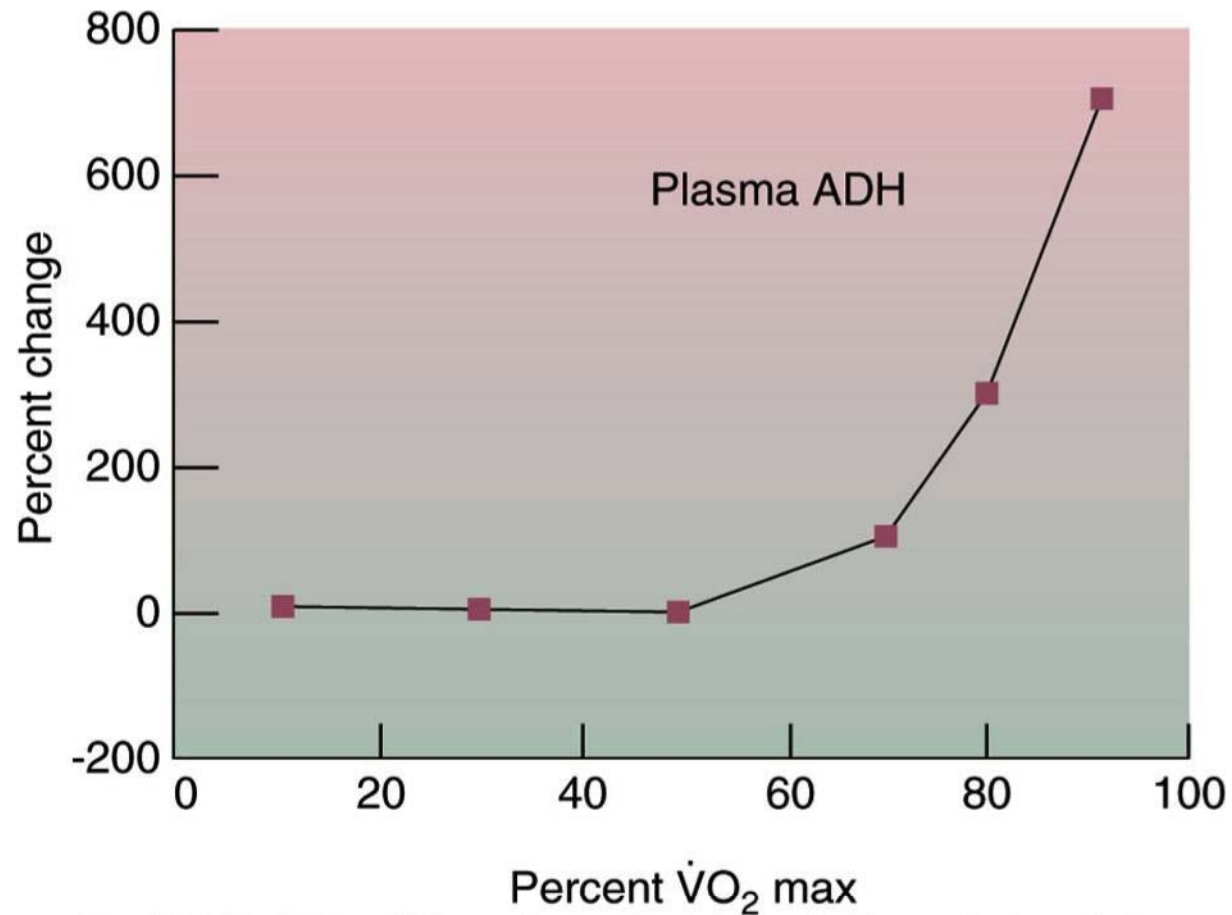
In Summary

- The hypothalamus controls the activity of both the anterior pituitary and posterior pituitary glands.
- GH is released from the anterior pituitary gland and is essential for normal growth.
- GH increases during exercise to mobilize free fatty acids from adipose tissue and to aid in the maintenance of blood glucose.

Posterior Pituitary Gland

- **Oxytocin**
- **Antidiuretic hormone (ADH)**
 - Reduces water loss from the body to maintain plasma volume
 - Favors reabsorption of water from kidney tubules to capillaries
 - Release stimulated by high plasma osmolality and low plasma volume
 - Due to sweat loss without water replacement
 - Increases during exercise $>60\%$ $\dot{V}O_2$ max
 - To maintain plasma volume

Change in Plasma ADH Concentration During Exercise

**Figure 5.7**

Thyroid Gland

- **Stimulated by TSH**
- **Triiodothyronine (T₃) and thyroxine (T₄)**
 - Establishment of metabolic rate
 - Permissive hormones
 - Permit full effect of other hormones
- **Calcitonin**
 - Regulation of plasma Ca⁺²
 - Blocks release from bone, stimulates excretion by kidneys
- **Parathyroid Hormone**
 - Primary hormone in plasma Ca⁺² regulation
 - Stimulates release from bone, stimulates reabsorption by kidneys

In Summary

- Thyroid hormones T_3 and T_4 are important for maintaining the metabolic rate and allowing other hormones to bring about their full effect.

Parathyroid Gland

- **Parathyroid hormone**
 - Primary hormone in plasma Ca^{+2} regulation
 - Stimulates Ca^{+2} release from bone
 - Stimulates reabsorption of Ca^{+2} by kidneys
 - Converts vitamin D_3 into a hormone that increase Ca^{+2} absorption from GI tract

Adrenal Medulla

- **Secretes the catecholamines**
 - Epinephrine (E) and norepinephrine (NE)
 - Fast-acting hormones
 - Part of “fight or flight” response
 - Bind to adrenergic receptors
 - Alpha (α)
 - Beta (β)
 - Effects depend on hormone used and receptor type

Effects of Epinephrine and Norepinephrine

TABLE 5.1 Physiological Responses to Epinephrine and Norepinephrine: Role of Adrenergic Receptor Type

Receptor Type	Effect of E/NE	Membrane-Bound Enzyme	Intracellular Mediator	Effects on Various Tissues
β_1	E = NE	Adenylate cyclase	↑cyclic AMP	↑Heart rate ↑Glycogenolysis ↑Lipolysis
β_2	E >>> NE	Adenylate cyclase	↑ cyclic AMP	↑Bronchodilation ↑Vasodilation
α_1	E ≥ NE	Phospholipase C	↑Ca ⁺⁺	↑Phosphodiesterase ↑Vasoconstriction
α_2	E ≥ NE	Adenylate cyclase	↓ cyclic AMP	Opposes action of β_1 and β_2 receptors

Adapted from J. Tepperman and H. M. Tepperman. 1987. *Metabolic and Endocrine Physiology*, 5th ed. Chicago: Year Book Medical Publishers.

In Summary

- The adrenal medulla secretes the catecholamines epinephrine (E) and norepinephrine (NE). E is the adrenal medulla's primary secretion (80%), while NE is primarily secreted from the adrenergic neurons of the sympathetic nervous system.
- Epinephrine and norepinephrine bind to α - and β -adrenergic receptors and bring about changes in cellular activity (e.g., increased heart rate, mobilization of fatty acids from adipose tissue) via second messengers.

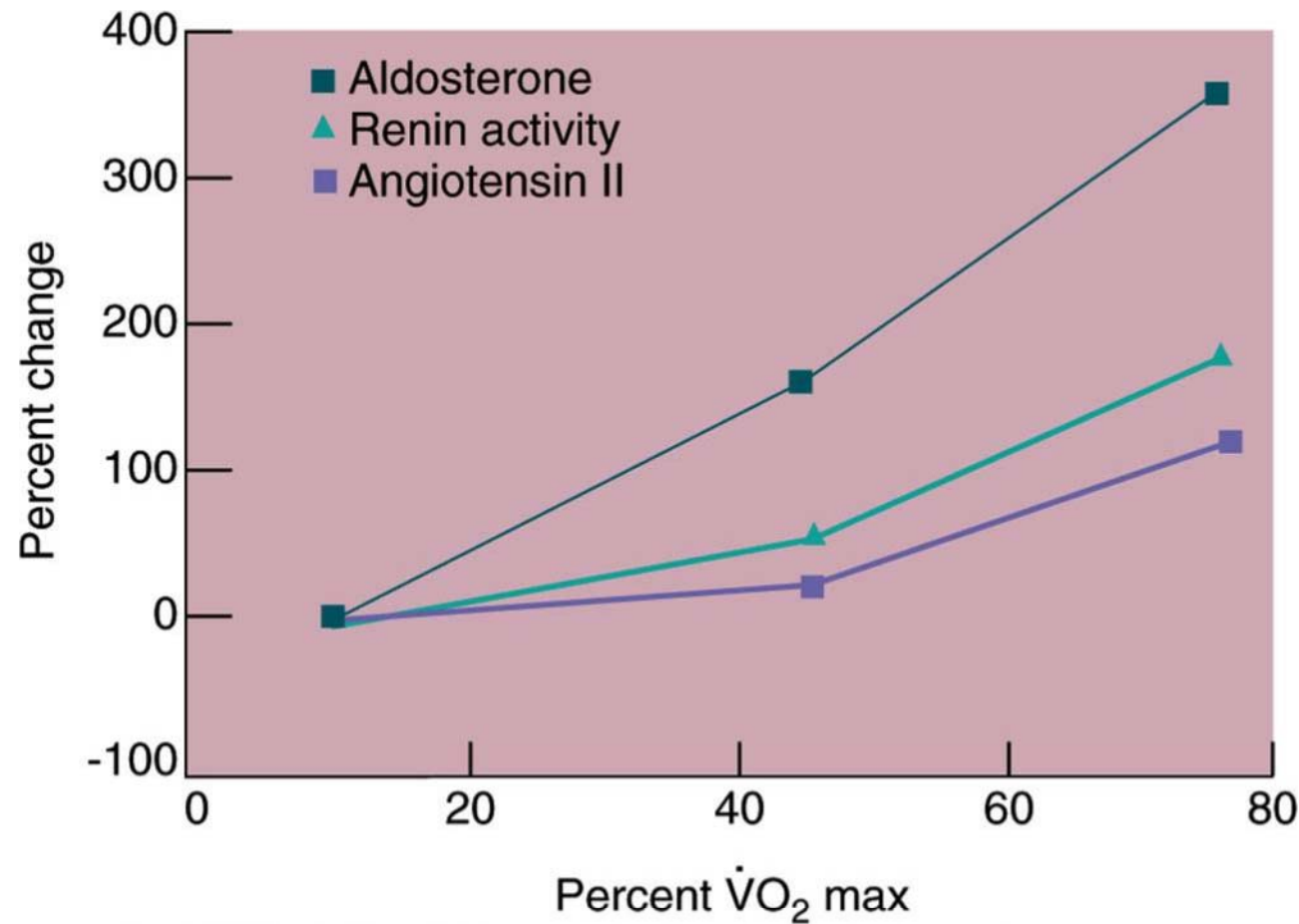
Adrenal Cortex

- **Secretes steroid hormones**
 - Derived from cholesterol
- **Mineralcorticoids**
 - Aldosterone
 - Maintenance of plasma Na⁺ and K⁺
- **Glucocorticoids**
 - Cortisol
 - Regulation of plasma glucose
- **Sex steroids**
 - Androgens and estrogens
 - Support prepubescent growth

Aldosterone

- **Control of Na⁺ reabsorption and K⁺ secretion**
 - Na⁺/H₂O balance
- **Regulation of blood volume and blood pressure**
 - Part of renin-angiotensin-aldosterone system
 - All three hormones increase during exercise
- **Stimulated by:**
 - Increased K⁺ concentration
 - Decreased plasma volume

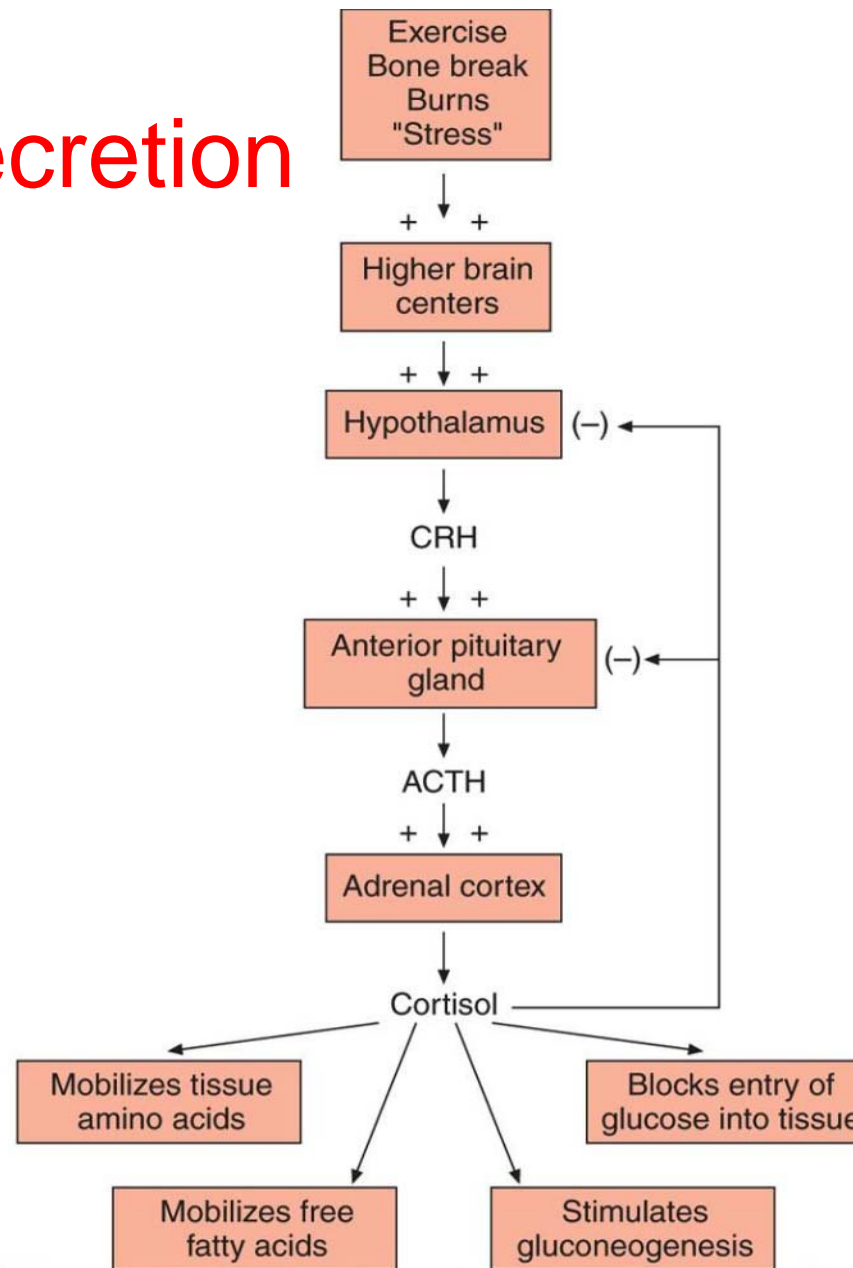
Change in Renin, Angiotensin II, and Aldosterone During Exercise

**Figure 5.8**

Cortisol

- **Maintenance of plasma glucose**
 - Promotes protein breakdown for gluconeogenesis
 - Stimulates FFA mobilization
 - Stimulates glucose synthesis
 - Blocks uptake of glucose into cells
 - Promotes the use of free fatty acids as fuel
- **Stimulated by:**
 - Stress, via ACTH
 - Part of General Adaptation Syndrome
 - Exercise

Control of Cortisol Secretion

**Figure 5.9**

In Summary

- The adrenal cortex secretes aldosterone (mineralcorticoid), cortisol (glucocorticoid), and estrogens and androgens (sex steroids).
- Aldosterone regulates Na^+ and K^+ balance. Aldosterone secretion increases with strenuous exercise, driven by the renin-angiotensin system.
- Cortisol responds to a variety of stressors, including exercise, to ensure that fuel (glucose and free fatty acids) is available, and to make amino acids available for tissue repair.

A Closer Look 5.2

Adipose Tissue Is an Endocrine Organ

- **In addition to storing triglycerides, adipose tissue also secretes hormones**
 - Leptin
 - Influences appetite through the hypothalamus
 - Enhances insulin sensitivity and fatty acid oxidation
 - Adiponectin
 - Increases insulin sensitivity and fatty acid oxidation
- **With increased fat mass (obesity)**
 - Higher leptin levels and lower adiponectin
 - Leads to type 2 diabetes and low-grade inflammation

Pancreas

- **Both exocrine and endocrine functions**
- **Secretes:**
 - Insulin (from β cells)
 - Promotes the storage of glucose, amino acids, and fats
 - Lack of insulin is called diabetes mellitus
 - Glucagon (from α cells)
 - Promotes the mobilization of fatty acids and glucose
 - Somatostatin (from δ cells)
 - Controls rate of entry of nutrients into the circulation
 - Digestive enzymes and bicarbonate
 - Into the small intestine

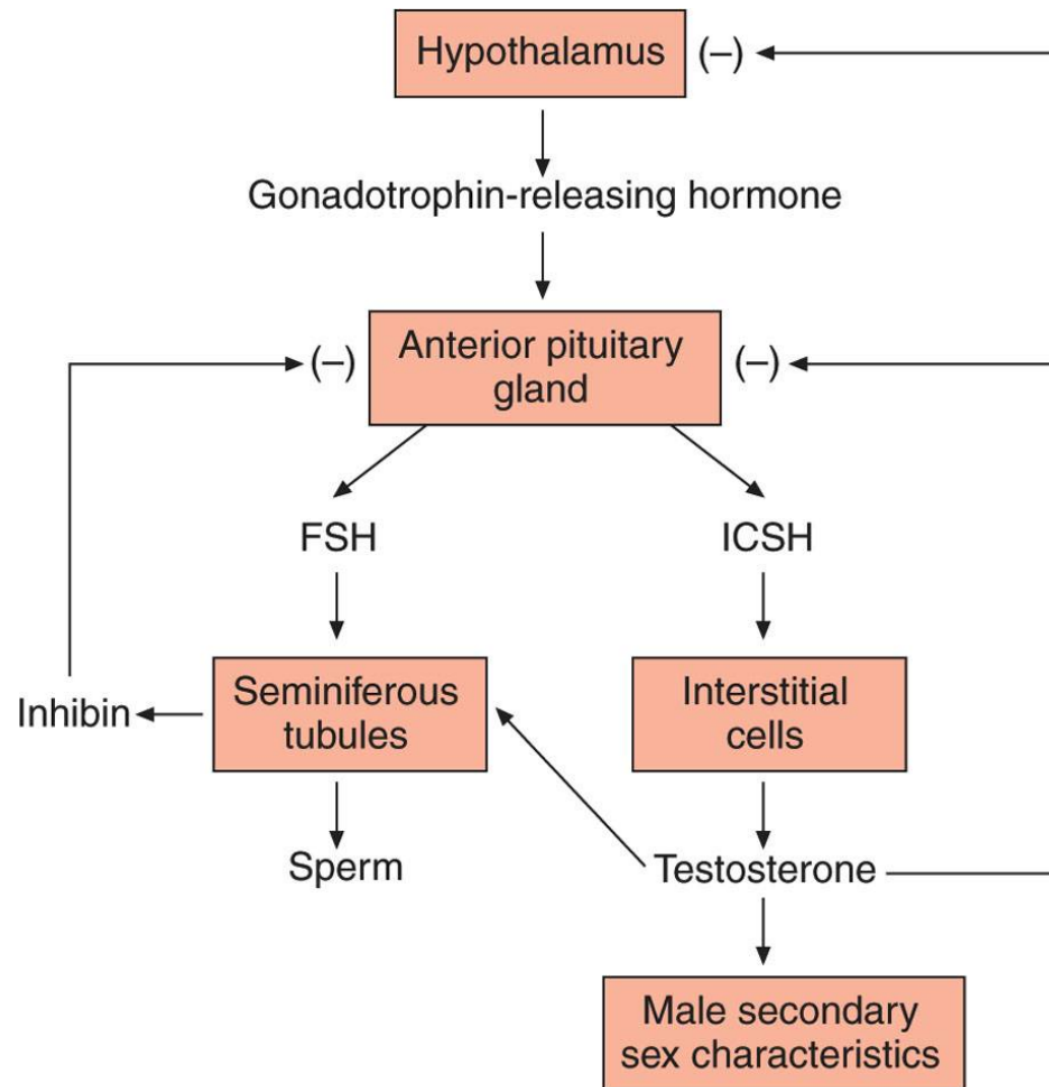
In Summary

- Insulin is secreted by the β cells of the islets of Langerhans in the pancreas and promotes the storage of glucose, amino acids, and fats.
- Glucagon is secreted by the α cells of the islets of Langerhans in the pancreas and promotes the mobilization of glucose and fats.

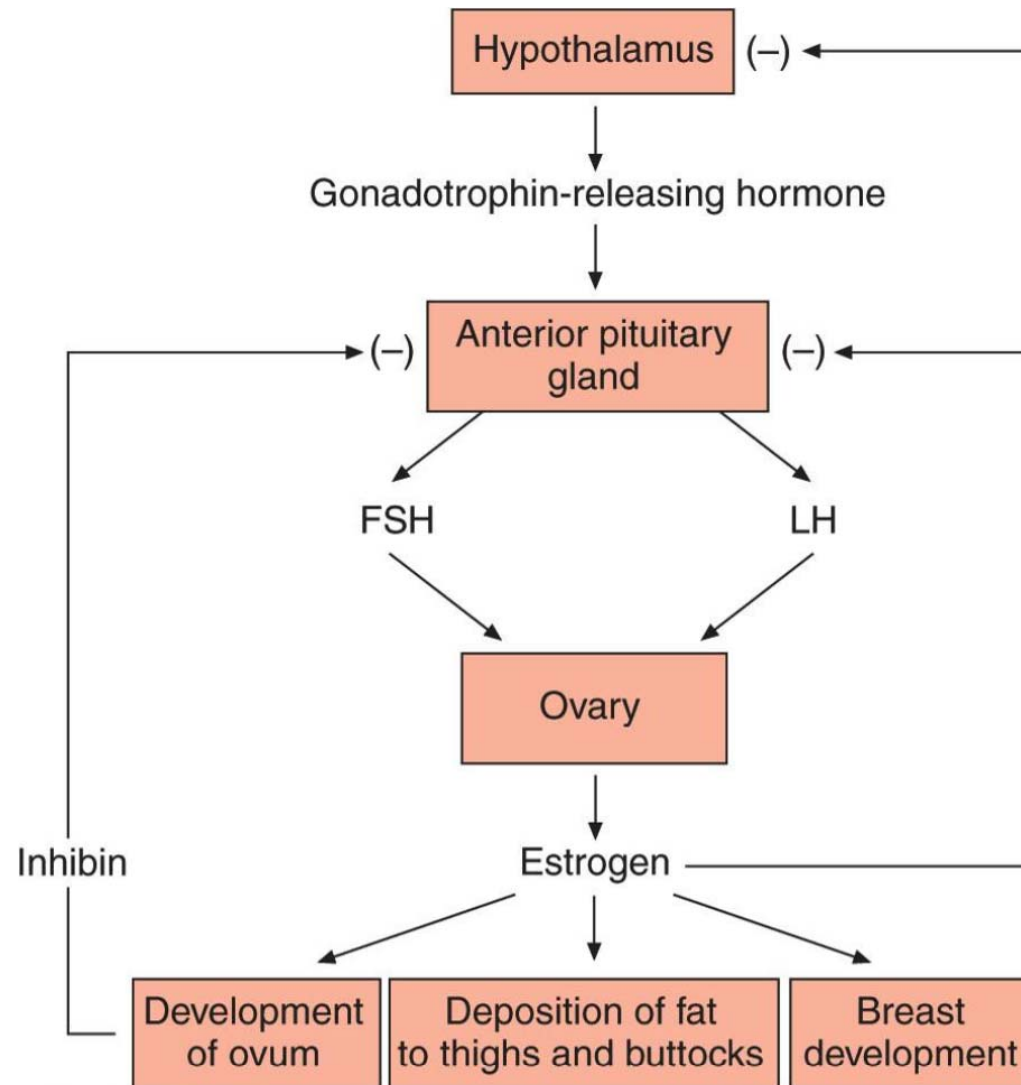
Testes and Ovaries

- **Testosterone**
 - Released from testes
 - Anabolic steroid
 - Promotes tissue (muscle) building
 - Performance enhancement
 - Androgenic steroid
 - Promotes masculine characteristics
- **Estrogen and Progesterone**
 - Released from ovaries
 - Establish and maintain reproductive function
 - Levels vary throughout the menstrual cycle

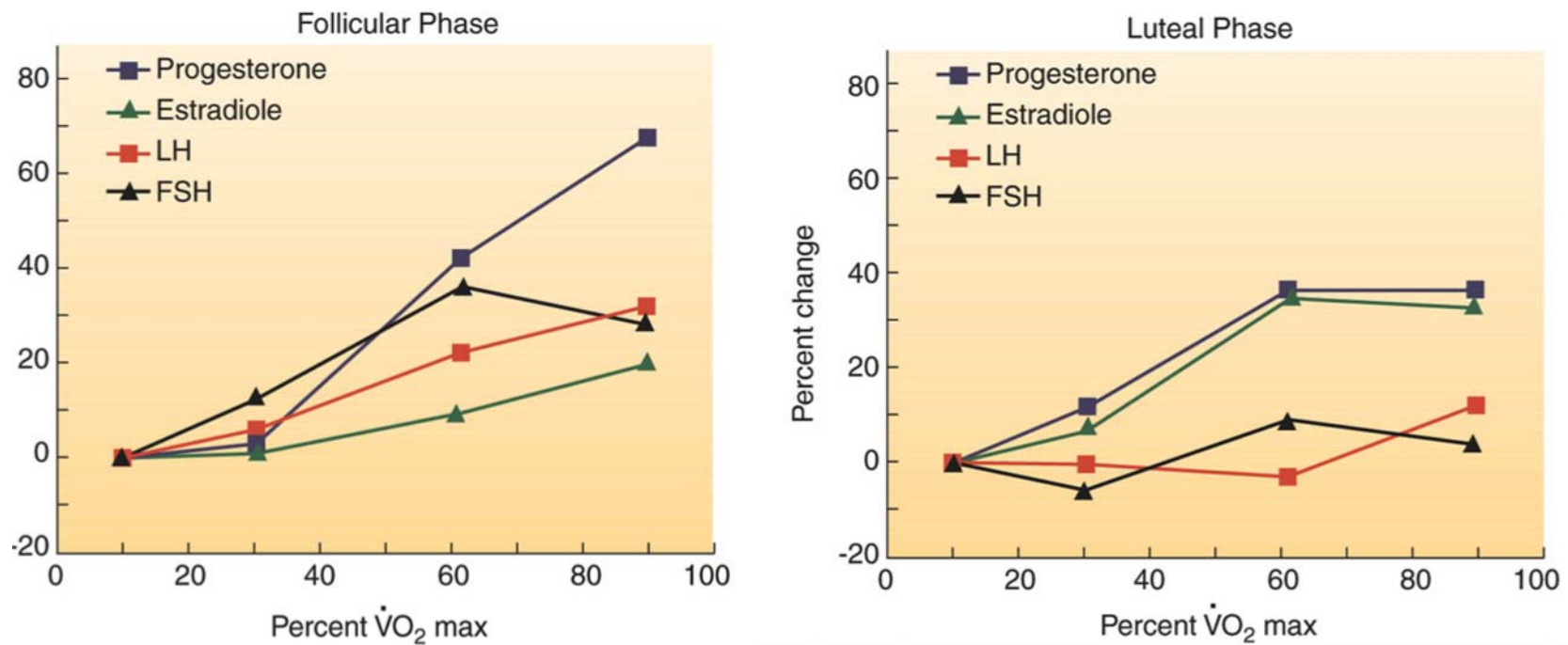
Control of Testosterone Secretion



Control of Estrogen Secretion



Change in FSH, LH, Progesterone, and Estradiol During Exercise



A Closer Look 5.3

Anabolic Steroids and Performance

- **Initial studies showed no benefit for developing muscle mass**
 - In contrast to real-world reports
 - “Subjects” used 10 to 100 times the recommended dosage
- **Also associated with negative side effects**
 - Revert to normal after discontinuation
- **Widespread use has led to testing of competitive athletes**
- **Most users are not competitive athletes**
 - Take more than one steroid in megadoses

In Summary

- Testosterone and estrogen establish and maintain reproductive function and determine secondary sex characteristics.
- Chronic exercise (training) can decrease testosterone levels in males and estrogen levels in females. The latter adaptation has potentially negative consequences related to osteoporosis.

Muscle Glycogen Utilization

- **Glycogenolysis is related to exercise intensity**
 - High-intensity exercise results in greater and more rapid glycogen depletion
- **Plasma epinephrine is a powerful simulator of glycogenolysis**
 - High-intensity exercise results in greater increases in plasma epinephrine

Glycogen Depletion During Exercise

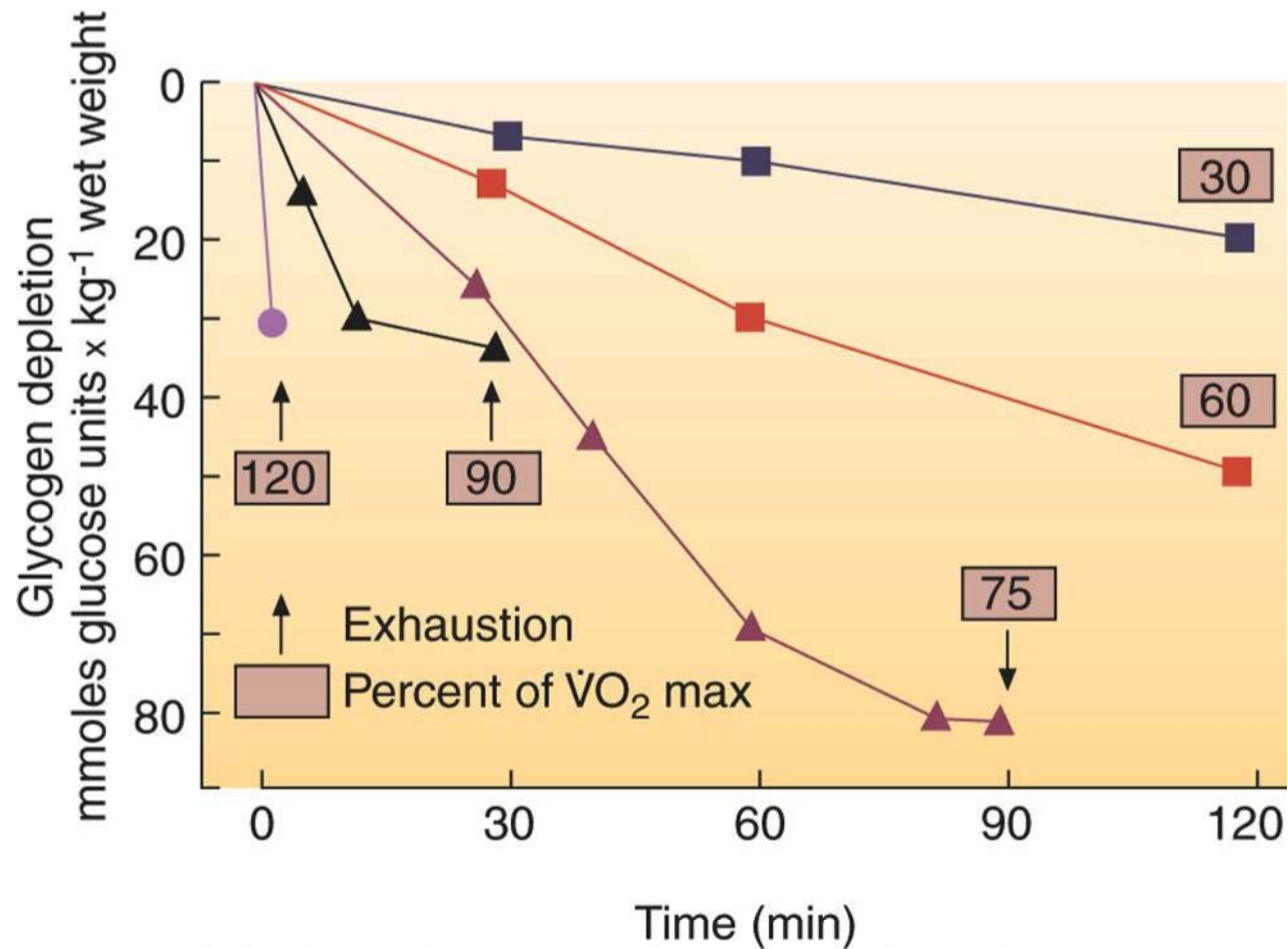
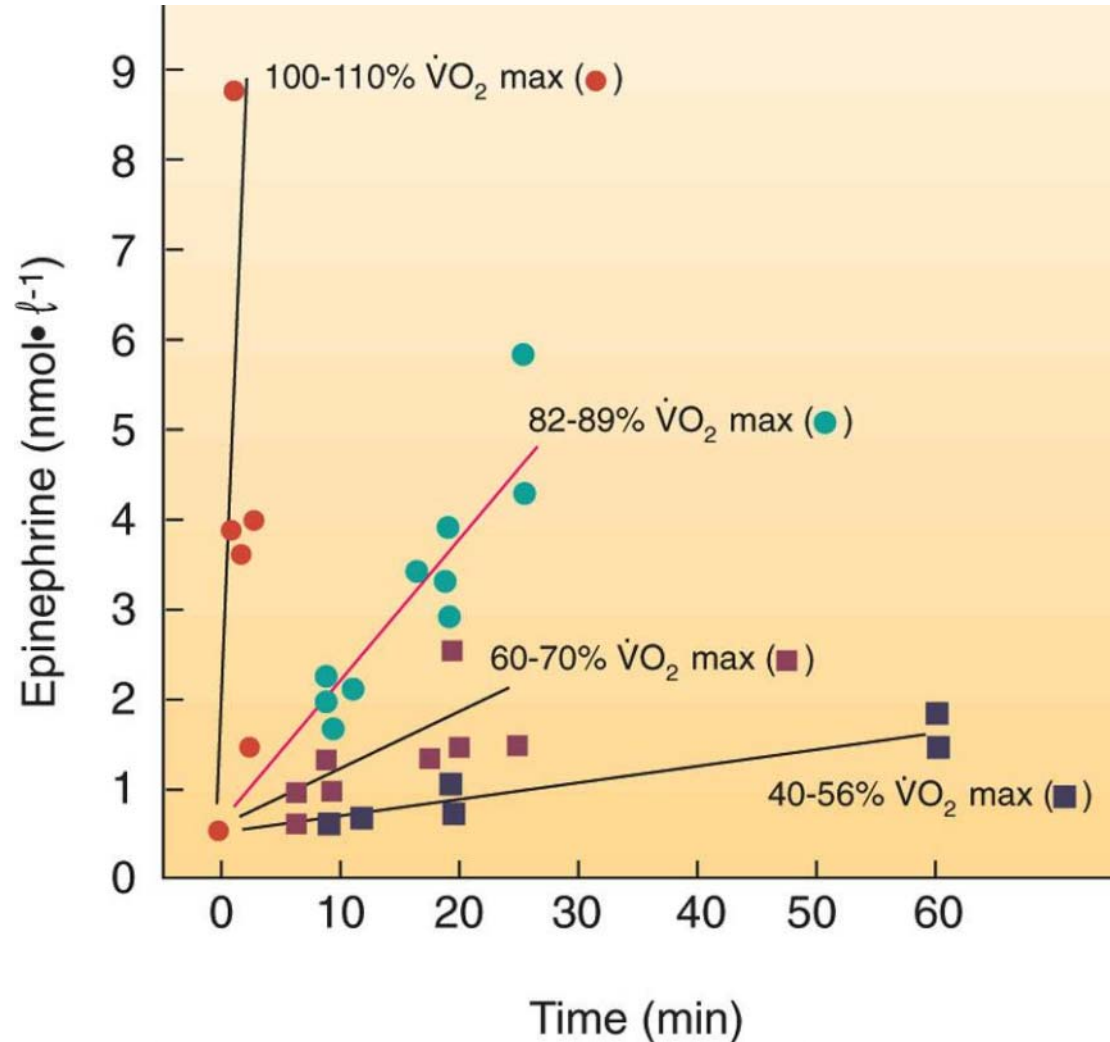


Figure 5.13

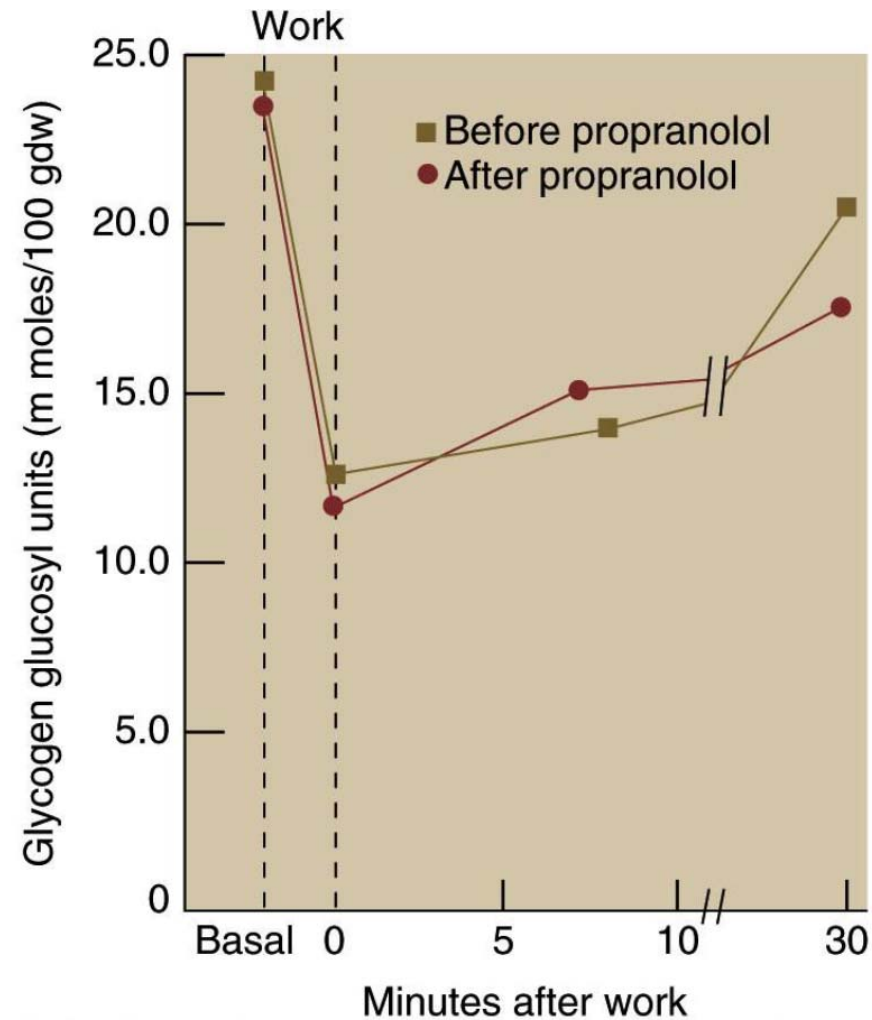
Plasma Epinephrine Concentration During Exercise



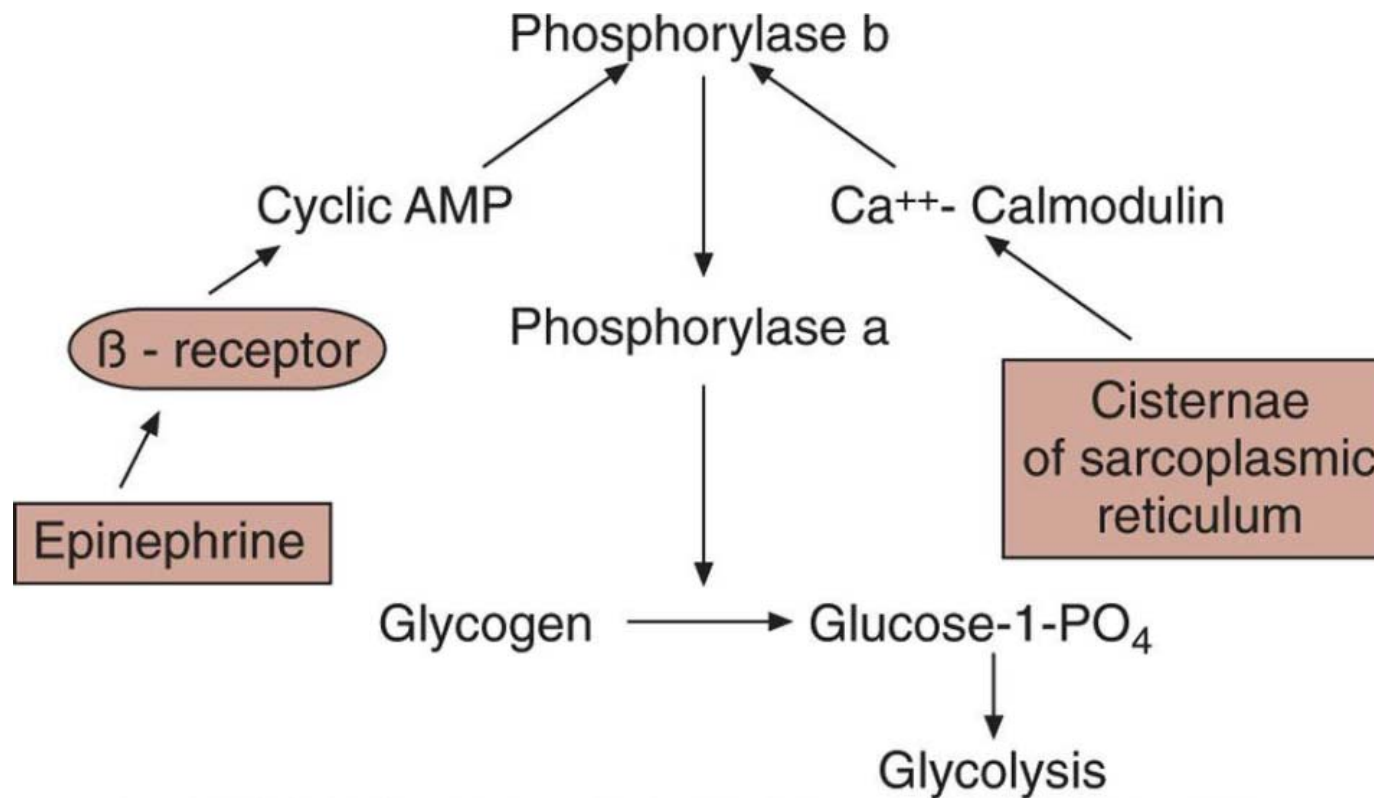
Control of Muscle Glycogen Utilization

- **Breakdown of muscle glycogen is under dual control**
 - Epinephrine-cyclic AMP
 - Via β -adrenergic receptors
 - Ca^{+2} -calmodulin
 - Enhanced during exercise due to Ca^{+2} release from sarcoplasmic reticulum
- **Evidence for role of Ca^{+2} -calmodulin in glycogenolysis**
 - Propranolol (β -receptor blocker) has no effect on muscle glycogen utilization

Changes in Muscle Glycogen Before and After Propranolol Administration

**Figure 5.15**

Control of Glycogenolysis



In Summary

- Glycogen breakdown to glucose in muscle is under the dual control of epinephrine-cyclic AMP and Ca^{+2} -calmodulin. The latter's role is enhanced during exercise due to the increase in Ca^{+2} from the sarcoplasmic reticulum. In this way, the delivery of fuel (glucose) parallels the activation of contraction.

Blood Glucose Homeostasis During Exercise

- **Plasma glucose maintained through four processes:**
 - Mobilization of glucose from liver glycogen stores
 - Mobilization of FFA from adipose tissue
 - Spares blood glucose
 - Gluconeogenesis from amino acids, lactic acid, and glycerol
 - Blocking the entry of glucose into cells
 - Forces use of FFA as a fuel
- **Controlled by hormones**
 - Permissive or slow-acting
 - Fast-acting

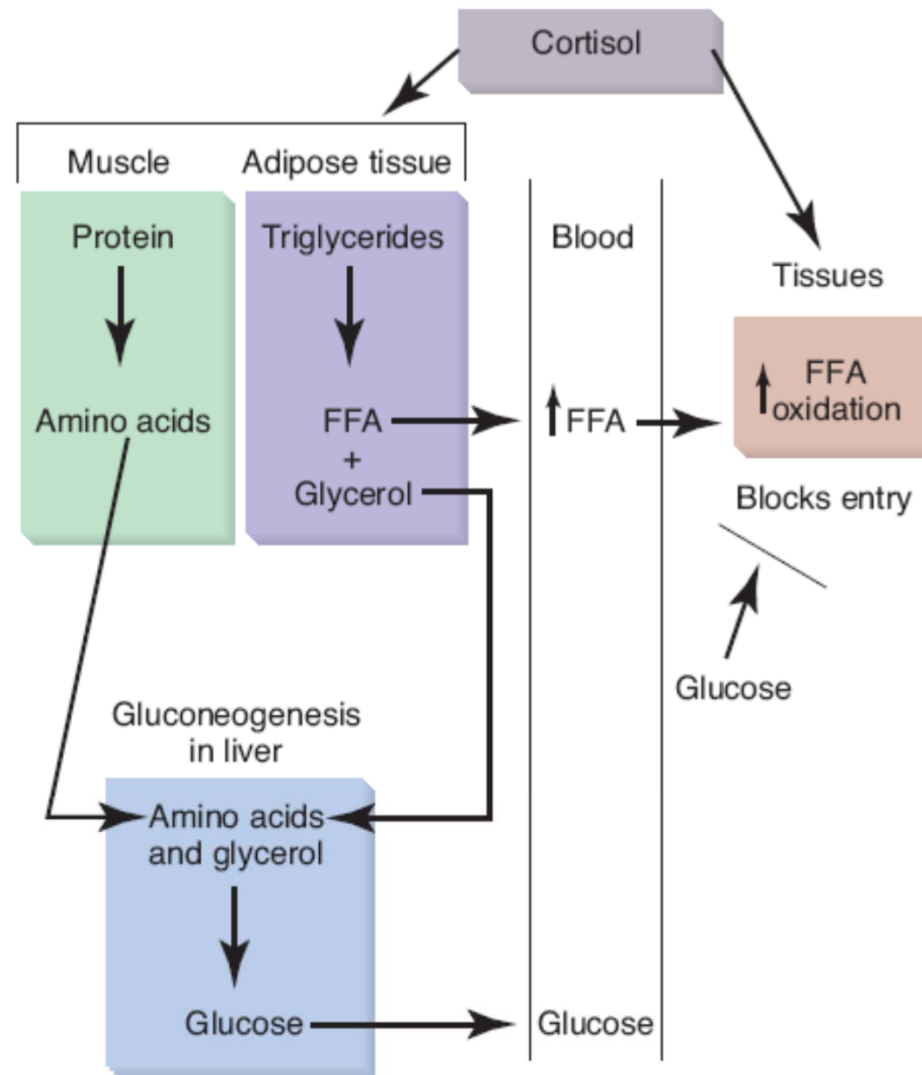
Thyroid Hormones

- **Act in a permissive manner to allow other hormones to exert their full effect**
 - T_3 enhances effect of epinephrine to mobilize free fatty acids from adipose tissue
- **No real change in T_3 and T_4 during exercise**

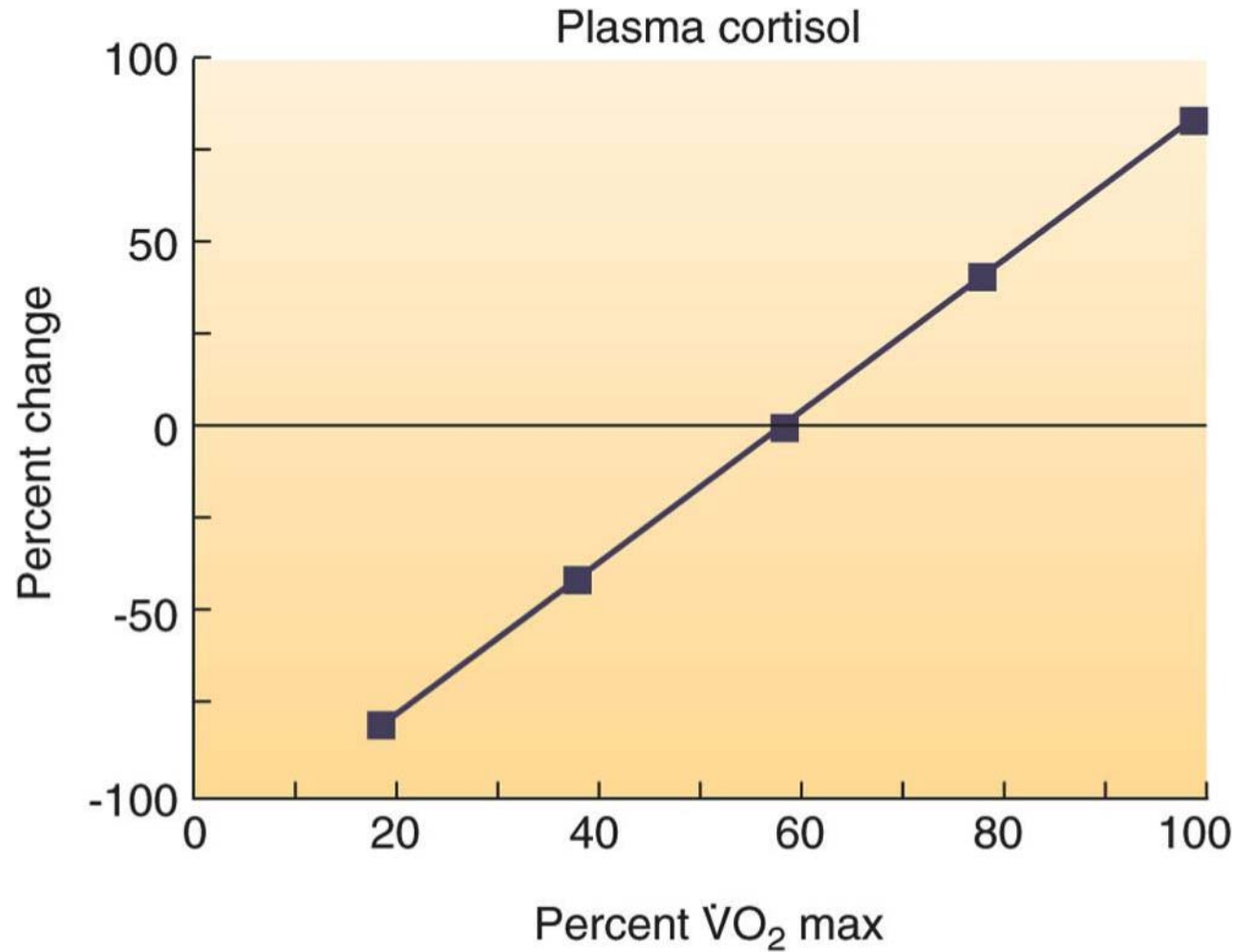
Cortisol

- **Slow-acting hormone**
- **Effects:**
 - Stimulate FFA mobilization from adipose tissue
 - Enhance gluconeogenesis in the liver
 - Decrease the rate of glucose utilization by cells
- **Effect of exercise**
 - Decrease during low-intensity exercise
 - Increase during high-intensity exercise
 - Above ~60% VO_2 max
- **Changes in cortisol may be related to repair of exercise-induced tissue damage**

Role of Cortisol in the Maintenance of Blood Glucose

**Figure 5.17**

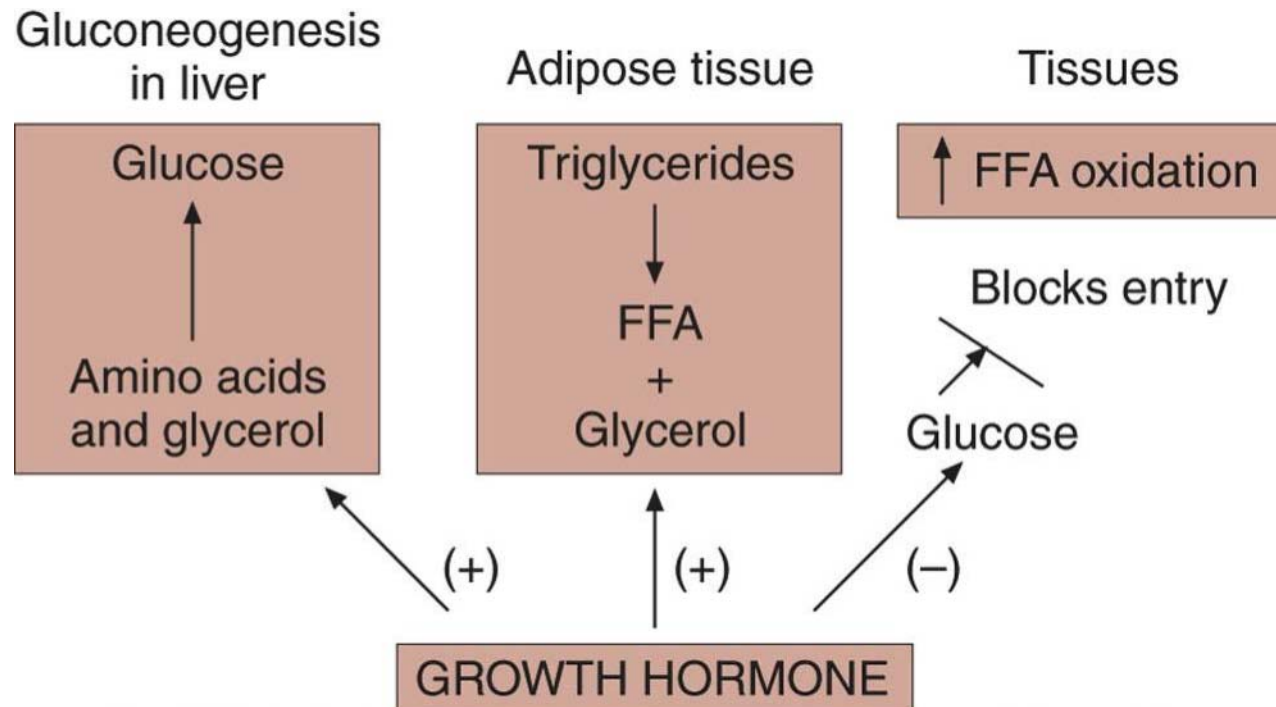
Changes in Plasma Cortisol During Exercise



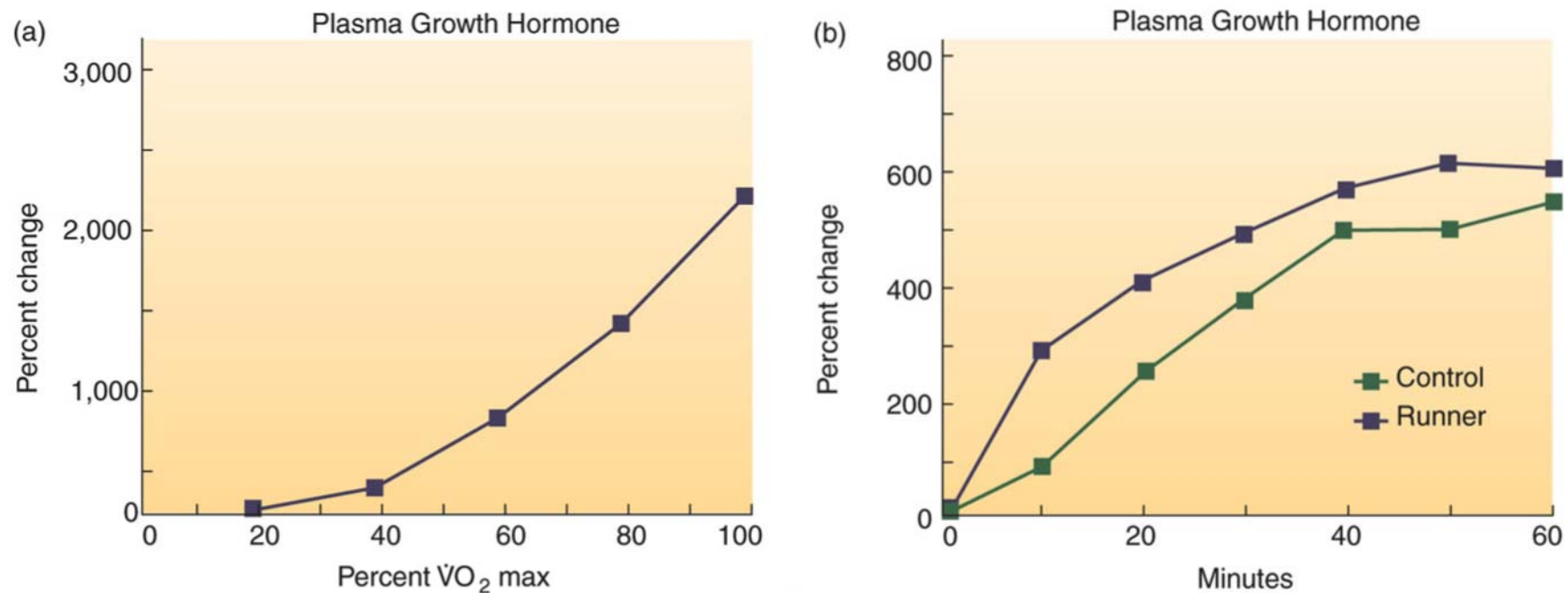
Growth Hormone

- **Slow-acting hormone**
- **Effects:**
 - Supports the action of cortisol
 - Decreases glucose uptake by tissues
 - Increases free fatty acid mobilization
 - Enhances gluconeogenesis in the liver
- **Exercise effect**
 - Increase in plasma GH with increased intensity
 - Greater response in trained runners

Role of Growth Hormone in the Maintenance of Plasma Glucose



Changes in Plasma Growth Hormone During Exercise



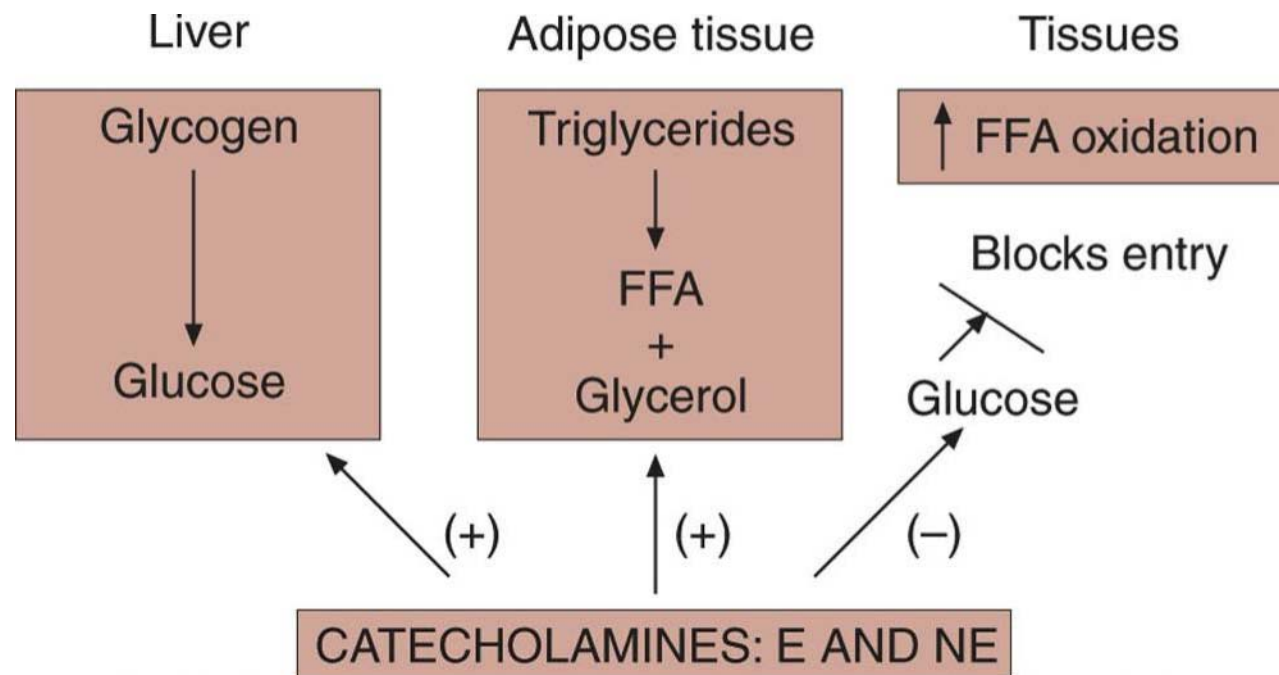
In Summary

- The hormones thyroxine, cortisol, and growth hormone act in a permissive manner to support the actions of other hormones during exercise.
- Growth hormone and cortisol also provide a “slow-acting” effect on carbohydrate and fat metabolism during exercise.

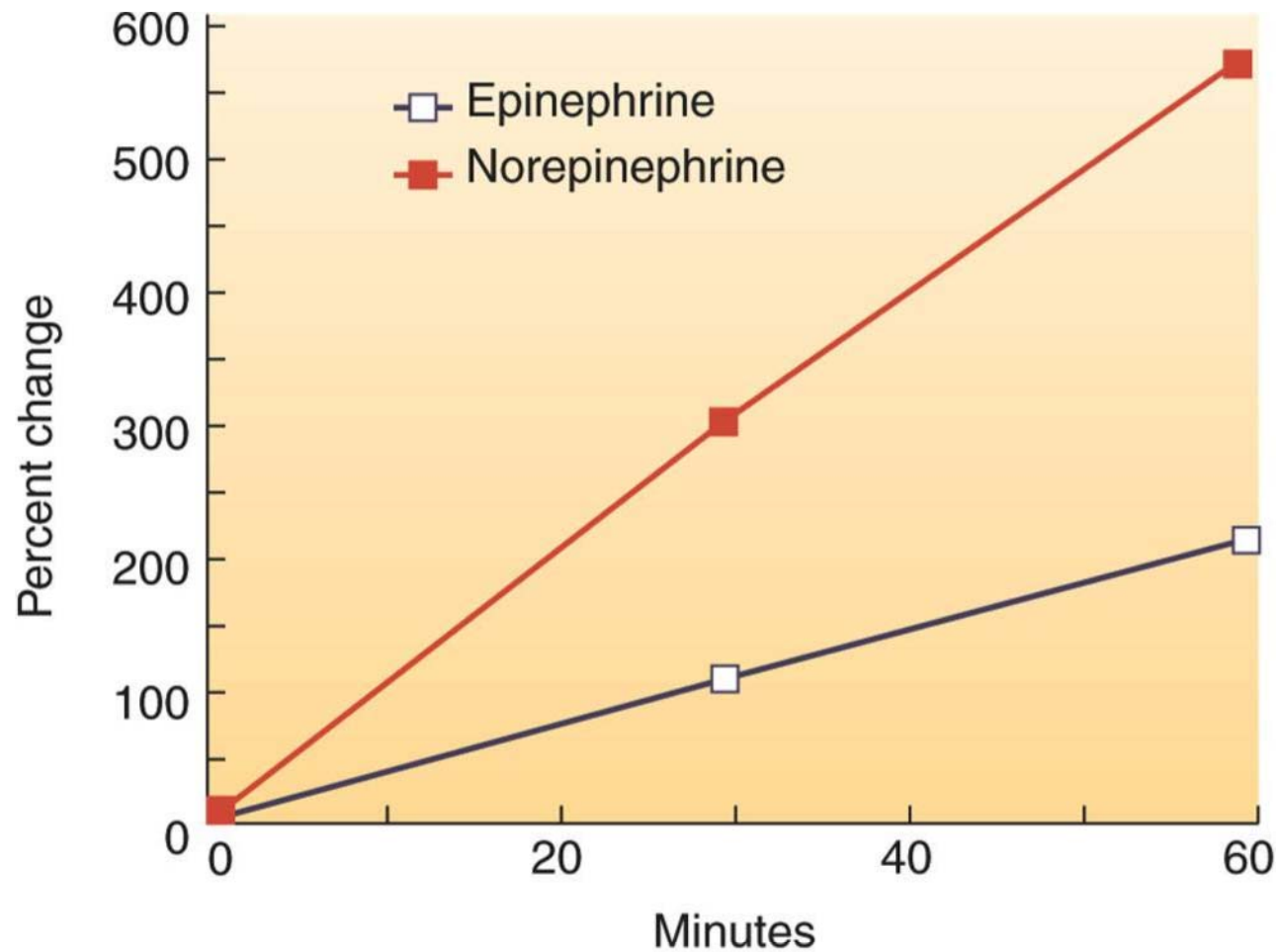
Epinephrine and Norepinephrine

- **Fast-acting hormones**
- **Maintain blood glucose during exercise**
 - Muscle glycogen mobilization
 - Increasing liver glucose mobilization
 - Increasing FFA mobilization
 - Interfere with glucose uptake
- **Plasma E and NE increase during exercise**
 - Also related to increased heart rate and blood pressure during exercise
- **Decreased plasma E and NE following training**

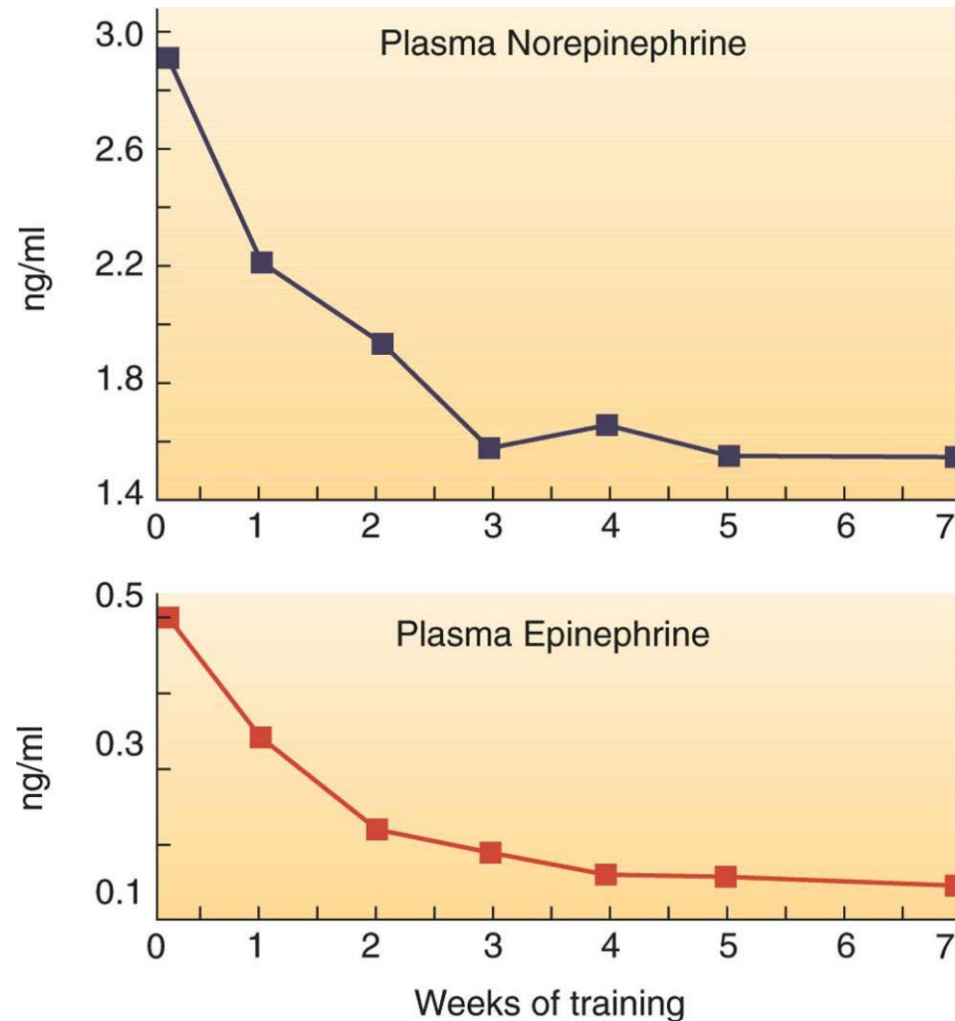
Role of Catecholamines in Substrate Mobilization



Change in Plasma Epinephrine and Norepinephrine During Exercise



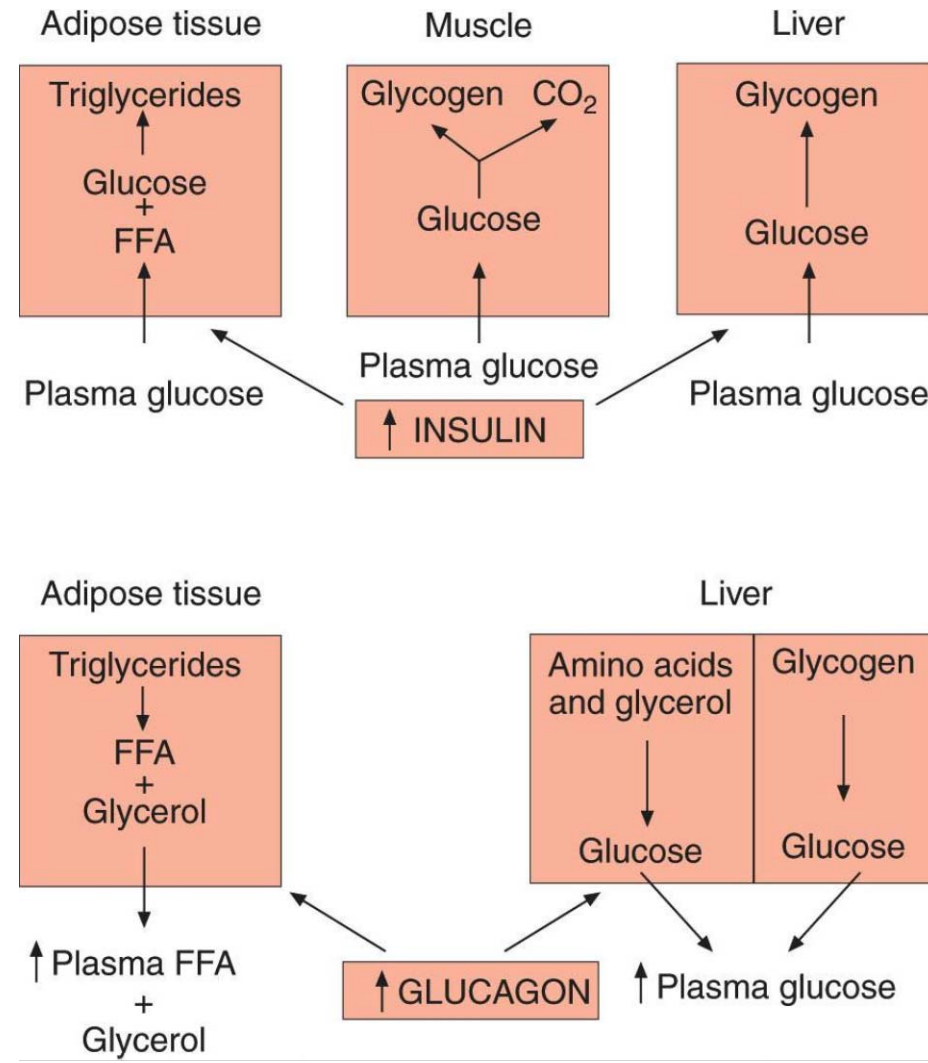
Plasma Catecholamines Responses to Exercise Following Training

**Figure 5.23**

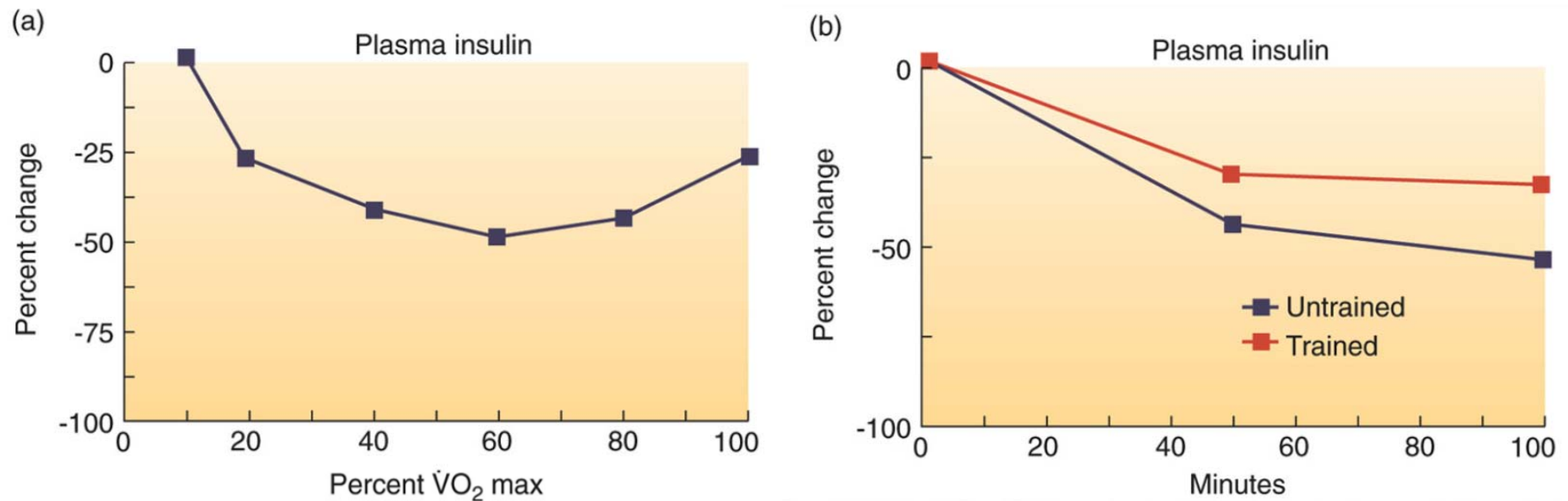
Fast-Acting Hormones

- **Insulin**
 - Uptake and storage of glucose and FFA
 - Plasma concentration decreases during exercise
 - Decreased insulin response following training
- **Glucagon**
 - Mobilization of glucose and FFA fuels
 - Plasma concentration increases during exercise
 - Decreased response following training
- **Insulin and glucagon secretion influenced by catecholamines**

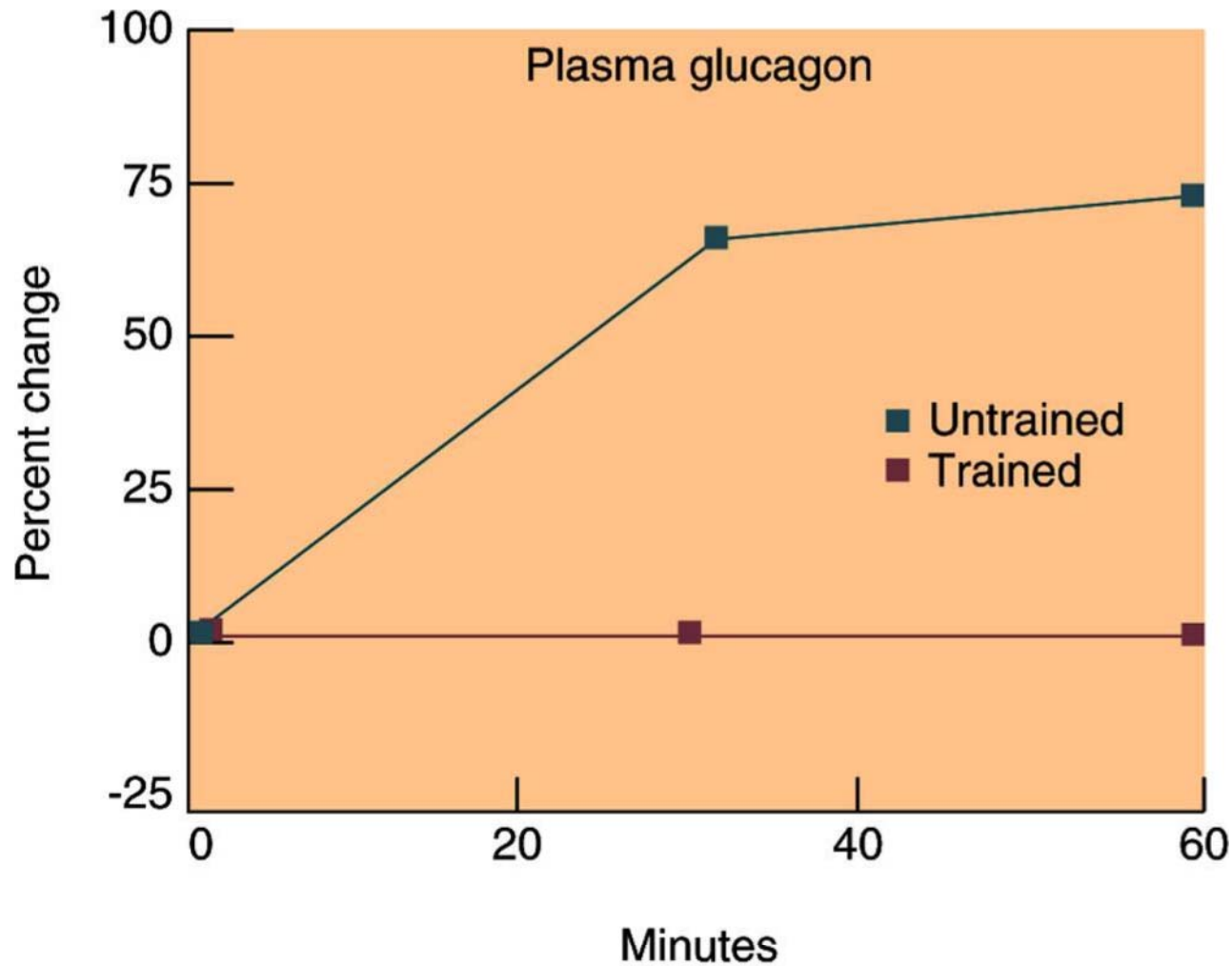
Effects of Insulin and Glucagon



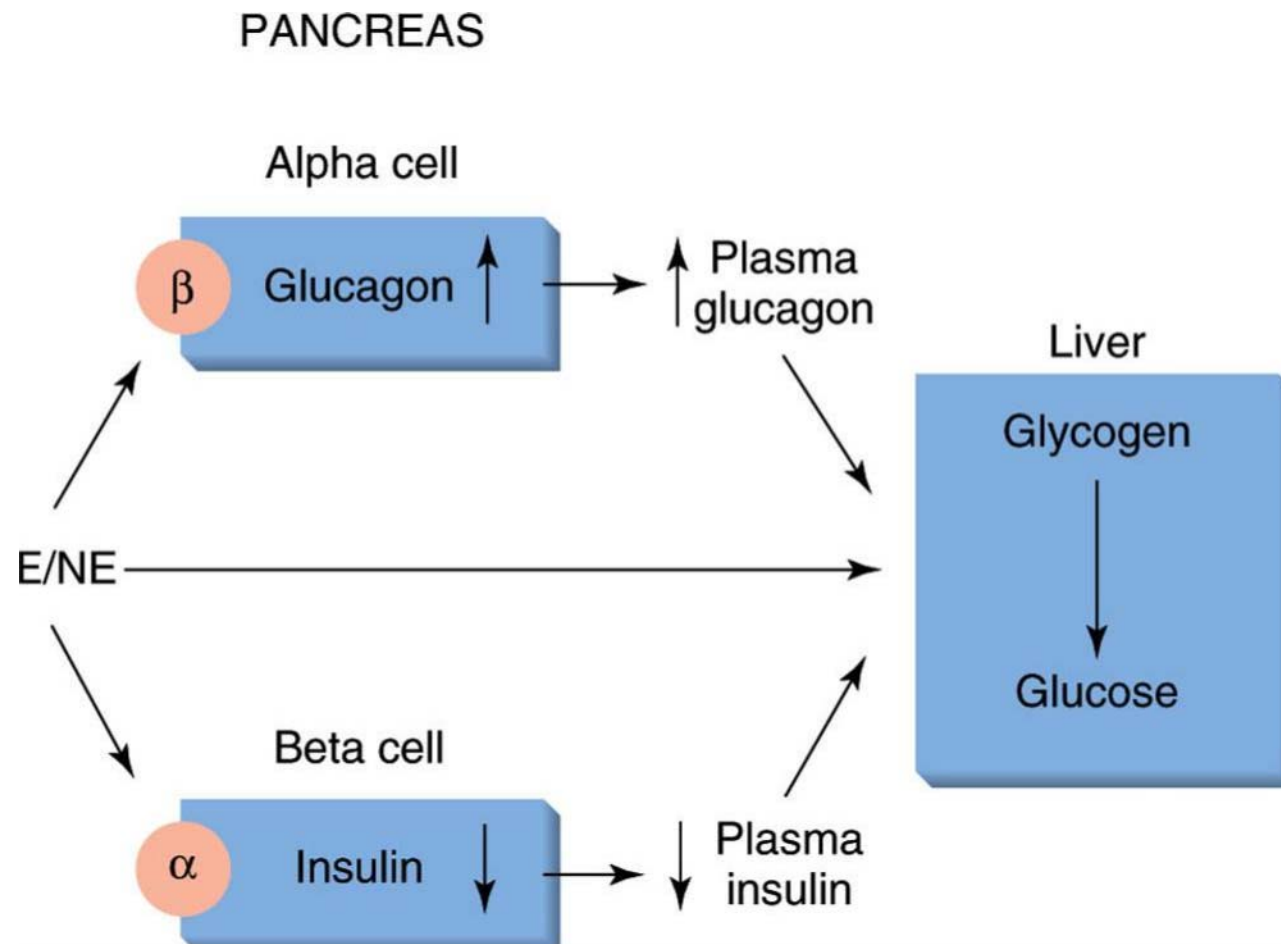
Changes in Plasma Insulin During Exercise



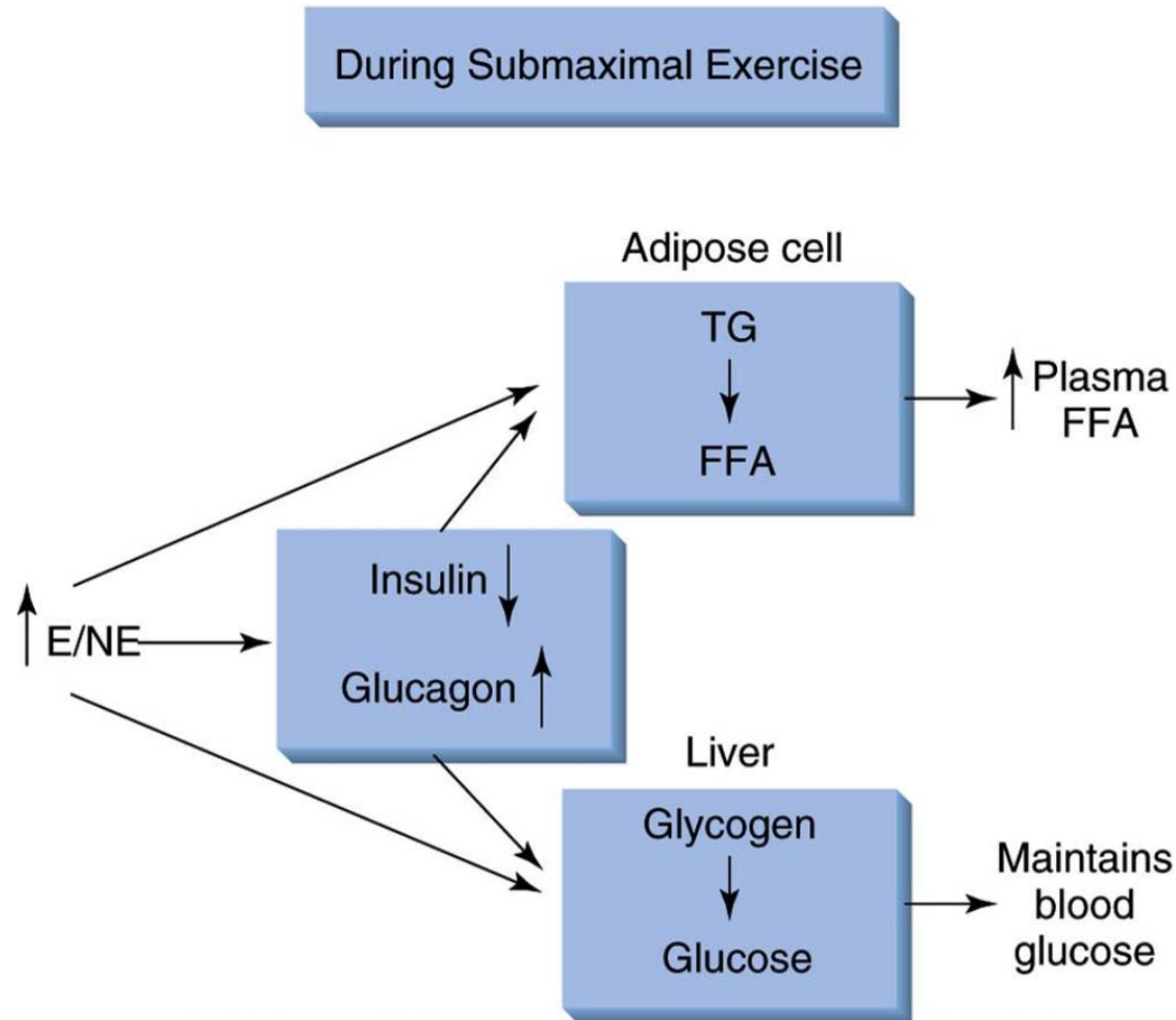
Changes in Plasma Glucagon During Exercise

**Figure 5.26**

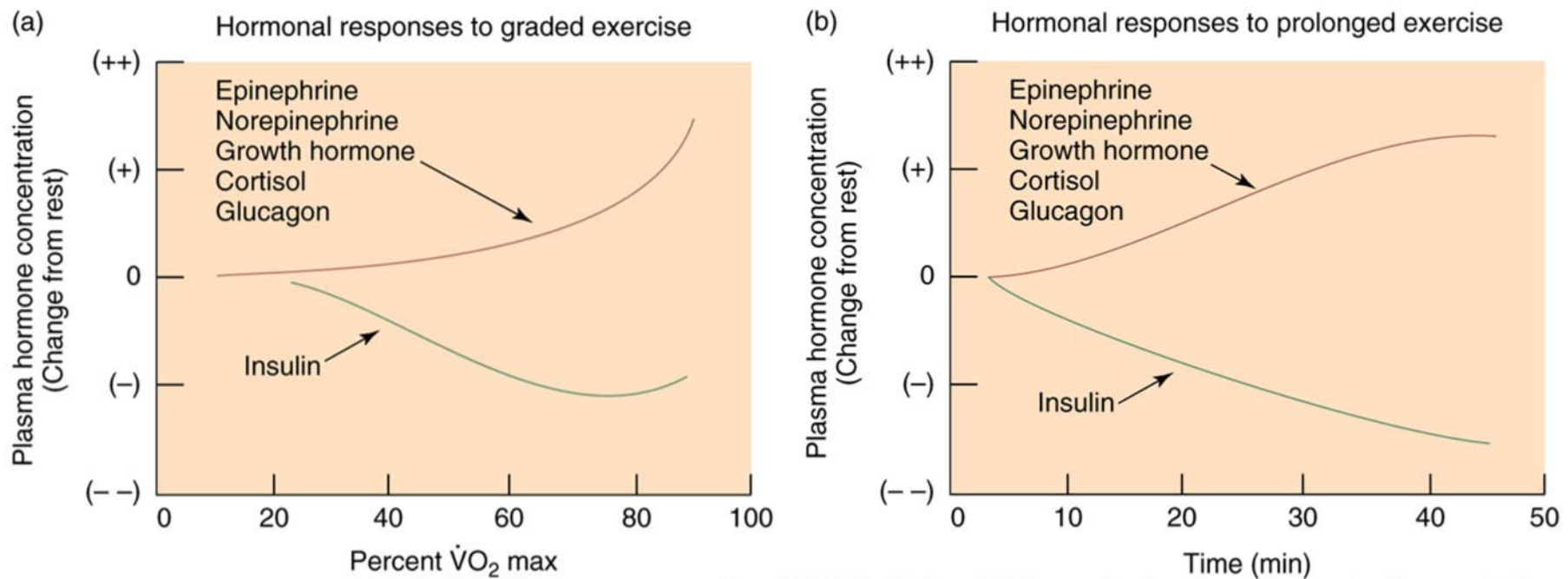
Effect of Epinephrine and Norepinephrine on Insulin and Glucagon Secretion



Effect of the SNS on Substrate Mobilization



Summary of the Hormonal Responses to Exercise



In Summary

- Plasma glucose is maintained during exercise by increasing liver glycogen mobilization, using more plasma FFA, increasing gluconeogenesis, and decreasing glucose uptake by tissues. The decrease in plasma insulin and the increase in plasma E, NE, GH, glucagon, and cortisol during exercise control these mechanisms to maintain the glucose concentration.

In Summary

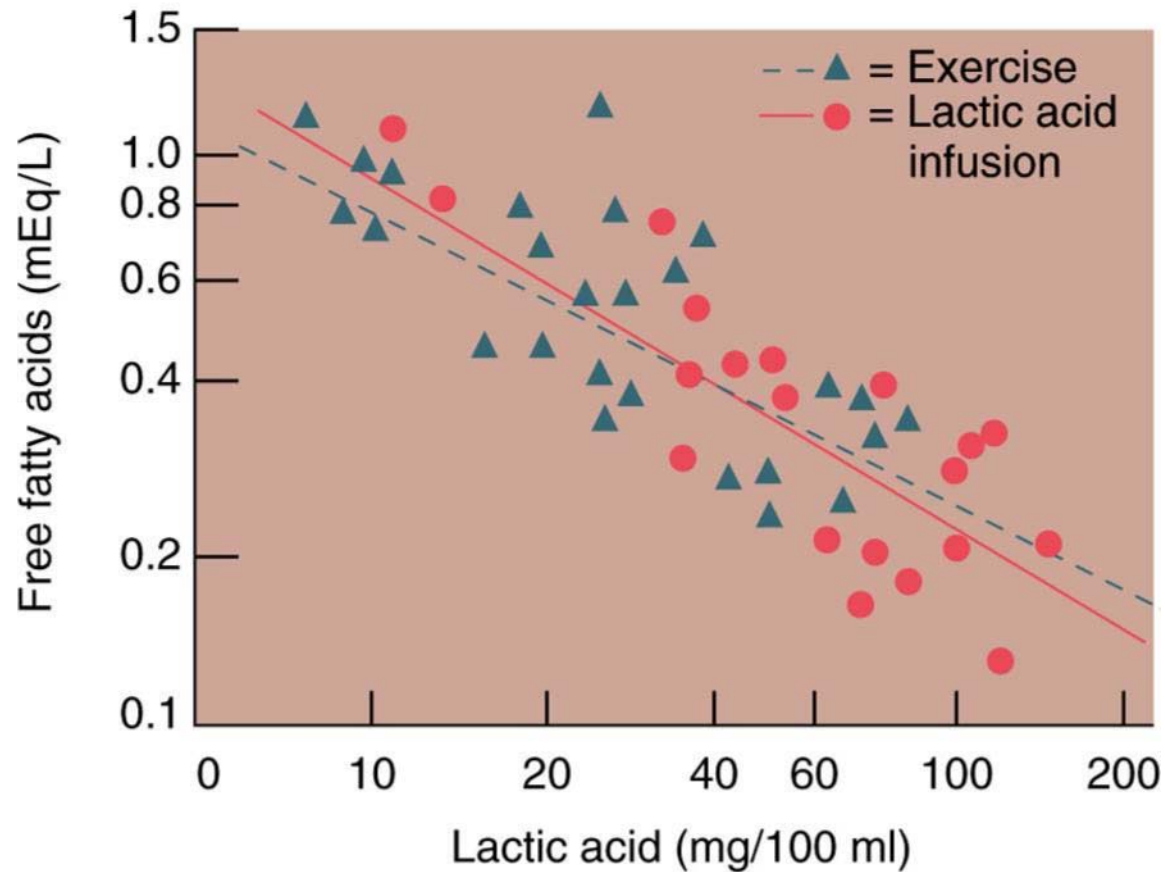
- Glucose is taken up seven to twenty times faster during exercise than at rest—even with the decrease in plasma insulin. The increases in intracellular Ca^{+2} and other factors are associated with an increase in the number of glucose transporters that increase the membrane transport of glucose.
- Training causes a reduction in E, NE, glucagon, and insulin responses to exercise.

Hormone-Substrate Interaction

- **FFA mobilization dependent on hormone sensitive lipase (HSL)**
- **FFA mobilization decreases during heavy exercise**
 - This occurs in spite of persisting hormonal stimulation for FFA mobilization
- **May be due to:**
 - High levels of lactic acid
 - Promotes resynthesis of triglycerides
 - Elevated H^+ concentration inhibits HSL
 - Inadequate blood flow to adipose tissue
 - Insufficient albumin to transport FFA in plasma

Changes in Plasma FFA Due to Lactic Acid

(a)

**Figure 5.30**

Effect of Lactic Acid on FFA Mobilization

(b)

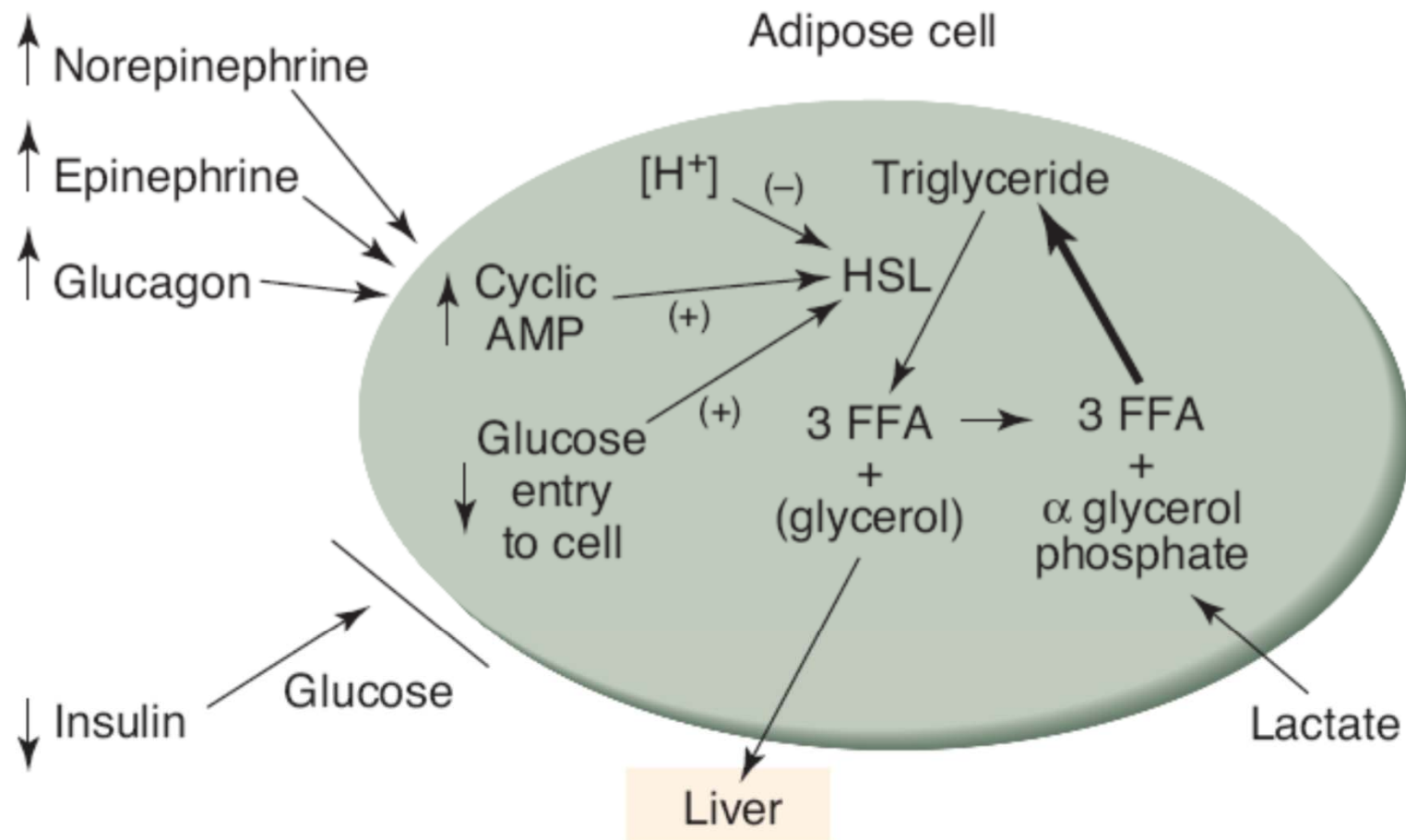


Figure 5.30

In Summary

- The plasma FFA concentration decreases during heavy exercise even though the adipose cell is stimulated by a variety of hormones to increase triglyceride breakdown to FFA and glycerol. This may be due to:
 - (a) the higher H^+ concentration inhibiting hormone sensitive lipase,
 - (b) the high levels of lactate during heavy exercise promoting the resynthesis of triglycerides,
 - (c) an inadequate blood flow to adipose tissue, or
 - (d) insufficient albumin needed to transport the FFA in the plasma.

Study Questions

- 1. Draw and label a diagram of a negative feedback mechanism for hormonal control using cortisol as an example.**
- 2. List the factors that can influence the blood concentration of a hormone.**
- 3. Discuss the use of testosterone and growth hormone as aids to increase muscle size and strength, and discuss the potential long-term consequences of such use.**
- 4. List each endocrine gland, the hormones(s) secreted from that gland, and its (their) action(s).**
- 5. Describe the two mechanisms by which muscle glycogen is broken down to glucose (glycogenolysis) for use in glycolysis. Which one is activated at the same time as muscle contraction?**

Study Questions

- 6. Identify the four mechanisms involved in maintaining the blood glucose concentration.**
- 7. Draw a summary graph of the changes in the following hormones with exercise of increasing intensity or duration: epinephrine, norepinephrine, cortisol growth hormone, insulin, and glucagon.**
- 8. What is the effect of training on the responses of epinephrine, norepinephrine, and glucagon to the same exercise task?**
- 9. Briefly explain how glucose can be taken into the muscle at a high rate during exercise when plasma insulin is reduced. Include the role of glucose transporters.**

Study Questions

- 10. Explain how free fatty acid mobilization from the adipose cell decreases during maximal work in spite of the cell being stimulated by all the hormones to break down triglycerides.**
- 11. Discuss the effect of glucose ingestion on the mobilization of free fatty acids during exercise.**