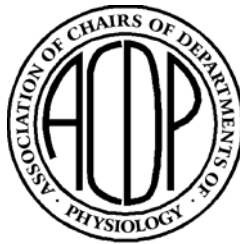


# Medical Physiology Learning Objectives



**Robert G. Carroll**  
**L. Gabriel Navar**  
**Mordecai P. Blaustein**

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The American Physiological Society (APS)

Education Office

9650 Rockville Pike

Bethesda, MD 20814-3991

301-634-7132

301-634-7098 (fax)

[education@the-aps.org](mailto:education@the-aps.org)

<http://www.the-aps.org>

Association of Chairs of Departments of  
Physiology (ACDP)

9650 Rockville Pike, Suite 314

Bethesda, MD 20814-3991

301-634-7785

301-634-7098 (fax)

[acdponline.org](mailto:acdponline.org)

<http://www.acdponline.org>

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# Introduction and Rationale

As medical and other professional schools in the health sciences continue to modify their curricula, a variety of approaches are being utilized to teach the students. These widely diversified approaches range from the traditional and systematic course in physiology and neuroscience to those in which there is not an identifiable course in physiology. While a systematic presentation of physiological concepts under the direction of physiology faculty continues to be the most efficient way to ensure appropriate depth and breadth, physiologically related topics are often spread out over several courses. It is, nevertheless, essential that all medical and health professional students receive sufficient exposure to the physiological concepts that provide the foundations needed for further studies in pharmacology, pathology, pathophysiology, and medicine. The mechanisms of deranged function cannot be appreciated without an in-depth understanding of basic biophysical and physiological mechanisms. The purpose of developing these core competency criteria is to provide guidelines for the breadth and depth of knowledge in the physiological principles and concepts that are considered minimal and essential for further progress in understanding mechanisms of disease and body defenses. Regardless of the specific didactic or educational approach used by any given institution, that institution must develop mechanisms to assure that the students are being inculcated with these basic principles and concepts at appropriate depth of understanding. The development of these core learning objectives will allow all programs to determine if their students are achieving at least this basic level of understanding.

By necessity, the objectives define content to be taught. Not addressed in this document are issues related to the format in which this content should be presented. This will be dictated by factors and constraints (i.e., class size, number of faculty) unique to each institution. Nevertheless, all of the objectives can be attained using multiple teaching formats, and faculty need to the optimum teaching/learning format for their students. The curricular objectives are focused primarily on normal body function. However, it is recognized that this material must be presented in a context that prepares students for their roles as physicians. Accordingly, it is suggested that wherever possible clinical examples can and should be used to illustrate the underlying physiological principles.

This project has been endorsed by The American Physiological Society and the Association of Chairs of Departments of Physiology. The objectives will be revised and updated periodically – readers are asked to see the APS web site <http://www.the-aps.org/education/MedPhysObj/medcor.htm> or the ACDP web site [http://www.acdponline.org/med\\_phys\\_obj.htm](http://www.acdponline.org/med_phys_obj.htm) for future versions of this project. Details on the construction and evaluation of the objectives project are also on the APS web site, published in the journal *Advances in Physiology Education* (*Adv Physiol Educ* 25: 2-7, 2001).

Address all comments to:     Robert G. Carroll, Ph.D.  
  Department of Physiology  
  Brody School of Medicine  
  East Carolina University  
  600 Moyer Blvd.  
  Greenville, NC 27858-4354  
  (252) 816-2768

# Authoring Committee Membership

## **Cardiovascular**

2006 Revision: Ronald Tuma, Coordinator; Brian Duling, Irving Zucker  
Coordinator: Fred Peterson  
Members: Mike Andresen, Aubrey Taylor, Harvey Sparks

## **Cell and General**

Coordinator: Mordecai Blaustein  
Members: Emile Boulpaep, Nelson Escobales, Robert Gunn, Robert Rakowski, Luis Reuss,  
Stanley Schultz

## **Central Nervous System, Neural Control and Autonomic Regulation**

Coordinators: Ian Phillips, Richard Ray  
Member: Robert Foreman

## **Endocrinology and Metabolism**

Coordinators: H. Maurice Goodman, Owen McGuinness,  
Members: Phyllis Wise, Patti Hinkle, Robert Goodman, Irving Joshua, James Voogt

## **Exercise and Environmental Physiology**

Coordinators: David Robertshaw, Patricia Gwartz, Charles Tipton

## **Gastrointestinal**

Coordinators: John Williams, Leonard (Rusty) Johnson  
Members: Jackie Wood, Tom Smith

## **Renal, Water and Electrolyte Homeostasis**

2005 Revision: L. Gabriel Navar, Willam Dantzler  
Coordinators: L. Gabriel Navar, Bruce Koeppe  
Members: James Schafer, Randy Packer, Herbert Janssen, Noreen Rossi, Brian Jackson,  
Klaus Beyenbach, Kurt Amsler

## **Respiration**

2006 Revision: Michael Maron, O. Douglas Wangenstein  
Coordinator: Aubrey Taylor  
Members: Mary Townsley, David Beckman, Jim Parker

## **Muscle**

Coordinator: Jack Rall

# Special Thanks to Faculty at These Institutions

Brown University  
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University of Nebraska  
University of North Texas Health Science Center  
University of Puerto Rico  
University of South Alabama  
University of South Florida  
Vanderbilt University  
Wayne State University

# Learning Objective Format

## Purpose of Learning Objectives

Learning objectives communicate the expectations of the faculty member. Consequently, the learning objectives have to identify the knowledge base, the appropriate depth or detail, and how the students are to use the knowledge. For a traditional 50-minute lecture, usually three to seven learning objectives can be constructed. For integrated courses, the objectives are provided in a group and are expected to be mastered during that block of the course.

## Bloom's Taxonomy

In 1956, Bloom identified six distinct levels of cognitive understanding, and organized them into a taxonomy of objectives in the cognitive domain. From basic to complex, the taxonomy categories are: Knowledge, Comprehension, Application, Analysis, Synthesis, and Evaluation. The taxonomy levels can be coupled with general objectives, and specific outcome action verbs, which lead to that level.

Level of Taxonomy	General Objectives	Specific Outcome Action Verbs
Knowledge	Knows terms Knows specific facts Knows rules Knows classifications and categories Knows criteria Knows methods and procedures Knows principles and generalizations Knows theories and structure	Defines Names States Identifies Describes Distinguishes
Comprehension	Translates communications Interprets relationships Extrapolates from given data	Interprets Converts Explains Predicts Generalizes Infers
Application	Applies principles	Uses Solves Constructs Prepares Demonstrates
Analysis	Analyzes organizations and relationships	Discriminates Outlines Diagrams Differentiates Infers Explains
Synthesis	Produces new arrangements	Designs Organizes Rearranges Compiles Modifies Creates
Evaluation	Judges on the basis of external criteria Judges on the basis of evidence	Appraises Compares Contrasts Discriminates Criticizes Detects

# Learning Objectives and Template

Learning objectives provide a focal point for student learning efforts. Objectives should be constructed so that the student will know:

1. The knowledge base they are expected to learn
2. The depth or detail they are to learn it
3. How they are to use this knowledge

One advantage of learning objectives is that you can use them to direct students to material not covered in class.

## Tips for Constructing Learning Objectives

- Objectives should be stated in terms of student behavior and the level of specificity that is expected
- Objectives should use an action verb that indicates the depth of understanding expected (see table on previous page)
- Objectives should be stated precisely using terms that have uniform meaning and are consistent with their reading resources
- Objectives should be realistic

### EXAMPLES

The ECU Physiology Department committed to the use of learning objectives for all sections in 1994. Each instructor wrote objectives for the lecture. The objectives were reviewed by four other physiologists, and then the proposed objectives were revised to answer the concerns of the reviewers. The process is cumbersome, but the product is worth the effort. Here are sample objectives proposed for the lecture on microcirculation, followed by reviewers' comments, and finally the revised objectives.

#### Chapter 28 The Microcirculation and Lymphatics

**ORIGINAL 1.** Using Fick's Law for Diffusion, contrast the movement of oxygen and glucose from the plasma to the intracellular space. Based on their chemical properties, predict which of these substances would show diffusion limited movement and which would show flow limited movement.

AUTHOR: I expect the students to review the factors influencing diffusion (presented earlier in the course) and contrast the movement of two different agents from the blood to the cell. I also expect a working definition of flow-limited and diffusion-limited transport.

COMMITTEE: Glucose movement is tissue specific, and entry into the cell by any of a variety of glucose transporters further obscures my intent (transport from the blood to the cell). Identify

a tissue, and delete intracellular space. Finally transport is a poorly defined term, replace with exchange (the term used in the text).

**REVISED 1.** Using Fick's Law for Diffusion, contrast the movement of oxygen and glucose from the plasma to a skeletal muscle cell. Based on their chemical properties, predict which of these substances would show diffusion limited exchange and which would show flow limited exchange.

**ORIGINAL 2.** Calculate the balance of hydrostatic and osmotic forces controlling fluid movement at the arteriolar and venular ends of a capillary bed. How is this balance altered by pre-capillary arteriolar constriction?

**AUTHOR:** The Starling forces control fluid exchange between the plasma and the interstitial fluid. The drop in arterial pressure along the capillary allows filtration at one area of the microcirculation and reabsorption at the other end of the microcirculation. Any factors that alter capillary pressure will affect this exchange.

**COMMITTEE:** Calculation requires standard values. Reference to the text forces students to use and review the appropriate figure. Replace fluid movement with the more specific transcapillary fluid exchange. Reword last sentence as an objective, with an action verb. Expand the objective to include the effects of venous pressure on capillary fluid exchange, such as occurs in ascites.

**REVISED 2.** Given the estimates in figure 28-7, calculate the balance of hydrostatic and osmotic forces controlling transcapillary fluid exchange at the arteriolar and venular ends of a capillary bed. Predict how this balance is altered by pre-capillary and post-capillary resistance and pressure changes.

**ORIGINAL 3.** List four causes of edema, and describe how each results from the disruption of the balance of microcirculatory fluid exchange and lymph flow.

**AUTHOR:** Disruption of the Starling forces, permeability, or lymphatic drainage each can cause edema.

**COMMITTEE:** OK as written (a minor miracle)

**ORIGINAL 4.** Describe how the theory of metabolic regulation of blood flow accounts for the observed phenomena of autoregulation, active hyperemia, and reactive hyperemia.

**AUTHOR:** Three theories can account for autoregulation. I feel that understanding of the metabolic theory has the most practical advantages, and I want to focus the student's attention on that area.

**COMMITTEE:** OK as written (they must have gotten tired)

# Cell and General

## Biological Membranes, Solutes and Solutions

CE 1. Describe the polar structure of water, and explain how the formation of hydrogen bonds permits the dissociation of salts (such as NaCl), saccharides, and other polar molecules. Contrast the definitions of hydrophobic and hydrophilic related to water polarity.

CE 2. Describe the composition of a cell membrane. Diagram its cross section, and explain how the distribution of phospholipids and proteins influences the membrane permeability of ions, hydrophilic and hydrophobic compounds.

CE 3. Using a cell membrane as an example, define a reflection coefficient, and explain how the relative permeability of a cell to water and solutes will generate an osmotic pressure. Contrast the osmotic pressure generated across a cell membrane by a solution of particles that freely cross the membrane with that of a solution with the same osmolality, but particles that cannot cross the cell membrane.

CE 4. Contrast the following units used to describe concentration: mM, mEq/l, mg/dl, mg%. List the typical value and normal range for plasma  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{H}^+$  (pH),  $\text{HCO}_3^-$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ , and glucose, and the typical intracellular pH and concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ , and  $\text{HCO}_3^-$ .

CE 5. Differentiate between the terms osmole, osmolarity, osmolality and tonicity. List the typical value and normal range for plasma osmolality.

CE 6. Understand that the difference in free energy of a solute or solvent between two components can have chemical, electrical and/or hydrostatic pressure components. At equilibrium, for a given component, the free energy difference between the two compartments is zero.

CE 7. Define the Donnan equilibrium and list the resulting characteristics.

CE 8. Describe the linear relationship between forces and flows (e.g., Ohm's Law, Fick's Law of diffusion, and the law of hydrodynamic flow).

CE 9. Write Fick's Law of diffusion, and explain how changes in the concentration gradient, surface area, time, and distance will influence the diffusional movement of a compound.

CE 10. Based on the principle of ionic attraction, explain how a potential difference across a membrane will influence the distribution of a cation and an anion.

CE 11. Define the term "steady state," and differentiate it from "equilibrium." Relate the pump-leak model of steady-state ion content to cell solute gradients and cell volume maintenance.

CE 12. Write the Nernst equation, and indicate how this equation accounts for both the chemical and electrical driving forces that act on an ion.

CE 13. Based on the Nernst equilibrium potential, predict the direction that an ion will move when the membrane potential a) is at its equilibrium potential, b) is higher than the equilibrium potential, or c) is less than the equilibrium potential. List values in a typical non-excitabile cell for the membrane potential, for  $E_{Na}$ ,  $E_K$ ,  $E_{Cl}$ , and  $E_{Ca}$ .

CE 14. Define the concepts of electrochemical equilibrium and equilibrium potential, and give internal and external ion concentrations. Be able to calculate an equilibrium potential for that ion using the Nernst equation. Contrast the difference in  $E_K$  (the Nernst potential for  $K^+$ ) caused by a 5 mEq/l increase in extracellular  $K^+$  with the change in  $E_{Na}$  (the Nernst potential for  $Na^+$ ) caused by a 5 mEq/l increase in extracellular  $Na^+$ .

CE 15. Explain how the resting membrane potential is generated and calculate membrane potential by using either a) the Goldman-Hodgkin-Katz equation or b) the chord conductance equation. Given an increase or decrease in the permeability of K, Na, or Cl, predict how the membrane potential would change.

CE 16. Differentiate the following terms based on the source of energy driving the process and the molecular pathway for: diffusion, facilitated diffusion, secondary active transport, and primary active transport.

CE 17. Describe how transport rates of certain molecules and ions are accelerated by specific membrane transport proteins (“carrier” and “channel” molecules).

CE 18. Describe how energy from ATP hydrolysis is used to transport ions such as  $Na^+$ ,  $K^+$ ,  $Ca^{2+}$ , and  $H^+$  against their electrochemical differences (e.g., via the  $Na^+$  pump, sarcoplasmic reticulum  $Ca^{2+}$  pump, and gastric  $H^+$  pump).

CE 19. Understand the role of ATP-binding cassette transporters in, for example, multi-drug resistance and its significance for cancer chemotherapy.

CE 20. Explain how energy from the  $Na^+$  and  $K^+$  electrochemical gradients across the plasma membrane can be used to drive the net “uphill” (against a gradient) movement of other solutes (e.g.,  $Na^+$ /glucose co-transport;  $Na^+$ / $Ca^{2+}$  exchange or counter-transport). Apply this principle to predict possible therapies for secretory diarrhea.

CE 21. Describe the role of water channels (aquaporins) in facilitating the movement of water across biological membranes.

## Excitable Cells

- CE 22. Define the following properties of ion channels: gating, activation, and inactivation.
- CE 23. State the cell properties that determine the rate of electronic conduction.
- CE 24. Differentiate between the properties of electrotonic conduction, conduction of an action potential, and saltatory conduction. Identify regions of a neuron where each type of electrical activity may be found.
- CE 25. Contrast the cell-to-cell spread of depolarization at a chemical synapse with that at a gap junction based on speed and fidelity (success rate). At the chemical synapse, contrast the terms temporal summation and spatial summation.
- CE 26. Understand the principle of the voltage clamp and how it is used to identify the ionic selectivity of channels.
- CE 27. Contrast the gating of ion-selective channels by extracellular ligands, intracellular ligands, stretch, and voltage.
- CE 28. Know the properties of voltage-gated  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  channels, and understand that voltage influences their gating, activation, and inactivation.
- CE 29. Understand how the activity of voltage-gated  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  channels generates an action potential and the roles of those channels in each phase (depolarization, overshoot, repolarization, hyperpolarization) of the action potential.
- CE 30. Contrast the mechanisms by which an action potential is propagated along both nonmyelinated and myelinated axons. Predict the consequence on action potential propagation in the early and late stages of demyelinating diseases, such as multiple sclerosis.

## Cell Volume Regulation, Intracellular pH, and Organelles

- CE 31. Understand how regulation of the concentrations of  $\text{K}^+$ ,  $\text{Cl}^-$ , and other  $\text{Na}^+$  solutes influence cell volume.
- CE 32. Understand how various transporters (e.g.  $\text{Na}^+/\text{H}^+$  exchange,  $\text{Cl}/\text{HCO}_3$  exchange,  $\text{Na}^+-\text{HCO}_3$  co-transport, etc.) contribute to the control of intracellular pH.
- CE 33. Describe  $\text{Ca}^{2+}$  accumulation in the sarcoplasmic and endoplasmic reticulum, mediated by  $\text{Ca}^{2+}$  ATPase.

## **Regulation of Cell Function**

CE 34. Describe how intracellular signaling pathways can influence the expression and function of proteins.

CE 35. Provide examples of how phosphorylation/dephosphorylation of proteins (e.g. channels and membrane receptors) can act as negative and positive effectors of signal transduction.

CE 36. Define the terms agonist and antagonist as related to membrane receptor ligands.

CE 37. Diagram the intracellular signaling pathways for cholinergic nicotinic, cholinergic muscarinic, alpha-1 adrenergic, alpha-2 adrenergic, beta-1 adrenergic, beta-2 adrenergic, and beta-3 adrenergic receptors.

CE 38. Contrast the receptor location and signaling pathways of peptide and steroid hormones. For peptide hormone receptors, describe the process of activation, inactivation, up-regulation, down-regulation, sensitization, and desensitization.

## **Epithelia**

CE 39. Draw an epithelium, labeling the tight junctions, the apical membrane, and the basolateral membrane. Trace the movement of a compound that travels across an epithelium by a transcellular pathway and a compound that travels via a paracellular pathway.

CE 40. Explain the role of the “tight” junctions in leaky and tight epithelia.

CE 41. Explain the functional significance of polarized distribution of various transport proteins to the apical or the basolateral cell membrane.

CE 42. Understand solute-solvent coupling in transport.

## **Cell Motors**

CE 43. Explain how cell molecular motors work to generate force and to transport organelles and other cargo.

CE 44. Explain how the mobilization of calcium initiates contractions in smooth, striated, and cardiac muscle. Explain the sliding filament model of muscle contraction and contrast the cellular and molecular basis of muscle contraction in smooth and striated muscle.

## **Transcapillary Transport**

CE 45. Differentiate the following terms: osmotic pressure, oncotic pressure, and hydrostatic pressure, as pertains to movement across the endothelium of the capillaries.

CE 46. Predict the permeability of cardiovascular capillaries to small ions/crystalloids (e.g., NaCl) and proteins (albumin) based on the capillary reflection coefficient.

CE 47. Based on the Starling hypothesis, explain how permeability, hydrostatic pressure and oncotic pressure influence transcapillary exchange of fluid.

# Cardiovascular

(revised 2006)

## Unique Characteristics of Cardiac Muscle

CV 1. Contrast the duration of the action potential and the refractory period in a cardiac muscle, a skeletal muscle, and a nerve. Sketch the temporal relationship between an action potential in a cardiac muscle cell and the resulting contraction (twitch) of that cell. On the basis of that graph, explain why cardiac muscle cannot remain in a state of sustained (tetanic) contraction.

CV 2. State the steps in excitation-contraction coupling in cardiac muscle. Outline the sequence of events that occurs between the initiation of an action potential in a cardiac muscle cell and the resulting contraction and then relaxation of that cell. Provide specific details about the special role of  $\text{Ca}^{2+}$  in the control of contraction and relaxation of cardiac muscle.

CV 3. Compare cardiac and skeletal muscle with respect to: cell size, electrical connections between cells, and arrangement of myofilaments. Based on ion permeability and electrical resistance describe role of gap junctions in creating a functional syncytium.

CV 4. Identify the role of extracellular calcium in cardiac muscle contraction. Identify other sources of calcium that mediate excitation-contraction coupling, and describe how intracellular calcium concentration modulates the strength of cardiac muscle contraction.

CV 5. Describe the role of Starling's Law of the Heart in keeping the output of the left and right ventricles equal.

CV 6. Describe the difference in the way changes in preload and changes in contractility influence ventricular force development. Compare the energetic consequences of these two separate mechanisms of force modulation.

## Electrophysiology of the Heart

CV 7. Sketch a typical action potential in a ventricular muscle and a pacemaker cell, labeling both the voltage and time axes accurately. Describe how ionic currents contribute to the four phases of the cardiac action potential. Use this information to explain differences in shapes of the action potentials of different cardiac cells.

CV 7A. Describe the ion channels that contribute to each phase of the cardiac action potential. How do differences in channel population influence the shape of the action potential in the nodal, atrial muscle, ventricular muscle, and Purkinje fiber cardiac cells.

CV 8. Explain what accounts for the long duration of the cardiac action potential and the resultant long refractory period. What is the advantage of the long plateau of the cardiac action potential and the long refractory period?

CV 9. Beginning in the SA node, diagram the normal sequence of cardiac activation (depolarization) and the role played by specialized cells. Predict the consequence of a failure to conduct the impulse through any of these areas.

CV 10. Explain why the AV node is the only normal electrical pathway between the atria and the ventricles, and explain the functional significance of the slow conduction through the AV node. Describe factors that influence conduction velocity through the AV node.

CV 11. Explain the ionic mechanism of pacemaker automaticity and rhythmicity, and identify cardiac cells that have pacemaker potential and their spontaneous rate. Identify neural and humoral factors that influence their rate.

CV 12. Discuss the significance of “overdrive suppression” and “ectopic pacemaker,” including the conditions necessary for each to occur.

CV 13. Contrast the sympathetic and parasympathetic nervous system influence on heart rate and cardiac excitation in general. Identify which arm of the autonomic nervous system is dominant at rest and during exercise. Discuss ionic mechanisms of these effects on both working myocardium and pacemaker cells.

CV 14. Describe how cell injury, resulting in a less negative resting potential, alters ionic events in depolarization and repolarization.

CV 15. Define the following terms: decremental conduction, reentry, and circus movement.

## **Cardiac Function**

CV 16. Draw and describe the length-tension relationship in a single cardiac cell. Correlate the cellular characteristics of length, tension, and velocity of shortening with the intact ventricle characteristics of end diastolic volume, pressure, and  $dP/dt$ .

CV17. Define preload and explain why ventricular end-diastolic pressure, atrial pressure and venous pressure all provide estimates of ventricular preload. Explain why ventricular end-diastolic pressure provides the most reliable estimate.

CV18. Define afterload and explain how arterial pressure influences afterload. Describe a condition when arterial pressure does not provide a good estimate of afterload.

CV 19. Define contractility and explain why  $dp/dt$  is a useful index of contractility. Explain how the calcium transient differs between cardiac and skeletal muscle and how this influences contractility.

CV 20. Define the difference between cardiac performance and cardiac contractility. Describe the impact of changes in preload, afterload, and contractility in determining cardiac performance.

CV 21. Explain how changes in sympathetic activity alter ventricular work, cardiac metabolism, oxygen consumption and cardiac output.

CV 22. Write the formulation of the Law of LaPlace. Describe how it applies to ventricular function in the normal and volume overloaded (failing) ventricle.

CV 23. Draw a ventricular pressure-volume loop and on it label the phases and events of the cardiac cycle (ECG, valve movement).

CV 24. Differentiate between stroke volume and stroke work. Identify stroke volume and stroke work from a pressure-volume loop.

CV 25. Define ejection fraction and be able to calculate it from end diastolic volume, end systolic volume, and/or stroke volume. Predict the change in ejection fraction that would result from a change in a) preload, b) afterload, and c) contractility.

CV 26. Draw the change in pressure-volume loops that would result from changes in a) afterload, b) preload, or c) contractility, for one cycle and the new steady state that is reached after 20 or more cycles.

## **Cardiac Cycle**

CV 27. Understand the basic functional anatomy of the atrioventricular and semilunar valves, and explain how they operate.

CV 28. Draw, in correct temporal relationship, the pressure, volume, heart sound, and ECG changes in the cardiac cycle. Identify the intervals of isovolumic contraction, rapid ejection, reduced ejection, isovolumic relaxation, rapid ventricle filling, reduced ventricular filling and atrial contraction.

CV 29. Know the various phases of ventricular systole and ventricular diastole. Contrast the relationship between pressure and flow into and out of the left and right ventricles during each phase of the cardiac cycle.

CV 30. Understand how and why left sided and right sided events differ in their timing.

## **Physiology of Cardiac Defects (Heart Sounds)**

CV 31. Deleted in 2006 revision.

CV32. Know the factors that contribute to the formation of turbulent flow.

CV 33. Describe the timing and causes of the four heart sounds.

CV34. Describe the expected auscultation sounds that define mitral stenosis, mitral insufficiency, aortic stenosis, and aortic insufficiency. Explain how these pathologic changes would affect cardiac mechanics and blood pressure.

## **The Normal Electrocardiogram (ECG) and the ECG in Cardiac Arrhythmias and Myopathies**

CV 35. Define the term dipole. Describe characteristics that define a vector. Describe how dipoles generated by the heart produce the waveforms of the ECG.

CV 36. Describe the electrode conventions used by clinicians to standardize ECG measurements. Know the electrode placements and polarities for the 12 leads of a 12-lead electrocardiogram and the standard values for pen amplitude calibration and paper speed.

CV 37. Name the parts of a typical bipolar (Lead II) ECG tracing and explain the relationship between each of the waves, intervals, and segments in relation to the electrical state of the heart.

CV 38. Explain why the ECG tracing looks different in each of the 12 leads.

CV 39. Define mean electrical vector (axis) of the heart and give the normal range. Determine the mean electrical axis from knowledge of the magnitude of the QRS complex in the standard limb leads.

CV 40. Describe the alteration in conduction responsible for most common arrhythmias: i.e., tachycardia, bradycardia, A-V block, Wolff-Parkinson-White (WPW) syndrome, bundle branch block, flutter, fibrillation.

CV 41. Describe electrocardiographic changes associated respectively with myocardial ischemia, injury, and death. Define injury current and describe how it alters the S-T segment of the ECG.

## **Cardiac Output and Venous Return**

CV 42. Understand the principles underlying cardiac output measurements using the Fick, dye dilution, and thermodilution methods.

CV 43. Know how cardiac function (output) curves are generated and how factors which cause hypereffective or hypoeffective changes (contractility) in the heart can alter the shape of cardiac function curves.

CV 44. Understand the concept of “mean systemic pressure,” its normal value, and how various factors can alter its value.

CV 45. Define venous return. Understand the concept of “resistance to venous return” and know what factors determine its value theoretically, what factors are most important in practice, and how various interventions would change the resistance to venous return.

CV46. Construct a vascular function curve. Predict how changes in total peripheral resistance, blood volume, and venous compliance influence this curve.

CV 46A. Explain why the intersection point of the cardiac function and vascular function curves represents the steady-state cardiac output and central venous pressure under the conditions represented in the graph.

CV 47 Use the intersection point of the cardiac function curve and vascular function curve to predict how interventions such as hemorrhage, heart failure, autonomic stimulation, and exercise will affect cardiac output and right atrial pressure. Predict how physiological compensatory changes would alter acute changes.

## **Fluid Dynamics**

CV 48. Describe the components of blood (cells, ions, proteins, platelets) giving their normal values. Relate the three red blood cell concentration estimates, red blood cell count, hematocrit, and hemoglobin concentration.

CV 49. Identify the source, stimulus for formation, and function of the hormone erythropoietin. Relate the rate of red blood cell synthesis to the normal red blood cell life span and the percentage of immature reticulocytes in the blood.

CV 50. Describe the functional consequence of the lack of a nucleus, ribosomes, and mitochondria for a) protein synthesis and b) energy production within the red blood cell.

CV 51. Discuss the normal balance of red blood cell synthesis and destruction, including how imbalances in each lead to anemia or polycythemia.

CV 52. Explain how red blood cell surface antigens account for typing of blood by the A B O system and rhesus factor. Based on these antigens, identify blood type of a “universal donor” and a “universal recipient.”

CV53 Know the factors that determine the total energy of the flowing blood and the relationship among these factors. Describe the usual reference point for physiological pressure.

CV 54. Be able to differentiate between flow and velocity in terms of units and concept.

CV 55. Understand the relationship between pressure, flow, and resistance in the vasculature and be able to calculate for one variable if the other two are known. Apply this relationship to the arteries, arterioles, capillaries, venules, and veins. Explain how blood flow to any organ is altered by changes in resistance to that organ.

CV 56. Explain how Poiseuille’s Law influences resistance to flow. Use it to calculate changes in resistance in a rigid tube (blood vessel). Explain the deviations from Poiseuille’s law predictions that occur in distensible blood vessels.

CV 57. Understand the relationship between flow, velocity, and cross-sectional area and the influence vascular compliance has on these variables. Explain how hemodynamics in blood vessels, especially microcirculation, deviate from theory due to anomalous viscosity, distensibility, and the glycocalyx.

CV 58. Define resistance and conductance. Understand the effects of adding resistance in series vs. in parallel on total resistance and flow. Apply this information to solving problems characterized by a) resistances in series and b) resistances in parallel. Apply this concept to the redistribution of flow from the aorta to the tissues during exercise.

CV 59. List the factors that shift laminar flow to turbulent flow. Describe the relationship between velocity, viscosity, and audible events, such as murmurs and bruits.

CV 60. Understand the principles of flow through collapsible tubes, the Starling resistor, and what pressure gradient determines flow for different relative values of inflow, surrounding, and outflow pressures.

CV 61. Explain how hemodynamics in blood vessels, especially microcirculation, deviates from theory due to anomalous viscosity, distensibility, axial streaming, and critical closing behavior.

## **Arterial Pressure and the Circulation**

CV 62. Describe the organization of the circulatory system and explain how the systemic and pulmonary circulations are linked physically and physiologically.

CV 63. Deleted in 2006 revision.

CV 64. Describe blood pressure measurement with a catheter and transducer and explain the components of blood pressure waveform. Contrast that with the indirect estimation of blood pressure with a sphygmomanometer. Explain how each approach provides estimates of systolic and diastolic pressures. Given systolic and diastolic blood pressures, calculate the pulse pressure and the mean arterial pressure.

CV 65. Describe how arterial systolic, diastolic, mean, and pulse pressure are affected by changes in a) stroke volume, b) heart rate, c) arterial compliance, and d) total peripheral resistance.

CV 66. Contrast pressures and oxygen saturations in the arteries, arterioles, capillaries, venules, and veins of both the systemic and pulmonary circulations. Repeat that process for velocity of blood flow and cross-sectional area, and volume.

CV 67. Identify the cell membrane receptors and second messenger systems mediating the contraction of vascular smooth muscle by norepinephrine, angiotensin II, and vasopressin.

CV 68. Identify the cell membrane receptors and second messenger systems mediating the relaxation of vascular smooth muscle by nitric oxide, bradykinin, prostaglandins, and histamine.

## **The Microcirculation and Lymphatics**

CV 69. Explain how water and solutes traverse the capillary wall. Use Fick's equation for diffusion to identify the factors that will affect the diffusion-mediated delivery of nutrients from the capillaries to the tissues. Define and give examples of diffusion-limited and flow-limited exchange.

CV 70. Describe how changes in capillary surface area affect the capacity for fluid exchange.

CV 71. Define the Starling equation and discuss how each component influences fluid movement across the capillary wall.

CV 72. Describe the pathway for leukocyte migration across the microcirculation, including leukocyte expression of cellular adhesion molecules, and recognition sites in the vascular endothelial cells.

CV 73. Starting at the post-capillary venule, describe the process of angiogenesis, including the stimulus that initiates new vessel growth.

CV 74. Describe the Donnan effect and its importance in capillary dynamics.

CV 74A. Describe how smooth muscle contractile mechanisms differ from the contractile mechanisms of skeletal and cardiac muscle.

CV 74B. Describe the involvement of G protein-coupled receptors and signal transduction pathways in the regulation of smooth muscle contraction.

CV 74C. Describe the involvement of endothelial cells in the regulation of vascular diameter and inflammatory responses.

CV 75. Predict how altering pressure or resistance in pre- and post-capillary regions alters capillary pressure and the consequence of this change on transmural fluid movement.

CV 76. Using the components of the Starling equation, explain why fluid does not usually accumulate in the interstitium of the lungs.

CV 77. Describe how histamine alters the permeability of the post-capillary venules, and how the loss of albumin into the interstitial space promotes localized edema.

CV 78. Describe the lymphatics, and explain how the structural characteristics of terminal lymphatics allow the reabsorption of large compounds, such as proteins.

CV 79. Contrast the structure of lymphatic capillaries and systemic capillaries, including the significance of the smooth muscle in the walls of the lymphatic vessels.

CV 80. Identify critical functions of the lymphatic system in fat absorption, interstitial fluid reabsorption, and clearing large proteins from the interstitial spaces.

CV 81. Diagram the relationship between interstitial pressure and lymph flow. Explain why edema does not normally develop as interstitial pressure increases.

CV 82. Explain how edema develops in response to: a) venous obstruction, b) lymphatic obstruction, c) increased capillary permeability, d) heart failure, e) tissue injury or allergic reaction, and f) malnutrition.

## **Regulation of Arterial Pressure**

CV 83. List the anatomical components of the baroreceptor reflex.

CV 84. Explain the sequence of events in the baroreflex that occur after an acute increase or decrease in arterial blood pressure. Include receptor response, afferent nerve activity, CNS integration, efferent nerve activity to the SA node, ventricles, arterioles, venules, and hypothalamus.

CV 85. Explain the sequence of events mediated by cardiopulmonary (volume) receptors that occur after an acute increase or decrease in arterial blood pressure. Include receptor response, afferent nerve activity, CNS integration, efferent nerve activity to the heart, kidney, hypothalamus, and vasculature.

CV 85A. Explain the sequence of events mediated by cardiopulmonary (volume) receptors that occur after an acute increase or decrease in central venous pressure. Include receptor response, afferent nerve activity, CNS integration, efferent nerve activity to the heart, kidney, hypothalamus, and vasculature.

CV 86. Contrast the sympathetic and parasympathetic nervous system control of heart rate, contractility, total peripheral resistance, and venous capacitance. Predict the cardiovascular consequence of altering sympathetic nerve activity and parasympathetic nerve activity.

CV 87. Contrast the relative contribution of short- and long-term mechanisms in blood pressure and blood volume regulation.

CV 88. Outline the cardiovascular reflexes initiated by decreases in blood O<sub>2</sub> and increases in blood CO<sub>2</sub>.

CV 89. Describe the release, cardiovascular target organs, and mechanisms of cardiovascular effects for angiotensin, atrial natriuretic factor, bradykinin, and nitric oxide.

## **Local Control of Blood Flow**

CV90 Define autoregulation of blood flow to the brain. Distinguish between short-term and long-term autoregulatory responses and the mechanisms responsible for each.

CV 91. Describe how the theory of metabolic regulation of blood flow accounts for active hyperemia and reactive hyperemia.

CV 92. Identify the role of  $PO_2$ ,  $PCO_2$ , pH, adenosine, and  $K^+$  in the metabolic control of blood flow to specific tissues.

CV 93. Diagram the synthetic pathway for nitric oxide (EDRF, endothelial derived relaxing factor), including substrate and the interplay between endothelium and vascular smooth muscle.

CV 94. Discuss the circumstances and the mechanisms whereby humoral substances contribute to regulation of the microcirculation.

CV95 Discuss the interaction of a) intrinsic (local), b) neural, and c) humoral control mechanisms and contrast their relative dominance in the CNS, coronary, splanchnic, renal, cutaneous, and skeletal muscle vascular beds.

CV 96. Describe the role of angiogenesis in providing a long-term match of tissue blood flow and metabolic need.

## **Fetal and Neonatal Circulation**

CV 97. Describe the progressive changes in maternal blood volume, cardiac output, and peripheral resistance during pregnancy and at delivery.

CV 98. Contrast the blood flow pattern in the fetus with that of a normal neonate, including the source of oxygenated blood.

CV 99. Describe the function in utero of the fetal ductus venosus, foramen ovale, and ductus arteriosus. Explain the mechanisms causing closure of these structures at birth.

CV 100. Discuss the relative differences in oxygen saturation and pressure for blood in the major blood vessels and cardiac chambers of the fetus. Explain how these values change at birth.

CV 101. Explain the unfavorable consequences to the neonate if either the ductus arteriosus or the foramen ovale fails to close.

## **Hemostasis and Injury, Hemorrhage, Shock**

CV 102. Diagram the enzymes and substrates involved in the formation of fibrin polymers, beginning at prothrombin. Contrast the initiation of thrombin formation by intrinsic and extrinsic pathways.

CV 103. Contrast the mechanisms of anticoagulation of a) heparin, b) EGTA, and c) coumadin. Identify clinical uses for each agent.

CV 104. Describe the mechanisms of fibrinolysis by TPA, tissue plasminogen activator and urokinase.

CV 105. Explain the role of the platelet release reaction on clot formation. Distinguish between a thrombus and an embolus.

CV 106. Explain why the activation of the clotting cascade does not coagulate all of the blood in the body.

CV 107. Describe the direct cardiovascular consequences of the loss of 30% of the circulating blood volume on cardiac output, central venous pressure, and arterial pressure. Describe the compensatory mechanisms activated by these changes.

CV 108. Explain three positive feedback mechanisms activated during severe hemorrhage that may lead to circulatory collapse and death.

CV 109. Contrast the change in plasma electrolytes, hematocrit, proteins, and colloid osmotic pressure following resuscitation from hemorrhage using a) water, b) 0.9% NaCl, c) plasma, and d) whole blood.

## Coronary Skeletal Muscle Circulation

CV 110. Describe the phasic flow of blood to the ventricular myocardium through an entire cardiac cycle. Contrast this cyclic variation in myocardial flow a) in the walls of the right and left ventricles and b) in the subendocardium and subepicardium of the left ventricle. Identify the area of the ventricle most susceptible to ischemic damage and why the risk is increased at high heart rates.

CV 111. Explain how arterio-venous  $O_2$  difference and oxygen extraction in the heart is unique when compared with other body organs.

CV 112. Explain the mechanism whereby coronary blood flow is coupled to myocardial workload, and identify stimuli that cause increases in coronary blood flow to occur.

CV 113. Explain how sympathetic stimulation alters heart rate, contractility, and coronary vascular resistance, as well as both directly and indirectly to change coronary blood flow. Identify the relative importance of the direct and indirect SNS effects in determining coronary blood flow during exercise.

CV 114. Describe what is meant by coronary vascular reserve and the role of collateral blood vessels. Discuss physiological and pathological events that decrease coronary vascular reserve.

CV 115. Contrast the neural and local control of skeletal muscle blood flow at rest and during exercise.

CV 116 Contrast the effect of phasic and sustained skeletal muscle contraction on extravascular compression of blood vessels and on central venous pressure.

## **Cerebral, Splanchnic, and Cutaneous Circulation**

CV 117. Contrast the local and neural control of cerebral blood flow. Discuss the relative importance of O<sub>2</sub>, CO<sub>2</sub>, and pH in regulating cerebral blood flow.

CV 118. Describe the structural components of the blood-brain barrier and how this barrier impedes the movement of gases, proteins, and lipids from the blood to neurons. Identify the differences in cerebrospinal fluid and plasma relative to protein concentration, and describe the function of cerebrospinal fluid.

CV 119. Contrast the mechanisms of the two major types of stroke, hemorrhagic and occlusive stroke.

CV 120. Contrast the local and neural control of the splanchnic circulation. Describe the role of the hepatic portal system and the hepatic artery in providing flow and oxygen to the liver.

CV 121: Describe the blood pressure in the hepatic portal vein, hepatic sinusoids, and the vena cava. Given an increase in central venous pressure, predict how hepatic microcirculatory fluid exchange will be altered, including the development of ascites.

CV 122. Describe how the GI circulation is adapted for secretion and absorption. Explain the enterohepatic circulation.

CV 123. Contrast local and neural control of cutaneous blood flow.

CV 124. Discuss the unique characteristics of skin blood flow that are adaptive for body temperature regulation.

### **Exercise** (also see Integration)

CV 125. Describe the cardiovascular consequences of exercise on peripheral resistance, cardiac output, A-V oxygen difference, and arterial pressure.

CV 126. Describe the redistribution of cardiac output during exercise to the CNS, coronary, splanchnic, cutaneous, and skeletal muscle vascular beds during sustained exercise (distance running). Explain the relative importance of neural and local control in each vascular bed.

CV 127. Discuss four adaptations to physical training on the cardiovascular system. Explain the mechanisms underlying each.

CV 128. Contrast the effects of static vs. dynamic exercise on blood pressure.

# Neurophysiology

## Electrophysiology

NEU 1. Define, and identify on a diagram of a neuron, the following regions: dendrites, axon, axon hillock, soma, and synaptic cleft.

NEU 2. Write the Nernst equation, and explain the effects of altering either the intracellular or extracellular  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ , or  $\text{Ca}^{2+}$  concentration on the equilibrium potential for that ion.

NEU 3. Describe the normal distribution of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{2+}$ , and  $\text{Cl}^-$  across the cell membrane, and using the chord conductance equation, explain how the relative permeabilities to these ions create a resting membrane potential.

NEU 4. Describe ionic basis of an action potential.

NEU 5. Contrast the generation and conduction of graded potentials with that of action potentials, identifying on the neuron the area in which each occurs.

NEU 6. Describe the basis for the calculation of the space constant and time constant of neuron process.

NEU 7. Define membrane capacitance and identify how membrane capacitance affects the spread of current in myelinated and demyelinated neurons.

NEU 8. Compare conduction velocities in a compound nerve, identifying how the diameter and myelination lead to differences in conduction velocity, and the use of these differences to classify neurons as group Ia, Ib, II, III, IV fibers or as  $A_{\alpha}$ ,  $A_{\beta}$ ,  $A_{\delta}$ , b, and c fibers.

NEU 9. Describe the ionic basis for inhibitory and excitatory post-synaptic potentials and how these changes can alter synaptic transmission.

NEU 10. Distinguish the effects of hyperkalemia, hypercalcemia, and hypoxia on the resting membrane and action potential.

NEU 11. Describe the effects of demyelination on action potential propagation and nerve conduction.

## **Neurochemistry**

NEU 12. Compare electrical and chemical synapses transmission based on velocity of conduction, fidelity, and the possibility for neuromodulation (facilitation or inhibition).

NEU 13. Describe chemical neurotransmission, listing in correct temporal sequence events beginning with the arrival of a wave of depolarization at the pre-synaptic membrane and ending with a graded potential generated at the post-synaptic membrane.

NEU 14. Define the characteristics of a neurotransmitter.

NEU 15. Learn the synthetic pathways, inactivation mechanisms and neurochemical anatomy and mechanisms of receptor transduction for the following neurotransmitters:

- |  |                 |
|--|-----------------|
| 1. Catecholamines (DA, NE, E)            | 6. Glutamate    |
| 2. Acetylcholine (ACh)                   | 7. Endorphins   |
| 3. Serotonin (5-hydroxytryptamine; 5-HT) | 8. Enkephalins  |
| 4. Histamine                             | 9. Dynorphins   |
| 5. GABA (gamma-aminobutyric acid)        | 10. Substance P |

NEU 16. Learn the major receptor classifications and representative receptor agonists and antagonists for the above transmitters.

NEU 17. Describe the relationships between neurotransmitter dysfunction and neuropathology.

## **Cerebrospinal Fluid, Blood Brain Barriers**

NEU 18. Diagram the adult ventricular system and relate it to its embryological development.

NEU 19. Identify on a diagram the meninges and subarachnoid spaces.

NEU 20. Describe formation and reabsorption of cerebral spinal fluid, including the anatomy and function of the choroid plexi.

NEU 21. Describe the normal pressure, volume, and composition of the CSF.

NEU 22. Describe how CSF can vary in certain pathological conditions.

NEU 23. Describe the endothelial basis of the blood-brain barrier, and predict the consequence of this barrier for the central nervous system distribution of intravenously administered hydrophilic and hydrophobic drugs.

## **Spinal Cord Physiology**

NEU 24. Distinguish between postsynaptic inhibition and presynaptic inhibition and provide examples of each.

NEU 25. Describe the anatomical location, function, and afferent neurotransmission of muscle spindle and Golgi tendon organs.

NEU 26. Trace the neuronal activity initiated by striking the patellar tendon with a percussion hammer (the patellar tendon reflex) that leads to contraction of a muscle. Contrast this reflex with the inverse myotactic reflex.

NEU 27. Describe the role of the gamma efferent system in the stretch reflex, and explain the significance of alpha-gamma co-activation.

NEU 28. Describe the properties of the flexor reflex initiated by touching a hot stove. Identify when pain is sensed, when flexor contraction occurs, and the neuronal connections and role of the crossed extensor reflex.

NEU 29. Describe the clinical tests and findings that allow a physician to distinguish between upper and lower motorneuron disorders, including the Babinski sign.

NEU 30. Describe the anatomy and functions of the major ascending and descending spinal cord tracts, including any crossing of midline.

NEU 31. Describe the use of dermatomes, sensory deficits, and motor deficits to identify local spinal cord lesions, and spinal cord hemisection. Describe the immediate and long-term consequences of spinal cord transection.

## **Nerve Conduction/EMG Studies**

NEU 32. Describe the procedure used for measuring nerve conduction velocity.

NEU 33. Describe the repetitive nerve stimulation procedure for assessing the integrity of the neuromuscular junction.

NEU 34. Compare the different EMG findings in neuropathy and myopathy.

NEU 35. Describe the physiological deficit and the consequence for patients with myasthenia gravis.

## **Autonomic Nervous System**

NEU 36. Contrast the sympathetic and parasympathetic branches of the autonomic nervous system based on: spinal cord division of origin, length of preganglionic and postganglionic neurons, neurotransmitters and receptors at the ganglionic and target organ synapse.

NEU 37. List the sensory input of the ANS.

NEU 38. List the major central nervous system control centers of the ANS.

NEU 39. Describe the functional effects of normal and abnormal ANS activity or lack of activity.

## **Brainstem Reflexes**

NEU 40. Describe the function of the following brain stem reflexes: cardiovascular baroreceptor, respiratory stretch receptor.

NEU 41. For each brain stem reflex, list the stimulus and its receptor, the afferent pathway, the brain stem nuclei involved, the efferent pathway and the resulting effect.

NEU 42. Contrast the effects of intra-axial and extra-axial brain stem lesions

## **Cerebrovascular System**

NEU 43. Describe the local factors affecting brain blood flow, and contrast their effectiveness with that of autonomic regulation of cerebral blood flow.

NEU 44. Describe cerebrovascular disorders (stroke, aneurysm, migraine headache) as to primary cause and effect, including how excitotoxic mechanisms can lead to neuronal death following stroke or injury.

## Somatosensory System

NEU 45. Define and contrast point localization and two-point discrimination in psychophysical and neurophysiological terms. Explain why the threshold for two-point discrimination changes in different areas of the body surface, e.g., lips, fingertips and back.

NEU 46. List the submodalities of discriminative touch.

NEU 47. Describe the following cutaneous and proprioceptive mechanoreceptors and their function: Pacinian corpuscles, Meissner's corpuscles, Ruffini endings, Merkel cell, A-delta and C free nerve endings, Golgi tendon organ, muscle spindle.

NEU 48. Describe functional organization at all levels and submodalities served by the dorsal column-medial lemniscal and the equivalent components of the trigeminal system.

NEU 49. Differentiate between feed-forward and feedback inhibition within neuronal circuits, and provide physiological examples of each.

NEU 50. Contrast the proprioceptive pathways to the cerebellum with that to the cerebral cortex.

NEU 51. Differentiate the submodalities of nondiscriminative touch, temperature and nociception based on receptor transduction mechanism, localization within the spinal gray matter, and central termination of the pathways.

NEU 52. Describe functional organization at all levels and submodalities served by the anterolateral system and the equivalent components of the spinal trigeminal system.

NEU 53. Describe the control of pain perception, including central processing and the role of endorphins.

NEU 54. Describe gating mechanism theory for control of pain transmission, and relate it to the use of TENS (transcutaneous electrical nerve stimulation) and spinal cord stimulation.

NEU 55. Describe pain perception and the central pain syndrome, for example, the thalamic pain syndrome.

NEU 56. Describe the peripheral and central mechanisms of primary hyperalgesia and secondary hyperalgesia.

NEU 57. Describe the mechanism of referred pain of visceral origin.

## Visual System

- NEU 58. Describe the refraction of light as it passes through the eye to the retina, identifying the eye components that account for refraction of light at the center of the eye and away from the center.
- NEU 59. Describe the process of accommodation, contrasting the refraction of light by the lens in near vision and in far vision.
- NEU 60. Describe the refractive deficits that account for myopia, hyperopia, presbyopia, and astigmatism, and their correction by eyeglasses or contact lenses.
- NEU 61. Describe the electrical responses produced by bipolar cells, horizontal cells, amacrine cells, and ganglion cells, and comment on the function of each.
- NEU 62. Contrast the transduction process for rods and the three types of cones, including the range of spectral sensitivity, including the ionic basis of these responses.
- NEU 63. Describe the neuronal circuitry basis for antagonist center-surround receptive fields of retinal ganglion cells.
- NEU 64. Describe the receptive field properties of all neuron types in the visual pathway (retina to lateral geniculate to visual cortex). Describe how convergence, divergence, and afferent surround inhibition affect visual neuron receptive fields.
- NEU 65. Predict the visual field defects resulting from the following lesions in the visual pathway: retinal lesion, optic nerve lesion, optic chiasm, optic tract, lateral geniculate nucleus, optic radiations, primary visual cortex.
- NEU 66. Describe the topographic representation of the visual field within the primary visual cortex, including the topics of retinotopic organization, orientation selectivity, and ocular dominance.
- NEU 67. Describe the processing of information in the visual cortex, and the consequence of a lesion in the higher visual association areas.
- NEU 68. List and compare four functional properties of scotopic and photopic vision.
- NEU 69. Explain the differing light sensitivities of the fovea and optic disk.

## **Smell and Taste**

NEU 70. Describe the olfactory receptors and transduction mechanisms.

NEU 71. Describe olfactory pathways.

NEU 72. Describe taste receptors and transduction mechanisms.

NEU 73. Describe taste pathways.

## **Auditory System**

NEU 74. Describe the function of the outer ear, middle ear, and inner ear, listing in order the mechanical structures over which sound energy is transmitted to auditory receptors.

NEU 75. Draw the human audibility curve and explain the changes that occur with aging.

NEU 76. Explain the frequency analysis performed by the cochlea on the basis of its physical properties.

NEU 77. Explain how deformations of the basilar membrane are converted into action potentials in auditory nerve fibers.

NEU 78. Diagram the auditory pathway including all central connections.

NEU 79. Describe how pitch, loudness, and localization of sounds in space is coded by central auditory neurons.

NEU 80. Distinguish conductive, central, and sensorineural deafness, and list the tests used to assess them.

## **Vestibular System**

NEU 81. Describe the structure, normal stimulus, transduction at the receptor level, and function of the otolith organs.

NEU 82. Describe the structure, normal stimulus, transduction at the receptor level, and function of the semicircular canals.

NEU 83. Describe the central connections of the vestibular nerve (the two targets of first order afferents and the four targets of second order afferents), and relate these to the three major functions of the vestibular apparatus.

NEU 84. Describe the neural mechanisms of nystagmus, past pointing, and caloric testing, and relate the direction of the nystagmus to the direction of rotation or which ear (left or right) was irrigated with cold or warm water.

NEU 85. List and describe four clinical signs of vestibular system dysfunction.

NEU 86. Describe the different kinds of gaze (voluntary) eye movements and reflex eye movements.

## **Medial and Lateral System Control of Movement**

NEU 87. Draw a “box” diagram of motor control systems, including cerebral cortex, basal ganglia, cerebellum, thalamus, brainstem motor nuclei, and spinal cord. Indicate with arrows the flow of information among these structures and, ultimately, to the alpha and gamma motor neurons.

NEU 88. Draw a cross section of the spinal cord and discuss the organization of the sensory and motor components of gray matter. Describe the somatotopic arrangement of motor neuron pools.

NEU 89. List the medial and lateral motor systems. Describe their origin, pathway, and termination within the spinal cord. Compare their functions in motor control.

NEU 90. Describe the effects of lesions in medial and lateral systems.

## **Cerebellum and Basal Ganglia**

- NEU 91. Describe the roles of the cerebellum in the regulation of skilled movement.
- NEU 92. List three functional divisions of the cerebellum, detailing the input and output connections of each. Be able to differentiate the functions of each and their integration with lateral and medial motor systems.
- NEU 93. Draw and label the circuitry of the cerebellar cortex, assign the functional role of each neuron type and give its synaptic action (excitatory/inhibitory). Be able to describe how this circuit functions as a timing mechanism and how it produces synergy in opposing muscle groups.
- NEU 94. On the basis of input-output organization, somatotopic organization, and overall function, predict the neurological disturbances that can result from disease or damage in different regions of the cerebellum.
- NEU 95. Contrast the spinal proprioceptive pathways to the cerebellum with those to the cortex.
- NEU 96. List and describe the major interconnections between components of the basal ganglia and the motor cortex. Identify the neurotransmitters determining the flow of information in the system.
- NEU 97. Describe the overall function of the basal ganglia in movement control and initiation in association with medial and lateral motor systems.
- NEU 98. List the appropriate signs of rigidity, dyskinesias, akinesia, and tremor for Parkinsonism, chorea, hemiballism, and athetosis. Assign a likely lesion site or chemical system defect for each clinical syndrome.
- NEU 99. Describe the rationale for treatment of Parkinsonism with anticholinergic drugs, L-DOPA, or transplantation of catecholamine-producing cells.

## Cerebral Cortex

- NEU 100. Describe the medial to lateral, rostral to caudal, and surface to white matter organizations of the primary motor cortex and the premotor cortex. Draw those regions on a sketch of the brain and also locate the supplementary motor cortex.
- NEU 101. Compare the effects of electrical stimulation of motor cortex and premotor cortex, relating the expected results to the control of voluntary movement.
- NEU 102. Describe the origin, course, and termination of the pyramidal tract.
- NEU 103. Compare the consequences of upper motor neuron loss to lower motor neuron loss. Describe the consequences of pyramidal tract transection.
- NEU 104. Draw a “flow diagram” for the brain regions involved in planning, initiating, and properly executing a skilled voluntary movement.
- NEU 105. Identify Brodmann areas for visual, auditory, somatic sensory, motor, and speech areas.
- NEU 106. Identify the cortical areas that receive projections from the following thalamic nuclei: ventral lateral, dorsomedial, pulvinar, medial geniculate, lateral geniculate, ventral posterolateral, and posteromedial.
- NEU 107. Describe the cortical areas important for language.
- NEU 108. Describe the cortical area important for spatial relations.
- NEU 109. Describe the functions of the prefrontal association cortex.
- NEU 110. Define and explain the physiological basis of evoked potentials and the electroencephalogram (EEG). List the main clinical uses of each.
- NEU 111. Describe the primary types of rhythms that make up the EEG and the behavioral states that correlate with each.
- NEU 112. Describe the origin of spontaneous electrical activity of the cerebral cortex.
- NEU 113. Distinguish EEG activity from evoked potentials and the uses of evoked potentials.

## **Sleep**

NEU 114. Describe the behavioral, EEG, and other characteristics of the stages of slow-wave sleep and rapid-eye-movement (REM) sleep. Explain the changes in sleep stages associated with aging, drugs, and sleep deprivation.

NEU 115. Distinguish slow wave sleep and paradoxical sleep.

NEU 116. Describe the neural systems important for the regulation of sleep-waking.

NEU 117. Describe the neurochemical systems important for sleep and waking.

NEU 118. Describe narcolepsy and sleep apnea.

NEU 119. Describe the mechanisms important in the production of coma.

NEU 120. Describe the changes in the sleep cycle across the life cycle.

## **Seizure Disorders**

NEU 121. Recognize normal and abnormal EEG records.

NEU 122. Describe characteristics of generalized and partial seizures.

## **Hypothalamus**

NEU 123. Describe the structure of the hypothalamus, including the major hypothalamic nuclei and areas.

NEU 124. Describe the major functions of the hypothalamus and its nuclei/areas.

NEU 125. Describe the role and mechanisms of the hypothalamus as it relates to thirst, hunger, temperature regulation, and the defense mechanism.

## **Limbic System**

- NEU 126. Describe the major components of the limbic system.
- NEU 127. Describe the major afferent and efferent connections of the hippocampus.
- NEU 128. Describe the major afferent and efferent connections of the amygdala.
- NEU 129. Describe reinforcement functions of the limbic system.
- NEU 130. Describe the functions of the hippocampus.
- NEU 131. Describe the functions of the amygdala.
- NEU 132. Describe the role of dopamine in the limbic system in disorders of thought and disorders of mood.

## **Aging of the Brain**

- NEU 133. Describe the gross, histological and biochemical changes that occur in the brain through aging.
- NEU 134. Describe dementia.
- NEU 135. Describe the characteristics of Alzheimer's disease.

## **Memory and Lateralization**

- NEU 136. List the parts of the brain that appear to be involved in memory in mammals, and summarize the proposed role of each in memory processing and storage.
- NEU 137. Explain the mechanisms proposed for short term and long-term memory storage.
- NEU 138. List the major differences in hemispheric function in humans.

# **Endocrinology and Metabolism**

## **General Principles**

- EN 1. Explain the principle of negative feedback control of hormone secretion.
- EN 2. Explain the principles of positive feedback and feed forward control of hormone secretion.
- EN 3. Explain the bases of hormone measurements; e.g., radio-immuno assay, ELISA.
- EN 4. Contrast the terms endocrine, paracrine, and autocrine based on the site of hormone release and the pathway to the target tissue. Provide an example of each, and describe major differences in mechanisms of action of peptides working through membrane receptors and steroids, vitamin D, and thyroid hormones working through nuclear receptors.
- EN 5. Define hormone, target cell, and receptor.
- EN 6. Compare and contrast hormone actions that are exerted through changes in gene expression with those exerted through changes in protein phosphorylation.
- EN 7. Understand the effects of plasma hormone binding proteins on access of hormones to their sites of action and degradation and on the regulation of hormone secretion.
- EN 8. Explain the effects of secretion, excretion, degradation, and volume of distribution on the concentration of a hormone in blood plasma.

### **Pituitary Gland - Posterior**

- EN 9. Contrast the anterior and posterior pituitary lobes with respect to cell types, vascular supply, development, and innervation.
- EN 10. List the target organs or cell types for oxytocin and describe its effects on each.
- EN 11. Name the stimuli for oxytocin release during parturition or lactation.
- EN 12. List the target cells for vasopressin and explain why vasopressin is also known as antidiuretic hormone.
- EN 13. Describe the stimuli and mechanisms that control vasopressin secretion
- EN 14. Identify disease states caused by a) over-secretion, and b) under-secretion of vasopressin and list the principle symptoms of each.

## **Pituitary Gland - Anterior**

- EN 15. Describe the biosynthesis, structure, and actions of the glycoprotein hormones FSH, LH, and TSH.
- EN 16. Describe the biosynthesis, structure, actions, and metabolism of the GH/prolactin family.
- EN 17. Describe the biosynthesis, structure, and actions of the POMC family: ACTH, MSH,  $\beta$ -lipoprotein,  $\beta$ -endorphin.
- EN 18. Identify appropriate hypothalamic factors that control the secretion of each of the anterior pituitary hormones, and describe their route of transport from the hypothalamus to the anterior pituitary.
- EN 19. Diagram the short-loop and long-loop negative feedback control of anterior pituitary hormone secretion. Predict the changes in secretory rates of hypothalamic, anterior pituitary, and target gland hormones caused by over-secretion or under-secretion of any of these hormones or receptor deficit for any of these hormones.
- EN 20. Explain the importance of pulsatile and diurnal secretion.

## **Thyroid Gland**

- EN 21. Identify the steps in the biosynthesis, storage, and secretion of tri-iodothyronine ( $T_3$ ) and thyroxine ( $T_4$ ) and their regulation.
- EN 22. Define “iodine pool”. Describe the distribution of iodine and the iodide metabolic pathway. Relate the distribution of radioiodide in the body to thyroid hormone synthesis, metabolism, and excretion.
- EN 23. Describe factors that control the synthesis, storage, and release of thyroid hormones. Explain the importance of thyroid hormone binding in blood on free and total thyroid hormone levels.
- EN 24. Understand the significance of the conversion of  $T_4$  to  $T_3$  and reverse  $T_3$  ( $rT_3$ ) in extra-thyroidal tissues.
- EN 25. Describe the actions of thyroid hormones on development and metabolism.
- EN 26. Understand the causes and consequences of a) over-secretion and b) under-secretion of thyroid hormones. Explain why either condition can cause an enlargement of the thyroid gland.

## Parathyroid Gland

- EN 27. Know the cells of origin for parathyroid hormone, its biosynthesis, and mechanism of transport within the blood (bound or free).
- EN 28. List the target organs and cell types for parathyroid hormone and describe its effects on each.
- EN 29. Describe the functions of the osteoblasts and the osteoclasts in bone remodeling and the factors that regulate their activities.
- EN 30. Identify the time course for the onset and duration for each of the biological actions of parathyroid hormone.
- EN 31. Describe the regulation of parathyroid hormone secretion and the role of the calcium-sensing receptor.
- EN 32. Understand the causes and consequences of a) over-secretion, and b) under-secretion of parathyroid hormone.
- EN 33. Identify the sources of vitamin D and diagram the biosynthetic pathway and the organs involved in modifying it to the biologically active  $1,25(\text{OH})_2\text{D}_3$  (1-25 dihydroxy cholecalciferol).
- EN 34. Identify the target organs and cellular mechanisms of action for vitamin D.
- EN 35. Describe the negative feedback relationship between the parathyroid hormone and the biologically active form of vitamin D [ $1,25(\text{OH})_2\text{D}_3$ ].
- EN 36. Describe the consequences of vitamin D deficiency and vitamin D excess.
- EN 37. List the cell of origin and target organs or cell types for calcitonin.
- EN 38. Name the stimuli that can promote secretion of calcitonin.
- EN 39. Describe the actions of calcitonin and identify which (if any) are physiologically important.

## Adrenal Gland

- EN 40. Identify the functional zones (one medullary and three cortical zones), innervation, and blood supply of the adrenal glands and the principal hormones secreted from each zone.
- EN 41. Describe the biosynthesis of the adrenal steroid hormones (glucocorticoids, mineralocorticoids, and androgens) and the key structural features that distinguish each class.
- EN 42. Understand the cellular mechanism of action of adrenal cortical hormones.
- EN 43. Identify the major actions of glucocorticoids on metabolism and the target organs on which they are produced.
- EN 44. Describe the actions of glucocorticoid hormones in injury and stress.
- EN 45. Describe the components of the neuroendocrine axis that control glucocorticoid secretion and describe how factors in the internal and external environment influence the neuroendocrine axis.
- EN 46. Identify the causes and consequences of a) over-secretion and b) under-secretion of glucocorticoids and adrenal androgens.
- EN 47. List the major mineralocorticoids and identify their biological actions and target organs or tissues.
- EN 48. Name the physiological stimuli that cause increased mineralocorticoid secretion. Relate these stimuli to regulation of sodium and potassium excretion. List the factors that can modulate the secretory response and explain how they are detected.
- EN 49. Identify the causes and consequences of a) over-secretion and b) under-secretion of mineralocorticoids.
- EN 50. Diagram the negative feedback control of aldosterone secretion.
- EN 51. Identify the chemical nature of catecholamines, their biosynthesis, mechanism of transport within the blood, and how they are degraded and removed from the body. Identify how the structure of norepinephrine differs from epinephrine.
- EN 52. Describe the biological consequences of activation of the adrenal medulla and identify the target organs or tissues for catecholamines along with the receptor subtype that mediates the response. Understand the mechanism by which epinephrine and norepinephrine can produce different effects in the same tissues. Explain the change in the ratio of epinephrine to norepinephrine release from the adrenal medulla during sympathetic activation (fight and flight), or in prolonged food deprivation.

EN 53. Name the key stimuli causing catecholamine secretion. List the factors that can modulate a) the secretory response and b) the responses of target tissues.

EN 54. Describe the interactions of adrenal medullary and cortical hormones in response to stress.

EN 55. Identify disease states caused by an over-secretion of adrenal catecholamines.

## **Pancreas**

EN 56. Identify the major hormones secreted from the endocrine pancreas, their cells of origin, and their chemical nature.

EN 57. List the target organs or cell types for glucagon and describe its principal actions on each.

EN 58. Identify the time course for the onset and duration of the biological actions of glucagon.

EN 59. Describe the control of glucagon secretion.

EN 60. List the major target organs or cell types for insulin, the major effects of insulin on each, and the consequent changes in concentration of blood constituents.

EN 61. Identify the time course for the onset and duration for the biological actions of insulin.

EN 62. Understand the relationship between blood glucose concentrations and insulin secretion. Describe the roles of neural input and gastrointestinal hormones on insulin secretion. List the factors that modulate the secretory response.

EN 63. Identify disease states caused by: a) over-secretion, b) under-secretion of insulin, or c) decreased sensitivity to insulin, and describe the principal symptoms of each.

## **Growth**

EN 64. Describe the relationship between growth hormone and the insulin-like growth factors and their binding proteins in the regulation of growth.

EN 65. Understand the regulation of growth hormone secretion. Identify the roles of hypothalamic factors and IGF-I.

EN 66. Identify the target organs or cell types for insulin-like growth factors that account for longitudinal growth.

EN 67. Explain how thyroid, gonadal, and adrenal hormones modulate growth.

EN 68. Understand the nature and actions of local growth factors: epidermal growth factor, nerve growth factor, platelet-derived growth factor, and angiogenic and antiangiogenic factors.

### **Endocrine Integration of Energy and Electrolyte Balance**

EN 69. Identify the normal range of plasma glucose concentrations, and list the chemical forms and anatomical sites of storage pools for glucose and other metabolic substrates.

EN 70. Identify the hormones that promote the influx and efflux of glucose, fat, and protein into and out of energy storage pools and their impact on the uptake of glucose by tissues. Establish specific roles for insulin, glucagon, glucocorticoids, catecholamines, growth hormone, and thyroid hormone.

EN 71. Describe the changes in metabolic fuel utilization that occur in long- and short-term fasting and in acute and sustained exercise. Understand how increases or decreases in hormone secretion produce these changes.

EN 72. Describe the role of appetite and metabolic rate in the maintenance of long-term energy balance and fat storage. Identify the factors that regulate appetite and fuel oxidation.

EN 73. Identify the normal range of dietary sodium intake, sodium distribution in the body, and routes of sodium excretion. Explain the roles of antidiuretic hormone, aldosterone, angiotensin, and atrial natriuretic hormone in the regulation of sodium balance.

EN 74. Identify the normal range of dietary potassium intake, potassium distribution in the body, and routes of potassium excretion. Explain how acute changes in aldosterone, insulin, and acid/base concentrations affect the plasma potassium concentration and the movement of potassium into and out of the intracellular compartment. Explain the chronic regulation of body potassium balance and plasma potassium levels by aldosterone through its actions on renal excretion, intestinal excretion, and dietary appetite/absorption.

EN 75. Identify the normal range of dietary calcium intake, calcium distribution in the body, and routes of calcium excretion. Explain the regulation of the plasma calcium concentration by parathyroid hormone, vitamin D, and calcitonin based on exchange with bone, renal excretion, and intestinal excretion and/or absorption.

EN 76. Identify the normal range of dietary phosphate intake, phosphate distribution in the body, and routes of phosphate excretion. Explain the regulation of the plasma phosphate concentration by parathyroid hormone, vitamin D, and calcitonin based on exchange with bone, renal excretion, intestinal excretion and/or absorption.

## **Reproductive Physiology - Male**

EN 77. Describe the physiological functions of the major components of the male reproductive tract.

EN 78. Describe spermatogenesis and the role of different cell types in this process.

EN 79. Describe the endocrine regulation of testicular function: the role of the GnRH pulse generator, FSH, LH, testosterone, and inhibin.

EN 80. Identify the cell of origin for testosterone, its biosynthesis, mechanism of transport within the blood, how it is metabolized and how it is eliminated. List other physiologically produced androgens.

EN 81. List the target organs or cell types for testosterone and describe its effects on each.

EN 82. Describe the cellular mechanisms of action for testosterone.

EN 83. List the neural, vascular, and endocrine components of the erection and ejaculation response.

EN 84. Identify the causes and consequences of over-secretion and under-secretion of testosterone for a) prepubertal and b) postpubescent males.

EN 85. Compare and contrast the actions of testosterone, dihydrotestosterone, estradiol, and Müllerian inhibitory factor in the development of the male and female reproductive tracts.

## **Reproductive System - Female**

EN 86. Describe oogenesis and its relationship to changes in the ovarian follicle. Explain the roles of FSH, LH, estradiol, inhibin, and paracrine agents in oogenesis and follicular maturation.

EN 87. Describe ovulation and the formation and decline of the corpus luteum and the roles of pituitary hormones in each of these processes.

EN 88. Describe the hormonal regulation of estrogen and progesterone biosynthesis and secretion by the ovary. Identify the cells responsible for their biosynthesis, the mechanism of their transport in the blood, and how they are degraded and removed from the body.

EN 89. List the target organs or cell types for estrogen action and describe its effects on each.

EN 90. Describe the cellular mechanisms of action for estrogen.

EN 91. List the principal physiological actions of progesterone, its target organs or cell types, and describe its effects on each and the importance of “estrogen priming.”

EN 92. Describe the cellular mechanisms of action for progesterone.

EN 93. With time on the x-axis, diagram the changes in the endometrium and the ovary seen during the menstrual cycle and correlate these changes with changes in blood levels of FSH, LH, estradiol, progesterone, and inhibin. Describe how the changes in ovarian steroids produce the proliferative and secretory phases of the uterine endometrium and menstruation and the changes in basal body temperature during the menstrual cycle.

EN 94. Trace the pathways of sperm and egg transport that can result in fertilization and the movement of the fertilized embryo to the uterus.

EN 95. List the protein hormones secreted by the placenta and describe the role of human chorionic gonadotropin (hCG) in the rescue of the corpus luteum in maintaining pregnancy early post-implantation.

EN 96. Describe the interactions between the placenta and the fetal adrenal cortex in the production of estrogens during pregnancy.

EN 97. Discuss the roles of oxytocin, relaxin, and prostaglandins in the initiation and maintenance of parturition.

EN 98. Explain the role of estrogens, progesterone, placental lactogen, prolactin, and oxytocin in mammary gland development during puberty, pregnancy, and lactation.

EN 99. Explain the basis for the inhibition of milk secretion during pregnancy and the initiation of lactation after parturition.

EN 100. Differentiate between milk secretion and milk ejection, and describe the hormonal regulation of both during lactation, including the role of suckling.

EN 101. Explain the physiological bases for the antifertility actions of contraceptive steroid hormones.

EN 102. Describe the age-related changes in the male and female reproductive systems, including the mechanisms responsible for these changes, at the following times:

- a. In utero development
- b. Puberty
- c. Senescence

# **Respiration**

(revised 2006)

## **Pulmonary Mechanics**

PUL 1. Diagram how pleural pressure, alveolar pressure, airflow, and lung volume change during a normal quiet breathing cycle. Identify on the figure the onset of inspiration, cessation of inspiration, and cessation of expiration. Describe how differences in pressure between the atmosphere and alveoli cause air to move in and out of the lungs.

PUL 2. Draw a normal pulmonary pressure-volume (compliance) curve (starting from residual volume to total lung capacity and back to residual volume), labeling the inflation and deflation limbs. Explain the cause and significance of the hysteresis in the curves.

PUL 3. Define compliance and identify two common clinical conditions in which lung compliance is higher or lower than normal.

PUL 4. Draw the pressure-volume (compliance) curves for the lungs, chest wall, and respiratory system on the same set of axes. Show and explain the significance of the resting positions for each of these three structures.

PUL 5. Identify the forces that generate the negative intrapleural pressure when the lung is at functional residual capacity, and predict the direction that the lung and chest wall will move if air is introduced into the pleural cavity (pneumothorax).

PUL 6. Draw a normal spirogram, labeling the four lung volumes and four capacities. List the volumes that comprise each of the four capacities. Identify which volume and capacities cannot be measured by spirometry.

PUL 7. Define the factors that determine total lung capacity, functional residual capacity, and residual volume. Describe the mechanisms responsible for the changes in those volumes that occur in patients with emphysema and pulmonary fibrosis.

PUL 8. Define surface tension and describe how it applies to lung mechanics, including the effects of alveolar size and the role of surfactants. Define atelectasis and the role of surfactants in preventing it.

PUL 9. Describe the principal components of pulmonary surfactant and explain the roles of each.

PUL 10. Describe the effects of airway diameter and turbulent flow on airway resistance.

PUL 11. Describe how airway resistance alters dynamic lung compliance.

PUL 12. Draw a spirogram resulting from a maximal expiratory effort. Label the forced vital

capacity (FVC), timed forced expiratory volumes (FEVs), and the maximal expiratory flow rate between 25-75% of FVC (FEF25-75%).

PUL 13. Draw a normal maximal effort flow-volume curve, labeling the effort-dependent and -independent regions. Use the concept of dynamic compression of airways to explain why each point in the effort-independent region of the curve represents a maximal flow rate that is uniquely dependent on lung volume. Describe how and why the shape of the flow-volume curve is shifted in chronic obstructive lung disease (COPD).

PUL 14. Differentiate between the two broad categories of restrictive and obstructive lung disease, including the spirometric abnormalities associated with each category.

PUL 15. Describe the regional differences in alveolar ventilation in healthy and diseased lungs and explain the basis for these differences.

### **Alveolar Ventilation**

PUL 16. Define partial pressure and fractional concentration as they apply to gases in air. List the normal fractional concentrations and sea level partial pressures for O<sub>2</sub>, CO<sub>2</sub>, and N<sub>2</sub>.

PUL 17. List the normal airway, alveolar, arterial, and mixed venous PO<sub>2</sub> and PCO<sub>2</sub> values. List the normal arterial and mixed venous values for O<sub>2</sub> saturation, [HCO<sub>3</sub><sup>-</sup>], and pH.

PUL 18. Define and contrast the following terms: anatomic dead space, physiologic dead space, wasted (dead space) ventilation, total minute ventilation and alveolar minute ventilation.

PUL 19. Describe the concept by which physiological dead space can be measured.

PUL 20. Define and contrast the relationships between alveolar ventilation and the arterial PCO<sub>2</sub> and PO<sub>2</sub>.

PUL 21. Describe in quantitative terms the effect of ventilation on PCO<sub>2</sub> according to the alveolar ventilation equation.

PUL 22. Be able to estimate the alveolar oxygen partial pressure (P<sub>A</sub>O<sub>2</sub>) using the simplified form of the alveolar gas equation. Be able to use the equation to calculate the amount of supplemental O<sub>2</sub> required to overcome a reduction in P<sub>A</sub>O<sub>2</sub> caused by hypoventilation or high altitude.

PUL 23. Define the following terms: hypoventilation, hyperventilation, hypercapnea, eupnea, hypopnea, and hyperpnea.

## **Pulmonary Circulation**

PUL 24. Contrast the systemic and pulmonary circulations with respect to pressures, resistance to blood flow, and response to hypoxia.

PUL 25. Describe the regional differences in pulmonary blood flow in an upright person. Define zones I, II, and III in the lung, with respect to pulmonary vascular pressure and alveolar pressure.

PUL 26. Describe how pulmonary vascular resistance changes with alterations in cardiac output or pulmonary arterial pressure. Explain in terms of distention and recruitment of pulmonary vessels. Identify the zones in which these two mechanisms apply.

PUL 27. Describe how pulmonary vascular resistance changes with lung volume. Explain in terms of alterations in alveolar and extra-alveolar blood vessels.

PUL 28. Describe the consequence of hypoxic pulmonary vasoconstriction on the distribution of pulmonary blood flow.

PUL 29. Describe the effects of inspired nitric oxide on pulmonary vascular resistance and hypoxic vasoconstriction.

PUL 30. Explain the development of pulmonary edema by a) increased hydrostatic pressure, b) increased permeability, c) impaired lymphatic outflow or increased central venous pressure, and d) hemodilution (e.g., with saline volume resuscitation).

PUL 31. Describe the major functions of the bronchial circulation.

## **Pulmonary Gas Exchange**

PUL 32. Name the factors that affect diffusive transport of a gas between alveolar gas and pulmonary capillary blood.

PUL 33. Describe the kinetics of oxygen transfer from alveolus to capillary and the concept of capillary reserve time (i.e., the portion of the erythrocyte transit time in which no further diffusion of oxygen occurs).

PUL 34. Define oxygen diffusing capacity, and describe the rationale and technique for the use of carbon monoxide to determine diffusing capacity.

PUL 35. Describe how the ventilation/perfusion (V/Q) ratio of an alveolar-capillary lung unit determines the PO<sub>2</sub> and PCO<sub>2</sub> of the blood emerging from that lung unit.

PUL 36. Identify the average V/Q ratio in a normal lung. Explain how V/Q is affected by the vertical distribution of ventilation and perfusion in the healthy lung.

PUL 37. Describe the normal relative differences from the apex to the base of the lung in alveolar and arterial PO<sub>2</sub>, PCO<sub>2</sub>, pH, and oxygen and carbon dioxide exchange.

PUL 38. Predict how the presence of abnormally low and high V/Q ratios in a person's lungs will affect arterial PO<sub>2</sub> and PCO<sub>2</sub>.

PUL 39. Describe two causes of abnormal V/Q distribution.

PUL 40. Define right-to-left shunts, anatomic and physiological shunts, and physiologic dead space (wasted ventilation). Describe the consequences of each for pulmonary gas exchange.

PUL 41. Describe the airway and vascular control mechanisms that help maintain a normal ventilation/perfusion ratio. Name two compensatory reflexes for V/Q inequality.

PUL 42. Be able to calculate the alveolar to arterial PO<sub>2</sub> difference, (A-a)DO<sub>2</sub>. Describe the normal value for (A-a) DO<sub>2</sub> and the significance of an elevated (A-a) DO<sub>2</sub>.

PUL 43. Name five causes of hypoxemia.

## **Oxygen and Carbon Dioxide Transport**

PUL 44. Define oxygen partial pressure (tension), oxygen content, and percent hemoglobin saturation as they pertain to blood.

PUL 45. Draw an oxyhemoglobin dissociation curve (hemoglobin oxygen equilibrium curve) showing the relationships between oxygen partial pressure, hemoglobin saturation, and blood oxygen content. On the same axes, draw the relationship between PO<sub>2</sub> and dissolved plasma O<sub>2</sub> content (Henry's Law). Compare the relative amounts of O<sub>2</sub> carried bound to hemoglobin with that carried in the dissolved form.

PUL 46. Describe how the shape of the oxyhemoglobin dissociation curve influences the uptake and delivery of oxygen.

PUL 47. Define P50.

PUL 48. Show how the oxyhemoglobin dissociation curve is affected by changes in blood temperature, pH, PCO<sub>2</sub>, and 2,3-DPG, and describe a situation where such changes have important physiological consequences.

PUL 49. Describe how anemia and carbon monoxide poisoning affect the shape of the oxyhemoglobin dissociation curve,  $\text{PaO}_2$ , and  $\text{SaO}_2$ .

PUL 50. List the forms in which carbon dioxide is carried in the blood. Identify the percentage of total  $\text{CO}_2$  transported as each form.

PUL 51. Describe the importance of the chloride shift in the transport of  $\text{CO}_2$  by the blood.

PUL 52. Identify the enzyme that is essential to normal carbon dioxide transport by the blood and its location.

PUL 53. Draw the carbon dioxide dissociation curves for oxy- and deoxyhemoglobin. Describe the interplay between  $\text{CO}_2$  and  $\text{O}_2$  binding on hemoglobin that causes the Haldane effect.

PUL 54. Explain why the total gas pressure of the venous blood is subatmospheric and why this situation is accentuated when breathing 100%  $\text{O}_2$ . Explain how breathing 100%  $\text{O}_2$  can result in further arterial  $\text{O}_2$  desaturation in hypoxemic patients who develop mucous plugging of their airways (absorption atelectasis).

PUL 55. Define respiratory acidosis and alkalosis and give clinical examples of each.

PUL 56. Describe the mechanism and function of respiratory acid base compensations.

## **Respiratory Control**

PUL 57. Identify the regions in the central nervous system that play important roles in the generation and control of cyclic breathing.

PUL 58. Give three examples of reflexes involving pulmonary receptors that influence breathing frequency and tidal volume. Describe the receptors and neural pathways involved.

PUL 59. List the anatomical locations of chemoreceptors sensitive to changes in arterial  $\text{PO}_2$ ,  $\text{PCO}_2$ , and pH that participate in the control of ventilation. Identify the relative importance of each in sensing alterations in blood gases.

PUL 60. Describe how changes in arterial  $\text{PO}_2$  and  $\text{PCO}_2$  alter alveolar ventilation, including the synergistic effects when  $\text{PO}_2$  and  $\text{PCO}_2$  both change.

PUL 61. Describe the respiratory drive in a COPD patient, and predict the change in respiratory drive when oxygen is given to a COPD patient.

PUL 62. Describe the mechanisms for the shift in alveolar ventilation that occur immediately upon ascent to high altitude, after remaining at altitude for two weeks, and immediately upon return to sea level.

PUL 63. Describe the physiological basis of shallow water blackout during a breath-hold dive.

PUL 64. Describe the significance of the feedforward control of ventilation (central command) during exercise, and the effects of exercise on arterial and mixed venous  $PCO_2$ ,  $PO_2$ , and pH.

### **Age Effects and Nonrespiratory Lung Functions**

PUL 65. Describe the effect of aging on lung volumes, lung and chest wall compliance, blood gases, and respiratory control.

PUL 66. Identify the mechanism by which particles are cleared from the airways.

PUL 67. Describe mechanisms for clearance of vasoactive substances from the blood during passage through the lung. Identify a substance that is almost completely cleared and one that is not cleared to any significant extent.

# **Gastrointestinal**

## **Functions and Regulation of GI Tract**

GI 1. Describe the overall role of the gastrointestinal system with respect to the whole body balance of water, electrolytes, carbohydrates, fats, and proteins. Include the processes of digestion, absorption, metabolic production, metabolic consumption, secretion, and excretion. Identify appropriate metabolic waste products present in the feces.

GI 2. For carbohydrates, differentiate the processes of ingestion, digestion, absorption, secretion, and excretion, including the location in the GI tract where each process occurs. Repeat the analysis for proteins and fats.

GI 3. Identify the approximate normal volumes of fluid entering and leaving the gastrointestinal tract daily.

GI 4. Define the major characteristics and temporally relate the cephalic, gastric, and intestinal phases of GI tract regulation.

GI 5. Describe the four classes of luminal stimuli that trigger GI reflexes.

GI 6. Describe the histoanatomical characteristics of the enteric nervous system. Given either a cross section or a longitudinal section of the intestine, name and locate the myenteric and submucosal plexus.

GI 7. Contrast the sympathetic and parasympathetic modulation of the enteric nervous system and the effector organs of the GI tract.

GI 8. Classify the following enteric nervous system neurotransmitters as excitatory or inhibitory: norepinephrine, acetylcholine, CCK, VIP, histamine, and somatostatin.

GI 9. Describe the terms “long reflex” and “short reflex” with respect to the GI tract.

GI 10. Describe the similarities and differences in regulating gastrointestinal function by nerves, hormones, and paracrine regulators. Include receptors, proximity, and local vs. global specificity.

GI 11. Identify the cell type and anatomical location of the endocrine cells secreting gastrin, secretin, and cholecystokinin (CCK), GIP, and motilin.

GI 12. Identify families to which gastrin, secretin, and CCK and other (non-GI) hormones belong.

GI 13. Define the concept of “incretins,” and state two gastrointestinal hormones believed to function in this manner.

GI 14. Describe function of somatostatin and histamine as paracrine regulators of acid secretion in the stomach.

### **Salivary Glands**

GI 15. Contrast the plasma and saliva concentrations of  $\text{Na}^+$ ,  $\text{Cl}^-$ , and  $\text{HCO}_3^-$  at low secretion rates and at high secretion rates and the principal cell types involved in each secretion rate.

GI 16. State the substrates and digestion products of salivary amylase (ptyalin).

GI 17. Identify the stimuli and cell types involved in GI secretion of mucous, and identify the function of salivary mucus.

GI 18. State three types of stimuli that increase salivary secretion.

GI 19. State the components of the saliva important in oral hygiene, and identify the role of salivary secretions in eliminating heavy metals.

### **Esophagus**

GI 20. Identify the normal resting esophageal pressure and explain why this pressure varies with the respiratory cycle.

GI 21. Describe the origin and consequence of the high basal tone found in the upper esophageal sphincter (UES) and lower esophageal sphincter (LES).

GI 22. State the stimulus that initiates the swallowing sequence. Identify the point at which the swallowing sequence becomes automatic (independent of voluntary control).

GI 23. Contrast the patterns of external and internal innervations of the upper, middle, and lower esophagus.

GI 24. Describe the pressure changes that occur in the esophagus as a bolus of food moves from the pharynx to the stomach, including the pressures immediately oral and aboral to the bolus, and the pressures in the upper and lower esophageal sphincters.

GI 25. Contrast primary and secondary peristalsis based on initiating event, voluntary control, reflex propagation, and regions of the pharynx and esophagus involved.

GI 26. Contrast the lower esophageal tone, innervation, and motility defects that lead to heartburn with those leading to achalasia.

## Stomach

- GI 27. Describe the storage, digestion, and motility roles of the stomach.
- GI 28. Contrast the  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Cl}^-$  concentrations of gastric secretion with that of plasma at low and at high gastric secretion rates. Identify the cell types that mediate this change.
- GI 29. Identify the protein component of chief cell secretions.
- GI 30. Describe the generation of an “alkaline tide” in the hepatic portal venous system following ingestion of a meal.
- GI 31. Describe the role, if any, of HCl in the gastric digestion of carbohydrates, proteins, and fats.
- GI 32. Describe the pH of the stomach in the fasted state, and outline the time course and causes of the pH changes in the two hours after ingestion of a protein meal.
- GI 33. State the stimuli for pepsinogen release and the mechanism for activating pepsinogen, and describe the digestion products of pepsin activity.
- GI 34. Describe the role of the stomach in preventing pernicious anemia.
- GI 35. Describe the regulation of  $\text{H}^+$ - $\text{K}^+$  ATPase, the stimuli for activation, and process of activation, including vesicular fusion with the luminal plasma membrane.
- GI 36. Describe the mechanism of gastric  $\text{H}^+$  generation and secretion, including the role of  $\text{K}^+$ ,  $\text{Cl}^-$ - $\text{HCO}_3^-$ , carbonic anhydrase,  $\text{H}^+$ - $\text{K}^+$  ATPase and  $\text{Na}^+$ - $\text{K}^+$  ATPase.
- GI 37. Describe the modulation of gastric acid secretion by the enterochromaffin-like cell (ECL cell) and the control of this process (including potentiation) by vagal stimulation, gastrin, histamine, and somatostatin.
- GI 38. Describe the pathways, if any, for the gastric absorption of electrolytes, water, lipids, amino acids, and carbohydrates.
- GI 39. State the mechanism for damage to the gastric mucosal barrier by aspirin, bile acids, and *Helicobacter pylori*.
- GI 40. Identify the stimuli that a) increase gastrin release and b) inhibit gastrin release.
- GI 41. State the effects of acid, fat, and solutions of high osmolarity in the duodenum on gastric secretion, and describe the mechanisms by which these effects regulate gastric secretion.

GI 42. Define receptive relaxation of the stomach and state mechanism and consequence.

GI 43. Describe origin and form of electrical activity and the progression of peristaltic waves across the body and antrum of the stomach. Include their role in mixing and propulsion of gastric contents and how the frequency is altered by the volume of gastric contents.

GI 44. Predict the effects of a) meal content (osmolarity, fat content, etc.), b) particle size, and c) volume on the rate of gastric emptying, including duodenal feedback.

GI 45. Describe the causes of peptic ulcer disease.

## **Pancreas**

GI 46. List the major ionic and peptide/protein components secreted by the pancreas. Contrast the plasma and pancreatic concentrations of  $\text{Na}^+$ ,  $\text{Cl}^-$ , and  $\text{HCO}_3^-$  at low secretion rates and at high secretion rates and the principal cell types involved in each secretion rate.

GI 47. Describe the mechanisms by which chyme from the stomach is neutralized in the duodenum.

GI 48. Describe the mechanism by which pancreatic zymogens are activated in the small intestine.

GI 49. List the stimuli that release a) secretin and b) CCK and the cellular mechanisms by which these agents control pancreatic secretion. Include any synergistic effects between CCK and secretin.

GI 50. Describes the role of CFTR in pancreatic ductular secretion, and predict the consequences of cystic fibrosis on the GI system.

GI 51. State the effects of the autonomic nerves to the pancreas and vago-vagal reflexes on pancreatic secretion.

## **Bile**

GI 52. List the water, ionic, bile salt, and bilirubin components of bile as secreted by the liver, and explain the modification of bile as it is stored in the gall bladder. Identify the role of secretin on the hepatic production of bile.

GI 53. Describe the cellular mechanisms for the hepatic uptake, conjugation, and secretion of bile salts and bilirubin.

GI 54. Describe the role of CCK in causing release of bile from the gall bladder, including the effects on the sphincter of Oddi.

GI 55. Describe the amphipathic structure of bile acids, and predict how this property assists the digestion of fats.

GI 56. State the difference between primary and secondary bile acids.

GI 57. Contrast the physical state of an emulsion with a micellar solution, and explain the conditions for the formation of emulsifications and micelles in the duodenum.

GI 58. Define enterohepatic circulation.

GI 59. Describe the mechanism of reabsorption of bile acids in the early portion of the small intestine with the mechanism found in the later part of the small intestine.

GI 60. Predict the effects of an increase in hepatic portal vein bile acid concentration on the rate of bile secretion, bile acid synthesis, and diseases of the gallbladder.

### **Small Intestine**

GI 61. Describe the role of the microvilli, the unstirred layer, and tight junctions in determining the rate at which glucose, amino acids, water, lipids, and electrolytes are absorbed.

GI 62. List the chemical classes of the carbohydrates entering the duodenum from the stomach, and identify mechanisms mediating further digestion and absorption across the apical and basolateral membranes of the intestinal epithelia. Include pancreatic secretions and brush-border enzymes.

GI 63. Predict the small intestine and colonic consequence of a deficiency in the enzyme lactase, and identify ethnic groups who commonly exhibit this deficiency.

GI 64. List the chemical classes of the proteins entering the duodenum from the stomach, and identify mechanisms mediating further digestion and absorption across the apical and basolateral membranes of the intestinal epithelia. Include pancreatic secretions and brush-border enzymes.

GI 65. Contrast the secondary active transport of amino acids with that of di- and tri-peptides, including the ion used as the energy source.

GI 66. List the chemical classes of the lipids entering the duodenum from the stomach, and identify mechanisms mediating further digestion and absorption across the apical and basolateral membranes of the intestinal epithelia. Include the roles of pancreatic lipase, colipase, and micelles.

GI 67. Describe the role of the endoplasmic reticulum in processing lipids absorbed across the apical membrane of enterocytes.

GI 68. Describe the composition and formation of chylomicrons, their movement across the enterocyte basolateral membrane, and the route of entry into the cardiovascular system.

GI 69. Define steatorrhea, and predict the effects of steatorrhea on the absorption of fat-soluble vitamins.

GI 70. Describe the absorption of water-soluble vitamins, including the role of intrinsic factor in the absorption of vitamin B<sub>12</sub>.

GI 71. Describe the changes in osmolarity that occur in chyme as it passes from the stomach through the duodenum and colon, and identify the cause of this change.

GI 72. Describe the pathways, if any, by which sodium ions, water, iron, and calcium are absorbed in the small intestine and colon.

### **Large Intestine**

GI 73. Diagram the cellular mechanisms of colonic sodium, potassium, and bicarbonate secretion and the regulation of this process by aldosterone.

GI 74. Define “dietary fiber” and list sources commonly found in the US diet.

GI 75. Identify substrates and products of colonic bacterial metabolism, and predict the impact of metabolites on the rate and composition of intestinal gas formation (flatus).

GI 76. Describe the production and absorption of short chain fatty acids in the colon.

### **Intestinal Motility**

GI 77. Describe the characteristics of the basic electrical rhythm (BER) of the small intestine and its relation to smooth muscle contractile activity.

GI 78. Describe the role of “interstitial cells of Cajal” in generation of electrical slow waves, and predict the consequence of the frequency gradients of electrical slow waves occurring within the intestinal tract.

GI 79. Explain the functional significance of ongoing activity of enteric inhibitory motor neurons to intestinal circular muscle.

GI 80. Contrast the patterns of intestinal motility seen during the absorptive phase (segmentation) with that of the post-absorptive phase between meals [the migrating motility complex (MMC)].

GI 81. Contrast the effects of parasympathetic and sympathetic nervous activity in modulating small intestinal motility.

GI 82. Describe the effects of distension on small intestinal motility.

GI 83. State effects of increased pressure in the ileum and cecum on the ileocecal sphincter, including defining the term “gastroileal reflex.”

GI 84. Compare colonic motor activity with the motor activity in the small intestine.

GI 85. Contrast the colonic motor activity during a “mass movement” with that during haustral shuttling and the consequence of each type of colonic motility.

GI 86. Describe the sequence of events occurring during reflexive defecation, differentiating those movements under voluntary control and those under intrinsic control.

# **Renal**

## **(Revised 2004)**

### **Body Fluids**

R 1. Given the body weight and percent body fat, estimate the a) total body water, b) lean body mass, c) extracellular fluid volume, d) intracellular fluid volume, e) blood volume, and f) plasma volume. Identify normal extracellular fluid (plasma) osmolality and concentrations of  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$ ,  $\text{HCO}_3^-$ , proteins, creatinine, and urea, and contrast these values with those for intracellular fluids.

R 2. Using the volumes/compartments identified in objective R 1, contrast the movement between intracellular and extracellular compartments caused by increases or decreases in extracellular fluid osmolality.

R 3. Given the composition and osmolality of a fluid, identify it as hypertonic, isotonic, or hypotonic. Predict the change in transcellular fluid exchange that would be caused by placing a red blood cell in solutions with varying tonicities.

R 4. Identify major routes and normal ranges for water intake and loss, and predict how changes in intake and loss affect the distribution of total body water.

R 5. Demonstrate the ability to use the indicator dilution principle to measure plasma volume, blood volume, extracellular fluid volume, and total body water, and identify compounds used to measure each volume.

R 6. Predict the changes in extracellular volume, extracellular osmolality, intracellular volume, and intracellular osmolality caused by infusion of three liters of 0.9% NaCl, lactated Ringer's solution, 0.45% NaCl, and 7.5% NaCl.

R 7. Identify the site of erythropoietin production, the adequate stimulus for erythropoietin release, and the target tissue for erythropoietin action.

### **Structure of the Kidney and Nephrons**

R 8. Given a cross section of a kidney, identify the renal cortex, renal medulla, renal calyces, medullary pyramids, renal pelvic space, renal artery, renal vein, and ureter.

R 9. Describe in sequence the tubular segments through which ultrafiltrate flows after it is formed at Bowman's capsule to when it enters the renal pelvis. Identify each structure as being located in the renal cortex or renal medulla. Based on the glomerulus location and the length of the loop of Henle, distinguish between cortical and juxtamedullary nephrons.

R 10. Describe in sequence the blood vessels through which blood flows when passing from the renal artery to the renal vein, including the glomerular blood vessels, peritubular capillaries, and the vasa recta.

R 11. On an electron micrograph and a line drawing, identify the following structures of the glomerular tuft: the afferent and efferent arterioles, glomerular capillary network, mesangium, Bowman's capsule, and the juxtaglomerular apparatus (including the specialized juxtaglomerular arteriole cells and the macula densa). Describe the three layers comprising the glomerular filtration barrier, and identify podocytes, foot processes, slits, and the basement membrane.

R 12. Explain the role of somatic, (pudendal) sympathetic, and parasympathetic nerves in the micturition reflex and in urination.

### **Renal Clearance**

R 13. Explain the clearance principle. Use the clearance equation and an appropriate compound to estimate the glomerular filtration rate, renal plasma flow, and renal blood flow.

R 14. Distinguish between the use of inulin and creatinine clearances as measures of the glomerular filtration rate.

R 15. Given the plasma and urine concentrations and the urine flow rate, calculate the filtered load, tubular transport, excretion rate, and clearance of inulin, creatinine, para-amino hippuric acid (PAH), glucose, and penicillin. Predict how changes in filtration, reabsorption, and secretion will affect renal excretion of each compound.

R 16. For each of the compounds listed in objective R 15, graph the urine excretion of a compound against the plasma concentration. Using this graph, identify the tubular load, tubular transport maximum ( $T_{max}$ ), and splay for each substance.

### **Glomerular Filtration Rate and Renal Hemodynamics**

R 17. Identify the filtration barriers, if any, which impede the filtration of  $H_2O$ ,  $Na^+$ , inulin, albumin, and red blood cells.

R 18. Define renal blood flow, renal plasma flow, glomerular filtration rate, and filtration fraction and list typical values.

R 19. Define the filtration coefficient at the glomerular capillary, describe the membrane properties that contribute to it, and explain its role in determining GFR.

R 20. Given the capillary and Bowman's capsule hydrostatic and oncotic pressures, calculate the net filtration force at the glomerular capillaries. Predict the changes in glomerular filtration caused by increases or decreases in any of those pressures.

- R 21. Describe the relative resistances of the afferent and efferent arterioles and the effects on renal blood flow and GFR of selective changes in each.
- R 22. Describe the myogenic and tubuloglomerular feedback mechanisms that mediate the autoregulation of renal plasma flow and glomerular filtration rate.
- R 23. Predict the change in renal blood flow and glomerular filtration rate caused by an increase in renal sympathetic nerve activity.
- R 24. Predict the change in renal blood flow and glomerular filtration caused by: a) increased synthesis of angiotensin II, b) increased release of atrial natriuretic peptide, c) increased prostaglandin formation, and d) increased nitric oxide formation.
- R 25. Identify which components of the filtration barrier whose damage would result in hematuria and proteinuria.
- R 26. Using the pressures described in objective R 20, predict the changes in net filtration force that occur as blood travels along the glomerular capillary and hydrostatic pressure falls and colloid osmotic pressure increases.
- R 27. Predict the change in renal blood flow and GFR caused by urinary tract obstruction, hypoalbuminemia, and diabetic nephropathy.
- R 28. Compare blood flow to, and oxygen consumption by, the kidneys with that of skeletal muscle and cardiac muscle.
- R 29. Describe the effects of changes in peritubular capillary hydrostatic and colloid osmotic pressures on net proximal tubular fluid reabsorption.

### **Transport Properties of Nephron Segments**

- R 30. Using glucose, para-amino hippuric acid (PAH), water, and  $\text{Cl}^-$ , contrast the transcellular and paracellular pathways for movement across proximal tubular epithelia.
- R 31. Distinguish between active (primary and secondary) transport, facilitated diffusion, and passive diffusion based on energy source and carrier protein involvement.
- R 32. Describe the contribution of the major nephron segments to the reabsorption of the filtered load of solute and water.
- R 33. Describe the cellular mechanisms for the transport of  $\text{Na}^+$ ,  $\text{Cl}^-$ ,  $\text{K}^+$ ,  $\text{HCO}_3^-$ ,  $\text{Ca}^{2+}$ , phosphate, organic solutes (e.g., glucose, amino acids, and urea), and water by the major tubular segments.

- R 34. Describe the function of the following renal transporters and their predominant localization along the tubules with regard to nephron segment and apical versus basolateral membranes
- Transport ATPases ( $\text{Na}^+/\text{K}^+$ -ATPase,  $\text{H}^+/\text{K}^+$ -ATPase,  $\text{H}^+$ -ATPase, and  $\text{Ca}^{2+}$ -ATPase)
  - Ion and water channels ( $\text{K}^+$ , ENaC,  $\text{Cl}^-$ ,  $\text{Ca}^{2+}$ , aquaporins)
  - Coupled transporters ( $\text{Na}^+$ -glucose,  $\text{Na}^+/\text{H}^+$ -antiporter,  $\text{Na}^+/\text{K}^+/\text{2Cl}^-$ -symporter,  $\text{Na}^+$ -phosphate symporter,  $\text{Na}^+/\text{Cl}^-$ -symporter,  $\text{Na}^+/\text{HCO}_3^-$ -symporter,  $\text{Cl}^-/\text{HCO}_3^-$ -antiporter)
- R 35. Describe the nephron sites and molecular mechanisms of action of the following classes of diuretics (osmotic, carbonic anhydrase inhibitors, loop, thiazide,  $\text{K}^+$ -sparing).
- R 36. Describe clinical syndromes related to defects in specific renal transporters (e.g., Bartter's, Gittelman's, Liddle's, etc.).
- R 37. Describe the effects of reductions in GFR on plasma creatinine concentrations and plot the relationship

### **Urine Concentration and Dilution**

- R 38. Using the intake and loss routes identified in objective R 4, predict the changes in body fluid volume and osmolality caused by a net water loss or gain in the body. Predict how each of these disturbances would alter the rate of urine production and the osmotic composition of the urine.
- R 39. Using the intake and loss routes identified in objective R 4, predict the changes in body fluid volume and osmolality caused by a net NaCl loss or gain in the body. Predict how each of these disturbances would alter the rate of urine production and the osmotic composition of the urine.
- R 40. Identify the two most powerful stimuli that cause ADH release, and describe the negative feedback control mechanisms for each.
- R 41. Describe the role of the ascending limb of the loop of Henle in producing a high renal interstitial fluid osmolality. Beginning with the loop of Henle, contrast the tubular fluid and interstitial fluid osmolality changes that allow either a dilute or a concentrated urine to be produced and excreted.
- R 42. Predict the consequence on urine concentrating ability if the medullary osmotic gradient is disrupted. Following disruption, describe how the osmotic gradient would be re-established.
- R 43. Identify the tubular section and cellular mechanism by which ADH increases permeability to water and urea. Describe the role of these changes on the ability of the kidney to produce either a dilute or a concentrated urine.

R 44. Given urine and plasma osmolarities and urine volume, calculate osmolar and free water clearance.

Identify expected free water clearance for an individual producing either a dilute or a concentrated urine.

R 45. Describe the actions of diuretics listed on objective R 35 on the ability of the kidneys to maximally concentrate and dilute urine.

R 46. Distinguish between central and nephrogenic diabetes insipidus based on plasma ADH levels and the response to an injection of ADH.

### **Na<sup>+</sup> Balance and Regulation of Extracellular Fluid Volume**

R 47. Identify the normal range of dietary Na<sup>+</sup> intake and major routes of Na<sup>+</sup> loss from the body. Define the role of Na in maintaining extracellular fluid volume.

R 48. Calculate the normal filtered load of Na<sup>+</sup>. Identify the tubular sites of Na reabsorption, and the alterations in Na<sup>+</sup> reabsorption in conditions of euvoemia, volume depletion, and volume expansion.

R 49. Describe the receptors involved in the monitoring of ECF volume (e.g., high-pressure baroreceptors and low-pressure cardiopulmonary stretch receptors), and diagram the neural reflex regulation of renal Na<sup>+</sup> and water excretion.

R 50. Diagram the formation and generation of angiotensin II, beginning with renin. Identify four factors that can promote renin release.

R 51. Describe the regulation of Na<sup>+</sup> reabsorption along the nephron, including the effects of sympathetic nerves, angiotensin II, aldosterone, and atrial natriuretic peptide.

R 52. Describe the effects of diuretics listed in objective R 35 on Na<sup>+</sup> handling by the kidneys and, thus, on ECF volume regulation.

R 53. Explain the contribution of the kidneys to progression of and/or the compensation for the altered fluid volume regulation characteristic of congestive heart failure and hepatic cirrhosis.

R 54. Describe the regulation of proximal tubule reabsorption that underlies the phenomenon of glomerulotubular balance.

R 55. Describe the role of the renin-angiotensin-aldosterone system in the regulation of systemic arterial blood pressure in volume-replete and volume-depleted states and in secondary forms of hypertension.

## **K<sup>+</sup> Balance**

R 56. Identify the normal range of dietary K<sup>+</sup> intake and major routes of K<sup>+</sup> loss from the body. Define the role of extracellular K<sup>+</sup> in maintaining normal nerve and muscle function.

R 57. Describe K<sup>+</sup> distribution within the body, extrarenal K<sup>+</sup> homeostasis, and the role insulin, epinephrine, and aldosterone play in the movement of K<sup>+</sup> between intracellular and extracellular pools. Describe the K<sup>+</sup> shift caused by acidosis.

R 58. Calculate the normal filtered load of K<sup>+</sup>. Identify the tubular sites of K<sup>+</sup> reabsorption and secretion.

R 59. Describe the factors that regulate K<sup>+</sup> secretion in the collecting duct (i.e., aldosterone, plasma K<sup>+</sup>) and distinguish these from factors that alter K<sup>+</sup> secretion at this site (i.e., luminal fluid flow rate, acid-base disturbances, anion delivery).

R 60. Contrast the tubular sites of action of K<sup>+</sup> wasting and K<sup>+</sup> sparing diuretics.

## **Ca<sup>2+</sup> and Phosphate Balance**

R 61. Identify the normal range of dietary Ca<sup>2+</sup> and phosphate intake, major storage pools of Ca and phosphate, and major routes of Ca<sup>2+</sup> and phosphate loss from the body. Describe the regulation of plasma Ca<sup>2+</sup> by calcitonin and phosphate by parathyroid hormone.

R 62. Calculate the normal filtered load of Ca<sup>2+</sup>. Identify the tubular sites of Ca<sup>2+</sup> reabsorption. Calculate the normal filtered load of phosphate. Identify the tubular sites of phosphate reabsorption.

R 63. Describe the renal regulation of Ca<sup>2+</sup> and phosphate transport by PTH, calcitonin, and 1,25-dihydroxy vitamin D (calcitriol), and distinguish from other factors that alter their transport (ECF volume, acid-base disorders).

R 64. Describe the role of the kidney in the production of 1,25-dihydroxy vitamin D (calcitriol).

R 65. Describe the effects of diuretics on Ca<sup>2+</sup> and phosphate excretion, especially noting the effect of thiazides to decrease Ca<sup>2+</sup> excretion and loop diuretics to increase Ca<sup>2+</sup> excretion.

## Acid-Base Balance

R 66. Identify the normal range of pH values, and the upper and lower limits compatible with life. Describe the role of buffers in maintaining pH, including the roles of the lungs and kidneys.

R 67. Describe the respiratory and renal regulation of the  $\text{CO}_2/\text{HCO}_3^-$  buffer system, which allows a buffer with a  $\text{pK}_a$  of 6.1 to be physiologically important in the maintenance of the normal plasma pH of 7.4.

R 68. Distinguish between  $\text{CO}_2$ -derived (volatile acid) and nonvolatile acid, the relative amounts produced each day through dietary intake and cellular metabolism, and the normal routes of loss from the body.

R 69. Calculate the filtered load of  $\text{HCO}_3^-$ , and identify the major sites of reabsorption (and secretion) along the nephron, emphasizing the importance of  $\text{H}^+$  secretory mechanisms in this process. Describe the cellular mechanisms responsible for net transepithelial movement of  $\text{HCO}_3^-$ .

R 70. Describe the adjustments in filtered load and  $\text{HCO}_3^-$  reabsorption ( $\text{H}^+$  secretion) by alterations in systemic acid-base balance and distinguish from factors that alter this process (i.e., ECF volume, aldosterone, and angiotensin II).

R 71. Describe net acid excretion by the kidneys, titratable acid, the importance of urinary buffers, and the production and excretion of ammonium. Distinguish between the reclamation of filtered bicarbonate and the formation of new bicarbonate.

R 72. Given a sudden increase or decrease in pH, identify the magnitude and the time course of the compensations that act to minimize change in pH of the body fluids, including a) buffers, b) respiratory adjustments, and c) renal adjustments.

R 73. From blood values, identify simple and mixed metabolic and respiratory acid-base disturbances. Distinguish between increased and normal anion gap metabolic acidosis, chloride-sensitive and -resistant metabolic alkalosis, and acute and chronic respiratory disturbances.

R 74. Describe processes that lead to acid-base disturbances and list common causes.

R 75. Describe the effects of carbonic anhydrase inhibitors and the other diuretics listed on objective R 35 on acid-base balance and the reabsorption of  $\text{HCO}_3^-$  by the nephron.

## **Integrative and Pathophysiological Aspects**

R 76. Describe the relationships between sodium balance and plasma volume as they contribute to cardiovascular hemodynamics and arterial pressure.

R 77. Describe the role of the renin-angiotensin-aldosterone systems in the regulation of sodium balance and arterial pressure with emphasis on the actions of angiotensin II on various target organs and tissues.

R 78. Describe pressure natriuresis and the mechanisms mediating and modulating this process.

R79. Describe how impairments in renal function and pressure natriuresis contribute to the long-term regulation of arterial pressure and the development and maintenance of hypertension.

# Muscle

## **Skeletal Muscle Structure and Mechanism of Contraction**

- MU 1. Draw and label a skeletal muscle at all anatomical levels, from the whole muscle to the molecular components of the sarcomere. At the sarcomere level, include at two different stages of myofilament overlap.
- MU 2. Draw a myosin molecule and label the subunits (heavy chains, light chains) and describe the function of the subunits.
- MU 3. Diagram the structure of the thick and thin myofilaments and label the constituent proteins.
- MU 4. Describe the relationship of the myosin-thick filament bare zone to the shape of the active length:force relationship.
- MU 5. Diagram the chemical and mechanical steps in the cross-bridge cycle, and explain how the cross-bridge cycle results in shortening of the muscle.

## **Control of Skeletal Muscle Contraction: Excitation-Contraction Coupling and Neuromuscular Transmission**

- MU 6. List the steps in excitation-contraction coupling in skeletal muscle, and describe the roles of the sarcolemma, transverse tubules, sarcoplasmic reticulum, thin filaments, and calcium ions.
- MU 7. Describe the roles of ATP in skeletal muscle contraction and relaxation.
- MU 8. Draw the structure of the neuromuscular junction.
- MU 9. List in sequence the steps involved in neuromuscular transmission in skeletal muscle and point out the location of each step on a diagram of the neuromuscular junction.
- MU 10. Distinguish between an endplate potential and an action potential in skeletal muscle.
- MU 11. List the possible sites for blocking neuromuscular transmission in skeletal muscle and provide an example of an agent that could cause blockage at each site.

## **Mechanics and Energetics of Skeletal Muscle Contraction**

MU 12. Explain the relationship of preload, afterload and total load in the time course of an isotonic contraction.

MU 13. Distinguish between an isometric and isotonic contraction.

MU 14. Distinguish between a twitch and a tetanus in skeletal muscle and explain why a twitch is smaller in amplitude than a tetanus.

MU 15. Draw the length versus force diagram for muscle and label the three lines that represent passive (resting), active, and total force. Describe the molecular origin of these forces.

MU 16. Explain the interaction of the length:force and the force:velocity relationships.

MU 17. Draw force versus velocity relationships for two skeletal muscles of equal maximum force generating capacity but of different maximum velocities of shortening.

MU 18. Using a diagram, relate the power output of skeletal muscle to its force versus velocity relationship.

MU 19 Describe the influence of skeletal muscle tendons on contractile function.

MU 20. List the energy sources of muscle contraction and rank the sources with respect to their relative speed and capacity to supply ATP for contraction.

MU 21. Define muscular fatigue. List some intracellular factors that can cause fatigue.

MU 22. Construct a table of structural, enzymatic, and functional features of fast-glycolytic and slow-oxidative fiber types from skeletal muscle.

MU 23. Describe the role of the myosin crossbridges acting in parallel to determine active force and the rate of crossbridge recycling to determine muscle speed of shortening and rate of ATP utilization during contraction.

MU 24. Discuss the functional consequences of the parallel and series arrangement of myofibrils in a skeletal muscle.

MU 25. Describe how the arrangement of a skeletal muscle to the skeleton can influence mechanical performance of the muscle.

MU 26. Define a motor unit and describe the order of recruitment of motor units during skeletal muscle contraction of varying strengths.

## **Smooth Muscle**

MU 27. Describe the differences in actomyosin regulation of, respectively, smooth and skeletal muscle and indicate the structural similarities in their respective contractile units.

MU 28. Compare and contrast the length versus force relationships in skeletal and smooth muscle. Describe the functional implications of the differences observed.

MU 29. Compare and contrast the force versus velocity relationships in skeletal and smooth muscle. Describe the primary cause for the observed differences in velocity of shortening.

MU 30. Explain why smooth muscles can develop and maintain force with a much lower rate of ATP hydrolysis than skeletal muscle.

MU 31. Distinguish between muscle relaxation from the contracted state and the phenomenon of stress relaxation and give examples of each process.

MU 32. Diagram the intracellular pathways that control contraction and relaxation in smooth muscle.

MU 33. Describe the distinguishing characteristics of multi-unit and unitary smooth muscles.

## **Cardiac Muscle**

MU 34. Describe the structure of cardiac muscle cells, comparing and contrasting it with that of smooth and skeletal muscle cells. Describe the physiological consequences of the low-resistance pathways between cardiac muscle cells.

MU 35. Diagram the relationship between the action potential and a twitch in cardiac muscle and explain why this prevents a tetanic contraction.

MU 36. Diagram the steps in the excitation-contraction coupling mechanism in cardiac muscle and compare with skeletal muscle.

MU 37. Diagram the length versus force curve for cardiac muscle and skeletal muscle, showing the active and passive relationships, and indicate the range over which each muscle type performs its physiological function.

MU 38. Define contractility in cardiac muscle. On the length versus force diagram, indicate the pathway for an isotonic contraction of cardiac muscle and show how an increase in contractility changes the relationship between afterload and amount of shortening.

MU 39. List some inotropic interventions that could change cardiac contractility.

# Exercise and Integration

## Thermoregulation

INT 1. Diagram the thermal balance for the body, including heat production (metabolism, exercise, shivering) and heat loss (convection, conduction, radiation, and evaporation). Identify those mechanisms that shift from heat production to heat loss when environmental temperature exceeds body core temperature.

INT 2. Define the thermoregulatory set point. Diagram the negative feedback control of body core temperature, including the role of the hypothalamic set point.

INT 3. Contrast the stability of body core with that of skin temperature. Include the role of cutaneous blood flow and sweating on skin temperature.

INT 4. Identify the mechanisms for maintaining thermal balance in the following environments: desert (120°F), snow skiing (10°F), falling through ice into a lake (water temp 37°F), and snorkeling in 80°F water.

INT 5. Explain how the change in core temperature that accompanies exercise differs from the change in core temperature produced by influenza, which alters the thermoregulatory set point.

INT 6. List and describe the physiological changes that occur as a result of acclimatization to heat and cold.

## Exercise

INT 7. Contrast the normal distribution of cardiac output with the distribution of cardiac output during aerobic (sustained) exercise and anaerobic (brief maximal burst) exercise. Include local regulation of blood flow and the role of capillary reserve in altering skeletal muscle blood flow.

INT 8. Define  $VO_{2MAX}$  and identify situations in which it is limited by cardiac output and by pulmonary gas exchange.

INT 9. Explain the control mechanism by which an increase in minute ventilation and heart rate accompanies exercise and how it can occur without any measurable change in arterial blood gas values.

INT 10. Define the effects of training on the heart and coronary circulation and how these changes contribute to an increase in  $VO_{2MAX}$ .

INT 11. Explain how each of the following can alter exercise performance: muscle fatigue,  $VO_{2MAX}$ , anaerobic threshold, gender, and age.

INT 12. Describe how chronic physical activity alters insulin sensitivity and glucose entry into cells.

INT 13. Describe the health benefits of exercise training on the cardiovascular, musculoskeletal, immune systems, and for weight control.