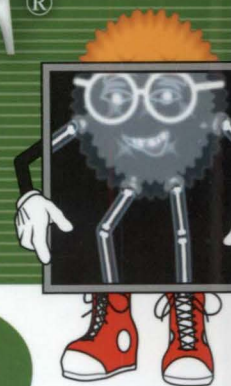


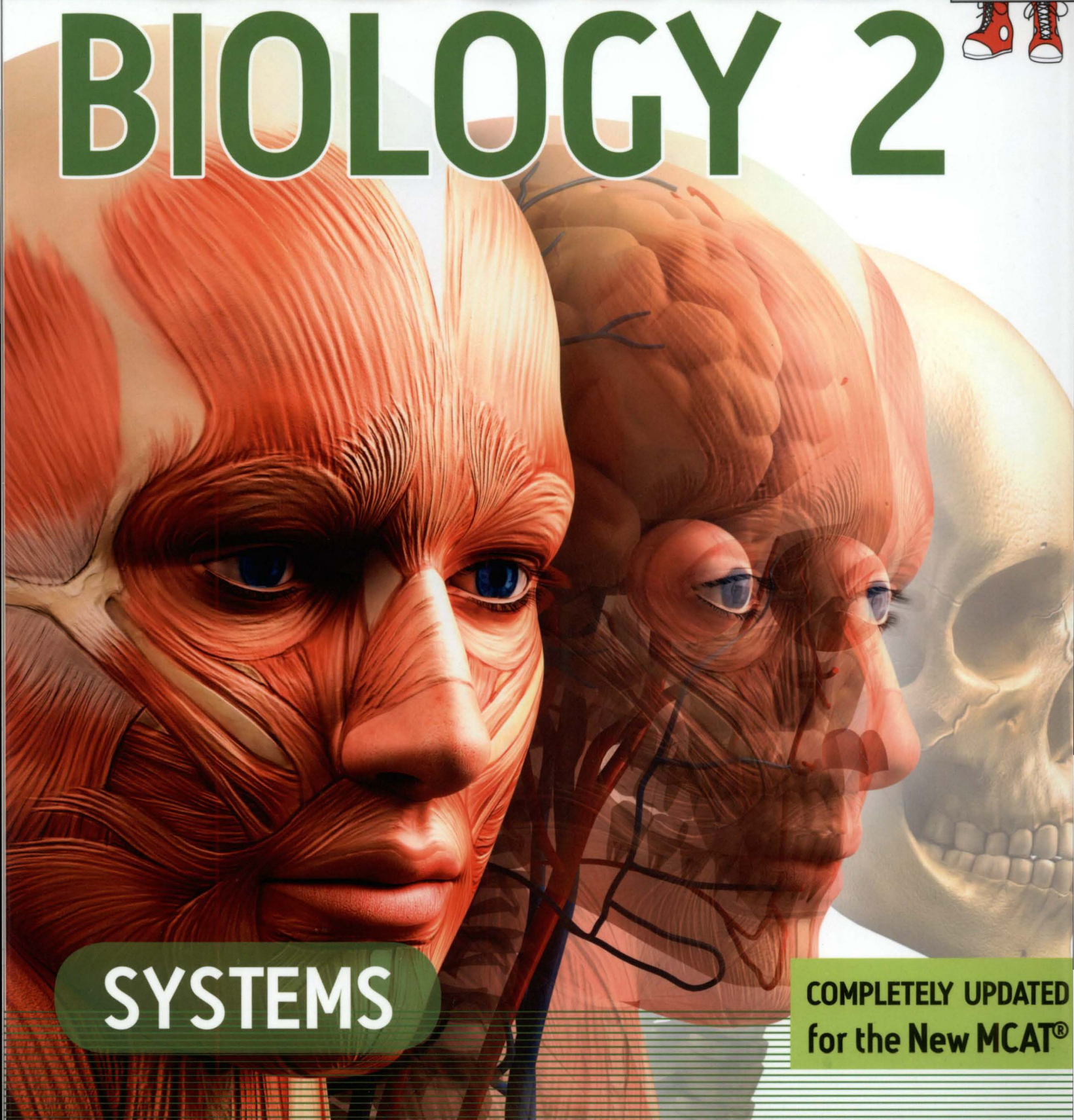


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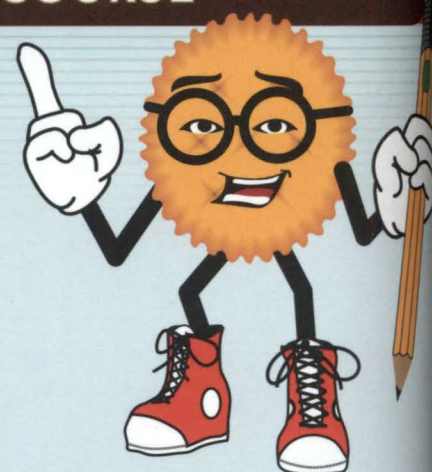


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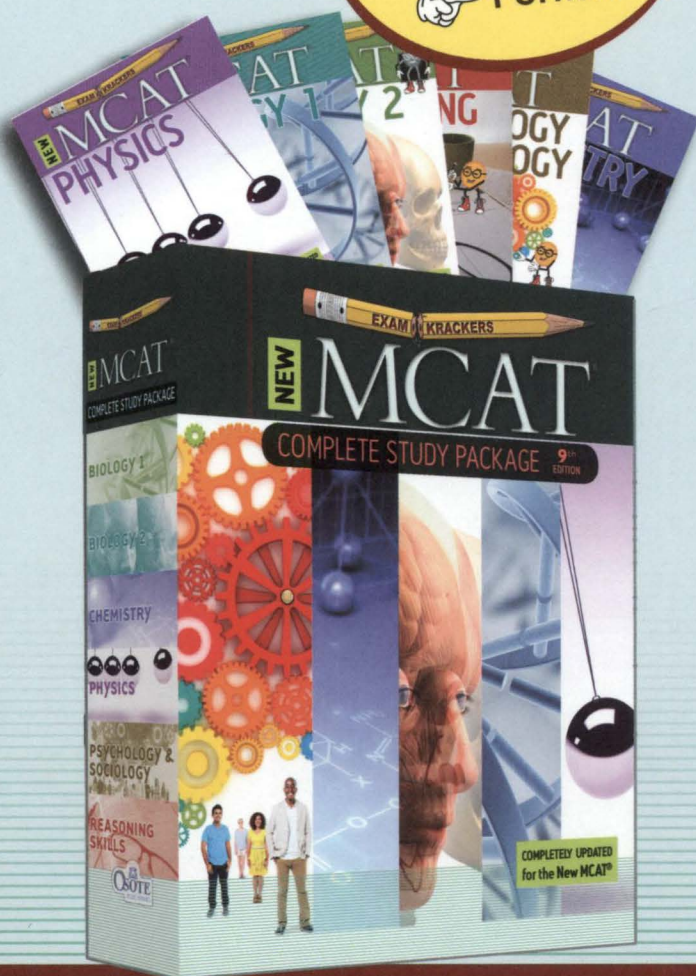
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EXAMKRACKERS MCAT®

BIOLOGY 2: SYSTEMS

9TH EDITION

JONATHAN ORSAY



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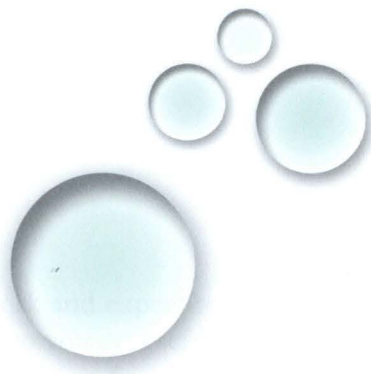
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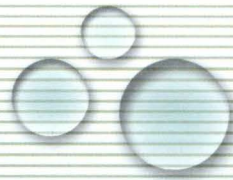
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Acknowledgements

The hard work and expertise of many individuals contributed to this book. The idea of writing in two voices, a science voice and an MCAT[®] voice, was the creative brainchild of my imaginative friend Jordan Zaretsky. I would like to thank Scott Calvin for lending his exceptional science talent and pedagogic skills to this project. I also must thank seventeen years worth of Examkrackers students for doggedly questioning every explanation, every sentence, every diagram, and every punctuation mark in the book, and for providing the creative inspiration that helped me find new ways to approach and teach biology. Finally, I wish to thank my wife, Silvia, for her support during the difficult times in the past and those that lie ahead.



Read this Section First!

Introduction to the Examrackers Manuals

The Examrackers books are designed to give you exactly the information you need to do well on the MCAT® while limiting extraneous information that will not be tested. This manual organizes all of the information on organ systems biology tested on the MCAT® conceptually. Concepts make the content both simple and portable for optimal application to MCAT® questions. Mastery of the organ systems biology covered in this manual will increase your confidence and allow you to succeed with seemingly difficult passages that are designed to intimidate. The MCAT® rewards your ability to read complex passages and questions through the lens of basic science concepts.

An in-depth introduction to the MCAT® is located in the Reasoning Skills manual. Read this introduction first to start thinking like the MCAT® and to learn critical mathematical skills. The second lecture of the Reasoning Skills manual addresses the research methods needed for success on 50% of questions on the science sections of the MCAT®. Once you have read those lectures, return to this manual to begin your study of the biology you will need to excel on the MCAT®.

How to Use This Manual

Examrackers MCAT® preparation experience has shown that you will get the most out of these manuals when you structure your studying as follows. Read each lecture three times: twice before the class lecture, and once immediately following the lecture. During the first reading, you should not write in the book. Instead, read purely for enjoyment. During the second reading, highlight and take notes in the margins. The third reading should be slow and thorough. Complete the twenty-four questions in each lecture during the second reading before coming to class. The in-class exams in the back of the manual are intended to be completed in class. Do not look at them before class.

Warning: Just attending the class will not raise your score. You must do the work. Not attending class will obstruct dramatic score increases.

If you are studying independently, read the lecture twice before taking the in-class exam and complete the in-lecture questions during the second reading. Then read the lecture once more after the in-class exam.

The thirty minute exams are designed to educate. They are similar to an MCAT® section, but are shortened and have most of the easy questions removed. We believe that you can answer most of the easy questions without too much help from us, so the best way to raise your score is to focus on the more difficult questions. This method is one of the reasons for the rapid and celebrated success of the Examrackers prep course and products.

A scaled score conversion chart for the in-class exams is provided on the answer page, but it is not meant to be an accurate representation of your score. Do not be discouraged by poor performance on these exams; they are not meant to predict your performance on the real MCAT®. **The questions that you get wrong or even guess correctly are most important. They represent your potential score increase. When you get a question wrong or have to guess, determine why and target these areas to improve your score.**

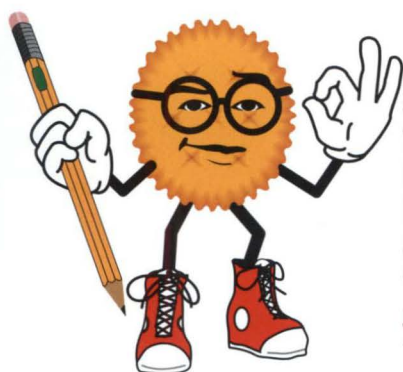
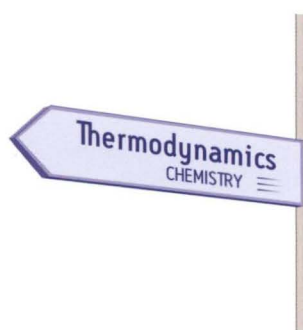
In order to study most efficiently, it is essential to know what topics are and are not tested directly in MCAT® questions. This manual uses the following conventions to make the distinction. Any topic listed in the AAMC's guide to the MCAT® is printed in **red, bold type**. You must thoroughly understand all topics printed in **red, bold type**. Any formula that must be memorized is also printed in **red, bold type**.

If a topic is not printed in **bold and red**, it may still be important. Understanding these topics may be helpful for putting other terms in context. Topics and equations that are not explicitly tested but are still useful to know are printed in *italics*. Knowledge of content printed in *italics* will enhance your ability to answer passage-based MCAT® questions, as MCAT® passages may cover topics beyond the AAMC's list of tested topics on the MCAT®.

Features of the Examcrackers Manuals

The Examcrackers books include several features to help you retain and integrate information for the MCAT®. Take advantage of these features to get the most out of your study time.

- **The 3 Keys** – The keys unlock the material and the MCAT®. Each lecture begins with 3 keys that organize by highlighting the most important things to remember from each chapter. Examine the 3 Keys before and after reading each lecture to make sure you have absorbed the most important messages. As you read, continue to develop your own key concepts that will guide your studying and performance.
- **Signposts** – The new MCAT® is fully integrated, asking you to apply the biological, physical, and social sciences simultaneously. The signposts alongside the text in this manual will help you build mental connections between topics and disciplines. This mental map will lead you to a high score on the MCAT®. The post of each sign "brackets" the paragraph to which it refers. When you see a signpost next to a topic, stop and consider how the topics are related. Soon you will begin making your own connections between concepts and topics within and between disciplines. This is an MCAT® skill that will improve your score. When answering questions, these connections give you multiple routes to find your way to the answer.
- **MCAT® Think** sidebars invite deeper consideration of certain topics. They provide helpful context for topics that are tested and will challenge you just like tough MCAT® passages. While MCAT® Think topics and their level of detail may not be explicitly tested on the MCAT®, read and consider each MCAT® Think to sharpen your MCAT® skills. These sidebars provide essential practice in managing seemingly complex and unfamiliar content, as you will need to do for passages on MCAT® day.



Text written in purple is me, Salty the Kracker. I will remind you what is and is not an absolute must for the MCAT®. I will help you develop your MCAT® intuition. I will offer mnemonics, simple methods of viewing a complex concept, and occasionally some comic relief. Don't ignore me, even if you think I am not funny, because my comedy is designed to help you understand and remember. If you think I am funny, tell the boss. I could use a raise.

Additional Resources

If you find yourself struggling with the science or just needing more practice, take advantage of the additional Examcrackers resources that are available. Examcrackers offers a 9-week Comprehensive MCAT® Course to help you achieve a high score on the MCAT®, including 66 hours with expert instructors, unique course format, and regular full-length MCAT® exams. Each class includes lecture, a practice exam, and review, designed to help you develop essential MCAT® skills. For locations and registration please visit Examcrackers.com or call 1-888-KRACKEM.

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Lecture 1	Lecture 3	Lecture 5		
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Lecture 1	Lecture 4	Lecture 6		
Lecture 2	Lecture 5	Lecture 7		
Lecture 3				
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Lecture 1	Lecture 3	Lecture 5		
Lecture 2	Lecture 4			

Your purchase of this book new will also give you access to the **Examkrackers Forums** at www.examkrackers.com/mcat/forum. These bulletin boards allows you to discuss any question in the book with an MCAT[®] expert at Examkrackers. All discussions are kept on file so you can refer back to previous discussions on any question in this book. Once you have purchased the books you can take advantage of this resource by calling 1-888-KRACKEM to register for the forums.

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Study diligently, trust this book to guide you, and you will reach your MCAT[®] goals.

Table of Contents

LECTURE

1

The Cell 1

- 1.1 Introduction.....1
- 1.2 Classification of Organisms.....2
- 1.3 Evolution: Genetics and Viruses.....3
- 1.4 Bacteria.....8

- 1.5 Eukaryotic Cells: Membrane Bound Organelles....15
- 1.6 Membrane Transport.....23
- 1.7 Tissues, Organ Systems, Organisms.....30

LECTURE

2

The Nervous System 37

- 2.1 Introduction.....37
- 2.2 Communication Within the Body.....38
- 2.3 Functions and Features of the Nervous System....39
- 2.4 Electrochemistry and the Neuron.....40
- 2.5 Communication Between
Neurons: The Synapse.....48

- 2.6 Supporting Cells: Glia.....50
- 2.7 The Structures of the Nervous System.....51
- 2.8 Sensing and Sensory Receptors.....60
- 2.9 The Eye and Vision.....61
- 2.10 The Ear and Hearing.....65
- 2.11 Smell, Taste, and Pain.....68

LECTURE

3

The Endocrine System 73

- 3.1 Introduction.....73
- 3.2 The Chemistry of Hormones.....74
- 3.3 Organizing the Endocrine System.....77
- 3.4 Regulation of Hormones.....81

- 3.5 Endocrine Glands and Their Hormones.....84
- 3.6 Homeostasis and Hormones.....90
- 3.7 Reproduction and Development.....94

LECTURE

4

The Circulatory, Respiratory, and Immune Systems 105

- 4.1 Introduction.....105
- 4.2 The Respiratory
System and Gas Exchange.....106
- 4.3 The Blood.....115

- 4.4 The Cardiovascular
System and Blood Pressure.....116
- 4.5 The Lymphatic System as Drainage.....126
- 4.6 The Immune System: Components and
Communication.....127

The Digestive and Excretory Systems 141

5.1 Introduction.....	141
5.2 Anatomy of the Digestive System	142
5.3 Gastrointestinal Hormones.....	150

5.4 Molecular Digestion and Absorption.....	153
5.5 The Liver: Storage, Distribution, and Detox.....	158
5.6 The Kidney: Excretion, Blood Pressure & Composition	162

Muscle, Bone and Skin 173

6.1 Introduction.....	173
6.2 Muscle.....	174
6.3 Skeletal Muscle: Physiology and Structure	174
6.4 Features of Cardiac Muscle.....	183

6.5 Smooth Muscle.....	184
6.6 Bone: Mineral Homeostasis and Structure.....	187
6.7 Cartilage and Joints.....	191
6.8 Skin	192

30-Minute In-Class Exams 197

In-Class Exam for Lecture 1.....	197
In-Class Exam for Lecture 2.....	203
In-Class Exam for Lecture 3.....	209

In-Class Exam for Lecture 4.....	217
In-Class Exam for Lecture 5.....	223
In-Class Exam for Lecture 6.....	231

Answers & Explanations to In-Class Exams 239

Answers and Scaled Score	
Conversion for In-Class Exams	240
Explanations to In-Class Exam for Lecture 1	241
Explanations to In-Class Exam for Lecture 2	244

Explanations to In-Class Exam for Lecture 3	248
Explanations to In-Class Exam for Lecture 4	250
Explanations to In-Class Exam for Lecture 5	254
Explanations to In-Class Exam for Lecture 6	258

Answers & Explanations to Questions in the Lectures 261

Answers to Questions in the Lectures.....	262
Explanations to Questions in Lecture 1	263
Explanations to Questions in Lecture 2	265
Explanations to Questions in Lecture 3	268

Explanations to Questions in Lecture 4	271
Explanations to Questions in Lecture 5	273
Explanations to Questions in Lecture 6	276

Photo Credits 279

BIOLOGICAL SCIENCES

DIRECTIONS. Most questions in the Biological Sciences test are organized into groups, each preceded by a descriptive passage. After studying the passage, select the one best answer to each question in the group. Some questions are not based on a descriptive passage and are also independent of each other. You must also select the one best answer to these questions. If you are not certain of an answer, eliminate the alternatives that you know to be incorrect and then select an answer from the remaining alternatives. A periodic table is provided for your use. You may consult it whenever you wish.

PERIODIC TABLE OF THE ELEMENTS

1 H 1.0																	2 He 4.0
3 Li 6.9	4 Be 9.0											5 B 10.8	6 C 12.0	7 N 14.0	8 O 16.0	9 F 19.0	10 Ne 20.2
11 Na 23.0	12 Mg 24.3											13 Al 27.0	14 Si 28.1	15 P 31.0	16 S 32.1	17 Cl 35.5	18 Ar 39.9
19 K 39.1	20 Ca 40.1	21 Sc 45.0	22 Ti 47.9	23 V 50.9	24 Cr 52.0	25 Mn 54.9	26 Fe 55.8	27 Co 58.9	28 Ni 58.7	29 Cu 63.5	30 Zn 65.4	31 Ga 69.7	32 Ge 72.6	33 As 74.9	34 Se 79.0	35 Br 79.9	36 Kr 83.8
37 Rb 85.5	38 Sr 87.6	39 Y 88.9	40 Zr 91.2	41 Nb 92.9	42 Mo 95.9	43 Tc (98)	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57 La* 138.9	72 Hf 178.5	73 Ta 180.9	74 W 183.9	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra 226.0	89 Ac* 227.0	104 Unq (261)	105 Unp (262)	106 Unh (263)	107 Uns (262)	108 Uno (265)	109 Une (267)									

*	58 Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm (145)	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
=	90 Th 232.0	91 Pa (231)	92 U 238.0	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (260)

For your convenience, a periodic table is also inserted in the back of the book.

The Cell

1.1 Introduction

This lecture discusses the cell, the basic unit of life. Evolution is used as a framework to discuss key principles of viruses, prokaryotic cells, and eukaryotic cells.

The lecture will first cover the organizational and naming scheme of living organisms. Then it will address evolution and how it explains changes in a genome over time, as well as how a species can become a new species altogether. Viruses, which have played a role in evolution and are dependent on living cells, will be described.

Next the lecture will discuss the structure and reproduction of bacteria, medically relevant prokaryotes. Bacteria reproduce asexually but are able to exchange genetic material among themselves. The cell walls of bacteria protect them from the outside environment, and thus are the target of many antibiotics.

Eukaryotic cells, including human cells, have two major types of organization. First, cells are organized by pathways. This lecture follows the flow of proteins after their initial synthesis; the Genetics Lecture in *Biology 1: Molecules* examines the flow of DNA and RNA; and the Metabolism Lecture in this same manual describes the flow of energy and biological molecules. Eukaryotic cells are also organized by chemical properties. Some compartments of the cell contain proteins, others lipids, and others acidic or basic environments. These compartments are surrounded by membranes that regulate the transport of substances.

The lecture concludes by considering how cells come together to form tissues and organs. Cells are held together by an extracellular matrix and communicate with each other so that the processes of these cells become synchronized. While an organ is more than the sum of its cells, the function of an organ depends on the functions of its cells. For example, organs that secrete proteins must have the organelles that make, synthesize, and secrete proteins. The remaining lectures in this manual will discuss systems of organs and how these systems work together to maintain the entire body.

The contents of a cell are in motion. When you see an organelle or cellular molecule, picture motion and identify what is moving and why.

Everything in the cell is in flux. Proteins are constantly being synthesized, modified, transported, and degraded. When the cell can no longer maintain these processes, the cell dies.

- 1.1 Introduction
- 1.2 Classification of Organisms
- 1.3 Evolution: Genetics and Viruses
- 1.4 Bacteria
- 1.5 Eukaryotic Cells: Membrane Bound Organelles
- 1.6 Membrane Transport
- 1.7 Tissues, Organ Systems, Organisms...

THE 3 KEYS

1. The cell has compartments to separate chemical properties and processes.
2. A cell is like an organism – understand the function of organelles by treating them as organs.
3. Transport in and out of a cell occurs through diffusion down the concentration gradient, by pumps against the diffusion gradient, or via endocytosis/exocytosis.



A horse and a zebra would be of the same species only if they could reproduce to create fertile offspring. Horses and zebras are not of the same species, so this horse/zebra hybrid cross is probably infertile.

1.2

Classification of Organisms

In biology, *taxonomy* is the organization of the naming system for living organisms. Most taxonomical classification systems are based upon genetic similarity resulting from shared phylogeny, or evolutionary history. The most commonly used classification system contains increasingly specific groupings in the following order: **Domain**, *Kingdom*, *Phylum*, *Class*, *Order*, *Family*, *Genus*, *Species*. There are three domains: Bacteria, Archaea, and Eukarya. The kingdoms of Protista, Fungi, Plantae, and Animalia are in the domain Eukarya. All mammals belong to the class *Mammalia* and the phylum *Chordata*; therefore, all mammals likely share a common genetic ancestor that they do not share with birds, which are also in the phylum *Chordata*, but in the class *Aves*.

A **species** is loosely limited to all organisms that can reproduce fertile offspring with one another. If two organisms can reproduce to create fertile offspring, they may be of the same species; if their gametes are incompatible, they are definitely not of the same species. Organisms may be prevented from producing fertile offspring for any number of reasons, such as living in different areas of the planet (*geographic isolation*), mating in different seasons (*temporal isolation*), and having gametes that do not form viable offspring (*genetic incompatibility*). This definition of a species is by no means perfect or all-inclusive. Bacteria, for example, do not reproduce sexually. Their classification system is entirely different and is beyond the scope of the MCAT®.

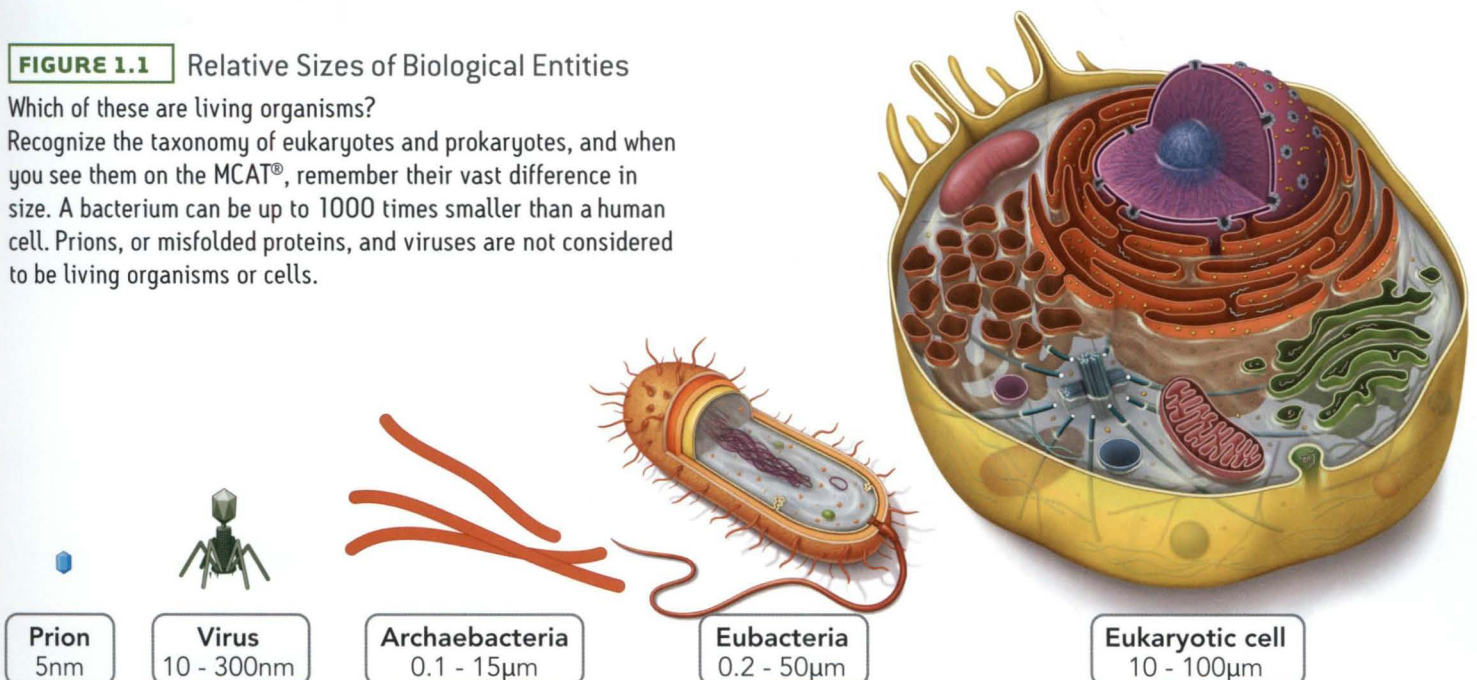
The evolutionary history of a single organism can be followed within its development from embryo to adult. That is, "ontogeny recapitulates phylogeny," or development retraces evolution. The human fetus, for example, has pharyngeal pouches, reflecting an ancestor with gills. Naming (taxonomy) makes sense when evolutionary or genetic history is considered.

As described by cell theory, the cell is the smallest basic unit of life and is shared by all living things; furthermore, cells give rise to other cells. When microscopes were invented, biologists were able to observe the similar organization of small units-- cells-- across different forms of life. No matter how different two organisms are in their taxonomies and evolutionary histories, they are both made up of cells.

FIGURE 1.1 Relative Sizes of Biological Entities

Which of these are living organisms?

Recognize the taxonomy of eukaryotes and prokaryotes, and when you see them on the MCAT®, remember their vast difference in size. A bacterium can be up to 1000 times smaller than a human cell. Prions, or misfolded proteins, and viruses are not considered to be living organisms or cells.



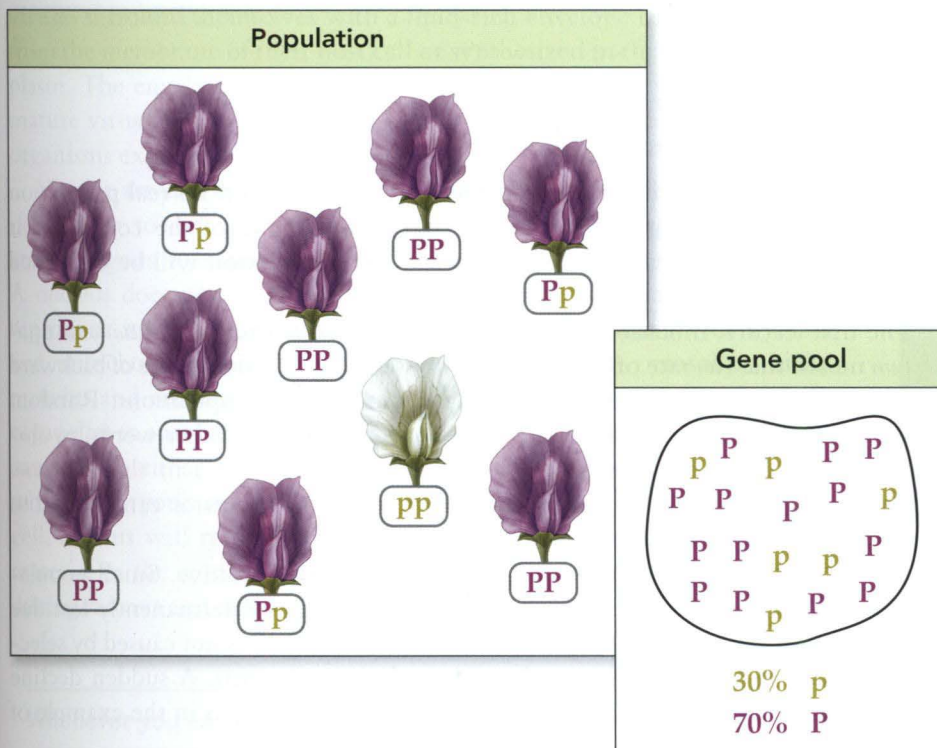
Evolution as Heritable Change in Genes

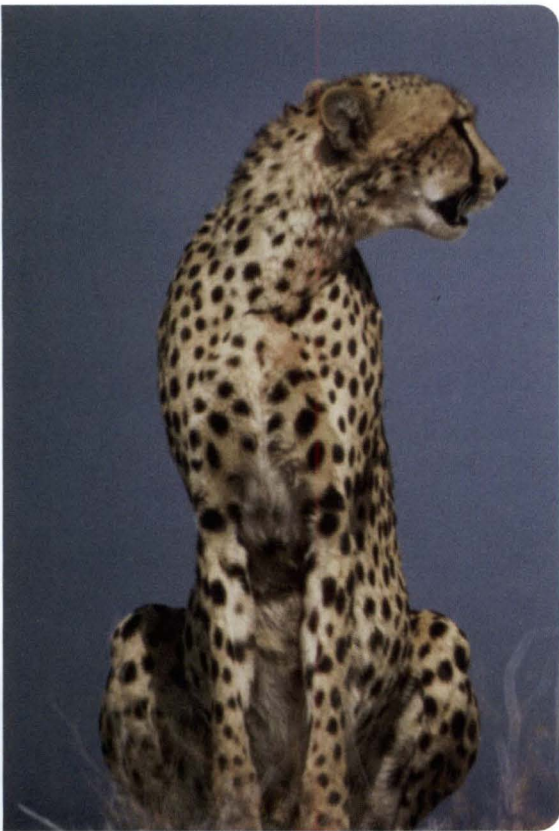
Our genome contains our entire evolutionary history. The genome is a patchwork of genetic material introduced through a variety of mechanisms including exchange with viruses.

An understanding of evolution requires terms used in genetics. Any particular trait has both a **genotype** and a **phenotype**. The genotype describes the chromosomes of an organism, while the phenotype describes the product of the genes that can be observed. Consider the flowers of a pea plant, which can be either purple or white. These colors comprise the phenotype and can be described as either dominant (purple) or recessive (white). On the chromosomal level, any dizygotic organism has two copies of each gene. For this flower, there are only two forms of the gene: P, which codes for purple, and p, which codes for white. P is the dominant form of the gene, so whenever it appears as one of the plant's genes, the flowers will be purple; thus either PP or Pp plants can be purple. Whenever P is absent, the flowers will be white. An **allele** is one form of a gene. In the simple example of flower color, there are only two possible alleles, P and p. Not all phenotypes are so simple. Some, such as height, vary gradually within a species.

A gene that has multiple alleles, corresponding to distinct forms of a phenotype, is called a **polymorphism**. The existence of polymorphisms in the population makes evolution and the related process of speciation possible. The **gene pool** is the total of all alleles in a population and **evolution** is a change in a population's gene pool. Figure 1.2 shows the flower color alleles for a small population. There are 70% P alleles and 30% p alleles. Even if the ratio of purple (PP and Pp) to white (pp) flowers changes temporarily, as long as the ratio of alleles remains 70 to 30, the population has not evolved. If the ratio does change, or if a new allele is formed by a mutation (such as a mutation coding for red flowers), evolution has occurred.

FIGURE 1.2 Gene Pool of a Population





Cheetahs have a very little genetic variation, due to an evolutionary bottleneck event experienced by the species. As a result, they are more vulnerable to environmental threats, such as disease.

Evolution can sometimes result in **speciation**, the formation of a new species. It is possible for a species to evolve into one or more new species. Since the definition of a species says that members of different species cannot produce fertile offspring, speciation is said to have occurred when a single species has evolved into different groups whose members can no longer interbreed to produce fertile offspring.

The MCAT® requires an understanding of a variety of mechanisms that can contribute to speciation. Polymorphisms provide the raw material for speciation. **Inbreeding**, the mating of relatives, increases the number of homozygous individuals in a population without changing the allele frequency. Inbreeding can lead to speciation under certain circumstances, such as if a population is geographically divided into groups and a mutation arises in one group but not the other. **Outbreeding**, or mating of nonrelatives, maintains genetic flow between populations and thus would not be expected to contribute to speciation.

Speciation can also occur due to random events. For example, a species may face a crisis so severe that there are few survivors, whose allelic frequencies are not representative of the original population. The result is that the allelic frequencies of the population are shifted. This situation, called a **bottleneck**, can ultimately lead to speciation.

Finally, specialization and adaptation are processes that can contribute to speciation. **Specialization** is the process by which the members of a species tailor their behaviors to exploit their environment. They carve out a particular role in the environment, including the use of certain resources and advantageous behaviors. When distinct groups within a population specialize such that they differ substantially, such as in their habits or locations, speciation may ultimately result. Similarly, genetic or behavioral changes that are advantageous in the given environment, or **adaptations**, can lead to speciation.

The Five Mechanisms of Evolution

Evolution can be understood by considering the circumstances that are required to prevent it from happening. The scientists Hardy and Weinberg defined a theoretical population in which no evolution would occur. This population is said to be in **Hardy-Weinberg equilibrium** and has the following features:

1. mutational equilibrium;
2. large population;
3. random mating;
4. immigration or emigration must not change the gene pool; and
5. no selection for the fittest organism.

Hardy-Weinberg equilibrium is an idealized concept, and no real population ever possesses these characteristics completely. When one of the conditions is broken, evolution occurs. The implications of each condition will be examined below.

The first feature, mutational equilibrium, is the most intuitive. *Mutational equilibrium* means that the rate of forward mutations exactly equals the rate of backward mutations. Mutational equilibrium rarely occurs in real populations. Random mutations can be used to track the progress of evolution. In other words, **evolutionary time can be measured by gradual random changes in the genome**. Comparing the genomes of species that share a common ancestor can be used to determine how long ago they diverged.

The second feature, a large population, is also fairly intuitive. Small populations are subject to **genetic drift**, where one allele may be permanently lost due to the death of all members having that allele. Genetic drift is not caused by selective pressure, so its results are random in evolutionary terms. A sudden decline in population size can also lead to changes in the gene pool, as in the example of bottlenecks.

The third feature, random mating, means that organisms are equally likely to mate with each other regardless of their phenotypes. Random mating can be described as the lack of selection for certain phenotypes in mating (*sexual selection*). In real populations, certain behavioral or physical phenotypes lead to increased mating success; as a result, the associated genotypes are preferentially passed on to the following generations, and evolution results.

The fourth feature, lack of immigration and emigration, is the requirement that new alleles are not introduced to the population by immigrating organisms, and that alleles are not decreased or eliminated by the emigration of organisms with those alleles. Either scenario could change the allelic makeup of a population.

In real populations, the fifth requirement, no selection of the fittest, is violated when certain members of a population exploit the environment more efficiently than others. According to the **fitness concept**, the “fittest” organism is the one that can best survive to reproduce offspring; these offspring will, in turn, reproduce offspring, and so on generation after generation.

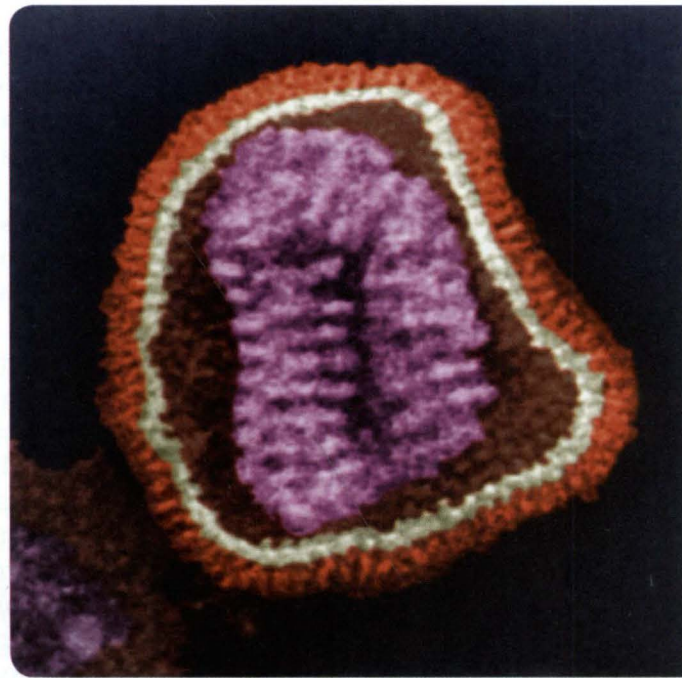
From an evolutionary standpoint, the success of a gene can be measured as its **increase in percent representation in the gene pool of the next generation**. The driving principle of **natural selection** is that genes that are advantageous in a given environment are preferentially passed down from generation to generation. At the core of natural selection is not how long an organism lives, but rather how well it can reproduce to contribute its genes to the next generation. Such selection therefore occurs by **differential reproduction**, which may include living beyond reproduction in order to give offspring a better chance to reproduce.

Viruses

Viruses are tiny infectious agents. They have the ability to transfer genetic material, which can have positive effects, as in gene therapy. Viruses have played a role in evolution by transferring genetic “information.”

Viruses are generally comparable in size to large proteins, although some are larger and some are much smaller. In its most basic form, a virus consists of a protein coat, called a **capsid**, and from one to several hundred genes in the form of DNA or RNA inside the capsid. No virus contains both DNA and RNA, and viruses do not contain organelles or nuclei. Most animal viruses, some plant viruses, and very few bacterial viruses surround themselves with a lipid-rich envelope that is borrowed from the membrane of their host cell or synthesized in the host cell cytoplasm. The envelope typically contains some virus-specific proteins. A mature virus outside the host cell is called a **viral particle** or virion. All organisms experience viral infections.

Viruses are not currently classified as living organisms and thus do not belong to any of the taxonomical kingdoms of organisms. They are analogous to a portion of a cell, namely the eukaryotic nucleus. A nucleus does not metabolize nutrients and cannot make proteins to reproduce itself. Instead it uses the ATP made available in the cytosol and mitochondria, and it uses the ribosomes in the cytosol to make proteins and enzymes to reproduce. Viruses similarly exploit the cell's organelles to survive. Viruses and eukaryotic nuclei differ in that a virus can contain either DNA or RNA as its inherited genome (never both), while eukaryotic nuclei use only DNA. Furthermore, when inside a cell, a virus will remove its capsid and envelope to expose its genetic material in the cytosol. The nucleus remains membrane bound except during mitosis and meiosis.



The transmission electron micrograph above shows the structure of an influenza virus particle. This virus has RNA as its genome and is an example of an enveloped virus.

Whenever you see a virus in a cell, think of it as an extra nucleus.

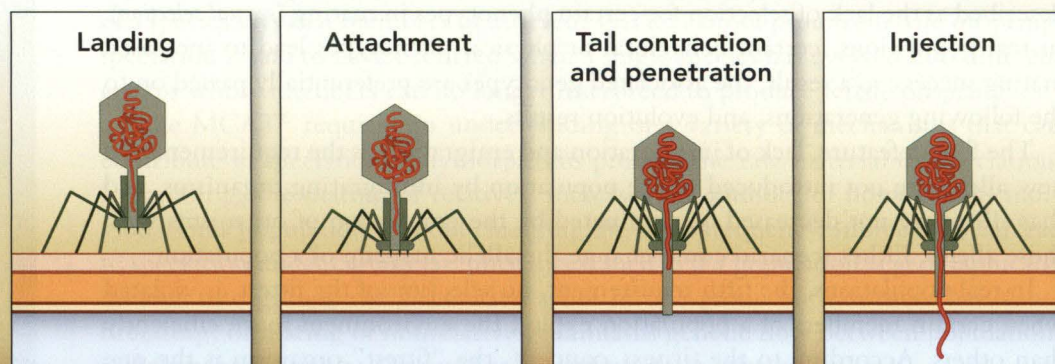
Capsid or Head
(Contains nucleic acid)

Tail

Tail fibers

Bacterium

FIGURE 1.3 Bacteriophage: Adsorption and Injection



It is important to know the structure of a virus: capsid, nucleic acid, and lipid-rich protein envelope for some viruses; and tail, base plate, and tail fibers for most bacteriophages. Viruses are very small. A bacterium is the size of a mitochondrion, and hundreds of viruses may fit within a bacterium.

Most animal viruses do not leave capsids outside the cell, but rather enter the cell through receptor-mediated endocytosis.

A viral infection begins when a virus binds to a specific chemical receptor site on the **host cell**, the cell that is being infected. The chemical **receptor** is usually a specific glycoprotein on the host cell membrane. A virus cannot infect a cell that does not have the specific receptor for that virus. Next, the nucleic acid of the virus penetrates into the cell. A **bacteriophage** (Greek: phagein: to eat), a virus that infects bacteria, typically injects nucleic acids into the host cell through its **tail** after viral enzymes have digested a hole in the cell wall, as shown in Figure 1.3. (Notice that this indicates that some viruses also include enzymes within their capsids.) Most viruses that infect eukaryotes are instead engulfed by an endocytotic process, meaning that the cell membrane surrounds the virus and brings it into the cell. Once inside the host, there are two possible paths: a lysogenic infection or a lytic infection (Figure 1.4).

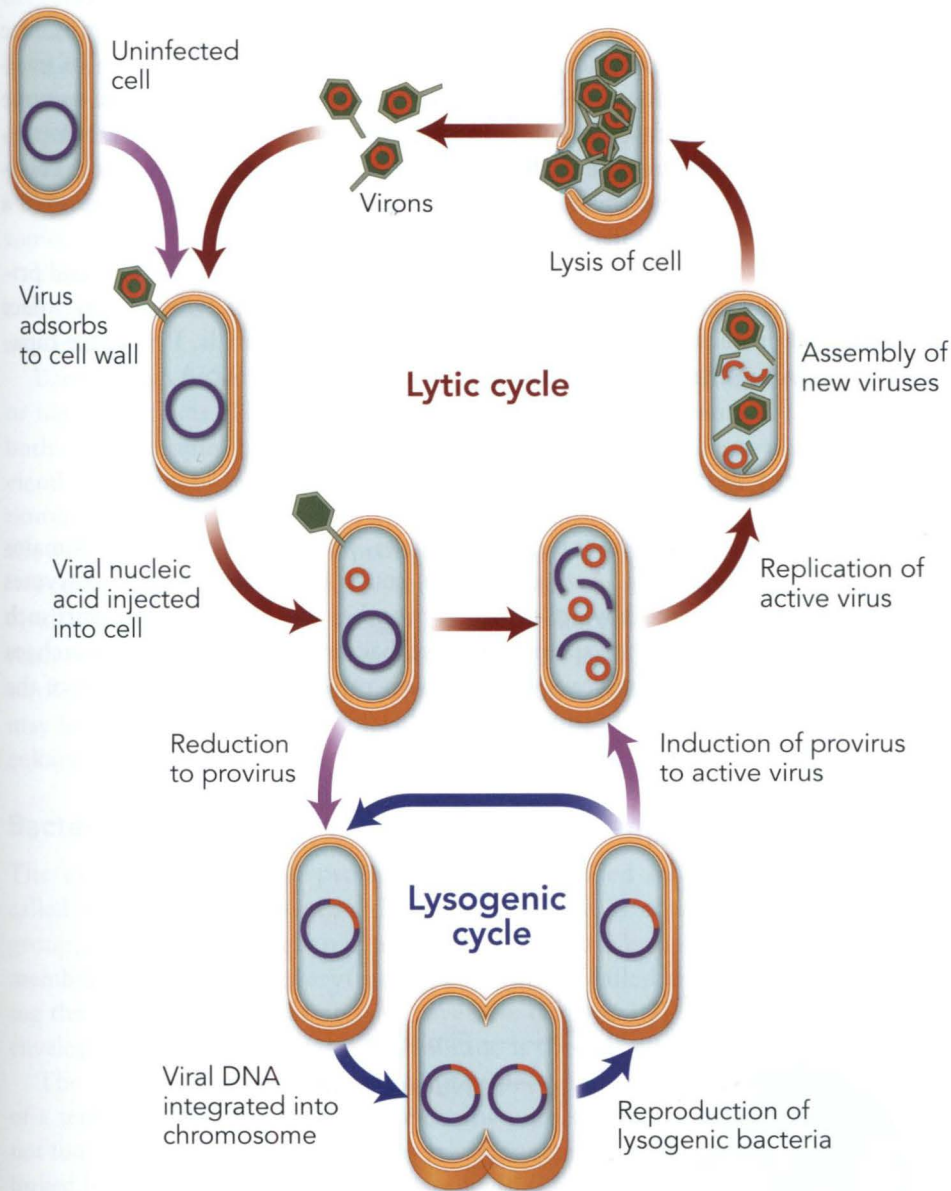
In a **lytic** (Greek: lysis → separation) infection, the virus commandeers the cell's **synthetic machinery**, which is normally used to produce proteins for the cell, to replicate viral components. The RNA (either directly from the virus or transcribed from viral DNA) is translated to form proteins. These proteins self-assemble to form a new virus. The cell may fill with new viruses until it lyses (bursts), or it may release new viruses one at a time in a reverse endocytotic process. The period from infection to lysis is called the *latent period*. A virus following a lytic cycle is a *virulent virus*, a virus that is capable of causing disease.

In a **lysogenic** infection, the viral DNA is incorporated into the host genome. When the host cell replicates its DNA, the viral DNA is replicated as well. A virus in a lysogenic cycle is called a *temperate virus*. A host cell infected with a temperate virus may show no symptoms of infection. While the viral DNA remains incorporated in the host DNA, the virus is said to be *dormant* or *latent*, and is called a *provirus* (a *prophage* [Greek: pro → before, phagein → eat] if the host cell is a bacterium). The dormant virus may become active when the host cell is under stress. When the virus becomes active, it becomes virulent.

As described previously, some viruses have **viral envelopes**, formed as they undergo exocytosis from the cell. These envelopes are pinched off pieces of host cellular membrane. To a certain extent, the envelope protects an **enveloped virus** from detection by the immune system. Even more importantly, the receptors on the envelope allow it to bind to a new host cell and start the process all over again. The original cell may not die right away, but due to degradation of its membrane and usable cellular machinery, it usually does die. By contrast to enveloped viruses, **nonenveloped viruses** typically do lyse a cell and cause cell death on their release.

Immune System
BIOLOGY 2

FIGURE 1.4 Viral Life Cycles



The replication and transcription of viral double stranded DNA (dsDNA) occurs as described in the Genetics Lecture in the *Biology 1: Molecules Manual*. After injection into a cell, the viral DNA translocates to the nucleus, where it hijacks the cellular machinery in order to replicate and translate its genetic material.

Almost all RNA viruses replicate via an *RNA-dependent RNA polymerase* (RdRP). This enzyme can synthesize a new strand of RNA from a previously existing RNA strand. Some RNA strands (+RNA) actually code for proteins. However, when RdRP makes a copy of this strand, it will create a complimentary strand that cannot code for protein products. This is a -RNA strand, which must undergo another replication with RdRP in order to form a new +RNA strand. All single stranded RNA viruses specifically carry either +RNA or -RNA. If a virus carries -RNA, it must undergo one replication by RdRP to form +RNA in order to code for proteins (as shown in Figure 1.5) and then another one to be packaged into its progeny.

Other genome types unique to viruses include single stranded DNA (ssDNA) and double stranded RNA (dsRNA). When a virus inserts ssDNA into a cell, it is translocated to the nucleus, where DNA polymerase transcribes a complimentary

Be sure to know the differences between the two viral life cycles. In particular, remember how the viral genetic material is converted into proteins and also how it can be incorporated into the host cell genome. See the Genetics Lecture for information about transcription and translation.

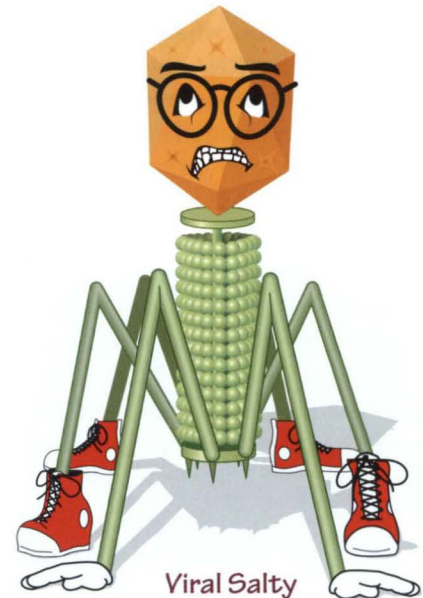


FIGURE 1.5 Viral RNA

A virus may have plus-strand or minus-strand RNA.

mRNA
UAGGCAUCUUUCGCA ↓ (translation) protein
Plus-strand RNA
UAGGCAUCUUUCGCA ↓ (translation) protein
Minus-strand RNA
AUCCGUAGAAAGCGU ↓ (transcription) UAGGCAUCUUUCGCA ↓ (translation) protein

You can remember that reverse transcriptase transcribes RNA into DNA because it *reverses* the usual process, where DNA is transcribed into RNA.

Don't get caught up in all the minute differences between Archaea and Bacteria. Just know that there is a distinction and that, although both Archaea and Bacteria are prokaryotes, Archaea have similarities to eukaryotes.

strand, thus forming dsDNA. The replication and transcription processes then proceed as they usually do for dsDNA. dsRNA in a cell simply separates to form a free +RNA and -RNA strand. These strands are then replicated by RdRP.

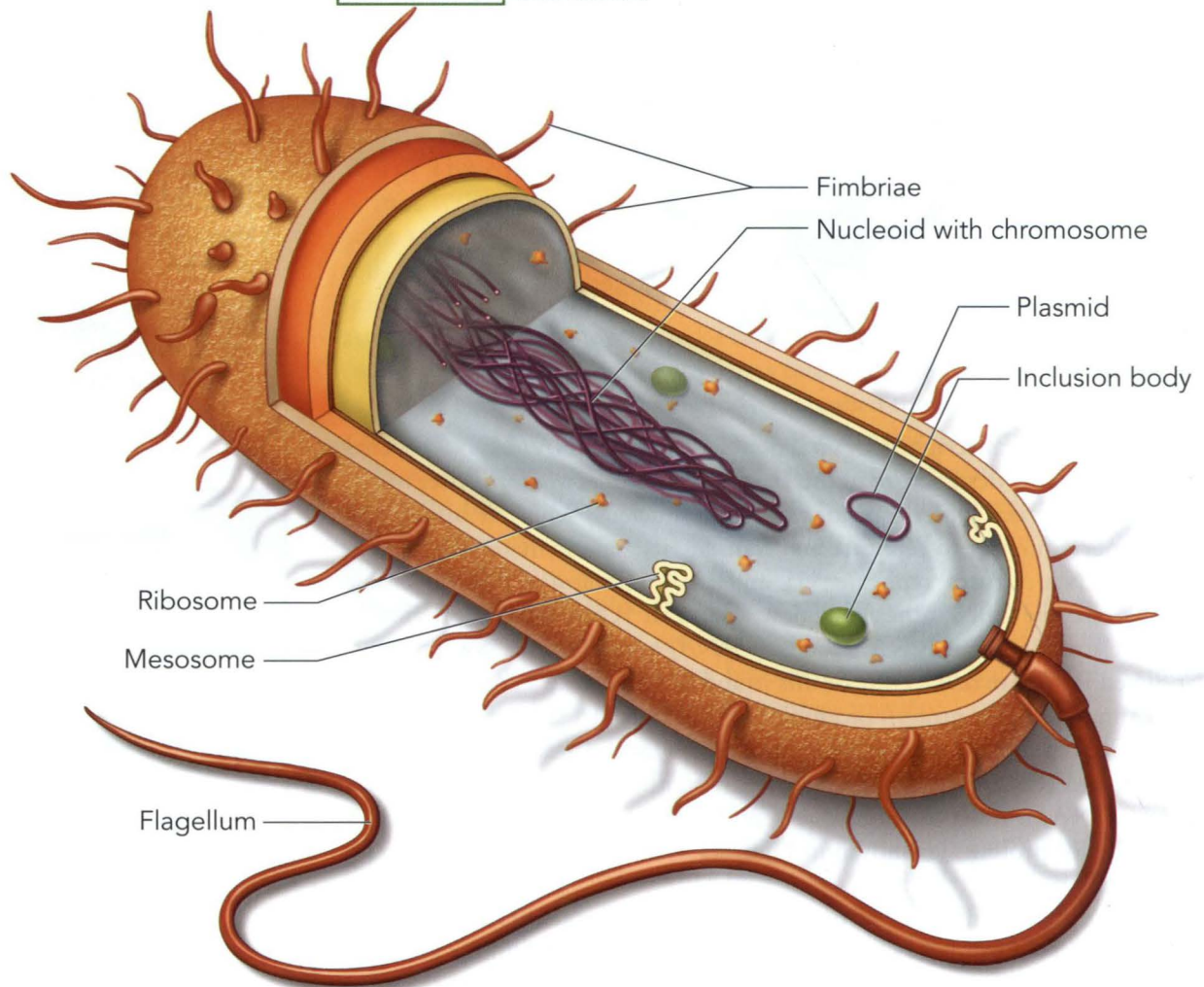
Some single-stranded RNA viruses, called **retroviruses**, are able to transcribe their RNA into double stranded DNA, in contrast to the usual process of transcription of DNA to produce RNA. The transcription is carried out by an enzyme called **reverse transcriptase**, which is carried by the retrovirus. The DNA produced by retroviruses can potentially be integrated into host DNA. It is exceedingly difficult to eradicate these viruses. **HIV** (*human immunodeficiency virus*) is a retrovirus that attacks cells involved in the immune response.

Subviral particles, infectious agents related to viruses, include viroids and prions. **Viroids** are small rings of naked RNA without capsids, which only infect plants. Naked proteins called **prions** cause infections in animals. Prions are capable of reproducing themselves, apparently without DNA or RNA.

1.4 Bacteria

Prokaryotes do not have membrane bound nuclei. They are split into two domains called Bacteria and Archaea. **Archaea** have as much in common with eukaryotes as they do with bacteria. They are typically found in extreme environments such as salty lakes and boiling hot springs. Unlike bacteria, the cell walls of archaea are not made from peptidoglycan. Most known prokaryotes are members of the domain **Bacteria** (Greek: bakterion: small rod).

FIGURE 1.6 Bacterium



The typical structure of prokaryotes (such as the bacterium shown in Figure 1.6) is simpler than that of eukaryotes. The most basic distinction between eukaryotes and prokaryotes is that prokaryotes do not have membrane bound organelles, including a nucleus, while eukaryotes do. Instead of a nucleus, prokaryotes usually have a single circular double stranded molecule of DNA. This molecule is twisted into *supercoils* and is associated with histones in Archaea and with proteins that are distinct from histones in Bacteria. The complex of DNA, RNA and proteins in prokaryotes forms a structure visible under the light microscope, called a *nucleoid*. Prokaryotes translate proteins and therefore have ribosomes. Prokaryotic ribosomes are smaller than eukaryotic ribosomes.

Bacteria come in three basic shapes: **cocci (spherical)**, **bacilli (rod-shaped)**, and **spirilli (spiral shaped)**. Spiral, or *helical*, bacteria are called *spirochetes* if they are flexible.

Bacteria can co-exist with other organisms, including humans, with beneficial or harmful effects. The relationship can be **symbiotic**, or mutually beneficial for both. For example, bacteria in the intestinal tract help humans digest food efficiently and benefit by receiving nutrients. Bacteria can also have a **parasitic** relationship with other organisms, where the relationship is beneficial to the bacteria, allowing them to grow and reproduce, but hurts the other organism.

Prokaryotes can be **anaerobic** (not dependent on oxygen for growth and survival) or **aerobic** (requiring oxygen). Early prokaryotes, which lived in an environment with no oxygen, were anaerobes. As atmospheric oxygen increased, aerobic prokaryotes evolved. A component of the eukaryotic cell, mitochondria, may have evolved from a symbiotic relationship between aerobic prokaryotes and eukaryotes.

Bacterial Envelopes: Protection and Movement

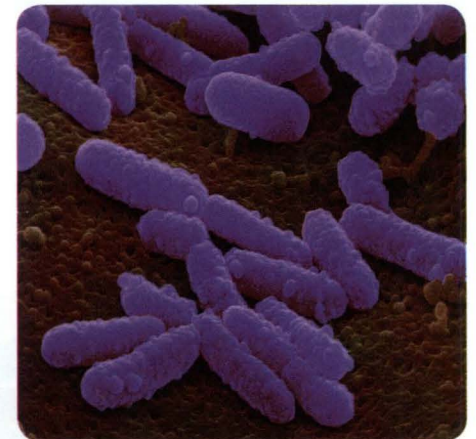
The cytosol of nearly all prokaryotes is surrounded by a phospholipid bilayer called the **plasma membrane**. Each phospholipid is composed of a **phosphate group**, two **fatty acid** chains, and a **glycerol backbone**. The bacterial plasma membrane, along with everything it contains, is called the *protoplast*. Surrounding the protoplast is the **bacterial envelope** (Figure 1.7). The component of the envelope adjacent to the plasma membrane is the cell wall.

The cell walls of bacteria are made of **peptidoglycan**. Peptidoglycan consists of a series of disaccharide polymer chains with amino acids, three of which are not found in proteins. These chains are connected by their amino acids, or cross-linked by an *interbridge* of more amino acids. The chains are continuous, forming a single molecular sac around the bacterium. The cell wall is also porous, so it allows large molecules to pass through. Many antibiotics such as *penicillin* attack the amino acid crosslinks of peptidoglycan. The cell wall is disrupted and the cell lyses, killing the bacterium. Some bacteria have been able to form new enzymes to attack penicillin, or even to change the molecular target so that penicillin can no longer recognize it. These bacteria gain penicillin resistance, an increasingly common problem in medicine.

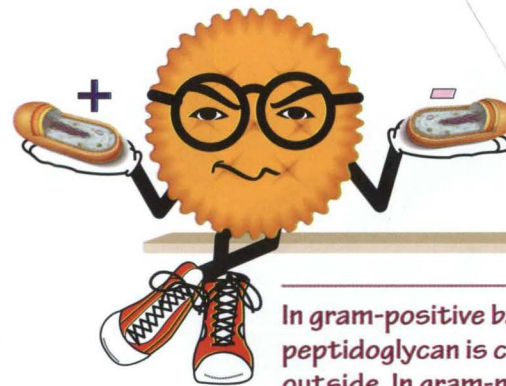
Bacteria can be classified according to the type of cell wall that they possess. *Gram staining* is a technique used to prepare bacteria for viewing under the light microscope, which stains two major cell wall types differently. Bacteria with one type are called *gram-positive bacteria* because the thick peptidoglycan cell wall prevents the gram stain from leaking out. These cells appear purple when they undergo gram staining. In gram positive bacteria, the cell wall is located just outside the cell membrane. The space between the plasma membrane and the cell wall is called the *periplasmic space*. The periplasmic space contains many proteins that help the bacteria acquire nutrition, such as hydrolytic enzymes.

Prokaryotes lack a nucleus. In fact, they have no complex, membrane-bound organelles. The key words are "complex" and "membrane-bound." They do have some organelles (e.g. ribosomes), but not complex, membrane-bound organelles like an endoplasmic reticulum or a Golgi complex.

The name of a bacterium often reveals the shape, like: *spiroplasma*, *staphylococcus*, or *streptococcus*.

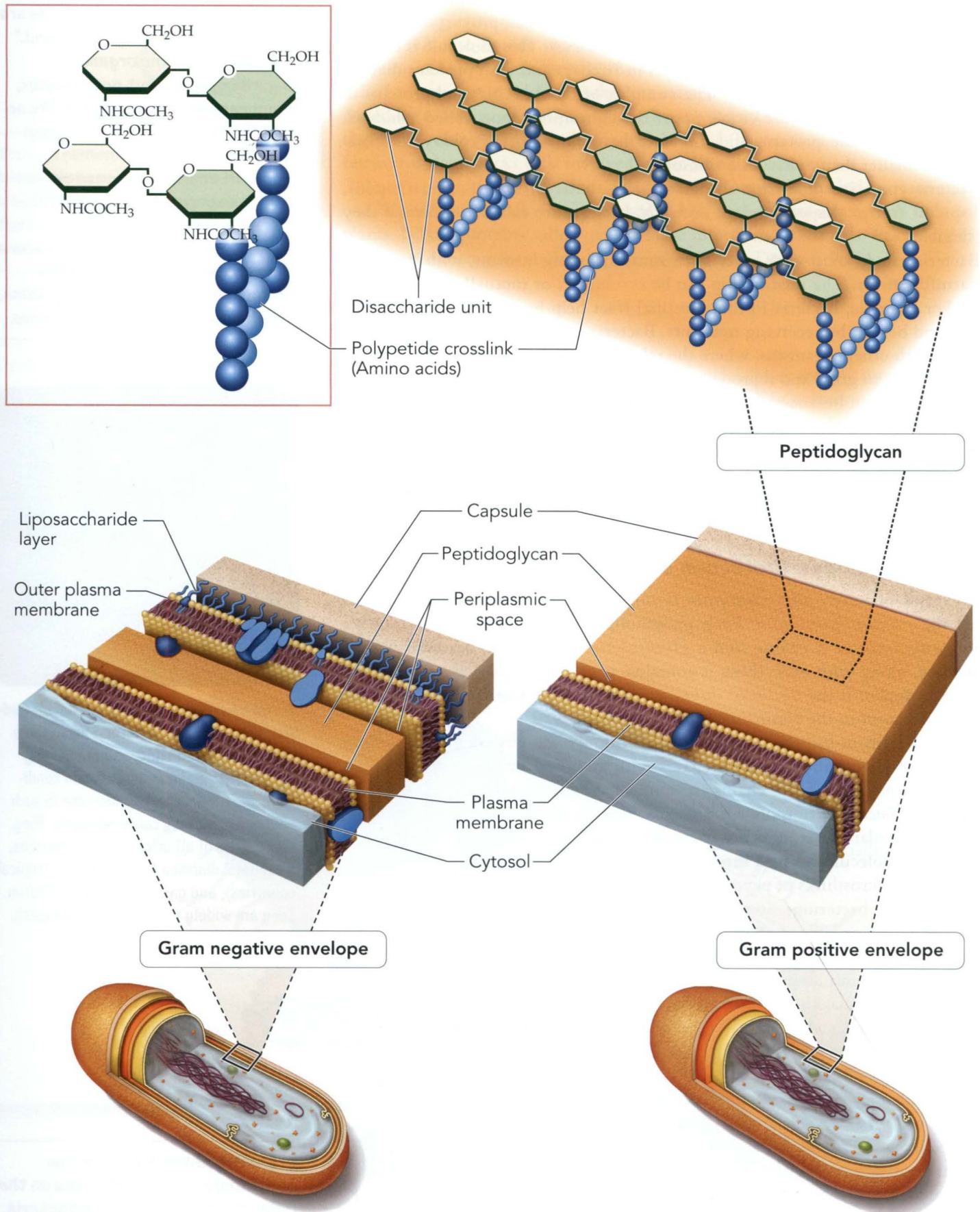


E. coli bacteria, gram-negative bacilli (rod-shaped) bacteria, are normal inhabitants of the human intestine, and are usually harmless. However, under certain conditions their numbers may increase to such an extent that they cause infection. They cause 80% of all urinary tract infections, travellers' diarrhea (particularly in tropical countries), and gastroenteritis in children. They are widely used in genetic research.



In gram-positive bacteria, the peptidoglycan is copious and on the outside. In gram-negative bacteria, a smaller amount of peptidoglycan is located between two membranes.

FIGURE 1.7 Bacterial Envelope



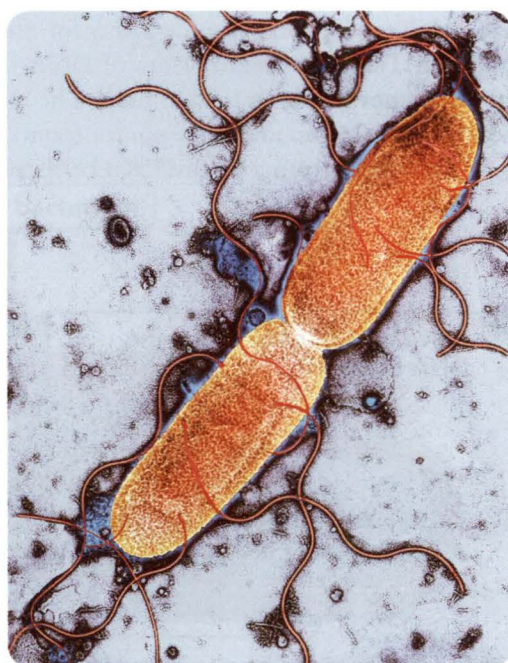
Gram-negative bacteria appear pink when gram stained. Their thin peptidoglycan cell walls allow most of the gram stain to be washed off. The small cell wall is located between two plasma membranes. The outer membrane is more permeable than the inner one, even allowing molecules the size of glucose to pass through easily. It also possesses *lipopolysaccharides*. The polysaccharide is a long chain of carbohydrates that protrudes outward from the cell. These polysaccharide chains can form a protective barrier from antibodies and many antibiotics. Some gram-negative bacteria possess *fimbriae*, or *pili*. Fimbriae are short tentacles that can attach a bacterium to a solid surface. They are not involved in cell movement.

Bacterial **flagella** are long, hollow, rigid, helical cylinders made from a globular protein called **flagellin**. Bacterial flagella rotate counterclockwise (from the point of view of looking at the cell from the outside) to propel the bacterium in a single direction. When they rotate clockwise, the bacterium *tumbles*. The tumbling changes the orientation of the bacterium, allowing it to move in a new direction. The flagellum is propelled using the energy from a proton gradient rather than from ATP. **Flagellar propulsion** allows bacteria to move toward favorable products, such as food sources. This directed movement toward substances that will promote the survival and growth of the bacterium is called **chemotaxis**.

Reproduction and Genetic Recombination

Bacteria do not undergo meiosis or mitosis. Instead they undergo cell division called **binary fission**, a type of asexual reproduction. (Sexual reproduction, by contrast, is one method of recombining genetic information between individuals of the same species to produce a genetically distinct individual.) Three alternative forms of **genetic recombination** allow bacteria to trade DNA: conjugation, transformation, and transduction.

In binary fission, circular DNA is replicated in a process similar to replication in eukaryotes. Two DNA polymerases begin at the same point on the circle (the **origin of replication**) and move in opposite directions, making complementary single strands that combine with their template strands to form two complete DNA double stranded circles. The cell then divides, leaving one circular chromosome in each daughter cell. The two daughter cells are genetically identical. Bacteria increase by **exponential growth**, meaning that each organism produces two offspring, which then each produce two offspring, and so on. They produce these organisms with little or no parental care until the essential nutrients of the environment are exhausted.



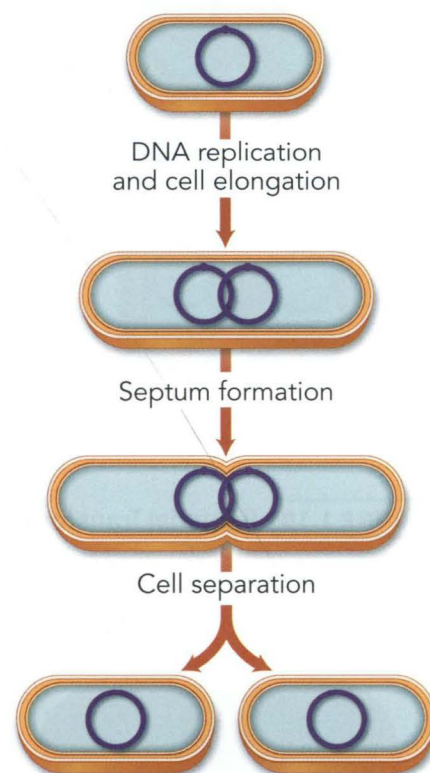
A single bacterium divides into identical daughter bacteria. Under optimal conditions, some bacteria can grow and divide extremely rapidly, and bacterial populations can double as quickly as every 10 minutes.

Return to these details when you read about mitochondria in the Metabolism Lecture. Mitochondria are similar to gram negative bacteria in that they also have two membranes and protons in their intermembrane space.



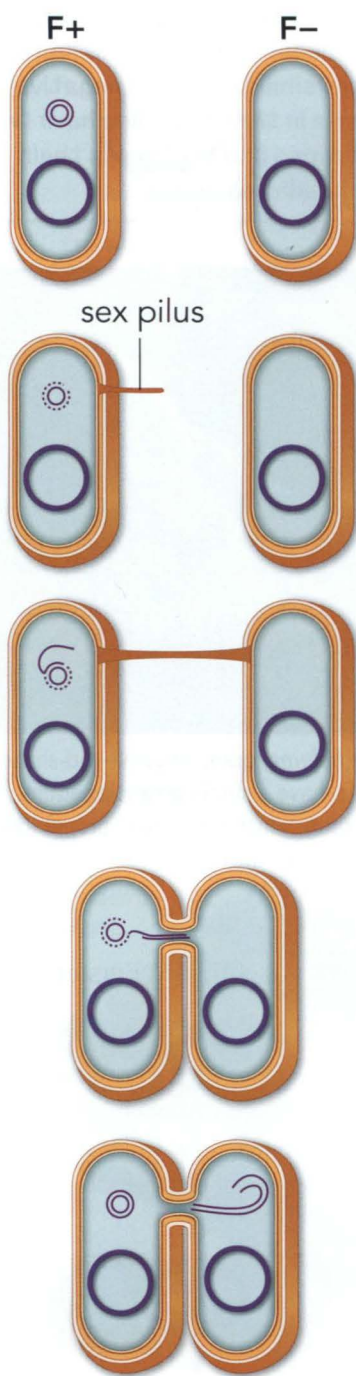
Vibrio cholerae, gram-negative rod-shaped bacteria, have a single polar flagellum (long, thin), which they use to propel themselves through water.

FIGURE 1.8 Binary Fission



Binary fission results in two genetically identical daughter cells.

FIGURE 1.9 Conjugation



The first method of genetic recombination, **conjugation** (Figure 1.9), involves the transfer of a **plasmid**. Plasmids are small circles of **extragenomic DNA**, meaning that they exist and replicate independently from the bacterial chromosome. If the plasmid can integrate into the chromosome, it is also called an *episome*. Plasmids are not essential to the survival of the bacteria that carry them.

Not all bacteria with plasmids can conjugate. In order for a bacterium to initiate conjugation, it must contain a *conjugative plasmid*. A conjugative plasmid possesses the gene for the *sex pilus*. The sex pilus is a hollow protein tube that connects two bacteria to allow the passage of the plasmid from one to the other. The passage of DNA is always from the cell that contains the conjugative plasmid to the cell that does not.

Two types of plasmids may be mentioned on the MCAT®: the *F plasmid* and the *R plasmid*. The F plasmid is called the *fertility factor* or *F factor* because it codes for the sex pilus. A bacterium with the F factor is called F+; one without the F factor is called F-. The F plasmid can be in the form of an episome, and if the pilus is made while the F factor is integrated into the chromosome, some or all of the rest of the chromosome may be replicated and transferred.

The R plasmid donates resistance to certain antibiotics. It is also a conjugative plasmid. It was once common practice to prescribe multiple antibiotics for patients to take simultaneously. Such treatment promotes conjugation of multiple R plasmids, producing a super-bacterium that contains many antibiotic resistances on one or more R plasmids. Some R plasmids are readily transferred between different species of bacteria, further promoting resistance and causing health problems for humans.

The second method of genetic recombination is transformation. **Transformation** is the process by which bacteria incorporate DNA from the external environment into their genomes. DNA may be added to the external environment in the lab, or it may be released by lyses of other bacteria. Transformation can be demonstrated by mixing heat-killed virulent bacteria with harmless living bacteria. The living bacteria can receive the genes of the heat-killed bacteria through transformation and thus become virulent.

The third type of genetic recombination, **transduction**, involves the transfer of genetic material by a virus. Transduction can occur when the capsid of a bacteriophage mistakenly encapsulates a DNA fragment of the host cell. When this virion infects a new bacterium, it injects harmless bacterial DNA fragments instead of virulent viral DNA fragments. The virus that mediates transduction is called a **vector**.

Within a bacterium, the genetic material of the chromosome is frequently rearranged. **Transposons** provide a way for nucleotides to move from one position to another. Transposons are pieces of DNA that are capable of "jumping" from one place to another along the genome. The enzyme *transposase* catalyzes the transposon's removal from and incorporation into the chromosome. Transposons are one way that genes from a plasmid can be incorporated into the genome.

FIGURE 1.10 Bacterial Transformation

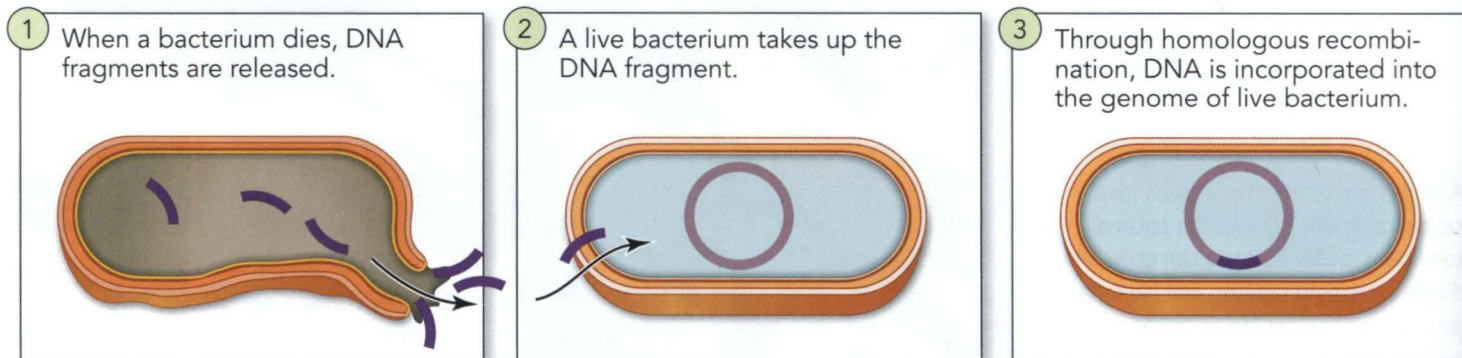
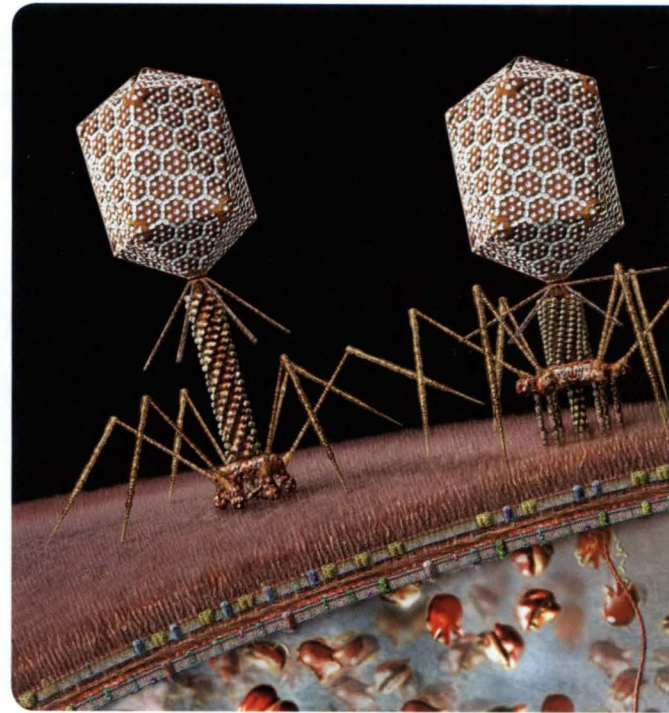
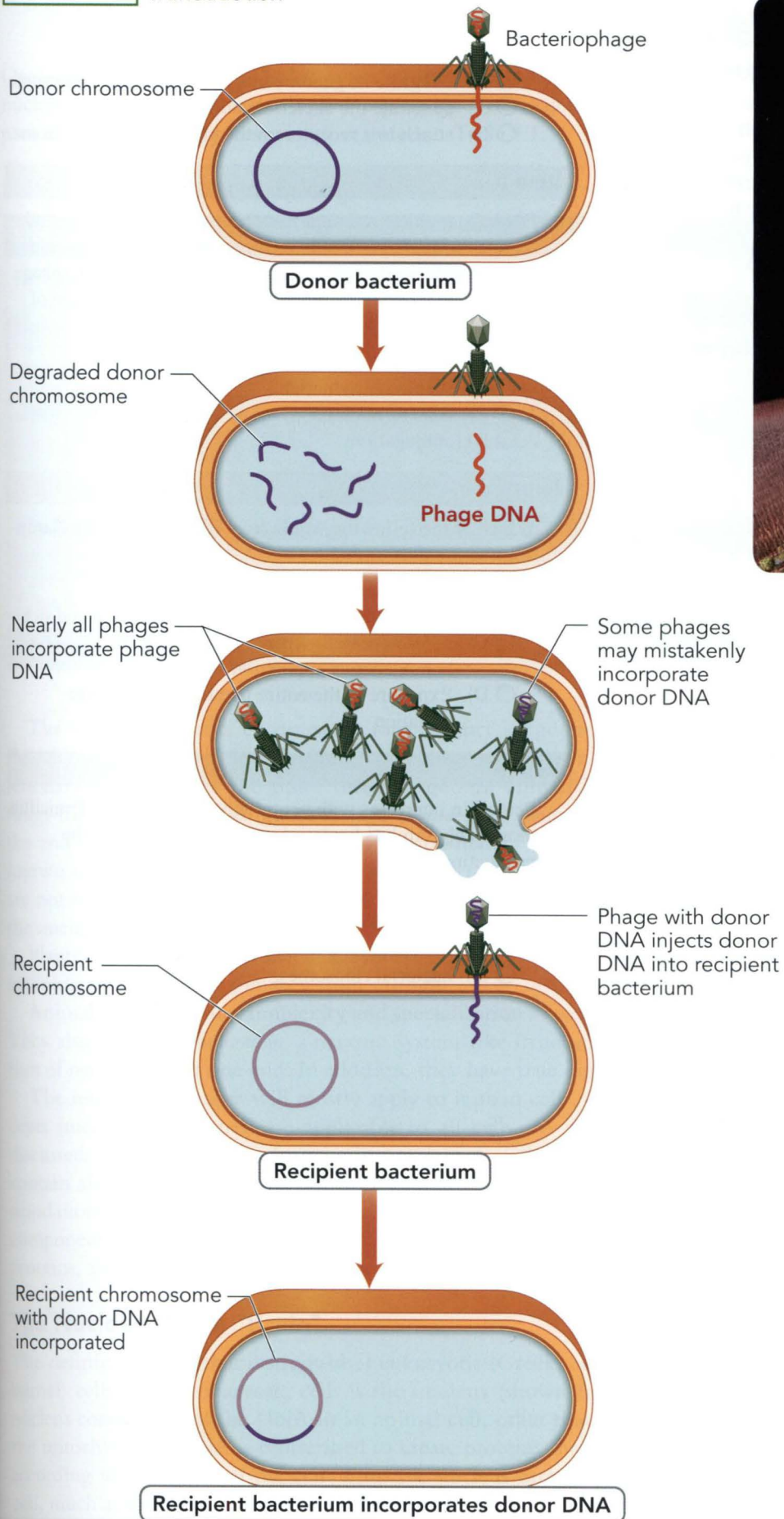


FIGURE 1.11 Transduction



A bacteriophage lands on the surface of a bacterium and injects its DNA into the cell.

These questions are NOT related to a passage.

Item 1

Which of the following events does NOT play a role in the life cycle of a typical retrovirus?

- ☐ A) Viral DNA is injected into the host cell.
- ☐ B) Viral DNA is integrated into the host genome.
- ☐ C) The gene for reverse transcriptase is transcribed and the mRNA is translated inside the host cell.
- ☐ D) Viral DNA incorporated into the host genome may be replicated along with the host DNA.

Item 2

If two species are members of the same order, they must also be members of the same:

- ☐ A) habitat.
- ☐ B) family.
- ☐ C) class.
- ☐ D) biome.

Item 3

Most viruses that infect animals:

- ☐ A) enter the host cell via endocytosis.
- ☐ B) do not require a receptor protein to recognize the host cell.
- ☐ C) leave their capsid outside the host cell.
- ☐ D) can reproduce independently of a host cell.

Item 4

Which of the following structures is (are) found in prokaryotes?

- I. A cell wall containing peptidoglycan.
 - II. A plasma membrane lacking cholesterol
 - III. Ribosomes
- ☐ A) I only
 - ☐ B) II only
 - ☐ C) I and II only
 - ☐ D) I, II, and III

Item 5

Prior to infecting a bacterium, a bacteriophage must:

- ☐ A) reproduce, making copies of the phage chromosome.
- ☐ B) integrate its genome into the bacterial chromosome.
- ☐ C) penetrate the bacterial cell wall completely.
- ☐ D) attach to a receptor on the bacterial cell membrane.

Item 6

DNA from phage resistant bacteria is extracted and placed on agar with phage-sensitive *E. coli*. After incubation it is determined that these *E. coli* are now also resistant to phage attack. The most likely mechanism for their acquisition of resistance is:

- ☐ A) transduction.
- ☐ B) sexual reproduction.
- ☐ C) transformation.
- ☐ D) conjugation.

Item 7

Which of the following would least likely disrupt the Hardy-Weinberg equilibrium?

- ☐ A) Emigration of part of a population
- ☐ B) A predator that selectively targets the old and sick
- ☐ C) A massive flood killing 15% of a large homogeneous population
- ☐ D) Exposure of the entire population to intense radiation

Item 8

Penicillin interferes with peptidoglycan formation. Penicillin most likely inhibits bacterial growth by disrupting the production of:

- ☐ A) bacterial plasma membranes.
- ☐ B) prokaryotic cell walls.
- ☐ C) the bacterial nucleus.
- ☐ D) bacterial ribosomes.

Eukaryotic Cells: Membrane Bound Organelles

Organisms in the domain Eukarya are characterized by cells that each have a nucleus and other membrane bound organelles. The major differences between prokaryotes and eukaryotes are summarized in Table 1.1.

TABLE 1.1 > Prokaryotes vs. Eukaryotes

Prokaryotes	Eukaryotes
No membrane bound nucleus	True membrane bound nucleus
No membrane bound organelles	Membrane bound organelles
"Naked" DNA, without histone proteins	DNA is coiled with histone proteins
mRNA does not undergo post-translational modifications	mRNA undergoes splicing, addition of Poly-A tail, and addition of 5' cap
Ribosomes are smaller	Ribosomes are larger
Cell walls are composed of peptidoglycan	Cell walls, if present, are composed of chitin (fungi) or cellulose (plants)
Flagella are made of flagellin	Flagella are made of microtubules
Division by binary fission	Division by mitosis

The domain Eukarya encompasses four distinct kingdoms. The kingdom of *Protista* contains the oldest organisms of the domain Eukarya, as well as the evolutionary precursors of the other three kingdoms: animal-like, plant-like, and fungi-like protists. The kingdoms *Fungi*, *Plantae*, and *Animalia* all separated from the end of this evolutionary branch at approximately the same time. Fungi are known for their filaments called *hyphae* that form masses of mycelium. Hyphae are not truly multicellular, but are divided by thin walls called *septa* that separate the nuclei.

Plants are true multicellular eukaryotes. They are all *photosynthetic autotrophs*, meaning that they obtain energy from sunlight.

Animals exhibit tissue complexity and specialization as well as body symmetry. They also exhibit *cephalization*, a nervous system-like structure with a concentration of nerve tissue at one end. In addition, they have true digestive tracts.

The rest of this lecture will mostly apply to human cells, although some concepts (such as membranes) are applicable to all cells. As cellular organelles are discussed, their roles in the functioning of organs will be emphasized. All cells contain all of these organelles, but organelle functions can sometimes be understood more clearly using specific organs as analogies or examples. Also, notice that components of the cell are organized according to their physical properties. DNA, proteins, and lipids are all stored and processed in separate places within the cell.

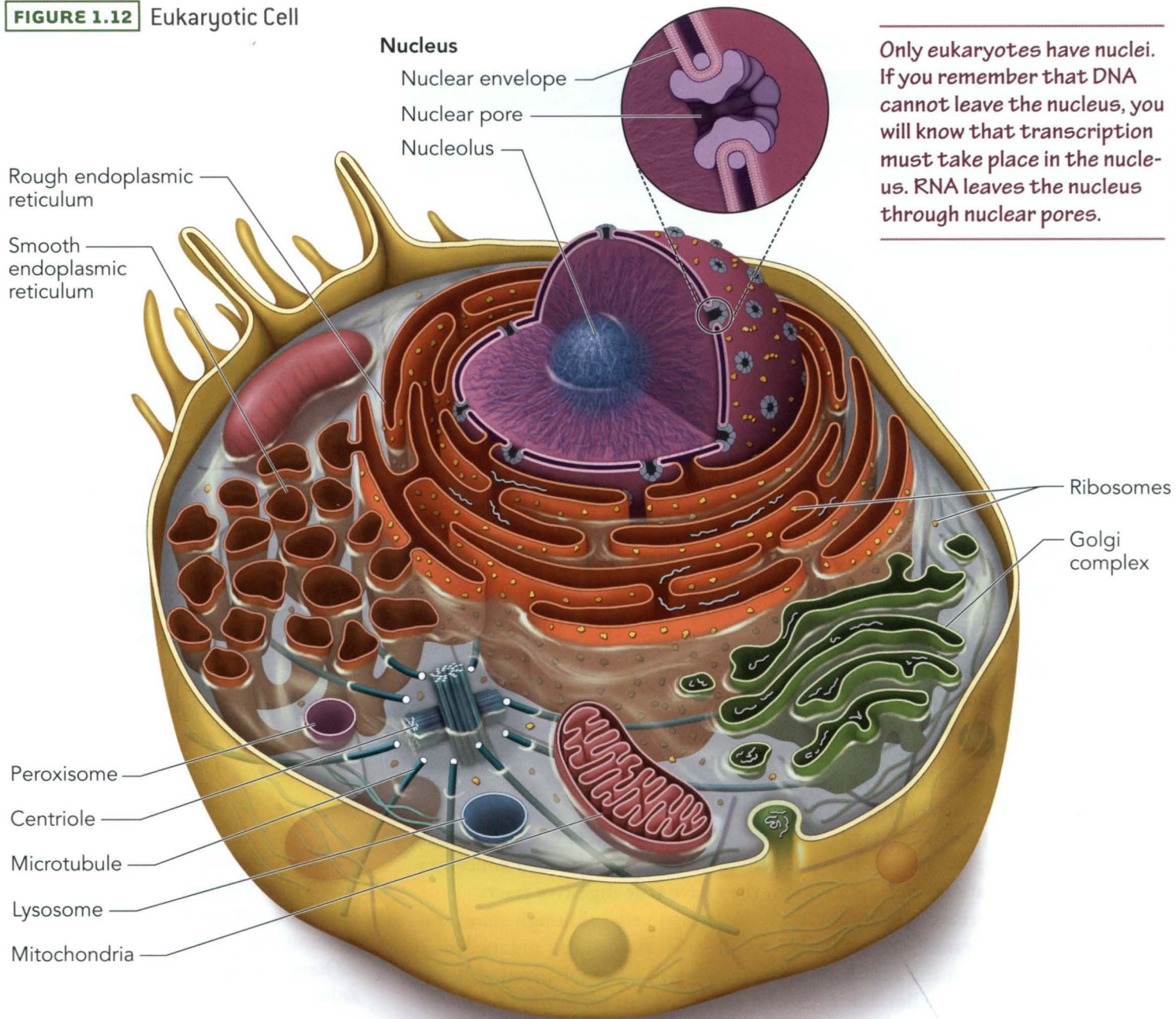
The Nucleus as the "Brain"

The defining feature that distinguishes eukaryotic (Greek: eu → well, karyos → kernel) cells from prokaryotic cells is the **nucleus** (shown in Figure 1.12). The nucleus contains all of the DNA in an animal cell, other than a small amount in the mitochondria. DNA is transcribed to create proteins that carry out functions according to the needs of the cell. Thus the nucleus directs the activities of the cell, much as the brain directs the activities of the body. Both the nucleus and the brain receive input from the environment and coordinate a response.

Don't worry about memorizing the features of the Fungi, Plantae, and Animalia kingdoms. They are included here to help you see what makes animals unique.

The aqueous fluid inside the nucleus is called the *nucleoplasm*. The nucleus is wrapped in a double phospholipid bilayer called the **nuclear envelope**, which is perforated with large holes called **nuclear pores**. RNA can exit the nucleus through the nuclear pores, but DNA cannot. The nucleus contains an area called the **nucleolus**, where ribosomal RNA (rRNA) is transcribed and the subunits of the ribosomes are assembled. The nucleolus is not separated from the rest of the nucleus by a membrane.

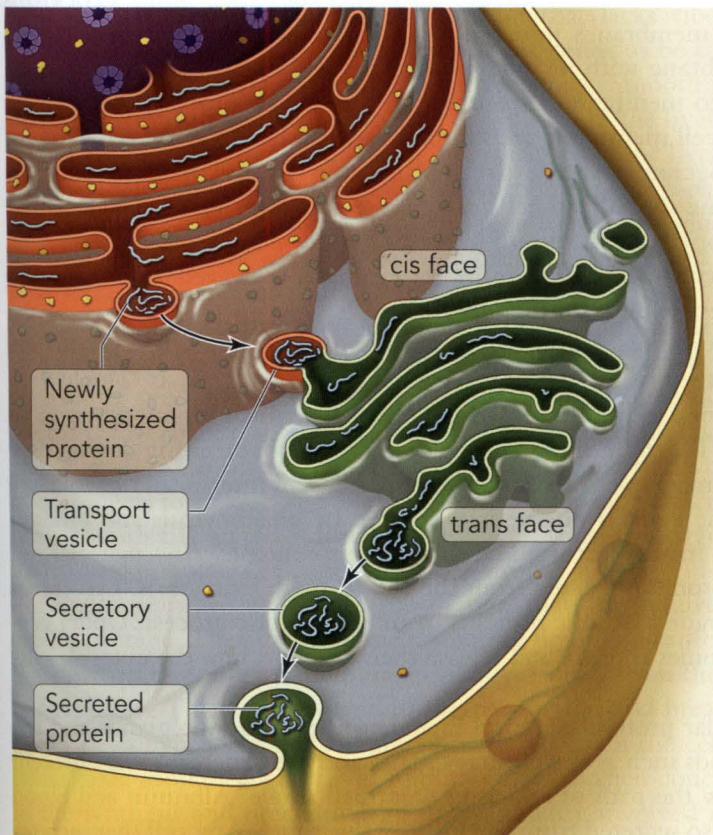
FIGURE 1.12 Eukaryotic Cell



Proteins and Vesicles

Protein synthesis begins on a ribosome, using mRNA as a template. As described in the Genetics Lecture, mRNA is transcribed from DNA in the nucleus and then exits the nucleus so that protein synthesis can occur in the cytosol. The mRNA is translated on a ribosome, which feeds the newly synthesized protein into the cytosol or the endoplasmic reticulum, depending on the protein's final destination.

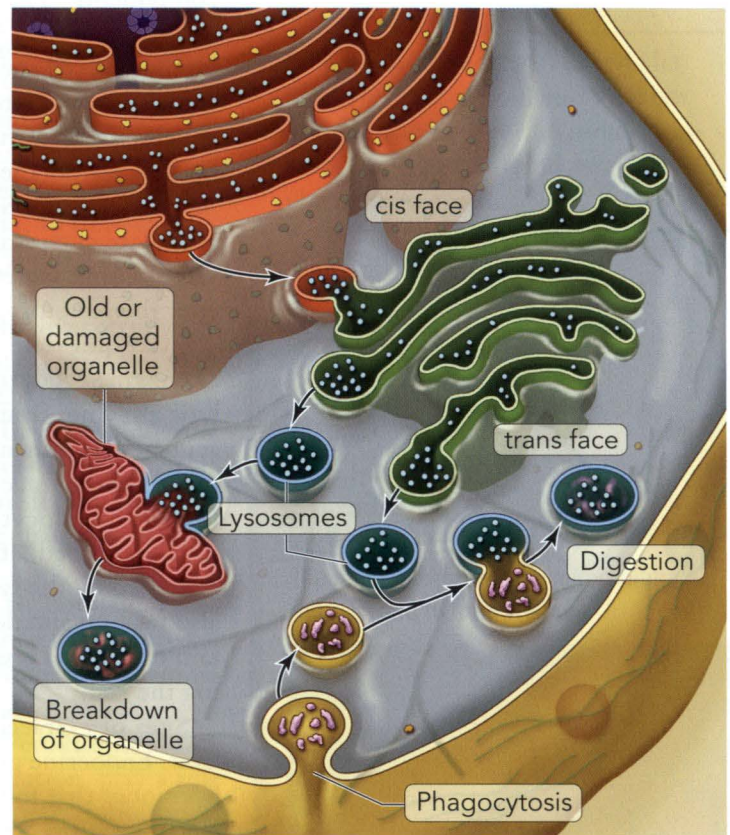
Genetics
BIOLOGY 1

FIGURE 1.13 Trafficking of Secretory Proteins

Proteins that will remain in the cytosol, the aqueous solution inside the cell, are translated in the cytosol. Examples of these proteins include the enzymes of glycolysis and actin filaments in muscle. Both are translated in the cytosol and remain there.

Proteins that will ultimately be exported from the cell or sequestered in a vesicle are translated on the **endoplasmic reticulum (ER)**. Proteins that are exported from the cell include protein hormones, such as ACTH, and bloodstream proteins, such as albumin. The ER is a thick maze of membranous walls in the eukaryotic cell separating the cytosol from the **ER lumen** or *cisternal space*. In some places the ER lumen is contiguous with the outer layer of the nuclear envelope. ER near the nucleus has many ribosomes attached to it on the cytosolic side, giving it a granular appearance, and thus is called the **rough ER**. As mRNA is translated, a particular sequence of amino acids known as a *signal sequence*, if present, directs the protein to the ER membrane for the completion of translation. Proteins that are translated on the rough ER are propelled into the ER lumen as they are created.

The newly synthesized proteins are moved through the lumen toward the **Golgi apparatus** or *Golgi complex*. The Golgi apparatus is a series of flattened, membrane bound sacs whose major functions are packaging and secreting proteins. Small *transport vesicles* bud off from the ER and carry proteins across the cytosol to the Golgi. The Golgi then organizes and concentrates the proteins as they are shuttled by transport vesicles progressively outward from one compartment to the next. Proteins are distinguished by their signal sequences and carbohydrate chains. The Golgi may alter proteins chemically by *glycosylation*, the addition of a carbohydrate, or by removing amino acids. The end-products of the Golgi are vesicles full of proteins. The vesicles may be expelled from the cell as secretory vesicles, released from the Golgi to mature into lysosomes, or transported to other parts of the cell such as the mitochondria or even back to the ER, as shown in Figures 1.13 and 1.14.

FIGURE 1.14 Transport and Fate of Lysosomal Proteins

The movement of a protein from the cytosol to the ER is just one example of the use of a signal sequence. Signal sequences direct molecules all around the cell – to lysosomes, the mitochondrion, and even to the nucleus.

The Golgi apparatus can be thought of as an assembly line. Proteins are passed from one compartment to the next and modified along the way.

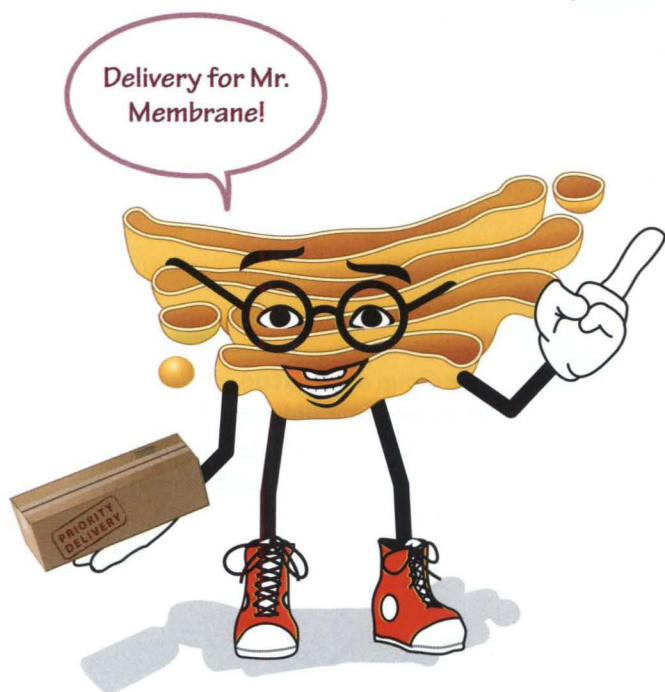
Secretory vesicles may contain enzymes, growth factors, or extracellular matrix components. They release their contents through exocytosis. Since exocytosis incorporates vesicle membranes into the cell membrane, secretory vesicles can supply the cell membrane with its integral proteins and lipids. Secretory vesicles can also contribute to membrane expansion. In the reverse process, endocytotic vesicles made at the cell membrane are shuttled back to the Golgi for recycling of the cell membrane. Secretory vesicles are continuously released by most cells (*constitutive secretion*). Some specialized cells can release secretory vesicles in response to certain chemical or electrical stimuli (*regulated secretion*). Some proteins are activated within secretory vesicles. Proinsulin, for example, is cleaved to insulin only after the secretory vesicle buds off the Golgi.

Lysosomes are a type of vesicle that contain **hydrolytic enzymes**. This type of enzyme catalyzes the breakdown of macromolecules by hydrolysis. The hydrolytic enzymes contained in lysosomes are *acid hydrolases*, which function best in an acidic environment. Together, these enzymes are capable of breaking down every major type of macromolecule. Lysosomes usually have an interior pH of 5. They fuse with endocytotic vesicles (the vesicles formed by phagocytosis and pinocytosis, described later in this lecture) and digest their contents. Any material not degraded by the lysosome is ejected from the cell through exocytosis. Lysosomes also take up and degrade cytosolic proteins in an endocytotic process. Under certain conditions lysosomes rupture and release their contents into the cytosol, killing the cell.

Sites of extracellular protein secretion include some endocrine glands and the liver. Endocrine glands such as the pituitary gland and the pancreas create protein hormones that follow the path of secretion described above. Albumin and blood clotting factors are also secreted from the liver by this route. Any cell that secretes proteins can be expected to have well-developed ER and Golgi bodies. However, lysosomes are not usually seen in high concentration in living cells. They exist in large concentrations in cells that are about to undergo **apoptosis**, also called **programmed cell death**. Apoptosis can contribute to development. For example, at one point during the development of a human embryo, the hands are webbed. The skin between the fingers eventually undergoes apoptosis, which is mediated by an increased concentration of lysosomes.

Biological Molecules
and Enzymes
BIOLOGY 1

Endocrine System
BIOLOGY 2



There is a lot of background information here that the MCAT® will not directly test. For the MCAT®, know the bolded terms and focus on the following points:

1. There are many internal compartments in a cell (organelles) separated from the cytosol by membranes.
2. Rough ER has ribosomes attached to its cytosolic side, and it synthesizes virtually all proteins that do not belong in the cytosol. Proteins synthesized on the rough ER are pushed into the ER lumen and sent to the Golgi apparatus.
3. The Golgi apparatus modifies and packages proteins for use in other parts of the cell and outside the cell.
4. Lysosomes contain hydrolytic enzymes that digest substances taken into the cell by endocytosis. Lysosomes come from the Golgi apparatus.

Smooth ER and Peroxisomes: Fat Storage and Toxin Breakdown

The portion of the endoplasmic reticulum that lacks ribosomes is called the **smooth endoplasmic reticulum**. Smooth ER tends to be tubular, in contrast to rough ER, which tends to resemble flattened sacs. Smooth ER has a number of functions that differ according to the type of cell. In the liver and kidney, smooth ER contains *glucose 6-phosphatase*, the enzyme used in the liver, intestinal epithelial cells, and renal tubule epithelial cells to hydrolyze *glucose 6-phosphate* to glucose, an important step in the breakdown of glycogen to produce glucose. In muscle cells, the smooth ER is known as the sarcoplasmic reticulum, and it sequesters calcium away from actin and myosin.

The smooth ER also plays a role in lipid metabolism. In the liver, triglycerides are produced in the smooth ER. These lipids are stored in **adipocytes**, cells containing predominantly fat droplets, again inside of smooth ER. Such cells contribute to energy storage and body temperature regulation. In some endocrine glands, such as the adrenal gland, the smooth ER and the cytosol share in the role of cholesterol formation and its subsequent conversion to various steroids. In addition, smooth ER oxidizes foreign substances, thus detoxifying drugs, pesticides, toxins, and pollutants.

Peroxisomes are vesicles in the cytosol that are involved in both lipid and protein storage. They grow by incorporating lipids and proteins from the cytosol. Rather than budding off membranes like lysosomes from the Golgi, peroxisomes self-replicate. They are involved in the production and breakdown of **hydrogen peroxide**, a byproduct that has the potential to harm the cell. Peroxisomes inactivate toxic substances such as alcohol, regulate oxygen concentration, play a role in the synthesis and breakdown of lipids, and are involved in the metabolism of nitrogenous bases and carbohydrates.

Mitochondria and Energy

Mitochondria (Figure 1.15) are the powerhouses of the eukaryotic cell. They are the site of ATP production, as described in the Metabolism Lecture. According to the *endosymbiotic theory*, mitochondria may have evolved from a symbiotic relationship between ancient prokaryotes and eukaryotes. Like prokaryotes, mitochondria contain circular DNA that replicates independently from the nuclear DNA. Mitochondrial DNA contains no histones or nucleosomes. Most animals have a few dozen to several hundred molecules of circular DNA in each mitochondrion.

The genes in mitochondrial DNA code for mitochondrial RNA that is distinct from the RNA in the rest of the cell. Thus mitochondria have their own ribosomes. However, most proteins used by mitochondria are coded for by nuclear DNA, not mitochondrial DNA. Antibiotics that block translation by prokaryotic ribosomes but not eukaryotic ribosomes also block translation by mitochondrial ribosomes. Some of the codons in mitochondria differ from the codons in the rest of the cell, an exception to the universal genetic code. Mitochondrial DNA is passed to offspring from the mother even in organisms in which male gametes contribute to the cytoplasm of the egg.

Like gram negative bacteria, mitochondria are surrounded by two phospholipid bilayers. The **inner membrane** invaginates (folds in on itself) to form *cristae*. The inner membrane holds the electron transport chain of aerobic respiration. Between the inner and **outer membrane** is the **intermembrane space**.

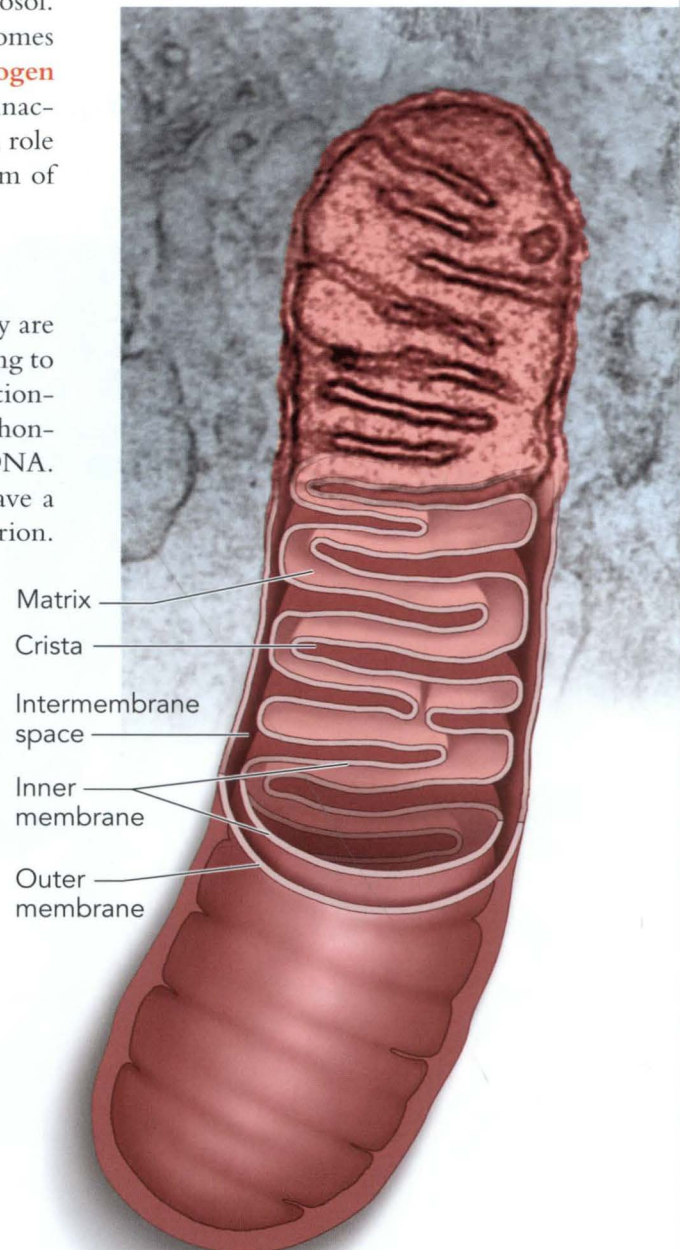
High concentrations of mitochondria are seen in the cell wherever energy needs are high. Muscle cells, for example, contain a large number of mitochondria.

When you see smooth ER on the MCAT®, think of lipid metabolism and storage as well as detoxification. Don't get carried away with the other details.

Metabolism BIOLOGY 1

FIGURE 1.15 Mitochondria

The inner membrane of a mitochondrion folds inward to form cristae.



The Cytoskeleton: Organizing Structure and Substances

The structure and motility of a cell is determined by a network of filaments called the **cytoskeleton**. The cytoskeleton anchors some membrane proteins and other cellular components, moves components within the cell, and moves the cell itself. The three basic parts of the cytoskeleton are microtubules, microfilaments, and intermediate filaments. Microtubules are larger than intermediate filaments, which are larger than microfilaments.

Microtubules provide a platform for **transport** within cells. For example, molecular motors can use microtubules to taxi secretory vesicles throughout the cell. The mitotic spindle that moves chromosomes around the cell is also made of microtubules. Furthermore, microtubules **support** the shape of the cell.

Structurally, microtubules are hollow tubes made from the protein *tubulin*. Tubulin is a globular protein that polymerizes into long straight filaments under certain conditions. Thirteen of these filaments lie alongside each other to form the tube. Microtubules have a + and – end. The – end attaches to a **microtubule-organizing center (MTOC)**. A microtubule grows away from an MTOC at its + end. The major MTOC in animal cells is the *centrosome*. The centrosome is composed of a pair of **centrioles**, which function in the production of flagella and cilia but are not necessary for microtubule production.

Don't confuse eukaryotic flagella with prokaryotic flagella. Eukaryotic flagella are made from a 9+2 microtubule configuration; a prokaryotic flagellum is a thin strand of a single protein called flagellin. Eukaryotic flagella undergo a whip-like action, while prokaryotic flagella rotate.

FIGURE 1.16 Structure of Flagella and Cilia

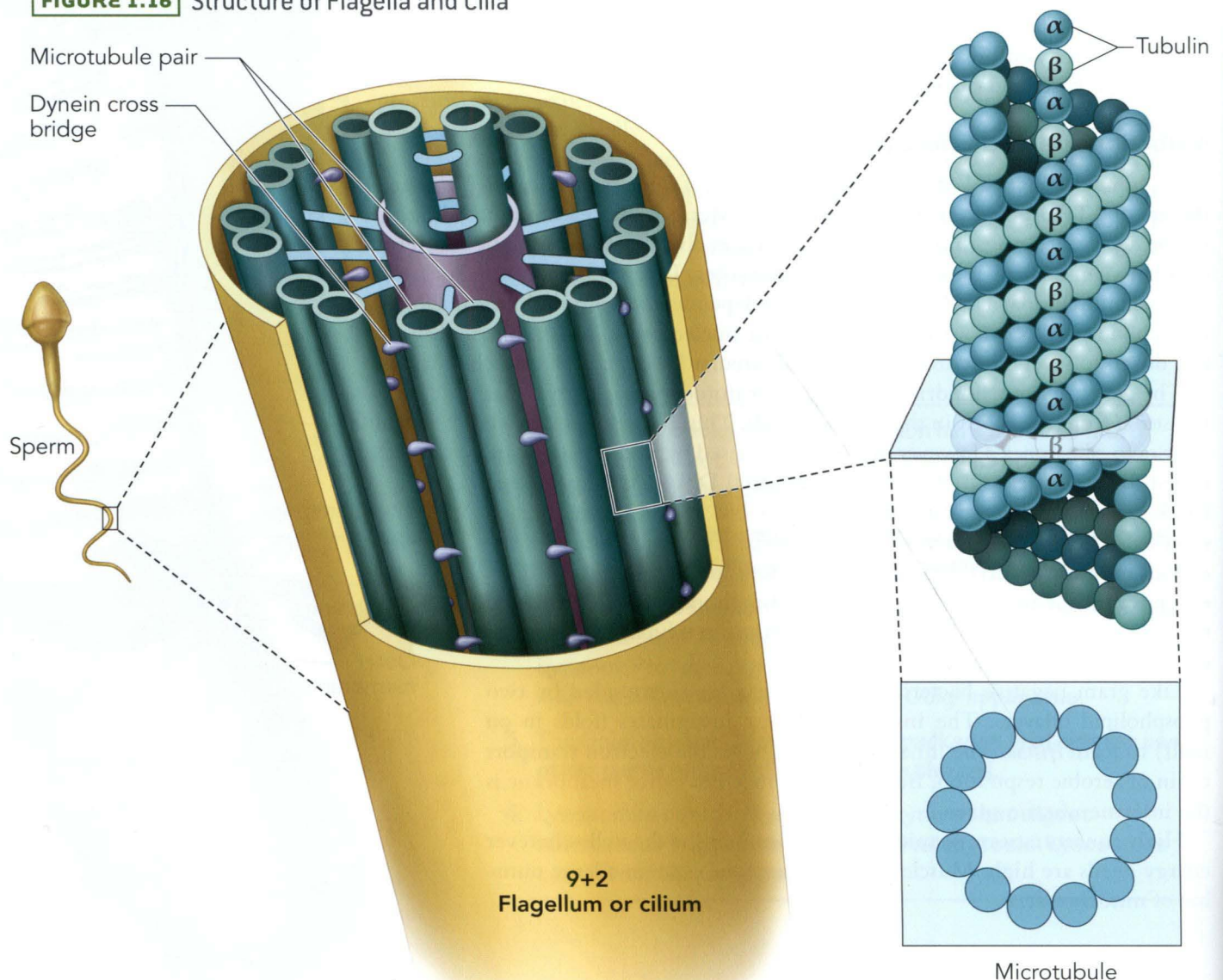
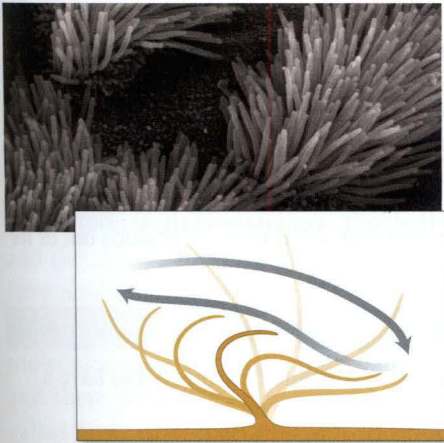
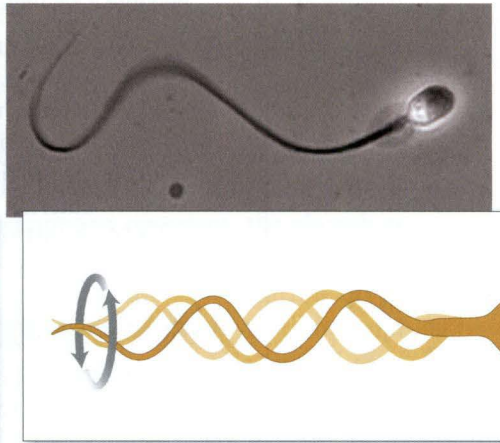


FIGURE 1.17 Motion of Flagella and Cilia

Lung and trachea cilia



Spermatozoan flagellum



Why would it be useful for a cell to be able to shift the fluid around it, other than for movement? One example is in the respiratory tract, where cilia move fluid and foreign substances so that they can be removed from the body.

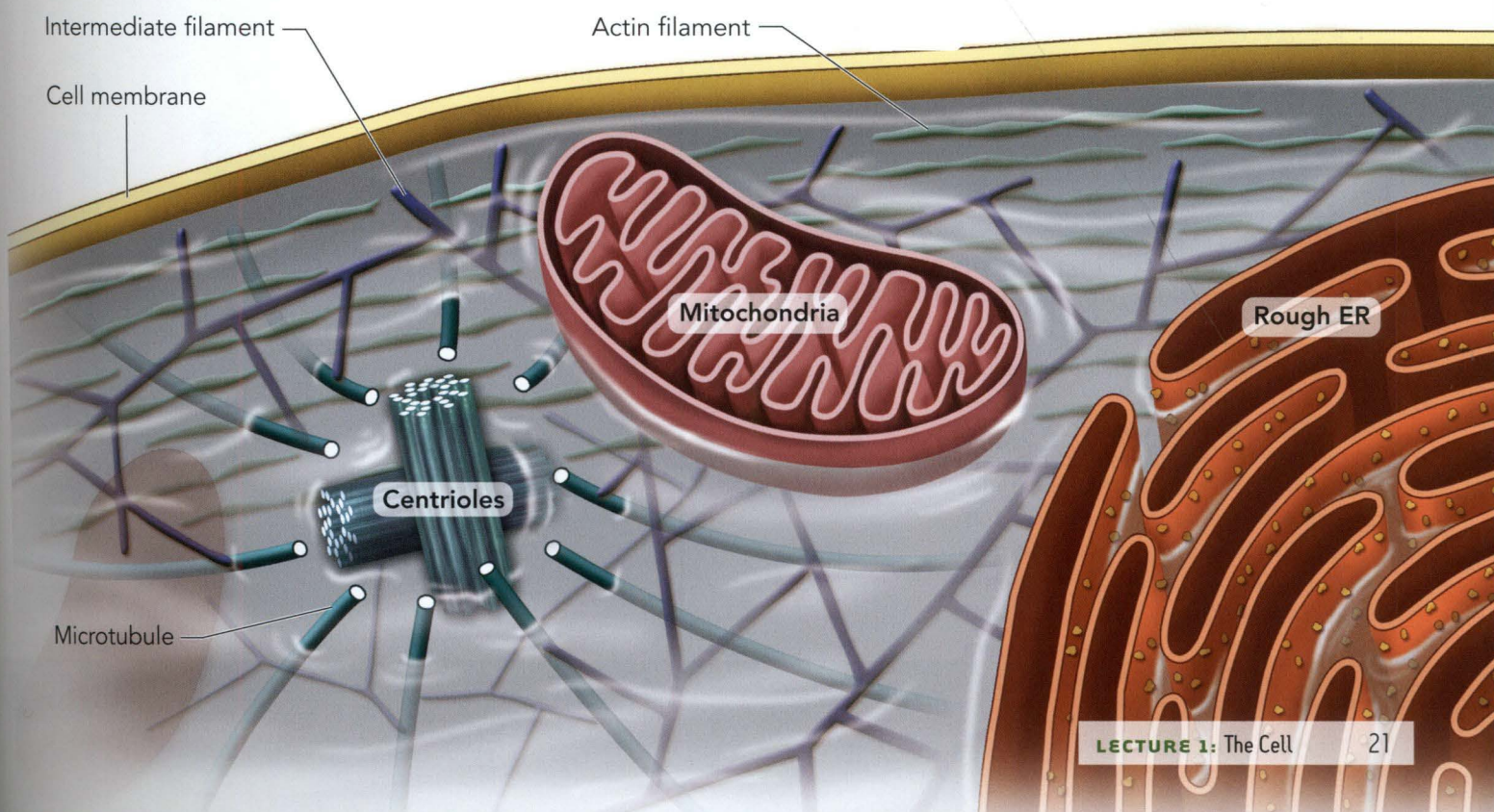
Flagella and **cilia** are specialized structures made from microtubules. They function to move fluid, causing the cell itself or nearby substances to move. The major portion of each flagellum and cilium contains nine pairs of microtubules that form a circle around two lone microtubules in a **9+2 arrangement**. Cross bridges made from the protein **dynein** connect each outer pair of microtubules to its neighbor. The cross bridges cause microtubule pairs to slide along their neighbors, creating a whip action in cilia that causes fluid to move laterally, or a wiggle action in flagella that causes fluid to move directly away from the cell.

Microfilaments are another name for actin filaments. They interact with myosin to cause muscle contraction. They are also responsible for the pinching of the cytoplasm during cytokinesis (**cleavage**). Notice that both of these actions reshape the cell membrane.

Intermediate filaments are the third portion of the cytoskeleton, which maintain the cell's shape. Intermediate filaments are not nearly as dynamic as microtubules or microfilaments and primarily serve to impart structural rigidity to the cell. Keratin, a type of intermediate filament found in epithelial cells, is associated with hair and skin.

Genetics
BIOLOGY 1

FIGURE 1.18 Cellular Filaments



These questions are NOT related to a passage.

Item 9

All of the following are composed of microtubules EXCEPT:

- ☐ A) the tail of a sperm cell.
- ☐ B) the spindle apparatus.
- ☐ C) the cilia of the fallopian tubes.
- ☐ D) the flagella of bacteria.

Item 10

Which of the following is true concerning the nucleolus?

- ☐ A) It is bound by a phospholipid membrane.
- ☐ B) It disappears during prophase.
- ☐ C) It is the site of translation of ribosomal RNA.
- ☐ D) It is found in most bacteria.

Item 11

In some specialized cells, glucose is transported against its concentration gradient via an integral protein using the energy of the sodium ion electrochemical gradient. If no ATP is used for this transport, it is most likely:

- ☐ A) active transport.
- ☐ B) facilitated transport.
- ☐ C) passive transport.
- ☐ D) osmosis.

Item 12

Which of the following cells would be expected to contain the most smooth endoplasmic reticulum?

- ☐ A) A liver cell
- ☐ B) An islet cell from the pancreas
- ☐ C) A mature sperm
- ☐ D) A zygote

Item 13

Which of the following is not a membrane bound organelle?

- ☐ A) The golgi body
- ☐ B) The nucleus
- ☐ C) The smooth endoplasmic reticulum
- ☐ D) The ribosome

Item 14

One function of the liver is to detoxify alcohol taken into the body. The organelle within the liver cell that most directly affects this process is:

- ☐ A) the smooth endoplasmic reticulum.
- ☐ B) the nucleus.
- ☐ C) the Golgi apparatus.
- ☐ D) the rough endoplasmic reticulum.

Item 15

When a primary lysosome fuses with a food vesicle to become a secondary lysosome:

- ☐ A) its pH drops via active pumping of protons into its interior.
- ☐ B) its pH drops via active pumping of protons out of its interior.
- ☐ C) its pH rises via active pumping of protons into its interior.
- ☐ D) its pH rises via active pumping of protons out of its interior.

Item 16

Which of the following cells would be expected to have a well-developed rough endoplasmic reticulum?

- ☐ A) Pancreatic cells
- ☐ B) Adipocytes
- ☐ C) Muscle cells
- ☐ D) Neurons

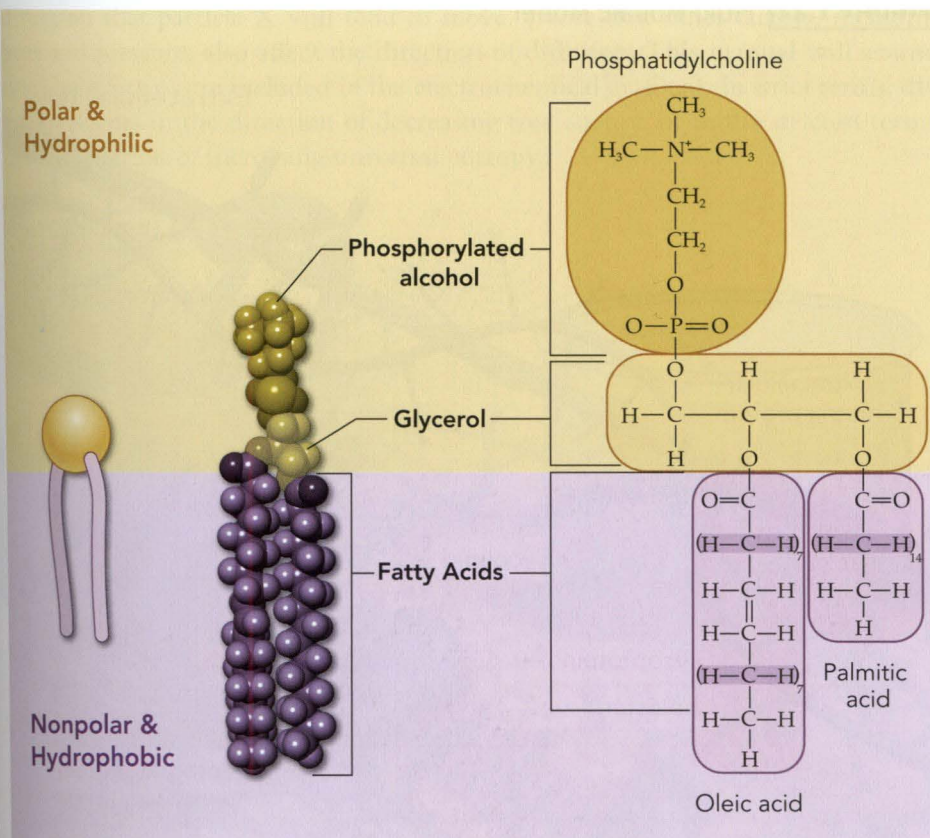
1.6 Membrane Transport

The eukaryotic cell, like the prokaryotic cell, has a phospholipid bilayer membrane surrounding the cytosol. A major function of the cell membrane is to regulate the substances that enter and leave the cell. Cell membranes also facilitate communication between cells.

A phospholipid (Figure 1.19) is made up of a glycerol backbone with a phosphate group and two fatty acid chains attached. The phospholipid is often drawn as a balloon with two strings. The balloon portion represents the phosphate group, and the strings represent the fatty acids. The phosphate group is polar, while the fatty acid chains are nonpolar, making the molecule **amphipathic** (having both a polar and a nonpolar portion). When placed in aqueous solution, amphipathic molecules spontaneously aggregate, turning their polar ends toward the solution and their nonpolar ends toward each other. The resulting spherical structure is called a **micelle** (Figure 1.20). If enough phospholipids are present in a solution that is subjected to ultrasonic vibrations, *liposomes* may form. A liposome is a vesicle surrounded by and filled with aqueous solution. It contains a lipid bilayer like that of a plasma membrane.

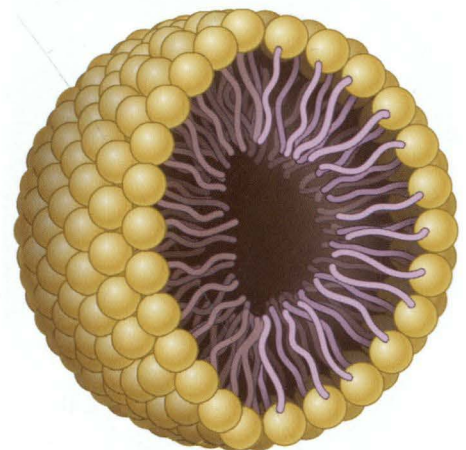
The inner and outer layers of a membrane are called *leaflets*. In addition to phospholipids, the plasma membrane contains other types of lipids such as glycolipids. Eukaryotic membranes, unlike prokaryotic plasma membranes, contain steroids such as cholesterol. Lipid types are arranged asymmetrically between the leaflets. For instance, glycolipids are found on the outer leaflet only.

FIGURE 1.19 Phospholipid Structure



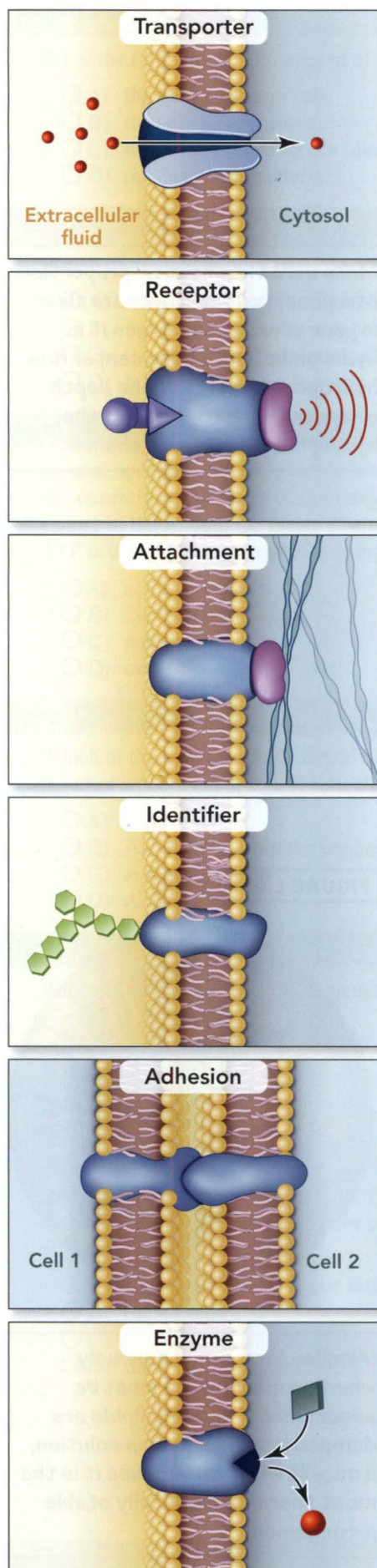
Make sure the chemical properties of a phospholipid bilayer are clear in your mind: at the edges it is hydrophilic, and at the center it is hydrophobic. Most of the depth of a membrane consists of the hydrophobic fatty acid chains.

FIGURE 1.20 Micelle



Micelles form spontaneously, whereas membranes must be assembled. If phospholipids are dumped into an aqueous solution, a micelle will form because it is the most thermodynamically stable arrangement.

FIGURE 1.21 Functions of Membrane Proteins

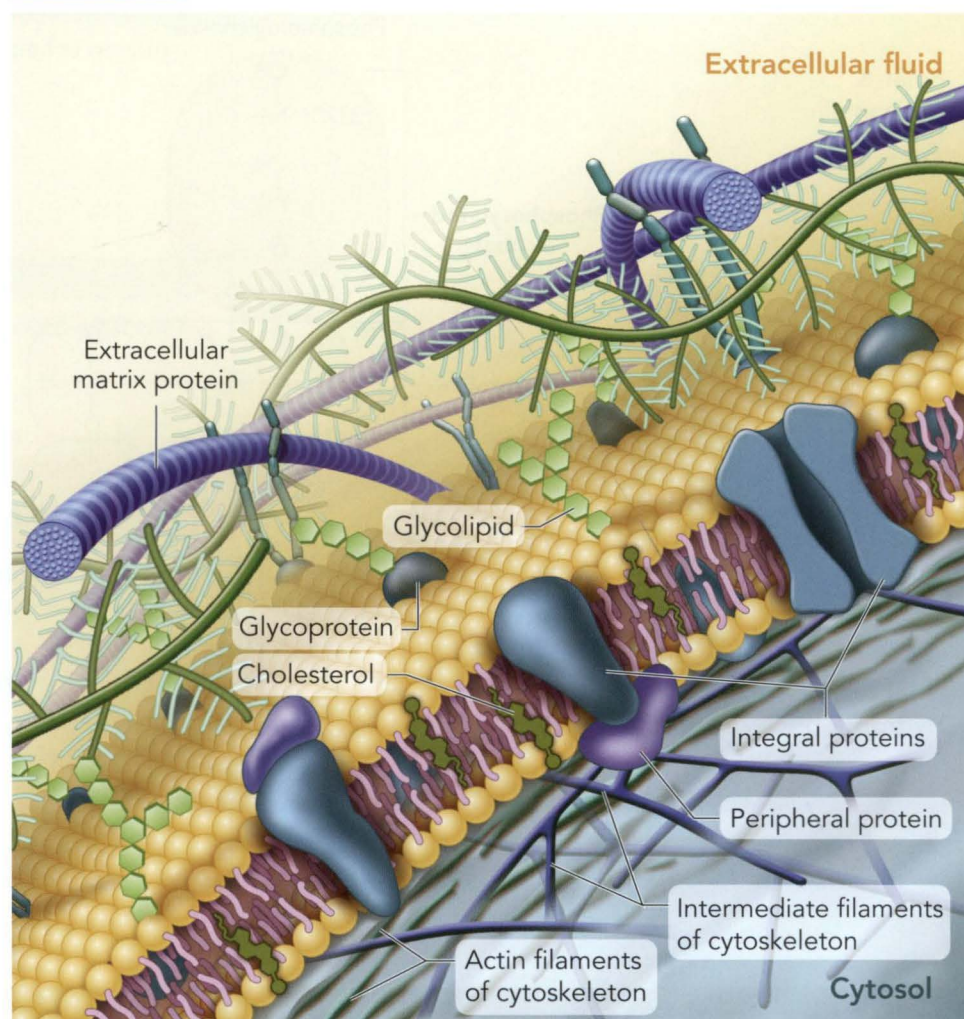


Proteins are also embedded within the plasma membrane. Amphipathic proteins can cross the membrane from the inside of the cell to the outside and are called **integral** or **intrinsic proteins**. By contrast, **peripheral** or **extrinsic proteins** are located on the surfaces of the membrane and are generally hydrophilic. They are ionically bonded to integral proteins or the polar group of a lipid. Both integral and peripheral proteins may contain carbohydrate chains, making them *glycoproteins*. The carbohydrate portion of a membrane glycoprotein always protrudes toward the outside of the cell. Membrane proteins are distributed asymmetrically throughout the membrane and between the leaflets. Neither proteins nor lipids flip easily from one leaflet to the other.

The model of the membrane just described is called the **fluid mosaic model** (Figure 1.22). The fluid part refers to the phospholipids and proteins, which can slide past each other. Since the forces holding the entire membrane together are intermolecular, the membrane is fluid; its parts can move laterally but cannot separate. The mosaic part refers to the asymmetrical layout of a membrane's lipids and proteins.

Most of the functions of membranes can be attributed to their proteins. Membrane proteins act as transporters, receptors, attachment sites, identifiers, adhesive proteins, and enzymes (Figure 1.21). As transporters, membrane proteins select which solutes enter and leave the cell. Other membrane proteins act as receptors by receiving chemical signals from the cellular environment. Some membrane proteins are attachment sites that anchor to the cytoskeleton. Membrane proteins can act as identifiers that other cells recognize. Adhesion by one cell to another is accomplished by membrane proteins. Many of the chemical reactions that occur within a cell are governed by membrane proteins on the inner surface.

FIGURE 1.22 Fluid Mosaic Model



A mosaic is a picture made by placing many small, colorful pieces side by side.

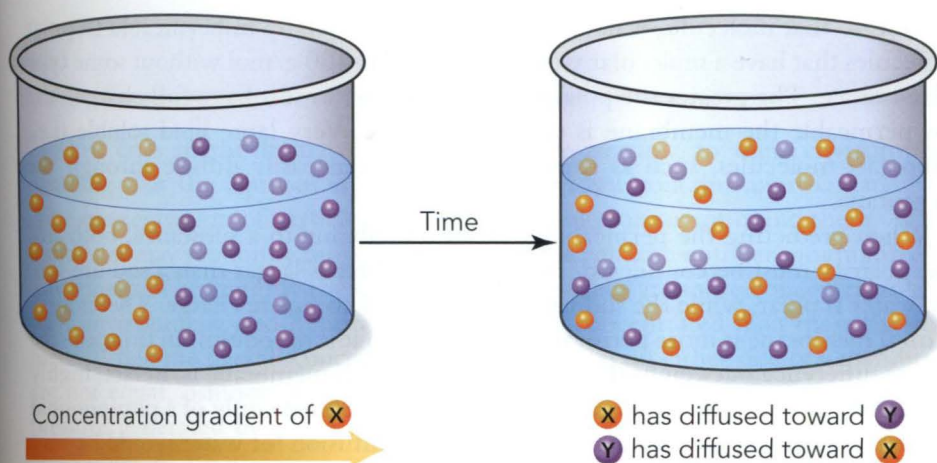
Membrane Transport and Solution Chemistry

The movement of a molecule across a membrane depends on two key factors: the electrochemical gradient experienced by the molecule and the chemical properties of the molecule.

A membrane is not just a barrier between two aqueous solutions of different compositions; it actually creates the difference in the compositions of the solutions. At normal temperatures for living organisms, all molecules move rapidly in random directions, frequently colliding with one another. This random movement is called *Brownian motion*. Brownian motion leads to the tendency of solutions to mix completely with each other over time. If solutions of two solutes, X and Y, are placed on opposite sides of the same container, the net movement of X will be toward Y. This movement is called **diffusion**. For solutes without an electric charge, diffusion occurs in the direction of lower concentration. In Figure 1.23, X diffuses toward the lower concentration of X, and Y diffuses toward the lower concentration of Y. A gradual change in the concentration of a compound over a distance is called a chemical concentration gradient.

The **chemical concentration gradient** is a series of vectors pointing in the direction of lower concentration. For charged solutes, there is also an **electrical gradient** pointing in the direction that a positively charged particle will tend to move. The two gradients can be added to form a single **electrochemical gradient** for a specific solute. The electrochemical gradient for compound X points in the direction that particle X will tend to move. (Note that other factors, including heat and pressure, also affect the direction of diffusion. This manual will assume that these factors are included in the electrochemical gradient. In strict terms, diffusion occurs in the direction of decreasing free energy, or in the strictest terms, in the direction of increasing universal entropy.)

FIGURE 1.23 Diffusion



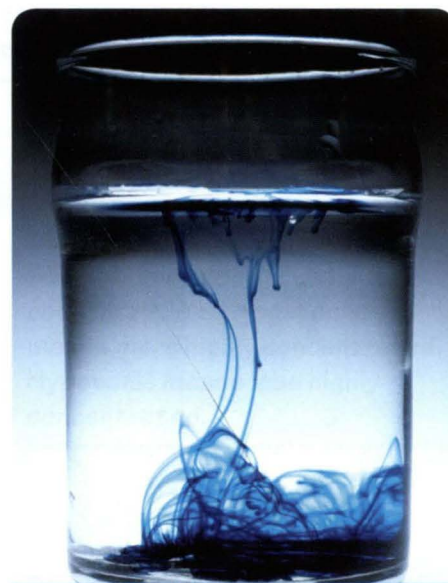
If compounds X and Y are separated by an impermeable membrane, diffusion stops. However, if the molecules of X can wiggle their way across the membrane, diffusion of X is only slowed. Since the membrane slows the diffusion of X but does not stop it, the membrane is **semipermeable** to compound X.

Figure 1.24 shows examples of membrane transport. Natural membranes are semipermeable to most compounds, but to varying degrees. Two characteristics of a compound, size and polarity, largely determine the permeability of the membrane to that compound. The bigger the molecule, the less permeable the mem-



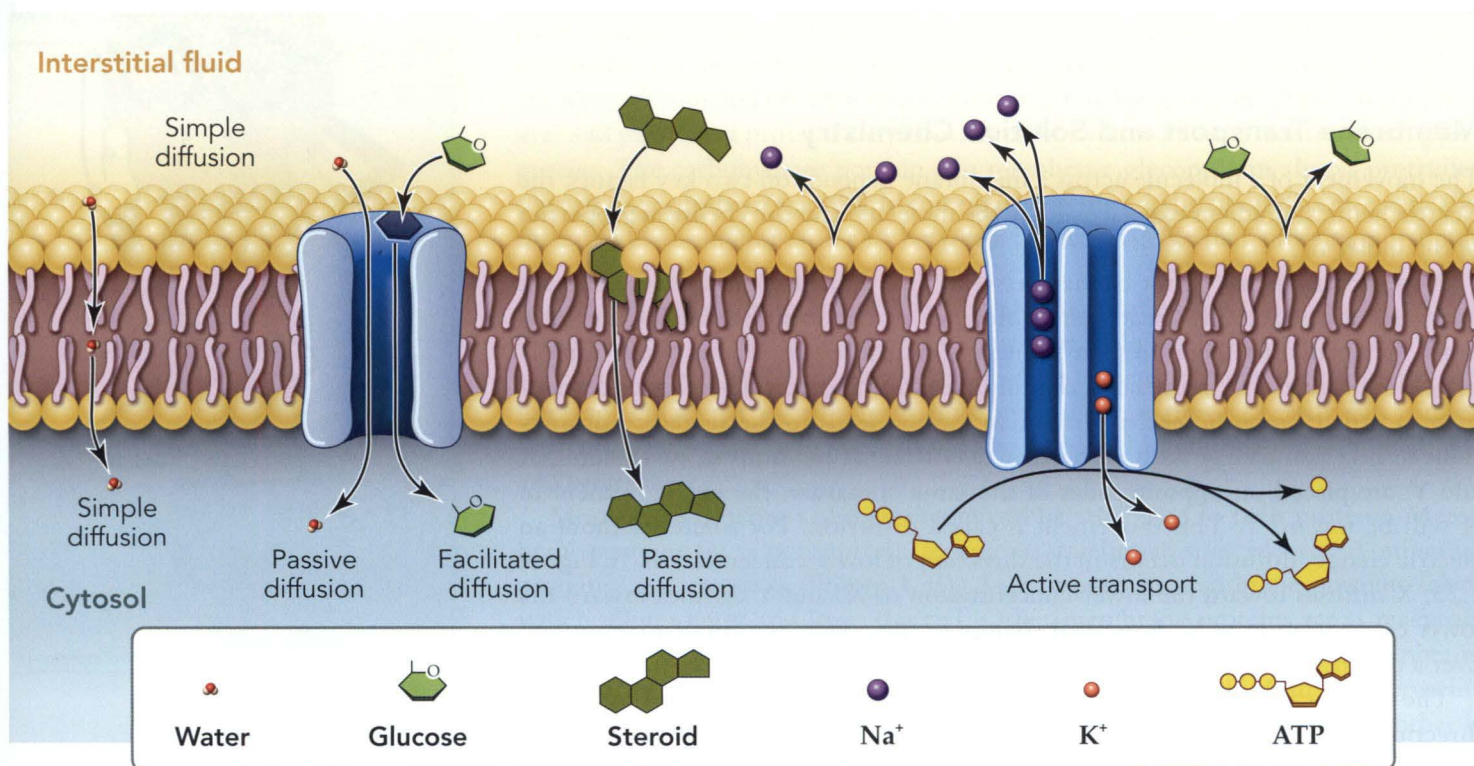
Nervous System
BIOLOGY 2

Thermodynamics
CHEMISTRY



Blue food coloring begins to diffuse in a beaker of water. Diffusion is caused by the tiny, random movements of solutes in a solution. Over a period of time these movements cause the dissolved substance to become evenly dispersed throughout the solvent.

FIGURE 1.24 Types of Membrane Transport



There are some important concepts here that require understanding and memorization. The membrane stuff is worth a second read through. For any molecule or ion, first determine whether it is moving against a gradient or with a gradient. If it is moving against a gradient, it requires active transport, regardless of size and charge. If it is moving with a chemical gradient, consider its chemical properties. Anything

that is lipid soluble (nonpolar enough to slide right through the phospholipid bilayer) and small enough to fit around the cracks in the integral proteins can pass through the membrane without the aid of a protein. If it meets these criteria, the molecule or ion crosses the membrane by passive diffusion. Otherwise it requires a protein to cross the plasma membrane. This type of transport is called facilitated diffusion.

brane is to that molecule. A natural membrane is generally impermeable to polar molecules that have a molecular weight greater than 100 g/mol without some type of assistance. The greater the polarity of a substance (or if it has a full charge), the less permeable the membrane is to that substance. Very large lipid soluble (i.e., nonpolar) molecules, such as steroid hormones, can easily diffuse through the membrane.

When predicting the permeability of the membrane to a substance, both size and polarity must be considered. For example, water is larger than a sodium ion, but water is polar, while the sodium ion possesses a complete charge. Therefore, a natural membrane is more permeable to water than it is to sodium. In this case, the charge difference outweighs the size difference. A cell membrane is, in fact, highly permeable to water. However, if the membrane were made only of a phospholipid bilayer, and did not contain proteins, the rate of diffusion for water would be very slow. Most of the diffusion of polar or charged molecules across a membrane takes place through incidental holes (sometimes called *leakage channels*) created by the irregular shapes of integral proteins. The function of these proteins is not to aid in diffusion. This is just an incidental contribution.

The diffusion described above, where molecules move through leakage channels across the membrane through random motion, is called **passive diffusion**. As mentioned previously, some molecules are too large or too polar to passively diffuse, yet they are needed for the survival of the cell. Proteins embedded into the cell membrane assist these molecules in moving across the membrane. These

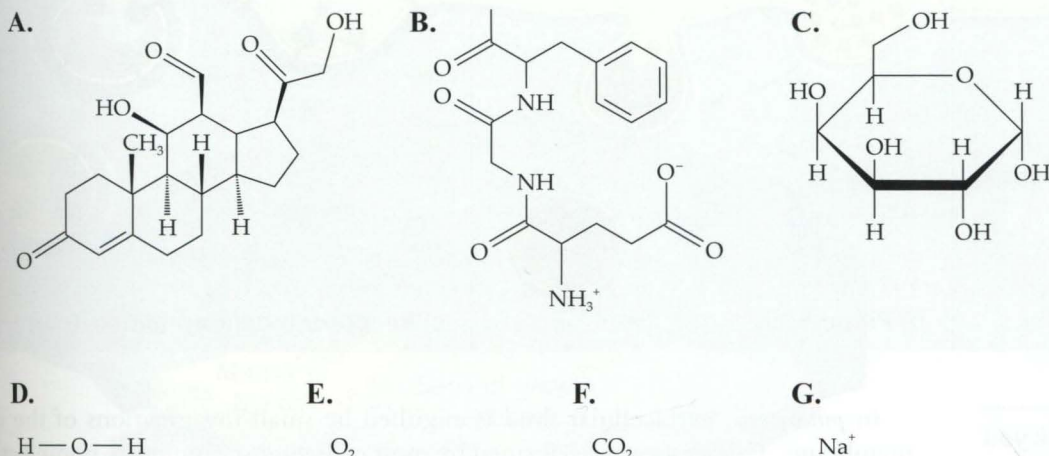
proteins, called **carrier proteins** or **membrane channels**, facilitate the diffusion of specific molecules or ions across the membrane. Several mechanisms are used by transport proteins in **facilitated diffusion**, but in order for the passage to be considered facilitated diffusion, the diffusion must occur down the electrochemical gradient of all species involved. Most, but not all, human cells rely on facilitated diffusion for their glucose supply. Facilitated diffusion contributes to the selective permeability of the membrane by selecting between molecules of similar size and charge.

A living organism must be able to transport some substances against their electrochemical gradients. Of course, such transport cannot be accomplished by diffusion. Movement of a compound against its electrochemical gradient occurs by **active transport**. Active transport requires expenditure of energy. It can be accomplished by the direct expenditure of ATP to acquire or expel a molecule against its electrochemical gradient. Active transport can also be powered indirectly by using ATP to create an electrochemical gradient, which is then used to acquire or expel a molecule. The latter method is called *secondary active transport*.

MCAT® THINK

Which of the following could cross through the cell membrane via passive diffusion?

(See answer on p. 36.)



Most cells in the human body are roughly **isotonic** to their environment, meaning that the aqueous solution of their cytosol contains approximately the same concentration of particles as the aqueous solution surrounding them. While molecules may randomly move into or out of the cell, the number moving in each direction will be roughly the same. **Hypertonic** cells are more concentrated than their environment, and **hypotonic** cells are less concentrated than their environment. When the overall concentrations of molecules on either side of a membrane are not equal, osmotic pressure is generated. **Osmotic pressure** is the "pulling" pressure generated by a concentration gradient, which encourages osmosis. It is an example of a **colligative property**, a property that is based on the number of particles present rather than the type of particle.

The body works to maintain an extracellular environment that is isotonic to its cells. If the extracellular environment suddenly became hypotonic with respect to the cell, a concentration gradient would be established. Recall that when there is a higher concentration of particles on one side of the cell membrane, the particles tend to move down their concentration gradient to the other side of the barrier. If the particles are prevented from crossing the barrier, perhaps because they are too large or charged, water will cross in the opposite direction, down its own electrochemical gradient. Since human cells have no rigid cell wall, the cell will fill until

When you see **tonic**, think **solute concentration**. **Hypertonic** means **more highly concentrated**. **Hypotonic** means **less highly concentrated**.

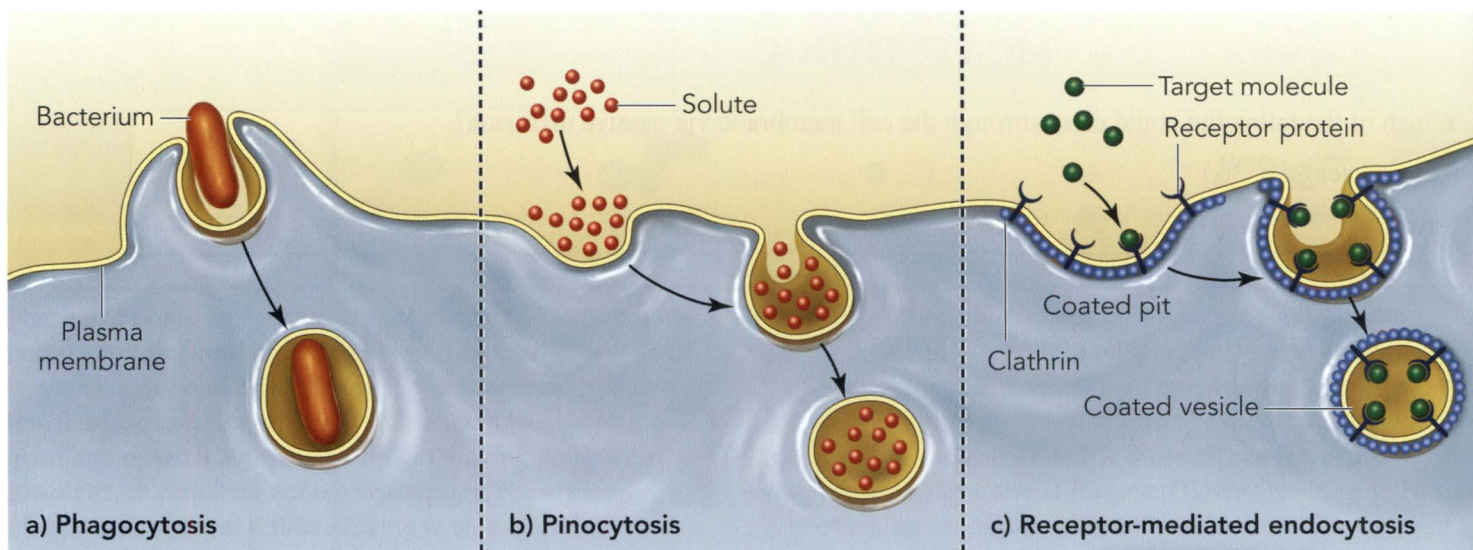
The opposite process can happen if a cell is hypotonic to its environment. Water will exit the cell, and the cell will shrivel.



the osmotic pressures are equal on the inside and outside of the cell. Water continues to move in and out of the cell very rapidly, but an equilibrium is reached. If the plasma membrane cannot withstand the pressure, the cell will burst.

Besides transport across the membrane by diffusion, cells can acquire substances from the extracellular environment through **endocytosis** (shown in Figure 1.25). There are several types of endocytosis: phagocytosis (Greek: phagein: to eat), pinocytosis (Greek: pinein: to drink), and receptor mediated endocytosis. In **phagocytosis**, the cell membrane protrudes outward to envelop and engulf particulate matter. Only a few specialized cells are capable of phagocytosis. Phagocytosis is triggered by the binding of particulate matter to protein receptors on the phagocytotic cell. In humans, antibodies or complement proteins bind to particles and stimulate receptor proteins on macrophages and neutrophils to initiate phagocytosis. Once the particulate matter is engulfed, the membrane bound body is called a *phagosome*.

FIGURE 1.25 Types of Endocytosis



The MCAT® probably will not ask you to distinguish between the types of endocytosis, but understand the basic concept and be aware that there are multiple methods for particles to gain access to the interior of the cell.

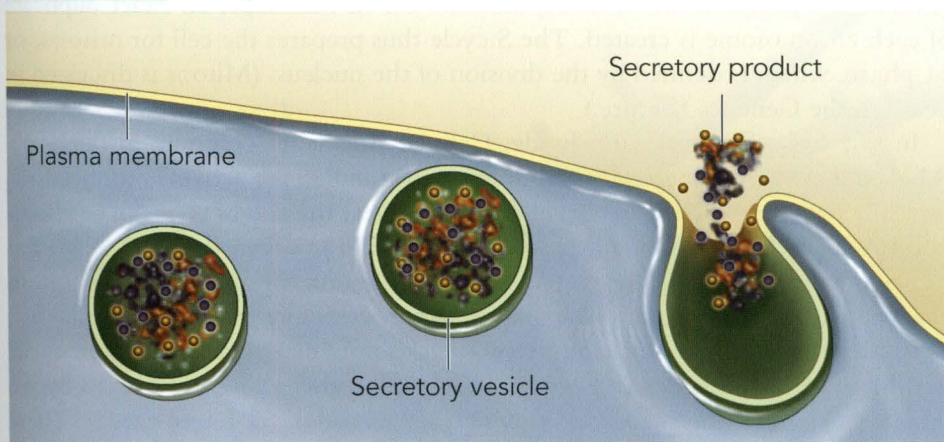
In *pinocytosis*, extracellular fluid is engulfed by small invaginations of the cell membrane. This process is performed by most cells, and in a random, nonselective fashion.

Receptor mediated endocytosis refers to specific uptake of macromolecules such as hormones and nutrients. In this process, the ligand binds to a receptor protein on the cell membrane and is then moved to a *clathrin coated pit*. Clathrin is a protein that forms a polymer, adding structure to the underside of the coated pit. The coated pit invaginates to form a *coated vesicle*. This process differs from phagocytosis in that its purpose is to absorb ligands, whereas ligands are only involved in phagocytosis as signals that initiate phagocytosis of other particles.

After endocytosis, the substance that was engulfed remains sequestered in a secretory vesicle. It moves backward along the route of proteins discussed earlier in this lecture. It can fuse back into the Golgi apparatus, or it can be targeted for destruction by a lysosome.

Exocytosis is simply the reverse of endocytosis. It provides a way for substances to leave the cell.

FIGURE 1.26 Exocytosis

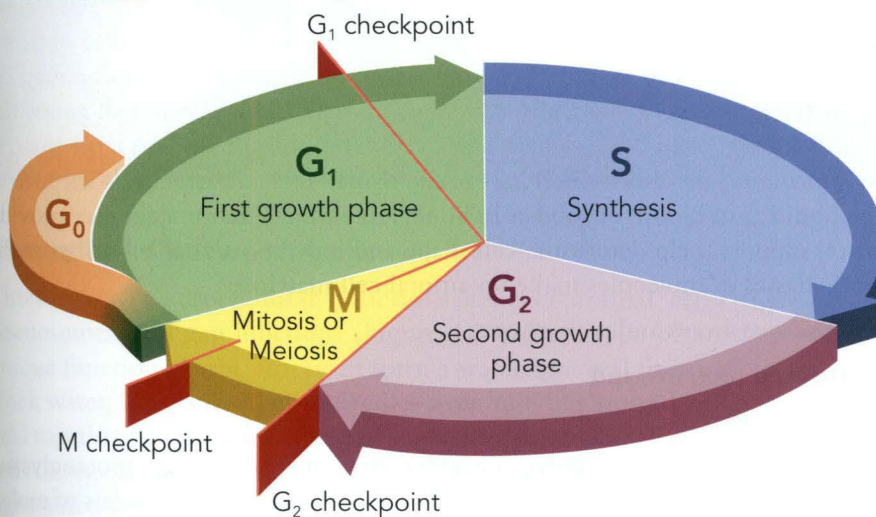


The Cell Cycle: Cell Growth and Division

Every cell has a life cycle (Figure 1.27) that begins with the birth of the cell and ends with the death or division of the cell. The life cycle of a typical somatic cell in a multicellular organism can be divided into four stages: the first growth phase (G_1); synthesis (S); the second growth phase (G_2); mitosis or meiosis (M); and cytokinesis (C). G_1 , S, and G_2 collectively are called **interphase**.

Genetics
BIOLOGY 1

FIGURE 1.27 The Cell Life Cycle



In G_1 , the cell has just divided, and begins to grow in size, producing new organelles and proteins. RNA synthesis and protein synthesis are highly active. The cell must reach a certain size and synthesize sufficient proteins in order to continue to the next stage. As it grows, the endoplasmic reticulum creates phospholipids and new portions of cell membrane as part of secretory vesicles. As these vesicles fuse with the membrane, the membrane grows. Cell growth is assessed at the G_1 checkpoint near the end of G_1 . If conditions are favorable for division, the cell enters the S phase; otherwise the cell enters the G_0 phase. The main factor in triggering the beginning of S is cell size, based upon the ratio of cytoplasm to DNA. G_1 is normally, but not always, the longest stage.

G_0 is a non-growing state distinct from interphase. The G_0 phase is responsible for variations in length of the cell cycle between different types of cells. In humans, enterocytes of the intestine divide more than twice per day, while liver cells spend a great deal of time in G_0 , dividing less than once per year. Mature neurons and muscle cells remain in G_0 permanently.

Cancer genes are like a car that is trying to get past a cop while speeding. If the cop is blinded, he can no longer check for the car. This is like the loss of a tumor repressor. If you paint the car a new color so that the cop can no longer recognize it, the car can also get by the cop. This is like the gain of an oncogene.

In **S**, the cell devotes most of its energy to DNA replication. Organelles and proteins are produced more slowly than in **G₁**. In this stage, an exact duplicate of each chromosome is created. The **S** cycle thus prepares the cell for **mitosis**, or **M phase**, which is defined by the division of the nucleus. (Mitosis is discussed in detail in the Genetics Lecture.)

In **G₂**, the cell prepares to divide. Cellular organelles continue to duplicate. RNA and proteins (especially tubulin for microtubules) are actively produced. **G₂** typically occupies 10–20% of the cell life cycle. Near the end of **G₂** is the **G₂ checkpoint**, which checks for *mitosis promoting factor* (MPF). When the level of MPF is sufficiently high, mitosis is triggered. An **M checkpoint** towards the end of mitosis ensures that the chromosomes are aligned correctly before the cell divides.

As described, there are a number of checkpoints that regulate the cell cycle, step by step. Sometimes a cell acquires a mutation that allows the cell to bypass these checkpoints. Such cells can grow unchecked and develop into **cancer**. There are two types of mutations that can cause cancer: the deactivation of a checkpoint protein (a *tumor repressor*) and the activation of a gene that causes the proliferation of the cell (an *oncogene*).

1.7 Tissues, Organ Systems, Organisms...

Muscle, Bone and Skin
BIOLOGY 2

Most cells in multicellular organisms form groups of similar cells that work together for a common purpose, called **tissue**. In some tissues, cells called **fibroblasts** secrete fibrous proteins such as elastin and collagen, which form a molecular network that holds tissue cells in place. This network is called an **extracellular matrix**. Different tissues form dramatically different matrices. The matrix can constitute most of the tissue, as in bone, where a few cells are interspersed in a large matrix, or the matrix may be only a small part of the tissue. The consistency of the matrix may be liquid as in blood, or solid as in bone. An extracellular matrix may provide structural support, help determine cell shape and motility, and affect cell growth.

Three classes of molecules make up animal cell matrices:

1. *glycosaminoglycans* and *proteoglycans*;
2. structural proteins; and
3. adhesive proteins.

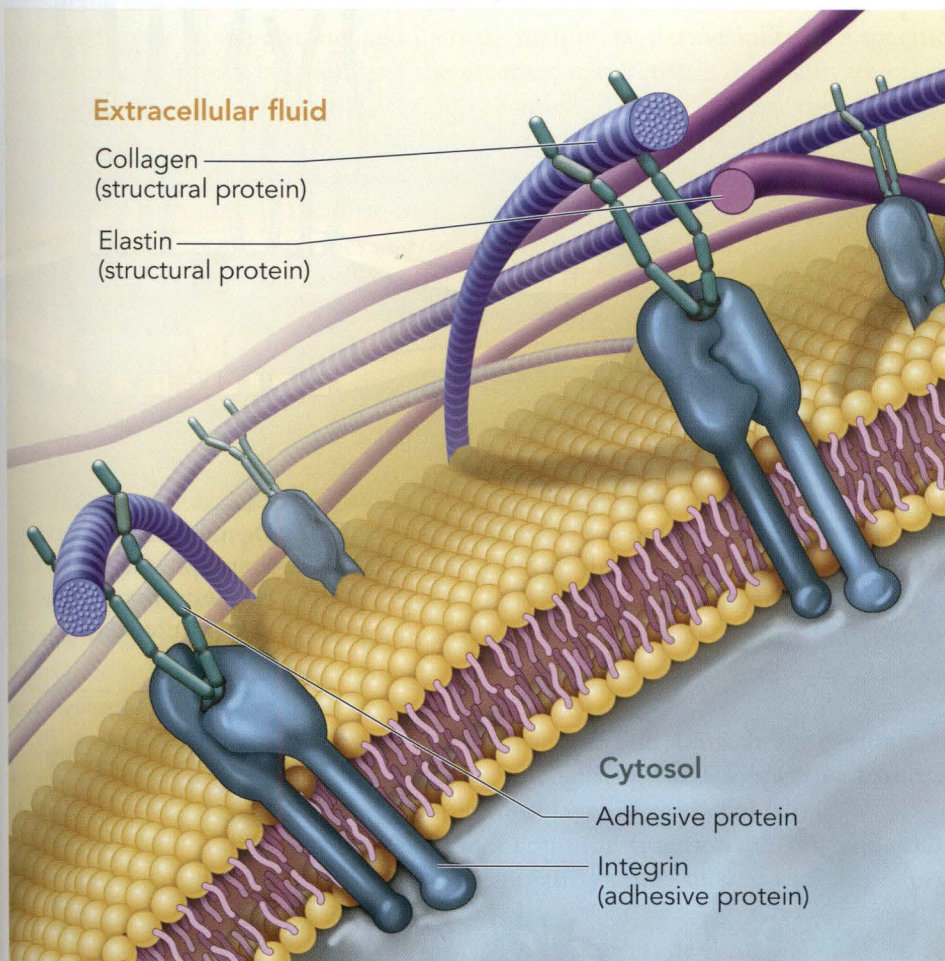
Glycosaminoglycans are polysaccharides that typically have proteoglycans attached. They make up over 90% of the matrix by mass. This first class of molecules provides pliability to the matrix. Structural proteins provide the matrix with strength. The most common extracellular matrix structural protein in the body is collagen. Collagen is particularly important to the strength of cartilage and bone. Adhesive proteins help individual cells within a tissue stick together.

The basal lamina (which, along with the reticular lamina, forms the basement membrane) could appear in an MCAT® passage. The *basal lamina* is a thin sheet of matrix material that separates epithelial cells from *support tissue*. (Epithelial cells separate the outside environment from the inside of the body. Support tissue is composed of the cells adjacent to epithelial cells on the inside of the body.) Basal lamina is also found around nerves, and muscle and fat cells. Basal lamina usually acts as a sieve type barrier, selectively allowing the passage of some molecules but not others.

Many animal cells contain a carbohydrate region analogous to the plant cell wall or bacterial cell wall, called the *glycocalyx*. The glycocalyx separates the cell membrane from the extracellular matrix. However, a part of the glycocalyx is made from the same material as the matrix, so the glycocalyx is often difficult to identify. The glycocalyx can be involved in cell-cell recognition, adhesion, cell surface protection, and permeability.

Don't worry about memorizing details about the extracellular matrix. Just know that is the material that surrounds the cell and that it is formed by the cell itself.

FIGURE 1.28 The Extracellular Matrix



Connections Between Cells

Three types of **intercellular junctions** connect animal cells: tight junctions, desmosomes, and gap junctions (Figure 1.29). Each type of junction performs a unique function. **Tight junctions** form a watertight seal from cell to cell that can block water, ions, and other molecules from moving around and past cells. Tissue held together by tight junctions can act as a complete fluid barrier. Epithelial tissue cells in organs like the bladder, the intestines, and the kidney are held together by tight junctions in order to prevent waste materials from seeping around the cells and into the body. Since proteins have some freedom to move laterally about the cell membrane, tight junctions also act as a barrier to protein movement between the *apical* and the *basolateral* surface of a cell. (The part of a cell facing the lumen of a cavity is called the apical surface. The opposite side of a cell is called the basolateral surface.)

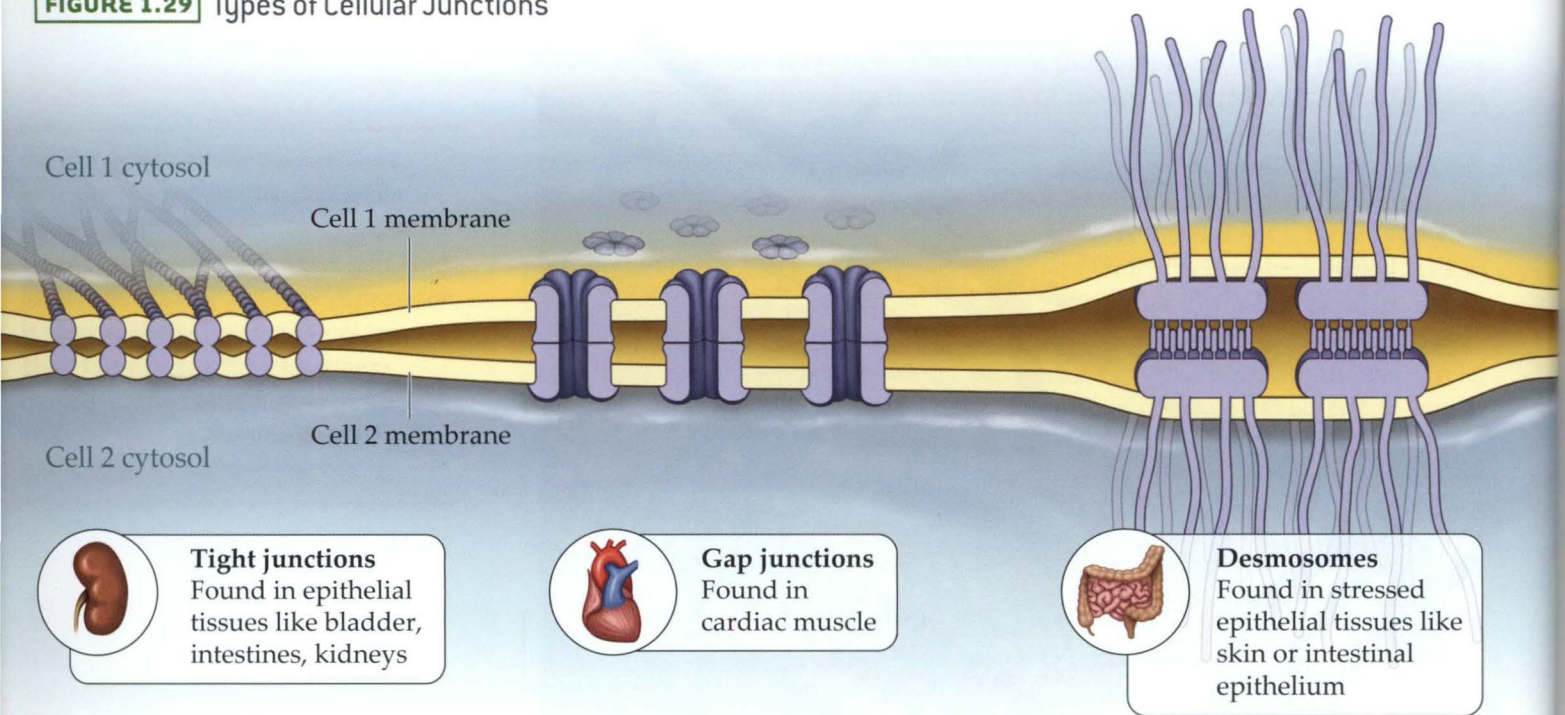
Desmosomes join two cells at a single point. They attach directly to the cytoskeleton of each cell. Desmosomes do not prevent fluid from circulating around the sides of a cell. They are found in tissues that normally experience a lot of stress due to sliding, like skin or intestinal epithelium. Desmosomes often accompany tight junctions.

Gap junctions are small tunnels that connect cells, facilitating the movement of small molecules and ions between the cells. Gap junctions in cardiac muscle allow the spread of the action potential from cell to cell. They also exist in some kinds of smooth muscle, allowing fibers to contract as a unit.

Tight junctions are like the plastic rings around a six pack of soda. The soda cans are the cells. The plastic rings hold the cans together and provide a watertight barrier around them. Although soda cans are impermeable to water, real cells may or may not be impermeable to water.

Muscle
BIOLOGY 2

FIGURE 1.29 Types of Cellular Junctions



Remember the three types of cellular junctions. Tight junctions act as a fluid barrier around cells. Desmosomes are like spot-welds holding cells together. Gap junctions are tunnels between cells that allow for the exchange of small molecules and ions.

Cell Communication Through Receptors

It is often the case that cells and tissues that are not directly connected must coordinate their activities. Gap junctions can only allow communication between adjacent cells. In the more common case where a cell has to communicate with a cell that is further away, the cell sends out a chemical message, or **hormone**, to be picked up by a receptor on another cell.

The location of the hormone receptor depends on the nature of the hormone. If a molecule is small and lipophilic, such as a steroid (cholesterol derivative), it can cross the cell membrane and bind to receptors inside of a cell. These receptors are located in the cytosol or the nucleus and act at the level of transcription. Thus, the typical effect of a steroid hormone is to increase certain membrane or cellular proteins within the target cell.

Endocrine System BIOLOGY 2

These receptors are like an ear for the nucleus. They receive input from the outside world and communicate it to the nucleus. The nucleus can then process this information and coordinate cell activities.

If a molecule is large and lipophobic, such as a protein, it cannot cross the cell membrane and instead binds to a receptor on the cell membrane. The receptor may itself act as an ion channel and increase membrane permeability to a specific ion in response to the hormone, or the receptor may activate or deactivate other intrinsic membrane proteins that act as ion channels. Another effect of the hormone binding to the receptor may be to activate an **intracellular second messenger** such as cAMP, cGMP, or calmodulin. These chemicals are called second messengers because the hormone is the first messenger to the cell. The second messenger activates or deactivates enzymes and/or ion channels and often creates a 'cascade' of chemical reactions that amplifies the effect of the hormone. Through a second messenger cascade, a small concentration of hormone can have a significant effect.

Types of hormones and their effects will be discussed in much greater detail in the Endocrine System Lecture. For now, focus on the fact that receptors allow cells to communicate with each other from a distance.

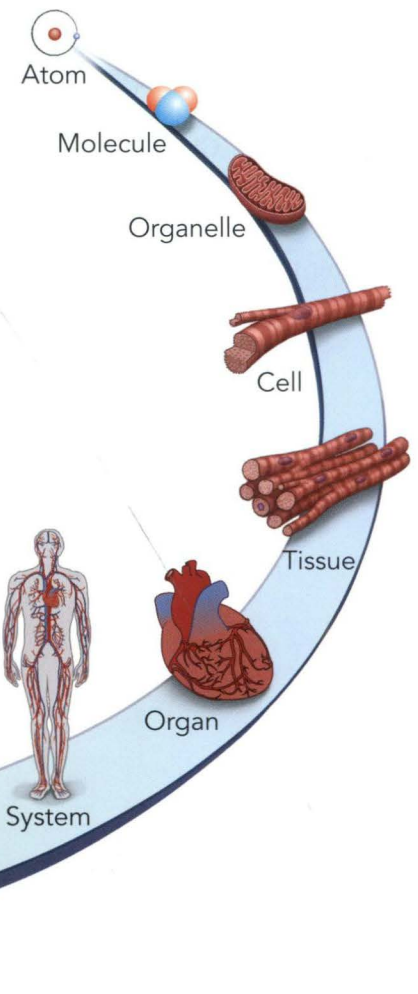
Cells in Context

The existence of tissues, where groups of cells work together with each type of cell performing a unique function that contributes to the specialized function of the group, is a defining feature of multicellular eukaryotes. There are four basic types of tissue in animals: *epithelial tissue*, *muscle tissue*, *connective tissue*, and *nervous tissue*. Epithelial tissue separates free body surfaces from their surroundings. Epithelium includes *endothelium*, which lines the vessels of the body, including the heart. Connective tissue is characterized by an extensive matrix. Examples include blood, lymph, bone, cartilage, and connective tissue proper, which makes up tendons and ligaments.

Various tissue types work together to form *organs*. The stomach, for example, is an organ with an outer layer made from epithelial tissue and connective tissue, a second layer of muscle tissue, and an innermost layer of epithelial tissue.

Organs that work together to perform a common function are called *systems*. This manual will discuss many significant organ systems, such as the respiratory system. Systems work together to create *organisms*.

Expanding outward, organisms live in social groups, as described in the *Psychology & Sociology Manual*. Biology includes the study of such groups. Humans live in families, which exist in communities. Just as the cells of a multicellular organism do not exist in isolation, humans and other organisms do not live independent of one another. The key to biology is not just understanding biological entities, but also understanding how these entities interact with their environments.



These questions are NOT related to a passage.

Item 17

The sodium-potassium ATPase hydrolyzes ATP to pump three sodium outside of the cell and two potassium into the cell. Which of the following is true about the sodium-potassium ATPase?

- I. It is an example of secondary active transport.
 - II. Sodium is pumped against its concentration gradient.
 - III. Potassium is pumped against its concentration gradient.
- ☐ A) I only
☐ B) II only
☐ C) II and III only
☐ D) I, II, and III

Item 18

Intestinal epithelium uses the diffusion of sodium down its concentration gradient to power the translocation of glucose inside of a cell. This is an example of:

- ☐ A) primary active transport.
☐ B) secondary active transport.
☐ C) passive diffusion.
☐ D) facilitated diffusion.

Item 19

Which of the following is least likely to require a protein to be transported into a cell?

- ☐ A) Protein
☐ B) Glucose
☐ C) Amino acids
☐ D) Carbon dioxide

Item 20

A protein hormone is least likely to act by which of the following mechanisms?

- ☐ A) Binding to a receptor in the nucleus
☐ B) Opening a membrane bound channel
☐ C) Activating a membrane bound enzyme
☐ D) Activating a G protein

Item 21

Which of the following statements is (are) true concerning tight junctions?

- I. They connect adjacent cells.
 - II. They may form a barrier to extracellular fluids.
 - III. They have the greatest strength of all cellular adhesions.
- ☐ A) I only
☐ B) I and II only
☐ C) II and III only
☐ D) I, II, and III

Item 22

What would be the likely consequence of adding pure water to a petri dish of human red blood cells?

- ☐ A) The cells would stay the same size.
☐ B) The cells would expand.
☐ C) The cells would burst.
☐ D) The cells should shrink.

Item 23

A neuron in an adult human is in which stage of the cell cycle?

- ☐ A) G₀
☐ B) G₁
☐ C) S
☐ D) G₂

Item 24

Which of the following is not involved in cell-to-cell communication?

- ☐ A) Gap junctions
☐ B) Desmosomes
☐ C) Membrane receptors
☐ D) Nuclear receptors

TERMS YOU NEED TO KNOW

9 + 2 arrangement	Exocytosis	Micelle
Active transport	Exponential growth	Microfilaments
Adaptations	Extracellular matrix	Microtubules: transport, support
Adipocytes	Extragenomic DNA	Microtubule-organizing center (MTOC)
Aerobic	Facilitated diffusion	Mitochondria
Allele	Fatty acid	Mitosis (M phase)
Amphipathic	Fibroblasts	Natural selection
Anaerobic	Fitness concept	Nonenveloped viruses
Apoptosis	Flagella	Nucleolus
Archaea	Flagellar propulsion	Nucleus
Bacilli (rod-shaped)	Flagellin	Nuclear envelope
Bacteria	Fluid mosaic model	Nuclear pores
Bacterial envelope	G ₁ , G ₂ , S, and G ₂ phases	Origin of replication
Bacteriophage	Gap junctions	Osmotic pressure
Binary fission	Gene pool	Outbreeding
Bottleneck	Genetic drift	Outer membrane
Cancer	Genetic recombination	Parasitic
Capsid	Genotype	Passive diffusion
Carrier protein	Glycerol backbone	Peptidoglycan
Centrioles	Golgi apparatus	Peroxisomes
Chemical concentration gradient	Hardy-Weinberg Equilibrium	Peripheral proteins (extrinsic proteins)
Chemotaxis	HIV	Phagocytosis
Cilia	Hormone	Phenotype
Cleavage	Host cell	Phosphate group
Cocci (spherical)	Hydrogen peroxide	Plasma membrane
Colligative property	Hydrolytic enzymes	Plasmid
Conjugation	Hypertonic cell	Polarity
Cytoskeleton	Hypotonic cell	Polymorphism
Desmosomes	Inbreeding	Prions
Differential Reproduction	Increase in percent representation	Programmed cell death
Diffusion	Inner membrane	Prokaryotes
Domain	Integral proteins (intrinsic proteins)	Receptor
Dynein	Intercellular junctions	Retroviruses
Electrical concentration gradient	Intermediate filaments	Reverse transcriptase
Electrochemical gradient	Intermembrane space	Rough ER
Endocytosis	Interphase	Size
Endoplasmic reticulum (ER)	Intracellular second messenger	Semipermeable membrane
Enveloped viruses	Isotonic	Smooth endoplasmic reticulum
ER lumen	Lysosomes	Speciation
Evolution	Lytic	
Evolutionary time	Membrane channels	

TERMS YOU NEED TO KNOW (CONTINUED)

Species	Tail	Vector
Specialization	Tight junctions	Viral envelopes
Spirill (spiral-shaped)	Tissue	Viral particle
Subviral particles	Transduction	Viroids
Symbiotic	Transformation	Viruses
Synthetic machinery	Transposons	

MCAT® THINK ANSWER

D, E, and F

Small, non-charged molecules such as O_2 and CO_2 can easily pass through the cell membrane via passive diffusion. Although H_2O is polar, it is small and does not have a full charge, so it can also pass through the membrane by passive diffusion. Ions that have a full charge, such as Na^+ , cannot diffuse passively through the membrane. Choices A, B, and C can all be eliminated because of their size; also note that the molecule shown in choice B has multiple full charges.



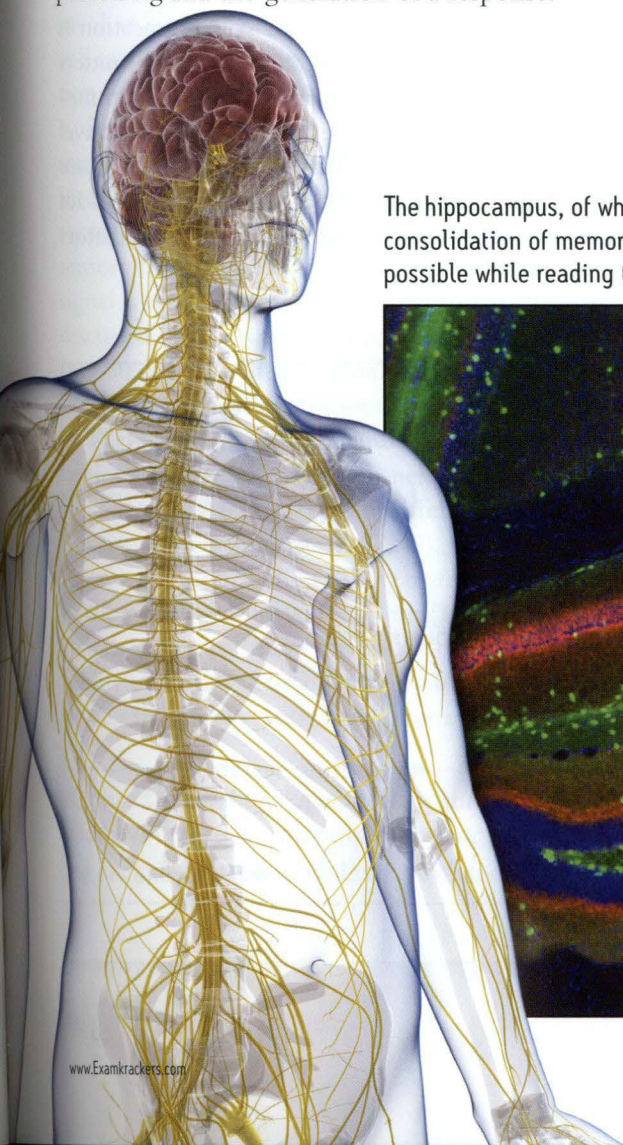
DON'T FORGET YOUR KEYS

1. The cell has compartments to separate chemical properties and processes.
3. A cell is like an organism – understand the function of organelles by treating them as organs.
3. Transport in and out of a cell occurs through diffusion down the concentration gradient, by pumps against the diffusion gradient, or via endocytosis/exocytosis.

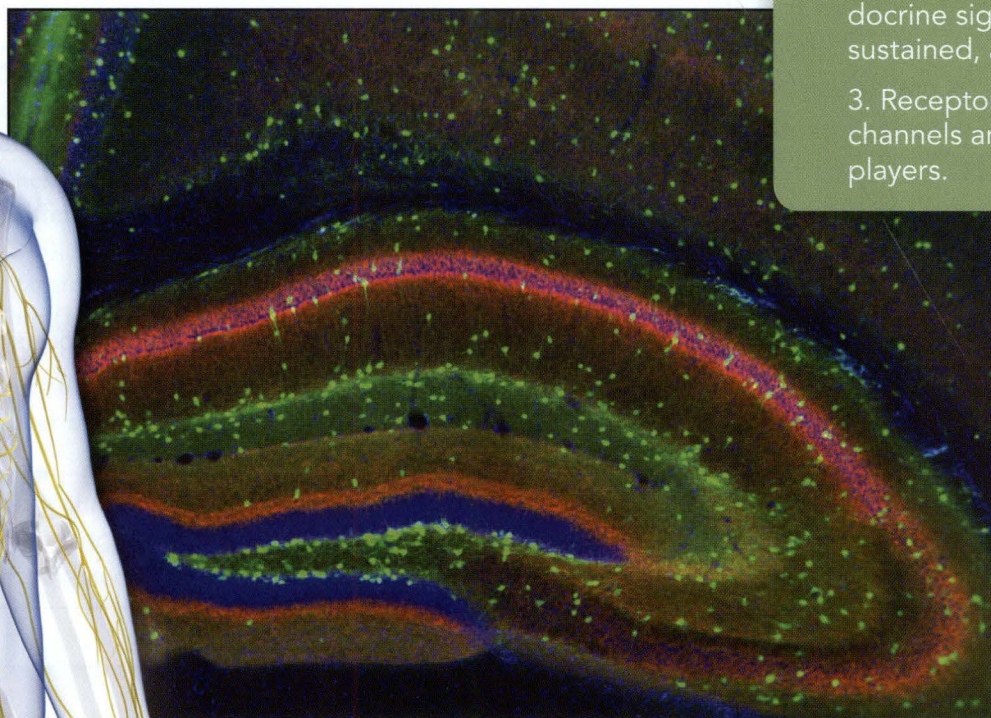
The Nervous System

2.1 Introduction

The nervous system is responsible for an organism's ability to sense stimuli, process information, and respond to changes in its environment. This lecture will review the nervous system and its functions on the molecular, structural, organ, and systemic levels. Following an introduction to the organization and essential functions of the nervous system, including the contrast with other communication systems in the body, the lecture will describe the smallest unit of the nervous system: the neuron. A review of the chemistry and physics of the neuron will elucidate the biological and physical principles involved in the transmission of a signal down the length of the cell. Next the site of interaction between neurons will be considered, including the conversion of information between a chemical and electrical state. These early sections provide the basis for understanding the higher-level organization and functions of the nervous system. Following a consideration of the major divisions of the nervous system and their unique characteristics, the lecture concludes by describing how each of the sensory systems of the body senses environmental stimuli and conveys this information to the central nervous system for processing and the generation of a response.



The hippocampus, of which a section is shown here, is critical for the consolidation of memory. The hippocampus should be used as much as possible while reading this lecture!



- 2.1 Introduction
- 2.2 Communication Within the Body
- 2.3 Functions and Features of the Nervous System
- 2.4 Electrochemistry and the Neuron
- 2.5 Communication Between Neurons: The Synapse
- 2.6 Supporting Cells: Glia
- 2.7 The Structures of the Nervous System
- 2.8 Sensing and Sensory Receptors
- 2.9 The Eye and Vision
- 2.10 The Ear and Hearing
- 2.11 Smell, Taste, and Pain

THE 3 KEYS

1. The nervous system senses the environment, processes information, and responds.
2. Neural signals are fast, fleeting, and specific; endocrine signals are slow, sustained, and general.
3. Receptors and channels are the hidden players.

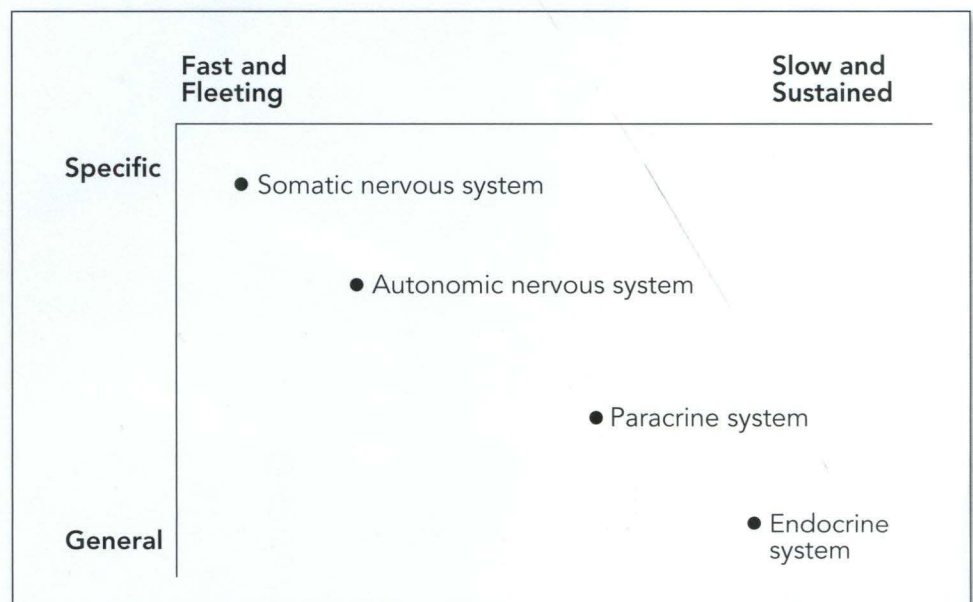
A consideration of the body's communication systems provides a basis for understanding the features of the nervous system. In multicellular organisms, cells must be able to communicate with each other so that the organism can function as a single unit. Communication is accomplished chemically via three types of molecules: 1. neurotransmitters; 2. local mediators; and 3. hormones. These methods of communication are governed by the nervous system, the paracrine system, and the endocrine system, respectively. These communication systems can be understood by looking at a few key characteristics: a signal can be fast or slow, specific or generalized, and fleeting or sustained in its effects. The specificity of a signal refers to the part of the body upon which the signal acts. A signal can be directed at a very specific site or can be more generalized, affecting multiple organs and systems. The category of fleeting or sustained has to do with how long the effect of the signal continues to influence the target. Usually a signal that is fast is also fleeting, whereas a signal that is slow is usually sustained: once it does get to the target, it stays around for a while and continues to exert an effect. The nervous, paracrine, and endocrine systems each have a unique position along these continuums, as shown in Figure 2.1.

The nervous system involves rapid and direct communication between specific parts of the body, allowing quick but generally short-lived changes in muscular contractions, organ functions, or glandular secretions in response to incoming stimuli. Thus, signals in the nervous system are generally specific, fast, and fleeting. By contrast, the endocrine system acts by releasing hormones into the bloodstream. The effects of the endocrine system are more generalized, slow, and sustained when compared to communication through the nervous system. The paracrine system lies somewhere between the extremes of the nervous and endocrine systems.

Another major distinction between the body's methods of communication is the distance traveled by the molecules used in each system. Neurotransmitters travel over very short intercellular gaps; local mediators function in the immediate area around the cell from which they were released; and hormones travel throughout the entire organism via the bloodstream. Thus neurotransmitters are released right at the target site, producing a quick and direct signal; hormones act on many areas throughout the body and take longer to arrive; and local mediators fall somewhere between these extremes.

FIGURE 2.1 Comparison of Communication Systems: Somatic and Autonomic NS

The motor and sensory neurons of the somatic nervous system have specific targets, allowing for fine control of movement and detailed mapping of sensory stimuli. The autonomic nervous system has more general actions involving multiple targets and longer-lasting effects. Signals in the endocrine system are much more general, slow, and sustained than those of the nervous system.



You can think about different types of signals in terms of modern communication systems. A slow and sustained signal is like a letter. It takes a while to arrive and then has a lasting effect, since the recipient can read it multiple times. A fast and fleeting signal is more like a short text. It arrives instantly and then can be read and forgotten just as quickly.

2.3 Functions and Features of the Nervous System

The characteristics that define the nervous system as a communication system allow it to carry out its most crucial functions in the body: sensing the environment, selecting and processing the most significant information, communicating it to different parts of the body, and coordinating a response. These actions allow the nervous system to play a key role in homeostasis. It is important to be aware that the nervous and endocrine systems often work together to sense the changing needs of various systems in the body and respond accordingly. The particular mechanisms by which the nervous system regulates functions in the organism are described in this lecture and throughout this manual, as well as in the *Psychology & Sociology Manual*.

Organisms perceive a huge amount of stimuli in their surroundings, but only the information that is most relevant is actually preserved by the conscious and unconscious mind for use. The nervous system selects the most important information based on past experience, preconceived ideas, and evolutionary instinct. While conscious perception of stimuli is a significant part of the function of the nervous system, homeostatic regulation that occurs outside of conscious awareness is also crucial to the functioning of the organism. Unconscious regulation involves simpler processing mechanisms than those of the conscious mind, but it still involves the gathering and integration of information, as well as the prioritization of the most important stimuli and functions of the body.

Sensory information is converted into different forms as it travels throughout the nervous system. First input from the environment, including the body's internal environment, reaches sensory receptors. Physical information stimulates sensory neurons and is then translated into an electrical signal that travels along sensory neurons. Electrical signals travel the length of neurons, while a chemical signal is required for information to pass between adjacent neurons. The synapse, discussed later in this lecture, is the junction between two neurons that allows the transfer of the chemical signal. The conversion of signals from one form to another will be described throughout this lecture.

The nervous system includes the brain, spinal cord, nerves, and neural support cells, as well as sense organs such as the eye and the ear. Several sets of nerves in the nervous system carry out different actions. The brain and spinal cord make up the central nervous system (CNS), which allows the highest level of integration of input and output. The CNS transmits information to the rest of the body by way of the peripheral nervous system (PNS), which is divided into two parts: one that signals voluntary movement and one that regulates unconscious and involuntary bodily functions. The overall organization and division of the nervous system will be described in greater detail later in this lecture.

Rather than being like a camera that records exactly what it sees, the nervous system is like a computer program that processes the image, enhancing certain parts and deleting others.

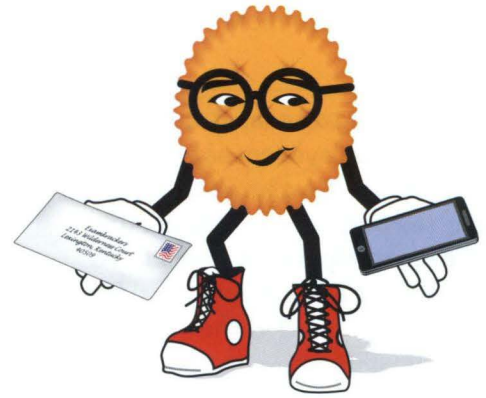
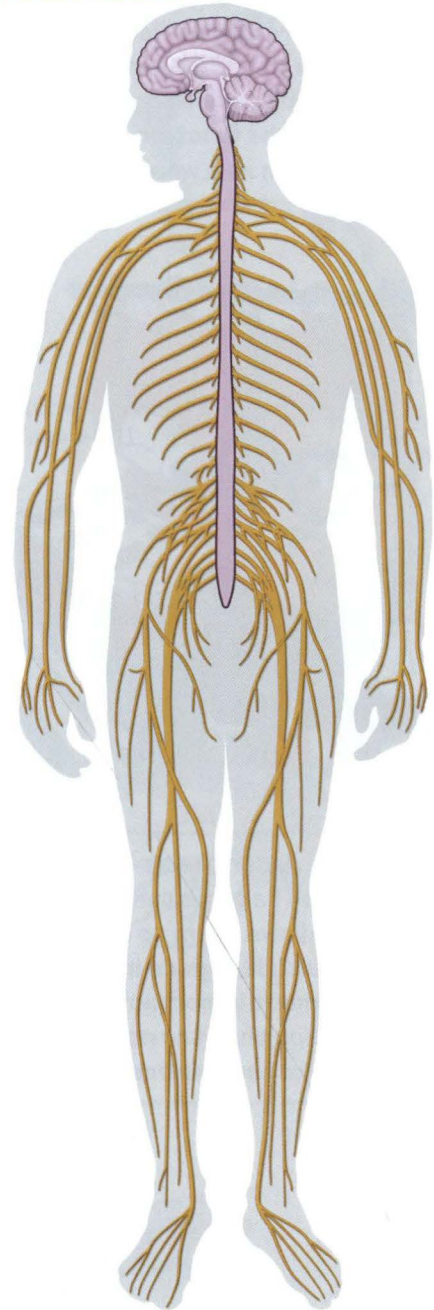


FIGURE 2.2 Nervous System



Central nervous system
Peripheral nervous system

It is crucial to understand that the nervous system acts at different levels of organization. For the purposes of the MCAT®, the most important levels to be aware of are the cellular level (the neuron); the level of the organ (i.e. the synapse between a neuron and organ); and the level of the system (the different systems are described in section 2.7). As you read this lecture and proceed from the neuron to the larger levels of organization, review earlier sections as necessary to understand how the different pieces fit together to determine the function of the nervous system as a whole.



Think of the dendrites as a voting machine. The structure of the dendrites allows them to collect and sum multiple signals in order to select the most important pieces of information that the neuron will transfer to other neurons.

The smallest functional unit of the nervous system is the **neuron**. A neuron is a highly specialized cell capable of transmitting a signal from one cell to another through a combination of electrical and chemical processes. Neurons join to form the higher-level divisions of the nervous system. The physical structure of the neuron and the mechanism by which it passes on a signal create the characteristic features of communication in the nervous system: fast, fleeting, and specific. The long axon of a neuron allows for contact with a specific site; the signal travels down the axon through a fast electrical mechanism; and the slowest (chemical) portion of the signal only has to cross a tiny space. Meanwhile, the effect of the signal is fleeting because the neurotransmitter is taken back up by the pre-synaptic neuron to prevent a sustained effect.

The neuron is so highly specialized that it has lost the ability to divide. In addition, it depends almost entirely upon glucose for its chemical energy. Although the neuron uses facilitated transport to move glucose from the blood into its cytosol, the neuron is not dependent upon insulin for this transport, unlike most other cells. The neuron depends heavily on the efficiency of aerobic respiration. However, it is not able to store significant amounts of glycogen and oxygen, and thus must rely on the blood to supply sufficient metabolic resources.

Neurons in different parts of the body have different physical appearances corresponding with their particular functions, but all neurons have a basic anatomy consisting of many **dendrites**, a single **cell body**, and usually one axon with many small branches (see Figure 2.3). The physical characteristics of each of these parts of the neuron correspond to its function, as described below.

The dendrites are stubby structures that receive a signal to be transmitted. Because a single neuron has many dendrites, each of which has multiple branches, inputs from many other neurons can be received simultaneously. **Summation** provides a way for the nervous system to screen for the most important stimuli. Spatial summation occurs when multiple dendrites receive signals at the same time, whereas temporal summation adds up the effects of signals that are received by a single dendrite in quick succession. The utility of summation is particularly evident in the gathering of sensory information by the central nervous system. Since the intensity of a stimulus can be coded by the **frequency of firing** of the sensory neuron or the number and type of receptors that respond, a stimulus of higher intensity will be more likely to trigger an action potential than a less intense stimulus.

The small size of the dendrites facilitates the quick transfer of an electrical signal to the cell body, to which the dendrites are attached. The cell body contains the organelles of the neuron, including the nucleus. Typically, the cytosol of the cell body is highly conductive and any electrical stimulus creates a disturbance in the electric field that is transferred immediately to the axon hillock. If the signals received by the dendrites sum to produce a large enough change in voltage across the membrane, the **axon hillock** (the site of connection between the cell body and the axon) generates an action potential in all directions, including down the **axon**. The membrane of the cell body usually does not contain enough ion channels to sustain an action potential. The axon, however, carries the action potential to a synapse, which passes the signal to another cell. The single axon is much longer than the dendrites, allowing the neuron to project to distant neurons or organs.

Some axons are extremely long (they can measure as much as a meter or even more!) Why have one long cell instead of several shorter ones? The answer is that having a single axon minimizes error and maximizes efficiency. Multiple synapses would provide opportunities for information to be transferred incorrectly and would also slow down the signal.

Receptors and **ion channels** are two types of molecules that are crucial to the function of neurons. Both are proteins that are embedded in the cellular membrane of neurons and determine what processes are possible at a given time or place along the membrane. Receptors bind substances (ligands) such as neurotransmitters and hormones, and respond by triggering processes within the cell. Different types of receptors are specialized to bind to particular chemicals. Some types of sensory receptors (cells that detect environmental stimuli, as described later in this lecture) have receptors in their membranes that bind chemicals in the environment. By contrast, ion channels open to allow ions to travel from one side of the membrane to the other, facilitating the transmission of signals. Different ion channels can specialize in terms of which ions they allow to pass through the membrane. In addition, ion channels vary in how quickly they open in response to changes in electrical potential. Some receptors are themselves ion channels and open in response to the binding of a ligand. These properties are crucial to the transfer of information between neurons. The role of receptors and ion channels in the nervous system will be discussed throughout this lecture.

It is important to know the basic anatomy of a neuron. Picture this basic structure to help you remember how neurons receive and convey information. Multiple branched dendrites receive multiple signals; the signals travel from the dendrites to the adjacent axon hillock; an action potential is generated at the axon hillock and moves down the axon to the synapse.

The Neuron as an Electrochemical Cell

The neuron is a biological example of an electrochemical **concentration cell** where differences in concentration initiate the moving of charge and thus create a voltage. This property of neurons, along with features of the surrounding environment, allows neurons to carry out their function of transferring information throughout the nervous system. The mechanism for the transfer of signals between neurons will be considered later in this lecture, but it is first necessary to understand how neurons generate voltage by acting like concentration cells.

FIGURE 2.4 Concentration Cell

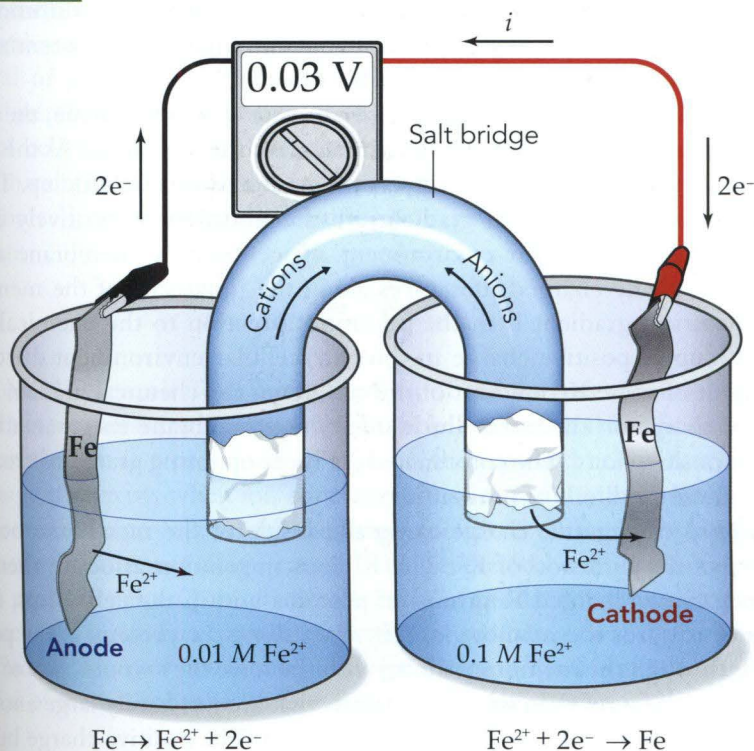
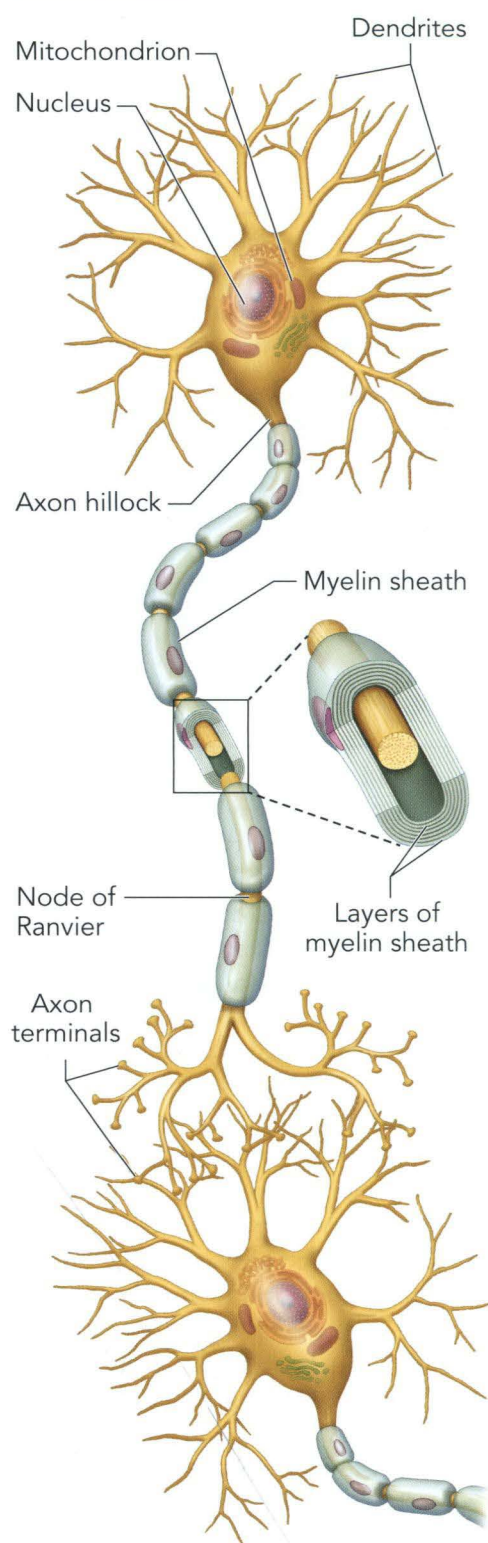


FIGURE 2.3 Myelinated Neuron

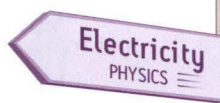


Electrochemistry
 CHEMISTRY

Remember the uneven distribution of Na^+ and K^+ across the membrane of a neuron: more Na^+ outside the cell than in, and more K^+ inside the cell than out.

As in all concentration cells, neurons use an insulating membrane to separate two conducting solutions. In the case of the neuron, the two solutions are the intracellular and extracellular fluids, and the insulating membrane is the cellular membrane. Concentration cells separate solutions that contain different concentrations of the same ion, generating an electrical potential. For the purpose of considering the neuron as a concentration cell, the two most important ions in solution are Na^+ and K^+ . The uneven distribution of these ions across the membrane, with a much higher extracellular concentration of Na^+ than the intracellular concentration and the reverse for K^+ , is responsible for the resting potential difference across the membrane, which is approximately -70 mV . There is a buildup of negative charge just inside the cell membrane, and a buildup of positive charge just outside the membrane. The voltage generated by the separation of different concentrations of an ion in solution can be calculated using the Nernst equation, as will be described.

The Resting Potential



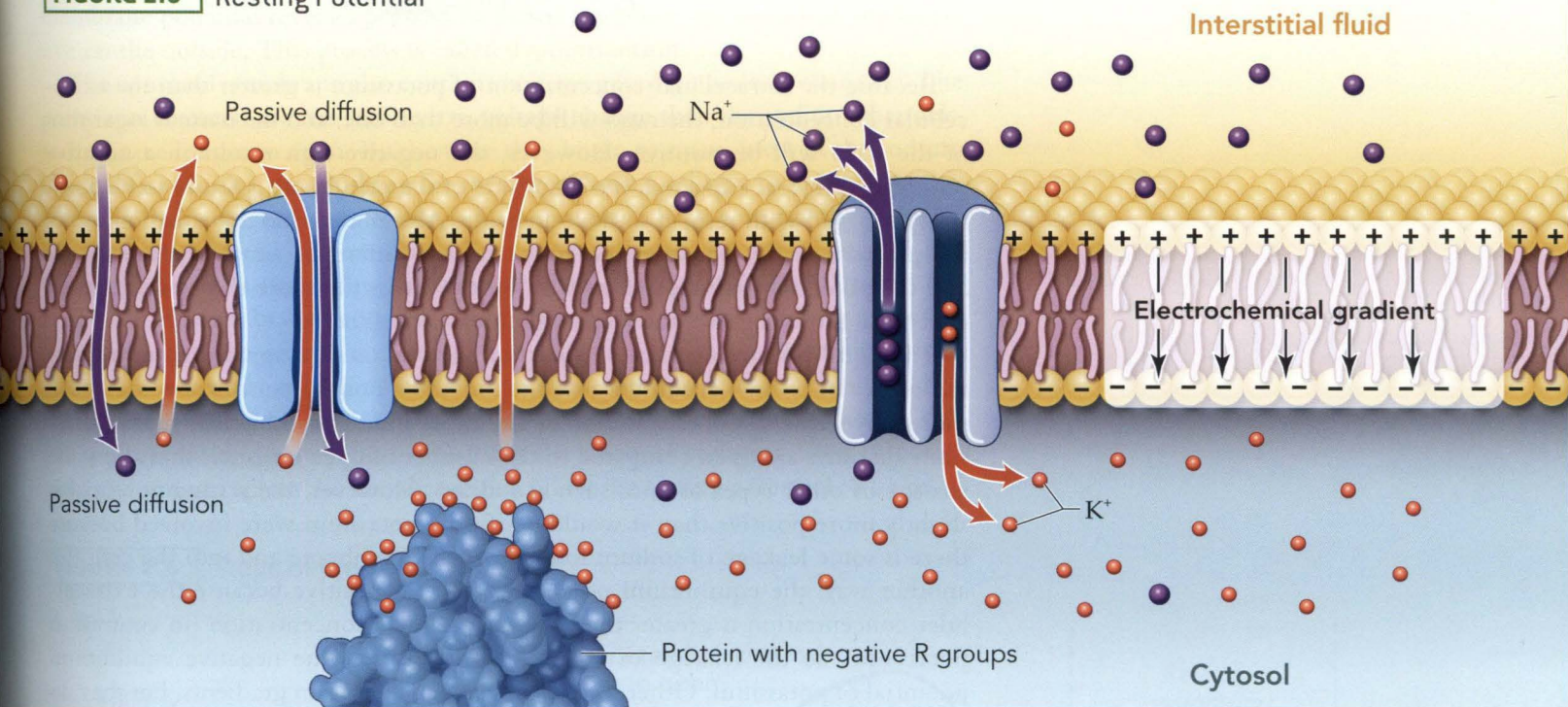
The **resting potential** is the electrical potential, or voltage, across the neuronal membrane at rest. It is the same as the voltage that is discussed in the context of electric charge and circuits in the *Physics Manual* and thus is related to potential energy. It can be thought of as a stored potential that is used by the neuron to transmit signals. A sufficient disruption in the balance of forces that maintain the resting potential leads to a cascade of events that constitute an action potential, as described in the next section. If a neuron loses the ability to establish the resting potential, it is no longer able to transmit action potentials.

The resting potential is established by the diffusion of potassium out of the cell through channels in the membrane. (Because the concentration of K^+ is much greater inside the cell, a chemical gradient is established that pushes potassium ions out of the cell.) When the K^+ ion approaches its chemical equilibrium, meaning that the concentrations of the ion on the inner and outer surfaces of the membrane start to equilibrate, there is an electric voltage created by the difference in charge between the ions that have crossed the membrane and the protein anions left behind. In the neuron at rest, the membrane is highly permeable to K^+ but almost completely impermeable to Na^+ . In other words, many more channels that allow the diffusion of K^+ are open compared to the number of channels specific to the passage of Na^+ . As a result, in the neuron at rest, the diffusion of K^+ across the membrane is the major determinant of the membrane potential across the membrane.

As with all chemical gradients, as K^+ diffuses across the membrane, the chemical gradient starts to equilibrate and the diffusional force decreases. As the chemical gradient starts to break down, an electrical gradient starts to build up. The two factors that cause this electrical gradient are the diffusion of positively charged K^+ ions into the extracellular environment adjacent to the membrane and the buildup of negatively charged substances along the inner side of the membrane. Thus the electrical gradient is in the opposing direction to the chemical gradient; the buildup of positive charge in the extracellular environment discourages the movement of more K^+ ions out of the cell down the chemical gradient, while the negative charge on the intracellular side of the membrane exerts an attractive force on the positive ions. The combination of these opposing gradients creates the **electrochemical gradient** of potassium.

The buildup of negative charge along the inside of the membrane occurs as a side effect of the diffusion of K^+ . The K^+ ions in solution associate themselves with the negatively charged R groups of proteins within the cell. Thus, as they start to move towards the membrane, they drag along the protein. If the proteins could move through the membrane along with the ions, they would. But of course proteins are much larger than the ion channels that are just barely large enough to allow the passage of K^+ ions, so they get left behind. The positive charge building

FIGURE 2.5 Resting Potential



up along the outside of the membrane as K^+ ions flow out of the cell attracts the negatively charged proteins, causing them to stay in their position near the membrane. Other anionic substances, particularly Cl^- , also contribute to the buildup of negative charge.

The membrane contains a pump called the **sodium/potassium** or **Na^+/K^+ pump** that functions to maintain or reestablish the chemical gradient that is lost by diffusion. The pump moves ions in the direction opposite to the flow of diffusion, so it uses an active transport mechanism and requires energy input from ATP. The Na^+/K^+ pump moves three positively charged sodium ions out of the cell while bringing two positively charged potassium ions back into the cell, preventing equilibrium and replenishing the concentration gradients of these ions. As a result, the resting potential stays constant when the neuron is at rest.

The value of the resting membrane potential is determined by the **equilibrium potential** of potassium. When different concentrations of an ion are separated across a membrane that is permeable to that ion, as in the case of K^+ across the neuronal cell membrane, an electrical gradient develops that precisely balances the chemical gradient caused by the unequal concentrations. As with any concentration cell, the value of the resulting voltage can be calculated by the **Nernst equation**:

$$E = E^{\circ} - \frac{RT}{nF} \ln(Q)$$

The MCAT® requires an understanding of the variables in the Nernst equation. When temperature is constant, the whole expression RT/F is a constant. The charge of the ion is represented by n . E_0 is the standard cell potential, meaning the voltage that exists when ion concentrations are equal in both parts of the cell. In any concentration cell, where the same reaction is taking place but proceeding in opposite directions, voltage can only be generated by unequal concentrations, so E_0 is equal to zero. Q stands for the ratio of products to reactants; in the case of the neuron, it can be represented by the ratio of the extracellular and intracellular concentrations of potassium. Thus for the purposes of calculating the resting potential of the neuron, the Nernst equation can be rewritten as:

You may be confused about how the resting membrane potential can be set up without dramatically altering the chemical environment of the cell. Students often ask whether the concentrations used in the Nernst equation refer to the intracellular and extracellular concentrations before or after the diffusion of K^+ to achieve its equilibrium potential. The answer is both! These processes occur locally, in the vicinity of the membrane. Only a small number of ions have to cross the membrane to set up the voltage. The overall concentration of ions on either side of the membrane is unaffected. Similarly, the negative and positive charge buildup also occurs right next to the membrane; the inside of the neuron does NOT have an overall negative charge.

$$E_{K^+} = -\frac{RT}{nF} \ln\left(\frac{[K^+]_{intracellular}}{[K^+]_{extracellular}}\right)$$

Because the intracellular concentration of potassium is greater than the extracellular concentration, the ratio will be more than one, and the natural logarithm of the ratio will be positive. However, the negative sign results in a negative potential. Thus, as expected, the inner side of the membrane is found to be negatively charged with respect to the outer side. Also notice that the equation shows the proportionality between the concentration difference across the membrane and the potential that is generated. In other words, the more the concentrations differ, the more negative the electrical potential will be.

The equilibrium potential of potassium can be used to approximate the resting potential of the neuron because the membrane of the neuron at rest is much more permeable to potassium than to any other ion. This is because many potassium channels are open compared to the number of open channels that allow the passage of other types of ions, such as sodium. However, the resting potential is slightly more positive than it would be if only potassium were involved because there is some leakage of sodium ions across the membrane and into the cell. Put another way, the equilibrium potential of Na^+ is positive because the extracellular concentration is greater than the intracellular concentration (in contrast to potassium), so the leakage of sodium slightly offsets the negative equilibrium potential of potassium. Other ions also have concentration gradients, but they do not significantly affect the resting potential due to the low permeability of the membrane for these ions.

MCAT® THINK

It may seem strange that neurons use such a complex process to transmit information. Why wouldn't electricity just flow down a neuron, as it does in a wire? The answer is that unlike wires, the membranes of axons are not conductive of electricity because they are primarily composed of lipids. Instead, the solution of the cell is made up of ions, also called electrolytes, which are conductors of electrical signals. The action potential is the evolved solution to the problem of how to convey an electrical signal. The signal can be transmitted down the axon exactly as fast as ions can travel and channels can open. Think of an axon as a revised wire that depends on the travel of ions rather than electrons. Note that ions are much larger than electrons. Drag slows the transmission of the signal if the cross-sectional area of the axon is too small.

The take home messages about the resting potential are: 1) Most importantly, the resting potential is set up by the diffusion of K^+ . 2) K^+ diffuses out of the cell, dragging along negatively charged proteins that get stuck along the inner side of the membrane. 3) When the chemical gradient of K^+ equilibrates, the inner side of the membrane is negatively charged compared to the outer side. The resulting potential across the membrane is very close to the equilibrium potential of K^+ . Another thing: understand the Nernst equation and its variables.

The Action Potential

The concentration gradients across the membrane, and the membrane potential that develops as those gradients equilibrate, are crucial for the generation of the action potential. The **action potential** is the mechanism by which a signal travels down the length of a neuron and ultimately is transferred to the next cell. It is generated by a change in voltage across the neuronal membrane. The entire mechanism of the action potential can be conceptualized as a flip between permeability to potassium and permeability to sodium. At first there are many more open potassium channels than sodium channels. The action potential begins when many sodium channels suddenly open up. The potential across the membrane moves towards the equilibrium potential of the ion to which the membrane is most permeable at any given moment, due to the unequal intracellular and extracellular concentrations of the ions. In the most common type of synapse, the end result of the action potential is the release of neurotransmitter from the end of the axon.

The membrane of a neuron contains integral membrane proteins called **voltage gated sodium channels**. These proteins change configuration when the voltage across the membrane is disturbed, allowing Na^+ to flow through the membrane for a fraction of a second. As Na^+ flows into the cell, the voltage changes still further, causing more sodium channels to change configuration, allowing still more sodium to flow into the cell in a positive feedback mechanism. Since the Na^+ concentration moves toward equilibrium (i.e. towards the positive equilibrium

potential of sodium) while the K^+ concentration remains higher inside the cell, the membrane potential reverses polarity so that it is positive on the inside and negative on the outside. This process is called **depolarization**.

The neuronal membrane also contains **voltage gated potassium channels**. The potassium channels are less sensitive to voltage change than the sodium channels, so they take longer to open. By the time they begin to open, most of the sodium channels are closing, diminishing the membrane's permeability to sodium. At this point K^+ flows out of the cell, moving the potential back towards the negative equilibrium potential of potassium. This process is called **repolarization**. The potassium channels are so slow to close that, for a fraction of a second, the potential across the membrane becomes even more negative than the resting potential. This portion of the process is called **hyperpolarization**. Passive diffusion returns the membrane to its resting potential. The entire process just described is called the action potential (Figure 2.6). Throughout the action potential, the Na^+/K^+ pump keeps working, helping to maintain the unequal concentrations of potassium and sodium across the membrane that allow the resting potential to be reset.

FIGURE 2.6 Steps of the Action Potential

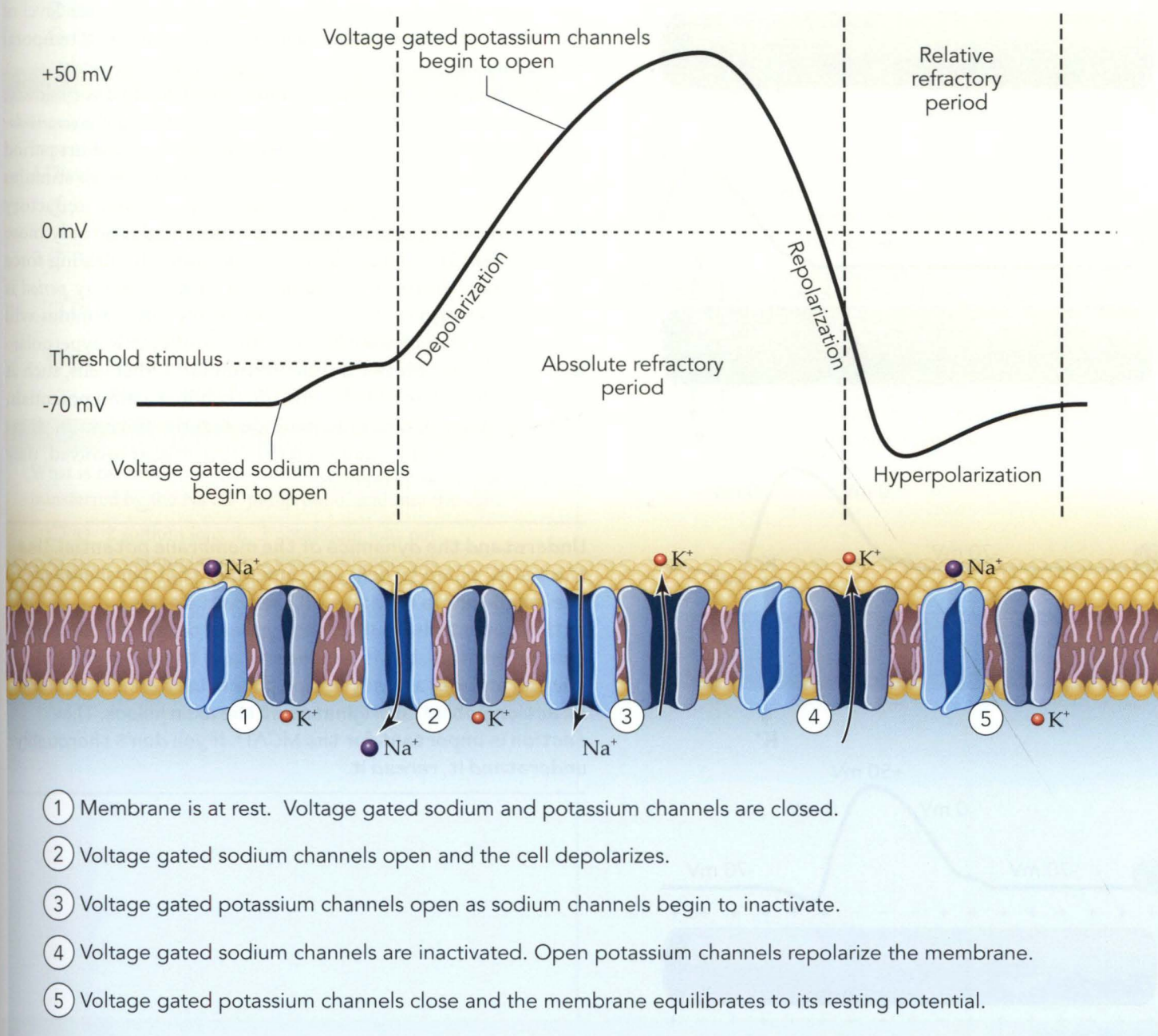
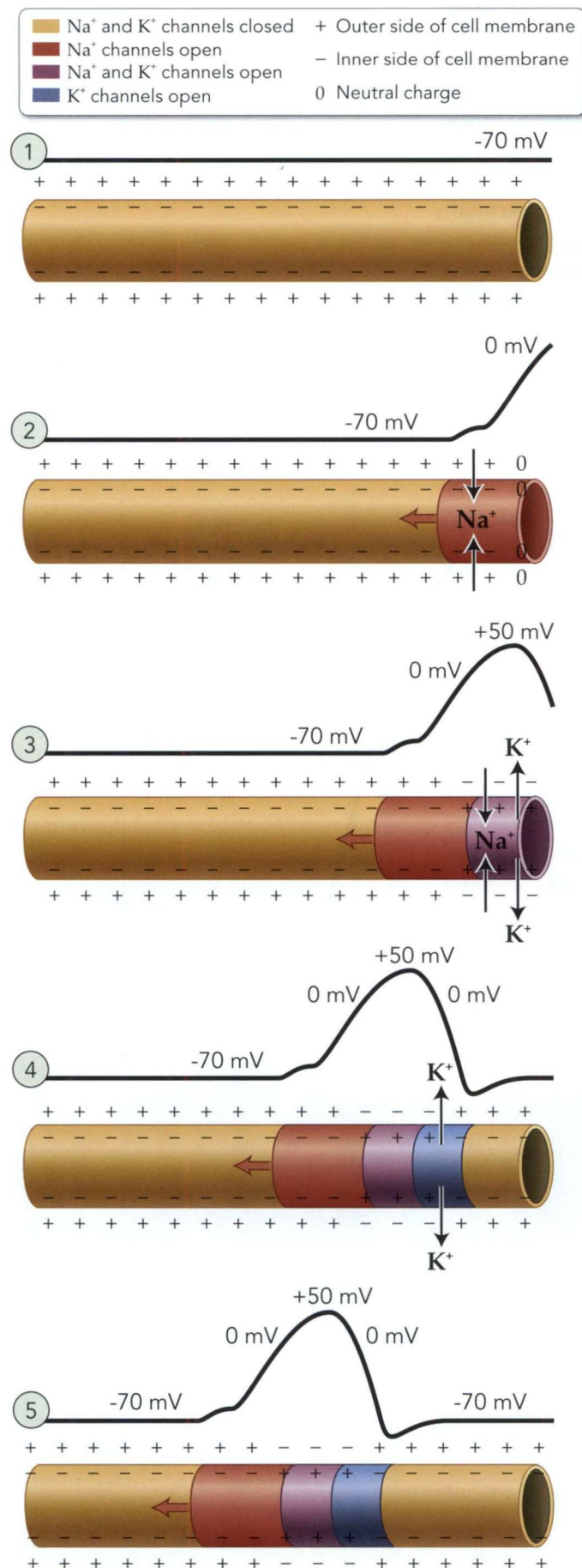


FIGURE 2.7 Unidirectional Propagation of an Action Potential



The action potential occurs at a point on the membrane and propagates by depolarizing the section of membrane immediately adjacent to it, which then causes the depolarization of the next adjacent section and so on down the membrane. Figure 2.7 shows an action potential propagating from right to left down the axon. The voltage at any given point on the membrane is indicated. The entire action potential as measured at one point on the membrane of a neuron takes place in a fraction of a millisecond.

An action potential is **all-or-none**, meaning that unless the membrane completely depolarizes, no action potential is generated. In order to create an action potential, the stimulus to the membrane must be greater than the **threshold stimulus**. Any stimulus greater than the threshold stimulus creates the same size action potential. The threshold stimulus is usually reached through the combination of many stimuli, each of which causes a small change in the membrane potential. Some have an **excitatory** (depolarizing) effect, while some have an **inhibitory** (hyperpolarizing) effect. An action potential is generated when the total effect of all inputs reaches the level of the threshold stimulus. The dendrites carry out both temporal and spatial summation of inputs, as described previously.

If the threshold stimulus is reached, but is reached very slowly, an action potential still may not occur. This is called *accommodation*. Once an action potential has begun, there is a short period of time called the *absolute refractory period* in which no stimulus will create another action potential. The absolute refractory period occurs because the membrane potential is already more positive than the resting potential, and thus the driving force of the action potential is absent. The *relative refractory period* is the time during which only an abnormally large stimulus will create an action potential because the membrane is hyperpolarized, requiring a greater threshold stimulus. Other cells, such as skeletal and cardiac muscle cells, also conduct action potentials. Although these action potentials are slightly different in duration, timing of stages, and even the types of ions involved, they work on the same principles.

Understand the dynamics of the membrane potential. Use the Na⁺/K⁺ pump to help you remember that the inside of the membrane is negative with respect to the outside. The action potentials of different types of cells have different characteristics, but if you understand the basic principle, you can understand any action potential. Remember that an action potential originates at the axon hillock. This section is important for the MCAT®. If you don't thoroughly understand it, reread it.

These questions are NOT related to a passage.

Item 25

Which of the following gives the normal direction of signal transmission in a neuron?

- ☐ A) From the axon to the cell body to the dendrites
- ☐ B) From the dendrites to the cell body to the axon
- ☐ C) From the cell body to the axon and dendrites
- ☐ D) From the dendrites to the axon to the cell body

Item 26

Novocaine is a local anesthetic used by many dentists. Novocaine most likely inhibits the action potential of a neuron by:

- ☐ A) stimulating calcium voltage gated channels at the synapse.
- ☐ B) increasing chloride ion efflux during an action potential.
- ☐ C) uncoiling Schwann cells wrapped around an axon.
- ☐ D) blocking sodium voltage gated channels.

Item 27

If a neuronal membrane were to become suddenly impermeable to potassium ions but retain an active Na^+/K^+ -ATPase, the neuron's resting potential would:

- ☐ A) become more positive because potassium ion concentration would increase inside the neuron.
- ☐ B) become more positive because potassium ion concentration would increase outside the neuron.
- ☐ C) become more negative because potassium ion concentration would increase inside the neuron.
- ☐ D) become more negative because potassium ion concentration would increase outside the neuron.

Item 28

What is the ratio of sodium ions to potassium ions transferred by the Na^+/K^+ pump out of and into the cell?

- ☐ A) 2 sodium ions in; 3 potassium ions out
- ☐ B) 3 sodium ions in; 2 potassium ions out
- ☐ C) 3 sodium ions out; 2 potassium ions in
- ☐ D) 2 sodium ions in; 3 potassium ions in

Item 29

Compared to the endocrine system, the nervous system is:

- ☐ A) faster and more specific.
- ☐ B) faster and more generalized.
- ☐ C) slower and more specific.
- ☐ D) slower and more generalized.

Item 30

The Nernst equation, when used to determine the resting membrane potential of a neuron, indicates that, as intracellular K^+ increases, the membrane potential:

- ☐ A) stays the same.
- ☐ B) changes, but not in a predictable way.
- ☐ C) becomes more positive.
- ☐ D) becomes more negative.

Item 31

Which of the following changes to the neuron at rest would be LEAST likely to prevent the formation of the normal resting membrane potential?

- ☐ A) Disruption of the electrochemical gradient of chlorine
- ☐ B) Disruption of the electrochemical gradient of sodium
- ☐ C) Disruption of the electrochemical gradient of potassium
- ☐ D) A change to the membrane resulting in impermeability to potassium

Item 32

During an action potential, the neuronal membrane:

- ☐ A) depolarizes, then hyperpolarizes, then repolarizes.
- ☐ B) depolarizes, then repolarizes, then hyperpolarizes.
- ☐ C) hyperpolarizes, then depolarizes, then repolarizes.
- ☐ D) hyperpolarizes, then repolarizes, then depolarizes.

Communication Between Neurons: The Synapse

Neural impulses are transmitted from one cell to another chemically or electrically via a synapse. The transmission of the signal from one cell to another is the slowest part of the process of nervous system cellular communication, yet it occurs in a fraction of a second.

Electrical synapses are uncommon. They are composed of gap junctions between cells. Cardiac muscle, visceral smooth muscle, and a very few neurons in the central nervous system contain electrical synapses. Since electrical synapses do not involve diffusion of chemicals, they transmit signals much more quickly than chemical synapses. In addition, the signal can propagate bidirectionally, meaning that both cells involved in the synapse can send and receive signals.

A more common type of synapse, the **chemical synapse** (Figure 2.8), consists of a space between two neurons that is crossed by neurotransmitters. Notice that unlike cells involved in electrical synapses, cells that are separated by a chemical synapse do not actually touch each other. Chemical synapses also differ from electrical synapses in that they are **unidirectional**; in a given chemical synapse, one cell always releases neurotransmitter and the other always receives it. An example of a chemical synapse is a **motor end plate**, which is the connection between a neuron and a muscle.

In a chemical synapse, small vesicles filled with neurotransmitter rest just inside the presynaptic membrane. **Neurotransmitters** are chemicals that are released into the synapse by a presynaptic neuron and attach to receptors on the postsynaptic cell. They are required because the electrical signal of the action potential cannot be transferred across the synapse between neurons. The membrane of the presynaptic neuron near the synapse contains a large number of Ca^{2+} voltage gated channels. When an action potential arrives at a synapse, these channels are activated, allowing Ca^{2+} to flow into the cell. In a mechanism that is not completely understood, the sudden influx of calcium ions causes some of the neurotransmitter vesicles to be released into the synaptic cleft through exocytosis. The neurotransmitter then diffuses across the synaptic cleft.

The postsynaptic membrane contains neurotransmitter receptor proteins. When the neurotransmitter attaches to the receptor proteins, the postsynaptic membrane becomes more permeable to ions. Ions move across the postsynaptic membrane through ion channels, completing the transfer of the neural impulse. In this way, the impulse is not attenuated by electrical resistance as it moves from one cell to the next. However, if a presynaptic cell is fired too often it will not be able to replenish its supply of neurotransmitter vesicles, resulting in *fatigue* (the impulse will not pass to the postsynaptic neuron).

FIGURE 2.8 Chemical Synapse

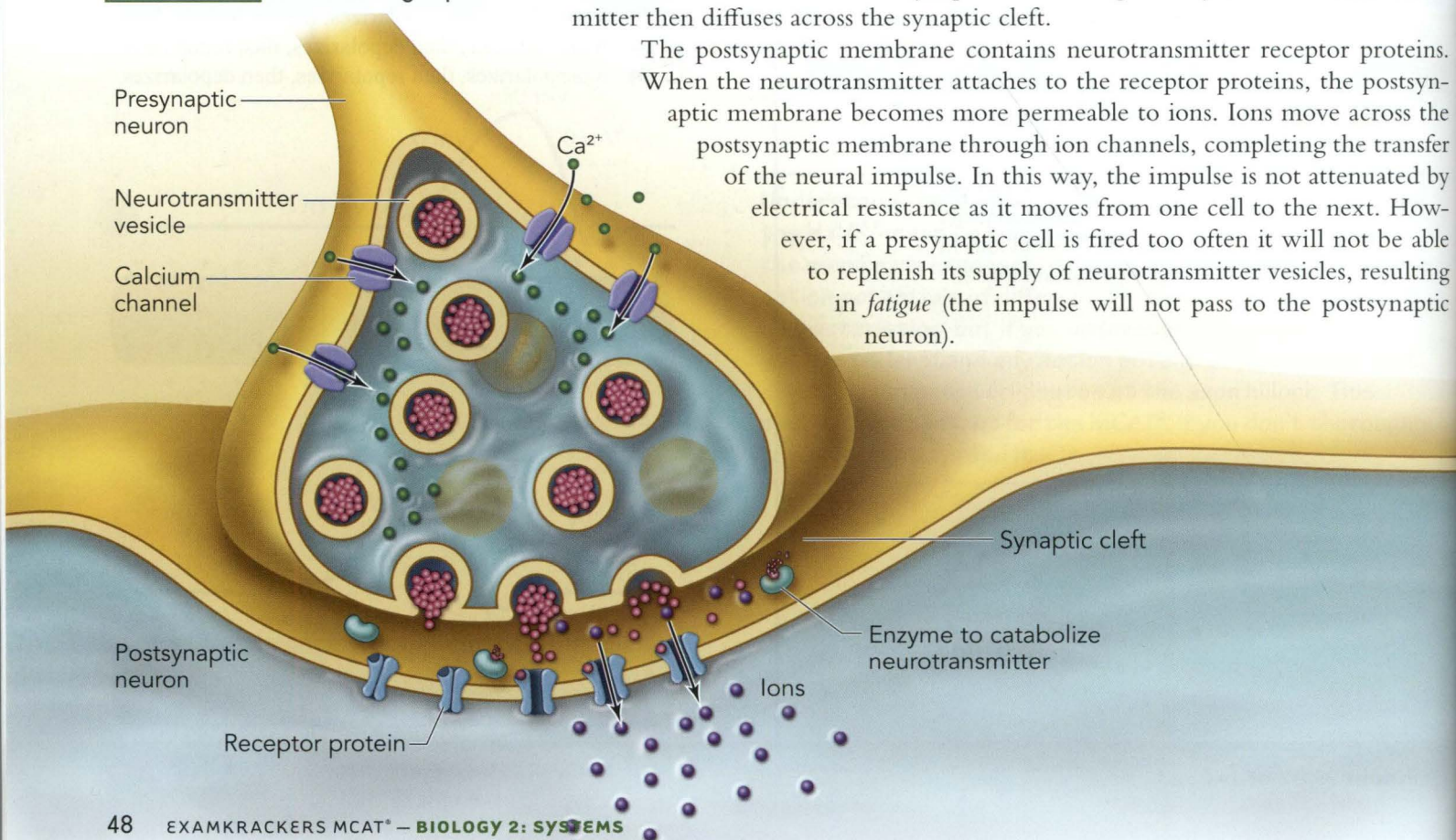
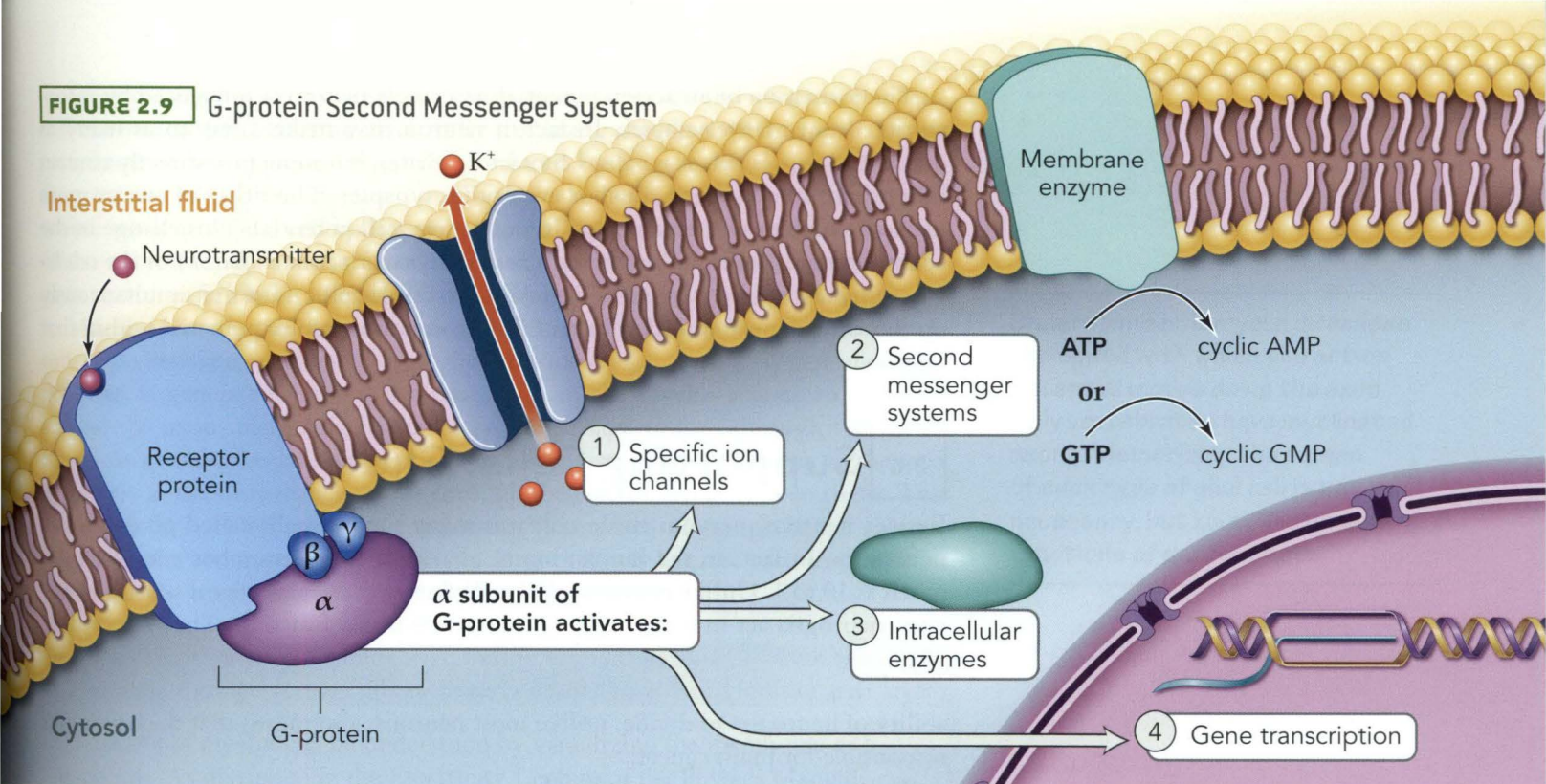


FIGURE 2.9 G-protein Second Messenger System



The neurotransmitter attaches to its receptor for only a fraction of a second and is then released back into the synaptic cleft. If the neurotransmitter remains in the synaptic cleft, the postsynaptic cell may be stimulated repeatedly. The cell uses several mechanisms to deal with this problem. The neurotransmitter may be destroyed by an enzyme in the matrix of the synaptic cleft and its parts recycled by the presynaptic cell; it may be directly absorbed by the presynaptic cell via active transport; or the neurotransmitter may diffuse out of the synaptic cleft.

Over 50 types of neurotransmitters have been identified. Different neurotransmitters are characteristic of different parts of the nervous system. A single neuron usually secretes only one type of neurotransmitter. Thus, rather than having to select different neurotransmitters for different purposes, a neuron can simply manufacture a single neurotransmitter for storage and release it when stimulated by an action potential. (However, a neuron may be able to respond to multiple types of neurotransmitter if its dendrites have the corresponding receptors.)

Any given synapse is designed either to inhibit or to excite, but not both. A single synapse cannot change from inhibitory to excitatory, or vice versa. On the other hand, some neurotransmitters can produce an inhibitory or excitatory effect depending on the type of receptor in the postsynaptic membrane. Acetylcholine, a common neurotransmitter, has an inhibitory effect on the heart, but an excitatory effect on the visceral smooth muscle of the intestines.

Receptors may be ion channels themselves, which open when their respective neurotransmitters attach, or they may act via a **second messenger system**, meaning that they activate another molecule inside the cell to make changes. For prolonged changes, such as those involved in memory formation, the second messenger system is preferred. *G-proteins* commonly initiate second messenger systems, as shown in Figure 2.9. A G-protein is attached to the receptor protein along the inside of the postsynaptic membrane. When the receptor is stimulated by a neurotransmitter, part of the G-protein, called the α subunit, breaks free. The α subunit may:

1. activate separate specific ion channels;
2. activate a second messenger (i.e. cyclic AMP or cyclic GMP);
3. activate intracellular enzymes; and
4. activate gene transcription.

Biological Correlates
PSYCH & SOC

Notice that the **second messenger system** allows nervous signals to have an effect on the expression of genes in target neurons.

The formation of an action potential in a single neuron is influenced by information from many synapses. In fact, a neuron may make a few to as many as 200,000 synapses. Most synapses contact dendrites, but some may directly contact other cell bodies, other axons, or even other synapses. The firing of one or more of these synapses creates a change in the neuron cell potential. This change in the cell potential is called either the *excitatory postsynaptic potential (EPSP)* or the *inhibitory postsynaptic potential (IPSP)*. Typically, 40–80 synapses must fire simultaneously on the same neuron in order for an EPSP to create an action potential within that neuron.

2.6

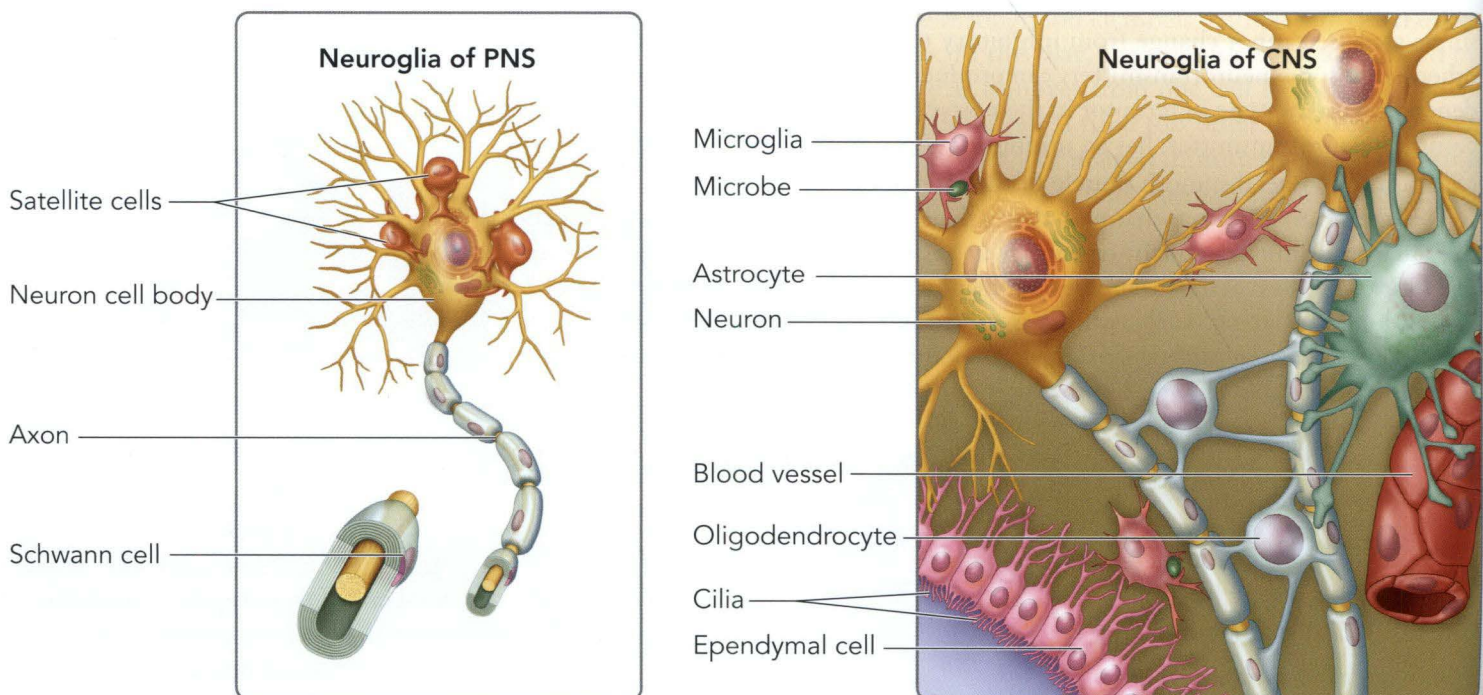
Supporting Cells: Glia

Besides neurons, nervous tissue contains many support cells called **glial cells** or **neuroglia**. In fact, in the human brain, glial cells can outnumber neurons by as much as 10 to 1. Unlike neurons, glial cells do not convey electrical signals. However, neuroglia act in many ways to support neuronal function. They are capable of cellular division, and, in the case of traumatic injury to the brain, it is the neuroglia that multiply to fill any space created in the central nervous system. The ability of neuroglia to divide, unlike most neurons, also means that they are often responsible for brain cancer.

There are six types of glial cells: microglia, ependymal cells, satellite cells, astrocytes, oligodendrocytes, and Schwann cells. *Microglia* are the central nervous system's macrophages. Like other macrophages, they arise from white blood cells called monocytes. They carry out an immune function, phagocytizing microbes and cellular debris. *Ependymal cells* are epithelial cells that line the space containing the cerebrospinal fluid. Ependymal cells use cilia to circulate the cerebrospinal fluid. *Satellite cells* support ganglia, which are groups of cell bodies in the peripheral nervous system. *Astrocytes* are star-shaped neuroglia in the central nervous system that give physical support to neurons and help maintain the mineral and nutrient balance in the interstitial space.



FIGURE 2.10 Glial Cells



Oligodendrocytes have processes that wrap many times around axons in the central nervous system, creating electrically insulating sheaths called **myelin**. In the peripheral nervous system, myelin is produced by **Schwann cells**, which wrap their entire cell bodies around axons. To the naked eye, myelinated axons appear white, while neuronal cell bodies appear gray. Thus, **white matter** refers to areas of the nervous system that are composed of myelinated axons of neurons, while **grey matter** refers to bundles of the cell bodies of neurons.

Myelin increases the rate at which signals can travel down an axon. There are tiny gaps between myelinated areas called **nodes of Ranvier**. When an action potential is generated down a myelinated axon, the myelin acts as an insulator around the axon, increasing resistance to the passage of ions through the membrane. As a result, the action potential jumps from one node of Ranvier to the next as quickly as the disturbance moves through the electric field between them. This phenomenon is called **saltatory conduction** (Latin *saltus*: a jump). In the absence of myelin, the action potential travels much more slowly because each tiny adjacent portion of the membrane must be depolarized in sequence.

MCAT® THINK

The effect of myelin can be understood by visualizing the membrane as a capacitor. As discussed in the Electricity Lecture of the Physics Manual, capacitance is defined as the amount of charge that a capacitor can store in a given area. Myelin is a non-conductive insulator and thus reduces the capacitance of the axon, which encourages ion flow just as the increased resistance does. Lowering capacitance also decreases the time required to charge a capacitor. In this biological example, the effect is that the speed of depolarization (and thus generation of the action potential) is increased at the nodes of Ranvier. This connection could appear in a physics passage on the MCAT®.

Understand how myelin increases the speed with which the action potential moves down the axon. Only vertebrates have myelinated axons. Memorizing the names of each type of glial cell is not necessary, but know the general functions of support cells.

2.7 The Structures of the Nervous System

Neurons may perform one of three functions:

1. **Sensory** (also called **sensor** or **afferent**) **neurons** receive signals from a receptor cell that interacts with the environment. The sensory neuron then transfers this signal to other neurons. The brain filters for the most relevant information and discards 99% of sensory input.
2. **Interneurons** transfer signals from neuron to neuron. 90% of neurons in the human body are interneurons.
3. **Motor** (also called **effector** or **efferent**) **neurons** carry signals to a muscle or gland called the **effector**. Sensory neurons are located dorsally (toward the back) on the spinal cord, while motor neurons are located ventrally (toward the front or abdomen). Thus, the neurons of the sensory and motor systems constitute physically separated systems, much like the parasympathetic and sympathetic divisions of the autonomic nervous system.

Neurons with these differing functions work in a coordinated fashion to sense incoming stimuli, communicate information to other neurons, and produce a response. Neuron processes (axons and dendrites) are typically bundled together to form **nerves** (called tracts in the CNS).

You can remember that **EFFerent** neurons are motor neurons because they cause the body to make an **EFFort** to respond to sensory information.

Figure 2.11 shows a simple **reflex arc** using all three types of neurons. A **reflex** is a quick response to a stimulus, such as one with the potential to cause tissue damage, that occurs without direction from the central nervous system. This adaptive response is what causes an organism to jerk away from a hot stimulus before having a conscious experience of pain. Some reflex arcs do not require an interneuron. For example, the *stretch reflex* involves direct communication between a motor and sensory neuron. In response to the stretching of a muscle, a sensory neuron signals a motor neuron in the spinal cord. The motor neurons respond such that the stretched muscle contracts to regain its resting length. The stretch reflex demonstrates how a reflex arc can act according to a **negative feedback loop**. The sensory neuron senses a change and stimulates a corresponding adjustment by the motor neuron that acts in opposition to the change, ensuring a return to the resting muscle length without the need for conscious control.

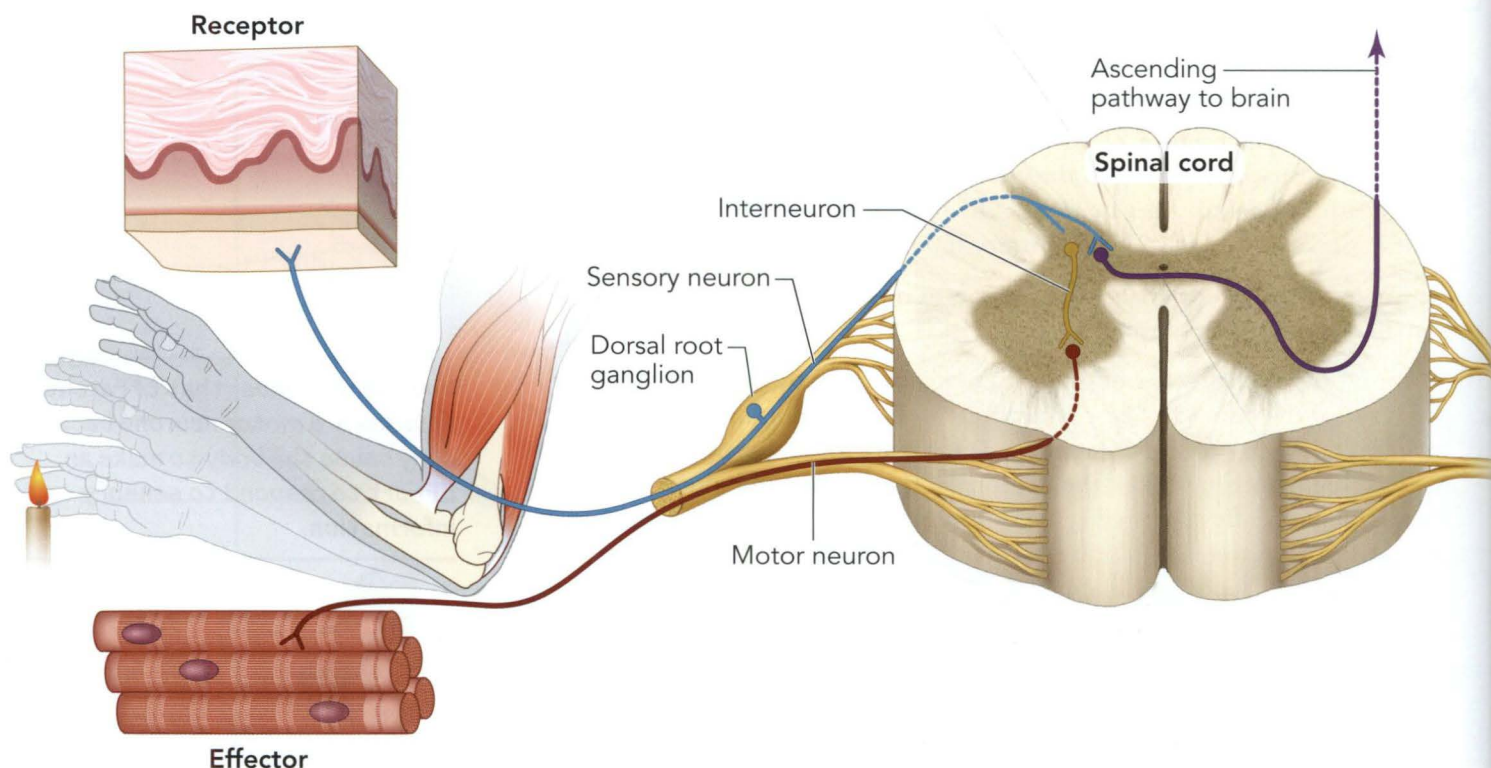
Even though reflexes do not require a higher-level command, they do not occur independently from the CNS. Information about the stimulus is sent to the CNS as the reflex is generated, allowing the perception of the stimulus and coordination of a more complex response. In addition, the CNS can send signals that dampen or enhance reflex responses according to the needs of the organism. In the example of the stretch reflex given above, inhibitory input from **supraspinal circuits** descending from the CNS can decrease the sensitivity and speed of the reflex so that it proceeds smoothly and only when needed.

As discussed previously, the nervous system has two major divisions: the **central nervous system (CNS)** and the **peripheral nervous system (PNS)**. The CNS consists of the neurons and support tissue within the brain and the spinal cord. A major function of the CNS is to integrate nervous signals between sensory and motor neurons.

The CNS is connected to the peripheral parts of the body by the PNS. Parts of the PNS, such as the *cranial nerves* and the *spinal nerves*, project into the brain and spinal cord. The PNS handles the sensory and motor functions of the nervous system. The PNS is further divided into the **somatic nervous system** and **autonomic nervous system (ANS)**. The somatic nervous system contains sensory and motor functions and primarily functions to respond to the external

For the MCAT®, think of the CNS as the brain and spinal cord, and the PNS as everything else.

FIGURE 2.11 Simple Reflex Arc of the Somatic Nervous System

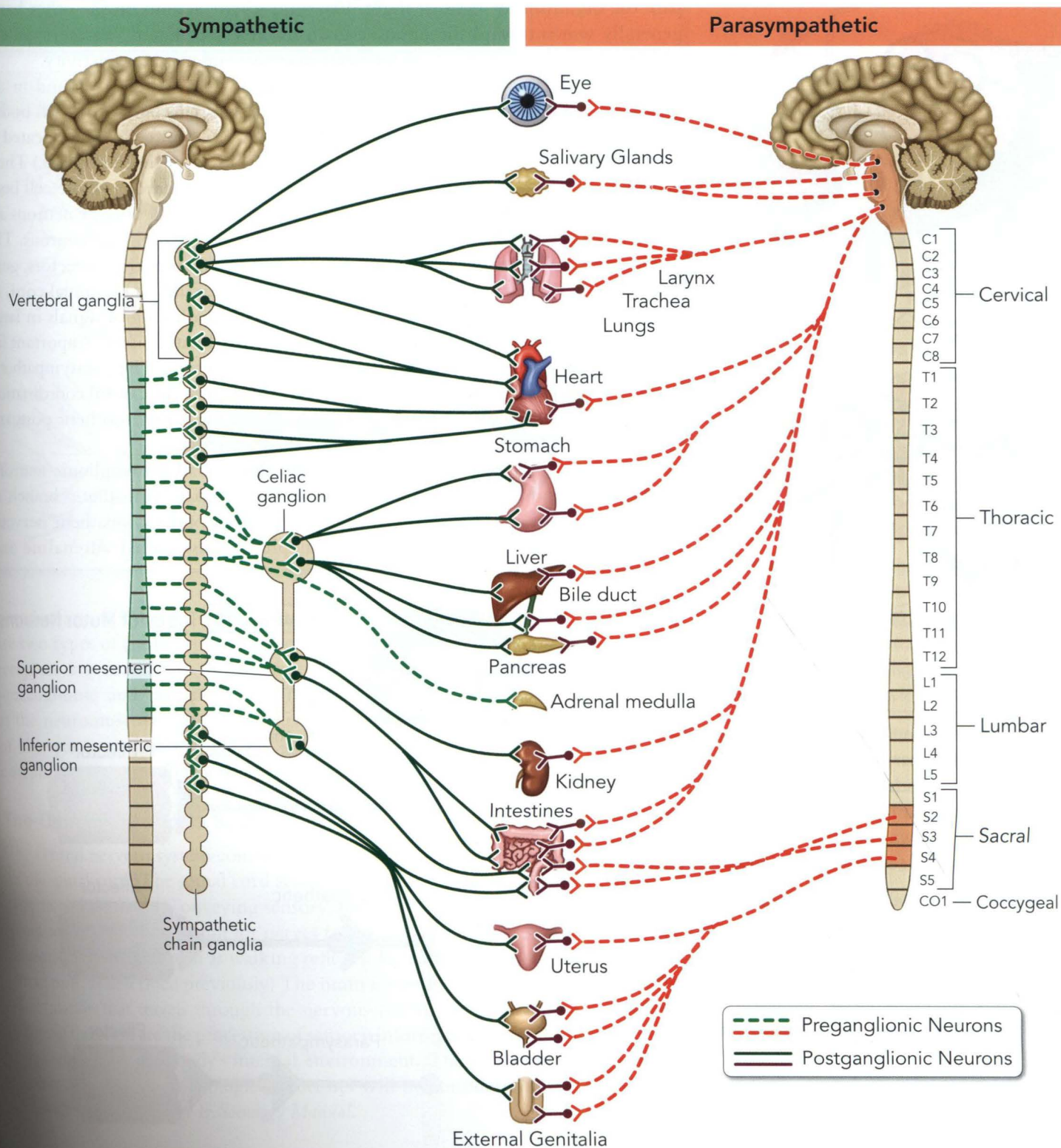


environment. The sensory neuron cell bodies are located in the *dorsal root ganglion*. The motor neurons innervate only skeletal muscle, which is involved in voluntary movement. The cell bodies of somatic motor neurons are located in the ventral horns of the spinal cord. These neurons synapse directly on their effectors and release the neurotransmitter acetylcholine. The motor functions of the somatic nervous system can be consciously controlled and are considered voluntary.

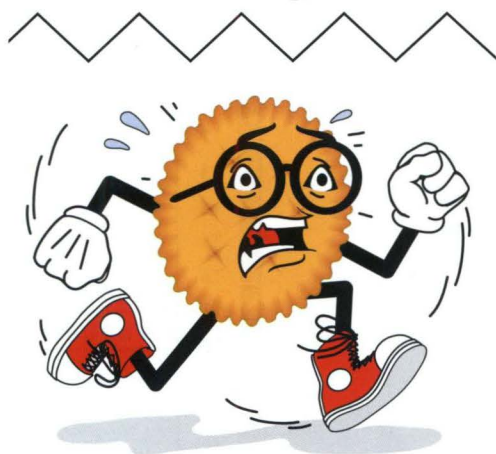
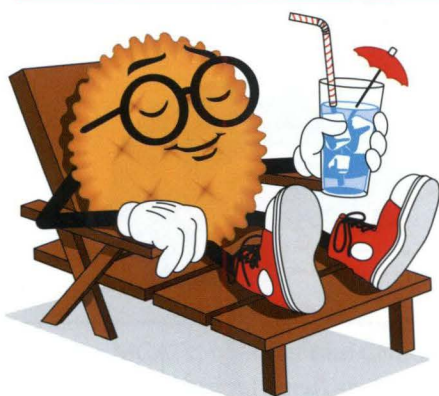
The ANS coordinates an involuntary response to environmental stimuli, altering processes within the body to produce the most adaptive physiological state and behavior. The sensory portion of the ANS receives signals primarily from the viscera (the organs inside the ventral body cavity). The motor portion of the ANS then

Associate the somatic nervous system with voluntary movement and conscious control. By contrast, when you think of the autonomic nervous system, think of involuntary processes that occur outside of conscious awareness.

FIGURE 2.12 The Autonomic Nervous System



Don't make the mistake of thinking that sympathetic stimulates and parasympathetic inhibits; this is **INCORRECT**. Their actions depend on the organs that they are innervating. For instance, parasympathetic neurons have an inhibitory effect on the heart but an excitatory effect on the digestive system. Use "fight or flight" and "rest or digest" to make predictions.



The autonomic nervous system is involuntary and innervates cardiac and smooth muscle, as well as some glands; the somatic nervous system is voluntary and innervates skeletal muscle. Autonomic pathways are controlled mainly by the hypothalamus (described in the next section).

Familiarize yourself with the following neurotransmitters: acetylcholine, epinephrine, and norepinephrine. Relate acetylcholine to both the somatic and parasympathetic nervous systems, and epinephrine and norepinephrine to the sympathetic nervous system only.

conducts these signals to smooth muscle, cardiac muscle, and glands. The motor portion of the ANS is divided into two systems: **sympathetic** and **parasympathetic** (see Figure 2.12). Most internal organs are innervated by both systems in a competitive manner. In other words, the two systems have opposing influences on the same organs and thus exert **antagonistic control**. The parasympathetic and sympathetic nervous systems are two physically separable sets of nerves, which are able to independently exert opposite influences on the same organs by each secreting their own neurotransmitter, as will be described.

The sympathetic ANS deals with "fight or flight" responses. For instance, it acts on the heart to increase heart rate and stroke volume. It also causes the constriction of blood vessels around organs of the digestive and excretory systems in order to divert more blood flow to skeletal muscles. Both of these effects help prepare the organism for fight or flight. Parasympathetic action, on the other hand, generally works toward the opposite goal, to "rest and digest." Parasympathetic activity slows the heart rate and increases digestive and excretory activity.

Sympathetic signals originate in neurons whose cell bodies are found in the spinal cord, while parasympathetic signals originate in neurons whose cell bodies can be found in both the brain and spinal cord. (A group of cell bodies located in the CNS is called a *nucleus*; if located outside the CNS, it is called a *ganglion*.) These neurons extend out from the spinal cord to synapse with neurons whose cell bodies are located outside the CNS. As shown in Figure 2.12, the former neurons are called preganglionic neurons, and the latter are called postganglionic neurons. The cell bodies of sympathetic postganglionic neurons lie far from their effectors, generally within the paravertebral ganglion, which runs parallel to the spinal cord, or within the prevertebral ganglia in the abdomen. The gathering of signals in large ganglia far from the effectors allows for a strong, coordinated signal, important for the sympathetic nervous system's "fight or flight" function. The parasympathetic nervous system's "rest and digest" functions do not require the careful coordination of signaling found in the SNS; thus the cell bodies of the parasympathetic postganglionic neurons lie in ganglia inside or near their effectors.

With few exceptions, the neurotransmitter used by all preganglionic neurons in the ANS and by postganglionic neurons in the parasympathetic branch is **acetylcholine**. In contrast, the postganglionic neurons of the sympathetic nervous system use either **epinephrine** or **norepinephrine** (also called **adrenaline** and

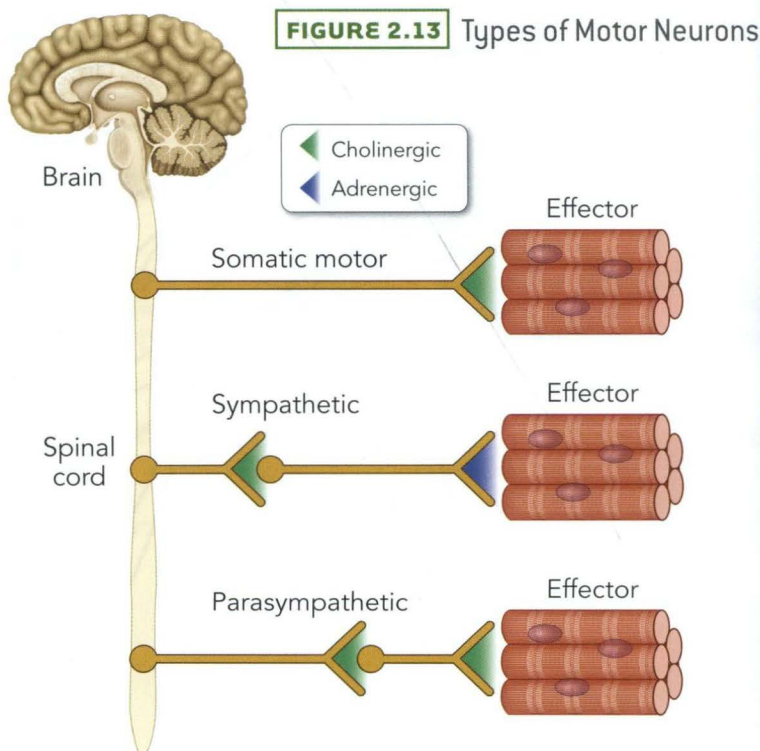
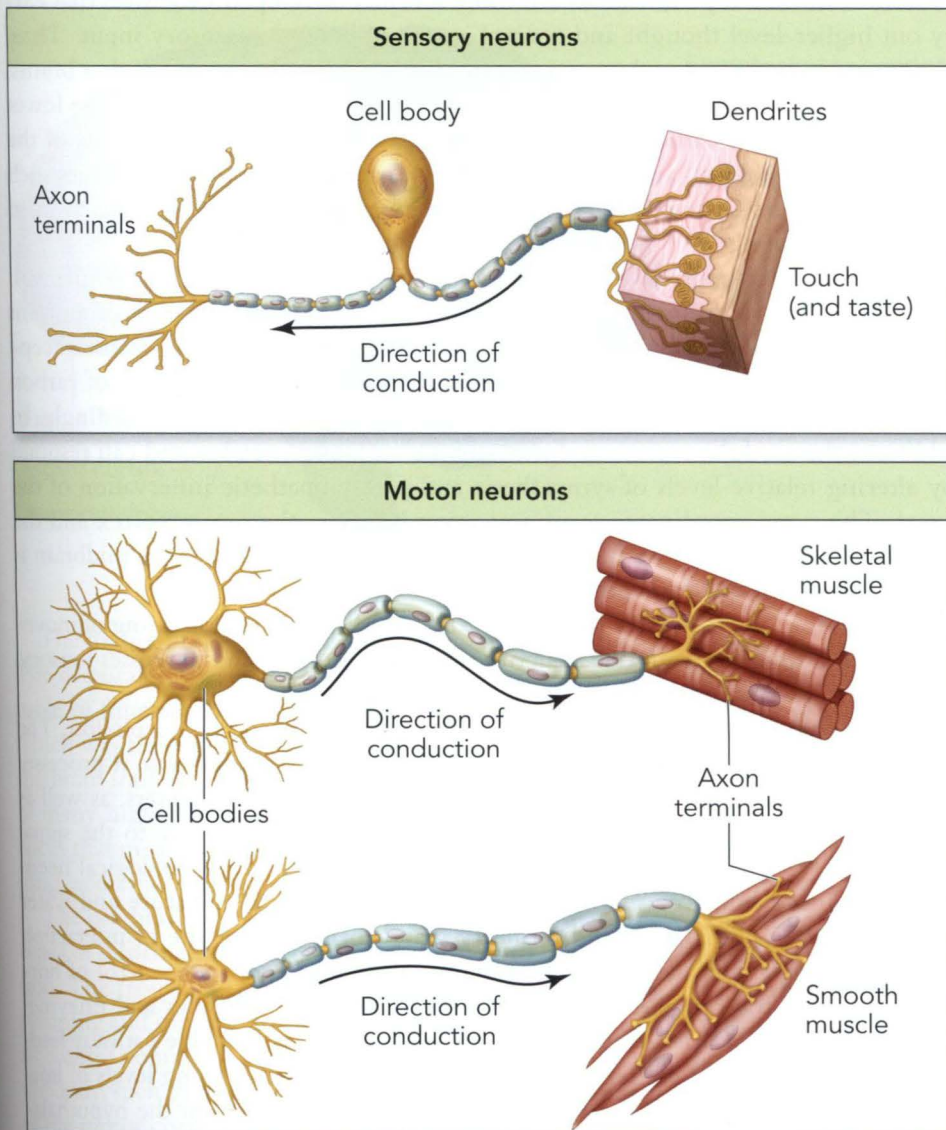


FIGURE 2.14 Sensory and Motor Neurons



noradrenaline). Receptors for acetylcholine are called *cholinergic receptors*. There are two types of cholinergic receptors: *nicotinic* and *muscarinic*. Generally, nicotinic receptors are found on the postsynaptic cells of the synapses between ANS preganglionic and postganglionic neurons and on skeletal muscle membranes at the neuromuscular junction. Muscarinic receptors are found on the effectors of the parasympathetic nervous system. The receptors for epinephrine and norepinephrine are called *adrenergic receptors*.

The Central Nervous System

The central nervous system consists of the lower brain, the higher brain, and some of the spinal cord. The spinal cord acts as a bridge between the peripheral nervous system and the brain, conveying sensory and motor signals. (Although the spinal cord acts mainly as a conduit for nerves to reach the brain, it does possess limited integrating functions such as walking reflexes, leg stiffening, and limb withdrawal from pain, as described previously) The brain is the site of integration for all of the information that travels through the nervous system. The most important functions of the brain are the processing of sensory information, responding to stimuli, and regulation of the body's internal environment. The connection between the nervous system and psychological processes will be considered further in the last lecture of the *Psychology & Sociology Manual*.

Think of **GANGlia** as gangs of cell bodies in the PNS. Recall that the cell bodies of neurons receive the electrical disturbances generated in dendrites at the synapse. As the interface between the input and output of the neuron, the cell body is the ideal location to gather together and integrate multiple signals. The axons of these neurons can then gather to form nerves.

Also, remember that groups of cell bodies that lie within the central nervous system are referred to as **nuclei**. You will see examples in the sections regarding processing of sensory information in the brain.

The areas of the CNS that originated in earlier stages of evolution control vital functions and convey information to more recently developed structures that carry out higher-level thought and control motor responses to sensory input. Thus, the brain can be considered in two sections known as the lower and higher brains, each of which contains areas that are specialized for certain functions. The lower brain represents an earlier stage of evolutionary development and consists of the brainstem, cerebellum, and diencephalon. It integrates unconscious activities such as the respiratory system, arterial pressure, salivation, emotions, and reaction to pain and pleasure.

The **brainstem** controls the basic involuntary functions necessary for survival. It includes the **medulla**, pons, and midbrain. The medulla plays an important role in the regulation of the cardiovascular and respiratory systems. Chemoreceptors (described in the following section) in the medulla monitor levels of carbon dioxide in the bloodstream and trigger changes in respiration rate accordingly. In addition, the medulla receives information about blood pressure and can respond by altering relative levels of sympathetic and parasympathetic innervation of the heart. The **pons** coordinates communication between the motor cortex and the cerebellum, facilitating the transfer of motor commands. Finally, the midbrain is a relay station for auditory and visual signals.

The **cerebellum** is heavily involved in the coordination and planning of movement. It is a highly integrative structure in that it receives and processes sensory, motor, and vestibular input.

The thalamus and hypothalamus are collectively called the **diencephalon**. The **thalamus** is often described as a control center or waystation because it processes almost all sensory information before it reaches higher cortical centers, as well as receiving motor commands from these cortical areas on their way to the spinal cord. The **hypothalamus** regulates many of the body's basic physiological needs by maintaining homeostasis in multiple systems such as temperature and water balance. The hypothalamus and pituitary gland form a major site of interaction between the nervous and endocrine systems, allowing **feedback control** of hormone levels in the body. As discussed in the Biological Molecules and Enzymes Lecture of *Biology 1: Molecules*, negative feedback within an enzyme pathway leads to down-regulation of earlier steps. In an analogous process, rising levels of hormones released by the pituitary gland in response to signals from the hypothalamus feed back to these structures to inhibit further hormone release. The next lecture in this manual will describe the hormones that are released by the anterior pituitary and thus participate in this mechanism of feedback control.

Endocrine System

BIOLOGY 2

FIGURE 2.15 Major Structures of the Lower Brain

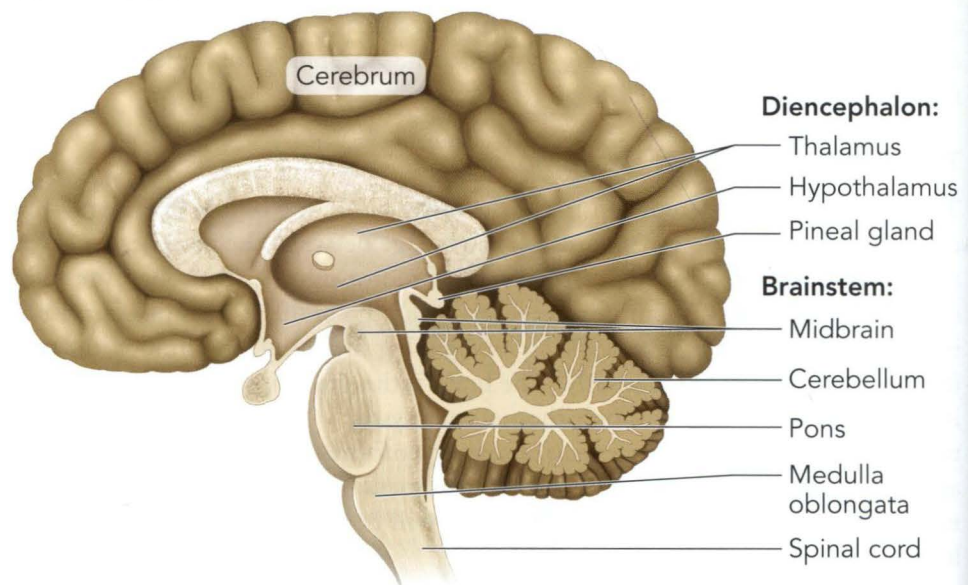
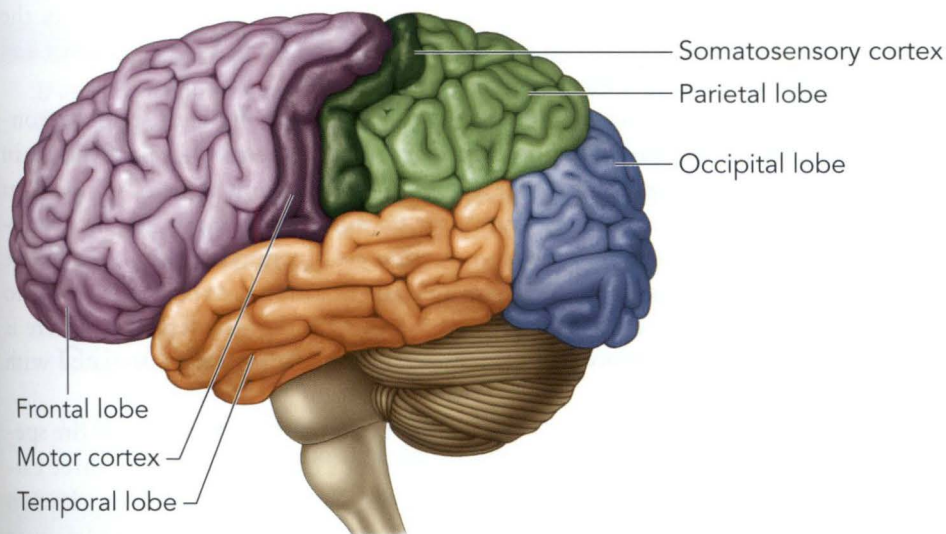


FIGURE 2.16 Lobes of the Cerebral Cortex



The higher brain, or cortical brain, contains the **cerebrum** or **cerebral cortex**. The cerebral cortex is the most recently evolved portion of the brain and is incapable of functioning without the lower brain. It has a folded, grooved structure, which was the evolutionary response to the problem of fitting a large new part of the brain into the restricted space of the skull. The cerebral cortex is the location of many higher-level functions of the nervous system that influence the experiences that most make us human, such as consciousness, memory, cognition, planning, and emotion.

The cerebral cortex can be divided into areas that receive and integrate specific types of information from the environment to achieve the highest level of perception. The **frontal lobe** is the location of higher-level (executive) functions such as planning and impulse inhibition. It includes the motor cortex, which sends signals to control voluntary movements. The **motor cortex** creates a map of the parts of the body, such that specific sets of neurons control certain body parts. The amount of the motor cortex that is devoted to each part of the body depends on the complexity of movement required. The **parietal lobe** contains the **somatosensory cortex**, which maps the body's sensation of touch. The somatosensory cortex is part of the **somatosensory system**, which involves the detection of physical stimuli such as touch, temperature, and pain. Like the motor cortex, the somatosensory cortex creates a map of the body. The devotion of comparatively large portions of the somatosensory cortex to particular parts of the body, such as the hands, makes these regions particularly sensitive to tactile stimuli.

The **occipital lobe** is the site where visual information is processed. Finally, the **temporal lobe** is primarily concerned with auditory and olfactory information. The cortical brain also contains the hippocampus and the amygdala. These structures are central to the function of the **limbic system**, which is primarily concerned with memory and emotion.

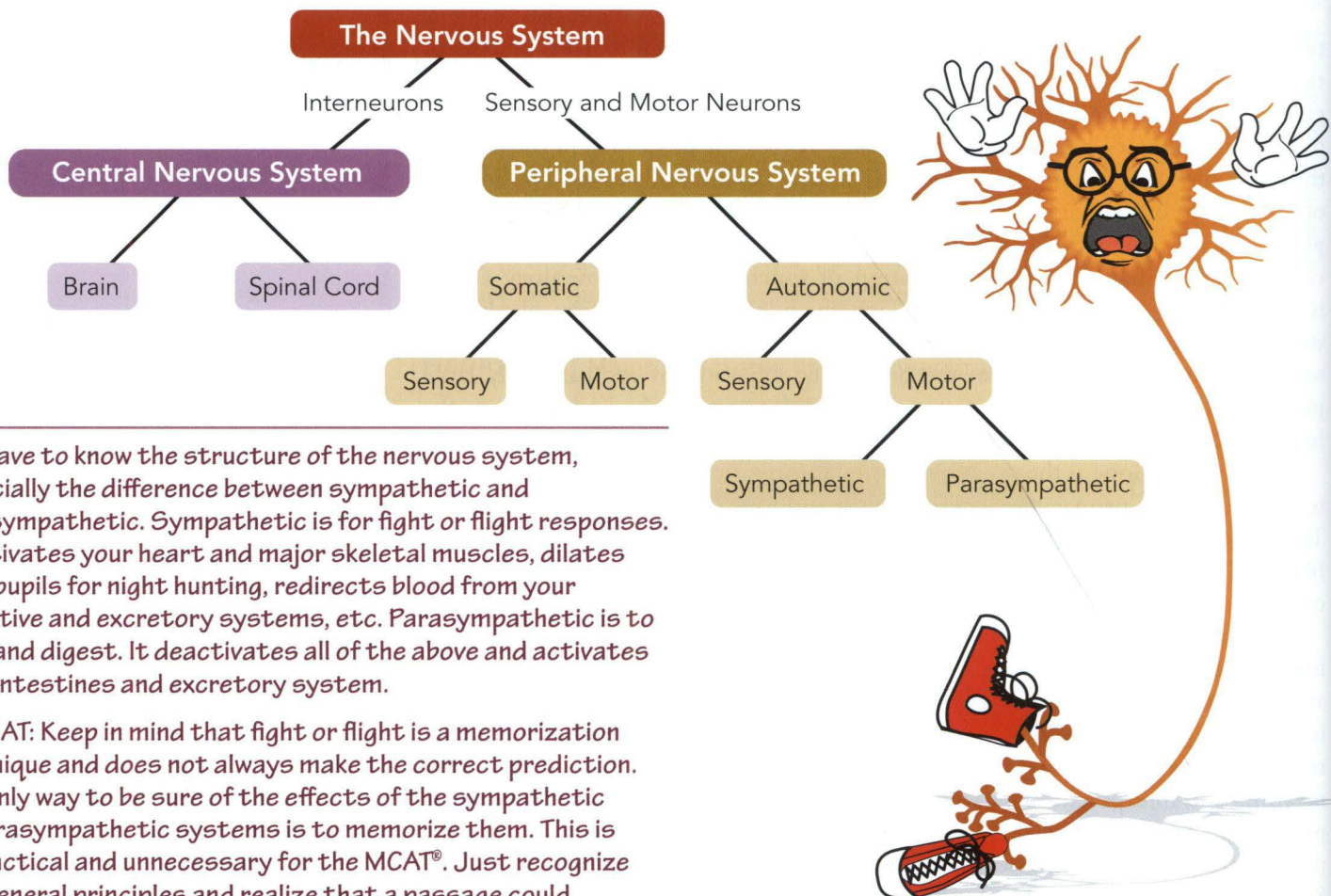
It is important to understand that the cerebrum does not simply receive information from the sensory system and coordinate a response (although this is an important part of its function). It also influences our experience of the world in two important ways. First, the cerebrum processes and interprets information received from the senses, integrating information and imposing higher-level meaning and interpretation based on previous experience. (The field of cognitive psychology describes the cerebrum's interpretation of stimuli using an **information processing model**, as discussed in Lecture 4 of the *Psychology & Sociology Manual*.) Second, it can exert a top-down influence on the sensory system, influencing what is considered most important and thus altering the perception of environmental

Both the limbic system and the interplay between the senses and higher-level interpretation will be considered further in the *Psychology & Sociology Manual*. It is likely that you would see questions about the different lobes of the cerebral cortex in the Psychosocial section of the MCAT®. Understand that the brain contains specialized areas for different sensory and motor functions, but realize that the brain also has plasticity. The brain can often partly compensate for damage to one part of the brain by recruiting neurons from adjacent areas to take over the functions of that area.

stimuli. For example, in addition to carrying signals from sensory receptors to the cerebrum, the thalamus is also a waystation for signals in the opposite direction. In some cases the cerebrum can even influence sensory receptors, such as in the auditory system, where signals can travel all the way from the cerebral cortex and through the thalamus to produce an effect on hair cells.

The cerebrum is physically divided into two halves (cerebral hemispheres), connected by the *corpus callosum*. For the most part the two hemispheres of the brain carry out the same functions. However, the brain does exhibit some **lateralization of cortical functions**. Lateralized functions take place primarily in one hemisphere or the other. For example, the production and comprehension of language are localized to two areas in the left hemisphere. Emotional experience seems to be roughly divided between the two hemispheres such that the left hemisphere is more involved in positive emotions while the right hemisphere is associated with negative emotions.

Many **methods of studying the brain** have been used to characterize the specific neural functions of certain areas. These methods can be placed into three categories: lesion studies, imaging, and recording of electrical activity. Many known areas of localized function, including the language centers mentioned above, were discovered by observation of people who had damage to those areas. It is now possible to carry out more direct observation of the brain in living organisms. Various methods of imaging, relying on the increased blood flow to areas of the brain that are active and thus have increased metabolic needs, can be used to examine the brain while the subject carries out tasks. In addition, it is possible to measure the firing of individual neurons (using electrodes in animal studies) or overall patterns of electrical activity at the scalp. However, none of these methods perfectly capture neurological activity. There is constant communication between different parts of the brain such that no one structure carries out its functions in isolation.



You have to know the structure of the nervous system, especially the difference between sympathetic and parasympathetic. Sympathetic is for fight or flight responses. It activates your heart and major skeletal muscles, dilates your pupils for night hunting, redirects blood from your digestive and excretory systems, etc. Parasympathetic is to rest and digest. It deactivates all of the above and activates your intestines and excretory system.

CAVEAT: Keep in mind that fight or flight is a memorization technique and does not always make the correct prediction. The only way to be sure of the effects of the sympathetic or parasympathetic systems is to memorize them. This is impractical and unnecessary for the MCAT®. Just recognize the general principles and realize that a passage could present other functions outside this framework.

These questions are NOT related to a passage.

Item 33

If an acetylcholinesterase inhibitor were administered into a cholinergic synapse, what would happen to the activity of the postsynaptic neuron?

- ☐ A) It would decrease, because acetylcholine would be degraded more rapidly than normal.
- ☐ B) It would decrease, because acetylcholinesterase would bind to postsynaptic membrane receptors less strongly.
- ☐ C) It would increase, because acetylcholine would be produced more rapidly than normal.
- ☐ D) It would increase, because acetylcholine would be degraded more slowly than normal.

Item 34

White matter in the brain and spinal cord appears white because:

- ☐ A) it contains large amounts of myelinated axons.
- ☐ B) it does not contain any myelinated axons.
- ☐ C) it is composed primarily of cell bodies.
- ☐ D) it contains a high concentration of white blood cells to protect the central nervous system from infection.

Item 35

Which of the following is found in vertebrates but NOT in invertebrates?

- ☐ A) A dorsal, hollow nerve chord
- ☐ B) Myelination to increase the speed of nervous impulse transmission along the axon
- ☐ C) Axons through which the nervous impulse is conducted
- ☐ D) An Na^+/K^+ - pump in the neuronal membrane

Item 36

Which of the following activities is controlled by the cerebellum?

- ☐ A) Involuntary breathing movements
- ☐ B) Fine muscular movements during a dance routine
- ☐ C) Contraction of the thigh muscles during the knee-jerk reflex
- ☐ D) Absorption of nutrients across the microvilli of the small intestine

Item 37

If an acetylcholine antagonist were administered generally into a person, all of the following would be affected EXCEPT:

- ☐ A) the neuroeffector synapse in the sympathetic nervous system.
- ☐ B) the neuroeffector synapse in the parasympathetic nervous system
- ☐ C) the neuromuscular junction in the somatic nervous system.
- ☐ D) the ganglionic synapse in the sympathetic nervous system.

Item 38

Which of the following occurs as a result of parasympathetic stimulation?

- ☐ A) Vasodilation of the arteries leading to the kidneys
- ☐ B) Increased rate of heart contraction
- ☐ C) Piloerection of the hair cells of the skin
- ☐ D) Contraction of the abdominal muscles during exercise

Item 39

Reflex arcs:

- ☐ A) involve motor neurons exiting the spinal cord dorsally.
- ☐ B) require fine control by the cerebral cortex.
- ☐ C) always occur independently of the central nervous system.
- ☐ D) often involve inhibition as well as excitation of muscle groups.

Item 40

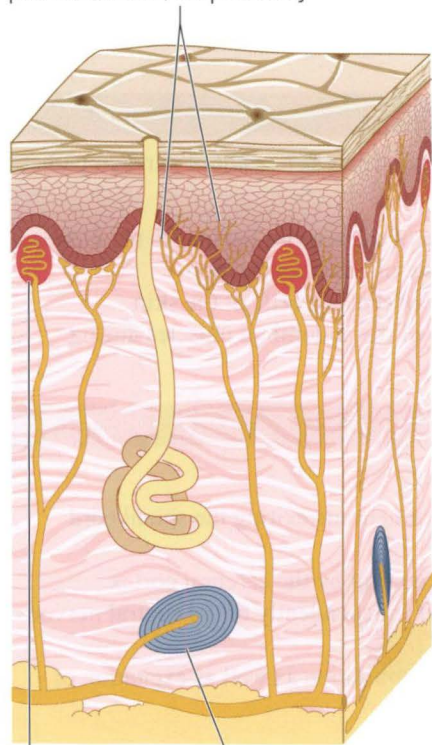
Which of the following structures is NOT part of the central nervous system?

- ☐ A) A parasympathetic effector
- ☐ B) The medulla
- ☐ C) The hypothalamus
- ☐ D) The cerebral cortex

FIGURE 2.17 Sensory Receptors of the Somatosensory System

Thermoreceptors and Nociceptors

Free nerve endings that detect changes in temperature and painful stimuli, respectively



Mechanoreceptors
Meissner's corpuscle detects superficial pressure
Pacinian corpuscle detects deep pressure

Sensing is bringing information into the nervous system from the outside. By contrast, motor neurons carry information out. The body uses cells called **sensory receptors** to detect internal and external stimuli. The sensory receptors communicate information by transducing physical stimuli to electrical signals that can then be conveyed to the central nervous system via sensory nerves for processing, integration, and interpretation. There are five types of sensory receptors:

1. **mechanoreceptors** for touch;
2. **thermoreceptors** for temperature change;
3. **nociceptors** for pain;
4. **electromagnetic receptors** for light; and
5. **chemoreceptors** for taste, smell and blood chemistry.

Some types of sensory receptors are actually part of sensory neurons rather than being separate cells. For example, the receptors associated with the somatosensory system are extensions of sensory neurons, as are the sensory receptors of the smell system. Sensory neurons that are themselves sensory receptors differ from other types of neurons in that they respond to environmental stimuli rather than to signals from other cells.

Since the somatosensory system processes the sensations of touch, temperature, and pain, the sensory receptors of the somatosensory system are mechanoreceptors, nociceptors, and thermoreceptors. Mechanoreceptors respond to the physical stimuli of touch and pressure change. (Mechanoreceptors are not only involved in the somatosensory system. As described later in this lecture, the hair cells of the organ of Corti are mechanoreceptors that send signals in response to the increased and decreased pressure of sound waves.) Nociceptors detect some of the same stimuli as the other types of receptors, such as temperature, pressure, and chemicals, but they are particularly sensitive to the extremes of these stimuli. Nociceptors specialize in the detection of stimuli that generate the experience of pain.

Photoreceptors are a type of electromagnetic receptor. They detect the physical stimulus of photons that enter the eye. Unlike other types of sensory receptors, they do not generate action potentials. Instead, in a similar but distinct process, the relative level of light in the environment affects the rate of neurotransmitter release by photoreceptors into the synapses that they share with sensory neurons. This unique setup will be described in the discussion of the visual system.

In contrast to the other types of receptors that detect and interpret non-chemical stimuli, chemoreceptors bind chemicals, acting as detectors of chemical levels in the external and internal environment. Chemoreceptors are extremely important for the maintenance of homeostasis throughout the body; for example, they are involved in the regulation of the cardiovascular and respiratory systems. Chemoreceptors are the type of sensory receptor used by the taste and smell systems, as described at the end of this lecture.

Each receptor responds strongly to its own type of stimulus and weakly or not at all to other types of stimuli. The sensory receptors transduce physical and chemical stimuli to neural signals that can then be conveyed by sensory neurons. Each type of receptor has its own neural pathway and termination point in the central nervous system, resulting in the various sensations.

Of course, it would not be particularly convenient if every little stimulus caused a response by sensory receptors. Just as small voltage disturbances in the neuronal resting potential caused by individual stimuli are summed to produce an overall excitatory or inhibitory effect, receptor potentials produced by outside stimuli each increase or decrease the likelihood that an action potential will be produced by the sensory receptor to transfer information to the associated sensory neurons. In addition, the sensory system codes information about the intensity of stimuli

through activation of different numbers of sensory receptors, activation of different types of receptors (e.g. nociceptors for pain and extreme stimuli), and the frequency of signaling by sensory neurons.

Just as the nervous system has mechanisms for distinguishing between stimuli of different intensity levels, it is able to tone down the response to a repeating stimulus. In a process known as **sensory adaptation**, a stimulus that occurs repeatedly at the same intensity level evokes fewer and fewer action potentials in the sensory receptors. Sensory adaptation is part of how the nervous system achieves its function of filtering out less important information, allowing the perception of changes in the environment. Some types of sensory receptors, called *phasic receptors*, adapt very quickly and thus specialize in the perception of changes in stimuli. By contrast, *tonic receptors* adapt more slowly. The length of time required for tonic receptors to stop producing action potentials provides information to the nervous system about the intensity of the stimulus.

The rest of this lecture is concerned with sensory systems that specialize in particular types of environmental input. Each of these systems can be characterized by the type(s) of receptors involved, the process by which the physical stimulus is converted into electrical information that can be transferred by the nervous system, and the interpretation of this information by higher brain centers. Within most of these systems, as will be described, the sensory receptors create a map of the surroundings that is preserved as the information travels throughout the nervous system.

2.9 The Eye and Vision

The **eye** detects patterns of light and transmits this information to the nervous system, ultimately resulting in the perception of vision. The eye can be thought of as a biological example of an optical instrument. Much like binoculars or a microscope, the eye can adjust to focus on objects of different sizes and distances. For the MCAT®, the test-taker must know the basic anatomy of the eye (as shown in Figure 2.19) and understand the function of a few of its parts. A good way to remember the basics of vision is to follow the path of light as it enters the eye.

Light reflects off an object in the external environment and first strikes the eye on the **cornea**. (Technically the light first encounters a very thin, protective layer known as the corneal epithelium.) The cornea is nonvascular and made largely from collagen. It is clear with a refractive index of about 1.4, which means that the incoming light is actually bent furthest at the interface of the air and the cornea rather than at the lens.

From the cornea, the light enters the *anterior chamber*, which is filled with **aqueous humor**. Aqueous humor is formed by the *ciliary bodies* and leaks out of the *canal of Schlemm*. Blockage of the canal of Schlemm increases intraocular pressure, resulting in one form of **glaucoma** and possibly blindness.

From the anterior chamber, light enters the **lens**. The lens naturally has a spherical shape, but stiff suspensory ligaments tug on it and tend to flatten it. Thus, the shape of the lens can be adjusted according to the focal length needed to ensure that the image produced by a given object will be focused precisely on the retina, rather than behind or in front of it. The suspensory ligaments are connected to the **ciliary muscle** circling the lens. When the ciliary muscle contracts, the opening of the circle decreases, allowing the lens to become more like a sphere and bringing its focal point closer to the lens; when the muscle

Why would the nervous system want to pay less attention to repeated stimuli? Imagine what would happen if I kept noticing these wool socks all day just as much as I did when I first put them on. I wouldn't be able to notice more important new information in my surroundings, like this hungry tiger.

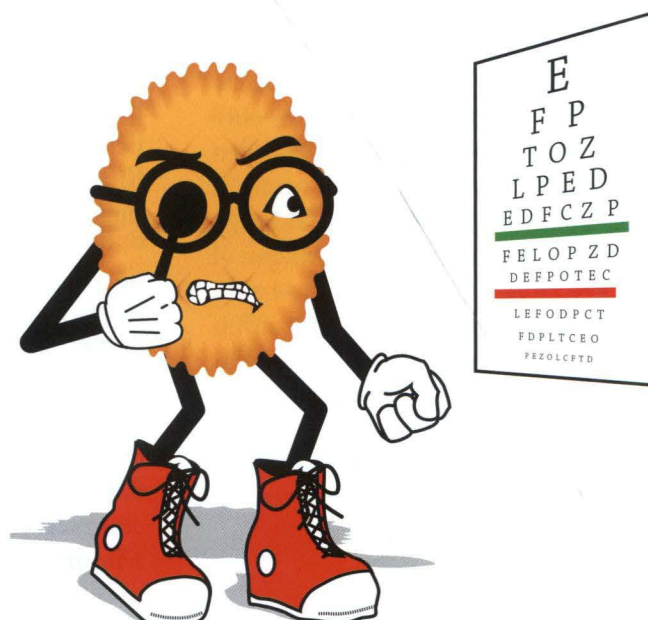
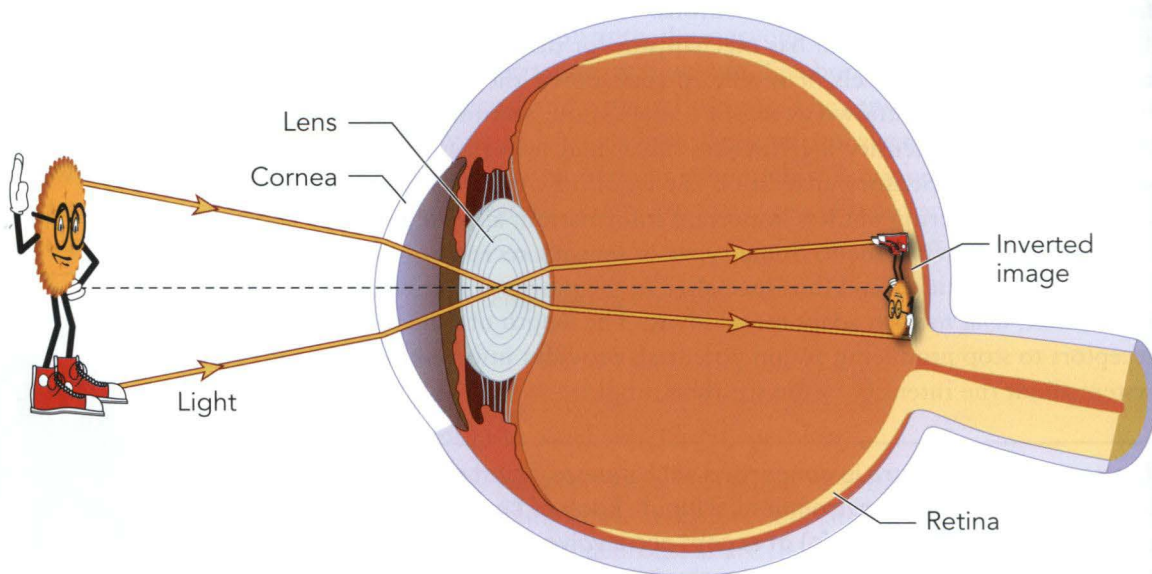


FIGURE 2.18 Image Formation on the Retina



relaxes, the lens flattens, increasing the focal distance. The elasticity of the lens declines with age, making it more difficult to decrease the focal length of the lens, with the result that it becomes harder to focus on nearby objects as one gets older.

When light passes through the structures described above, it is focused through the gel-like *vitreous humor* and onto the retina. Since the eye acts as a converging lens, and the object is outside the focal distance, the image on the retina is real and inverted (Figure 2.18).

The **retina** covers the inside of the back (distal portion) of the eye. It contains **rods** and **cones**, two types of photoreceptors named for their characteristic shapes. The tips of these cells contain light sensitive photochemicals called *pigments* that undergo a chemical change when one of their electrons is struck by a single photon. Vitamin A is a precursor to all the pigments in rods and cones. (As discussed in the Biological Molecules and Enzymes Lecture of *Biology 1: Molecules*, vitamin A is an example of a terpene.) The restricted range of wavelengths of light to which the pigments respond determines the spectrum of light visible to humans.

The pigment in rod cells is called *rhodopsin*. Rhodopsin is made of a protein bound to a prosthetic group called *retinal*, which is derived from vitamin A. The photon isomerizes retinal, causing the membrane of the rod cell to become less permeable to sodium ions, which in turn causes it to hyperpolarize. Rods respond to all photons with wavelengths in the visible spectrum (390 nm to 700 nm), so they cannot distinguish colors.

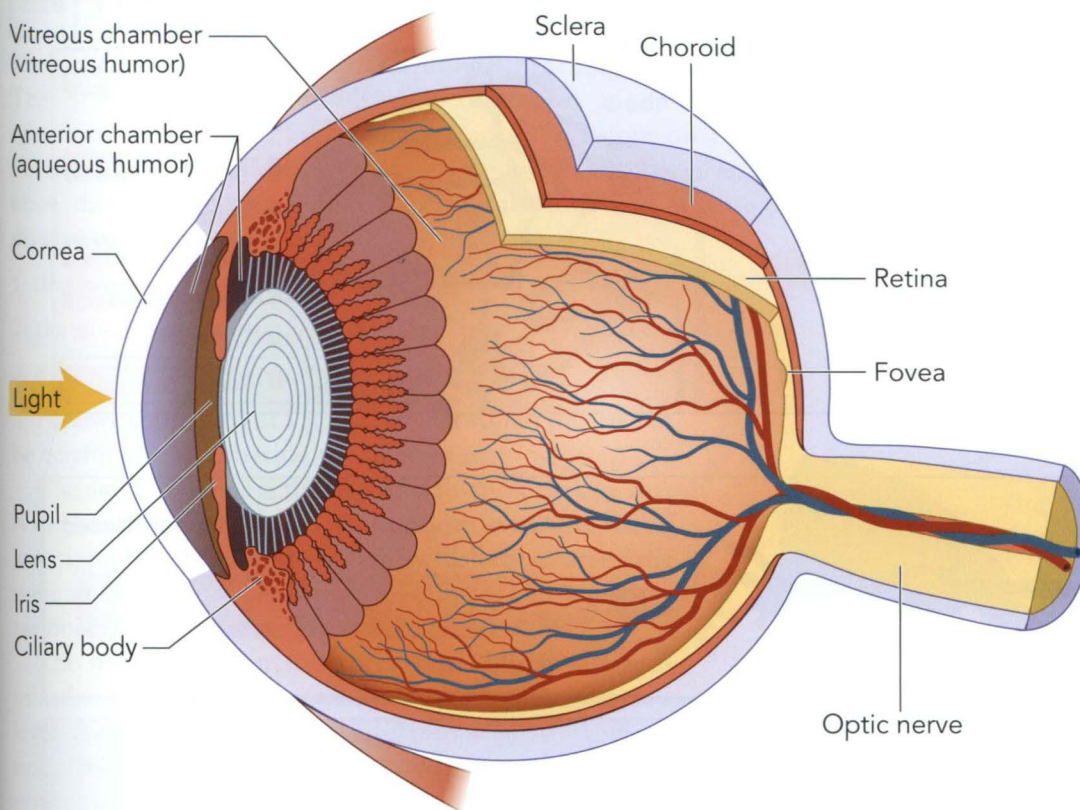
There are three types of cones, each with a different pigment that is stimulated by a slightly different spectrum of wavelengths. Thus cones, unlike rods, are able to distinguish colors.

The *fovea* is a small point on the retina containing mostly cones. This is the point on the retina where vision is most acute.

Another important feature of the eye is the **iris**. The iris is the colored portion of the eye that creates the opening called the **pupil**. The iris contains both circular and radial muscles. In a dark environment, the sympathetic nervous system contracts the iris, dilating the pupil and allowing more light to enter the eye. In a bright environment, the parasympathetic nervous system contracts the circular muscles of the iris, constricting the pupil and screening out light.

Remember that **cones** distinguish colors and **rods** don't.

FIGURE 2.19 Anatomy of the Eye



Processing of Visual Information

Once light travels through the eye and is detected by the photoreceptors, this information must be conveyed to higher levels of the nervous system. As described previously, light striking the photopigments contained in cone and rod cells triggers a series of events that lead to the hyperpolarization of the membrane of the photoreceptor. Photoreceptors do not generate action potentials, but hyperpolarization has an inhibitory effect by reducing the rate of neurotransmitter release. All photoreceptors release glutamate, which is usually an excitatory neurotransmitter. However, the cells that receive glutamate from photoreceptors respond to it differently.

The next step in the visual pathway after the photoreceptors is the passage of visual information to *bipolar cells*. Bipolar cells receive signals from their associated photoreceptors ("vertical" information). Depending on the type of glutamate receptor, a given bipolar cell may be inhibited or excited by changes in the amount of glutamate released by photoreceptors. Bipolar cells are also affected by signals from *horizontal cells*, which provide "horizontal" information from photoreceptors at the edge of the bipolar cell's *receptive field*, the distinct area of visual information to which the cell responds. The integration of horizontal and vertical information gives the eye the ability to focus on changes and edges in the visual field.

If the bipolar cells experience an overall excitatory effect from both the vertical and horizontal inputs, they release neurotransmitter at an increased rate (much like photoreceptors), producing an excitatory effect on the *ganglion cells*. These are the sensory neurons that finally produce action potentials.

The axons of the ganglion cells gather to form the **optic nerve**, which leaves the eye to convey visual information to the brain. Some of the axons from each eye cross to the opposite side of the brain. The optic nerve travels to the **lateral geniculate nucleus (LGN)** of the thalamus, which preserves the visual map created by the ganglion cells and projects this information to the **primary visual cortex**, located in the occipital lobe. Groups of neurons within the primary visual

Think about what would happen if all bipolar cells responded equally to stimuli in all areas of the visual field. This would be a very inefficient and metabolically expensive system! Just as the parasympathetic and sympathetic branches are physically separate systems that are thus able to complete separate tasks, different bipolar cells respond to different receptive fields. Subsequent levels of visual processing retain the use of these receptive fields.

FIGURE 2.20 Anatomy of the Retina

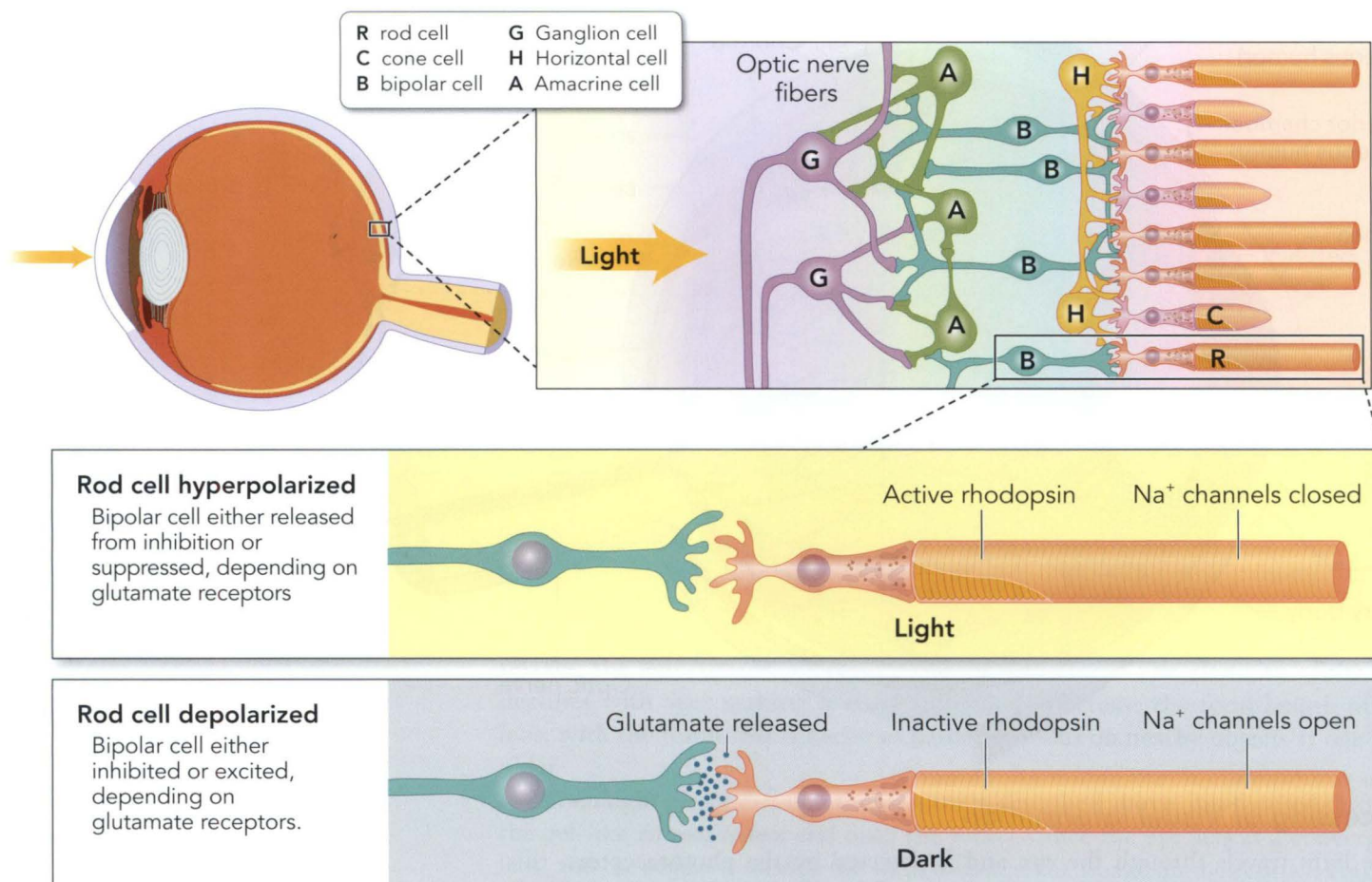
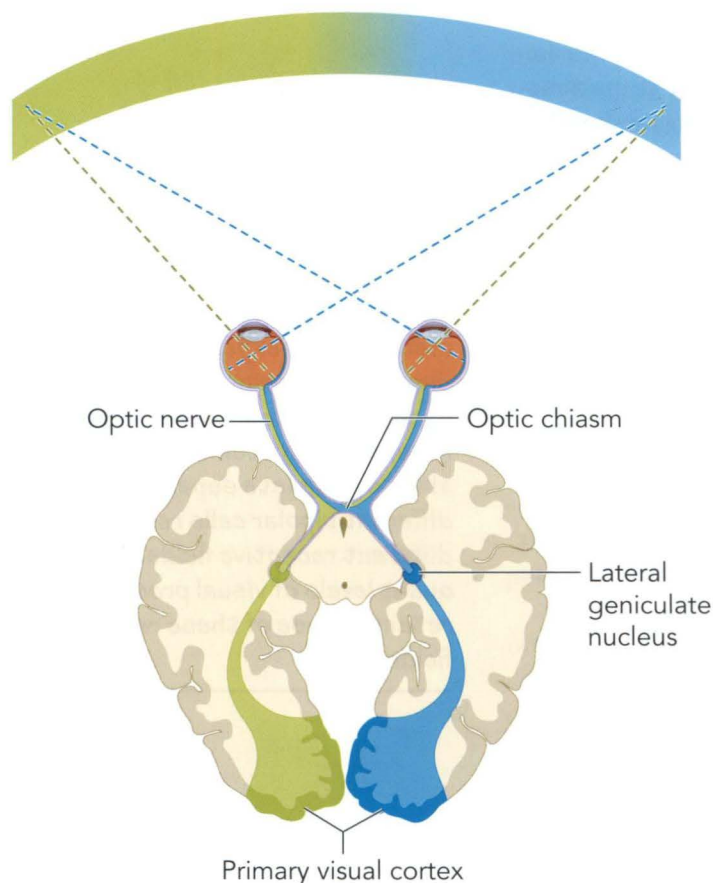


FIGURE 2.21 Visual Pathways in the Brain



cortex are specialized for the detection of specific aspects of visual stimuli, particularly lines and edges of different orientations.

Neurons project from the primary visual cortex along two visual pathways, which detect different features of visual stimuli. The **ventral ("what") pathway** travels to the temporal lobe towards the base of the brain and is involved in object recognition, while the **dorsal ("where") pathway** projects to the parietal cortex and is more involved in perceiving the location of objects. However, the two pathways communicate with each other, and information from both is ultimately integrated in other areas of the brain.

You probably won't be asked about the nitty gritty details of the visual pathways in the brain, but you should definitely know that visual information passes from the optic nerve to the thalamus and finally to the primary visual cortex. Also remember the "what" and "where" pathways. More will be said about specific psychological theories of visual processing in the Psychology & Sociology Manual.

2.10 The Ear and Hearing

The **ear** can be thought of as an instrument that condenses sound into a tiny space. The ear transforms sound from waves of pressure in the air (a gas) into physical vibrations, first in solid bone and then in fluid, before finally transforming the physical phenomenon into an electrical signal. As with the eye, it is important to know the basic parts (see Figure 2.22) and the functions of these parts. The ear is divided into three sections:

1. the **outer ear**;
2. the **middle ear**; and
3. the **inner ear**.

Following the path of a sound wave through the ear can be helpful in remembering the structures.

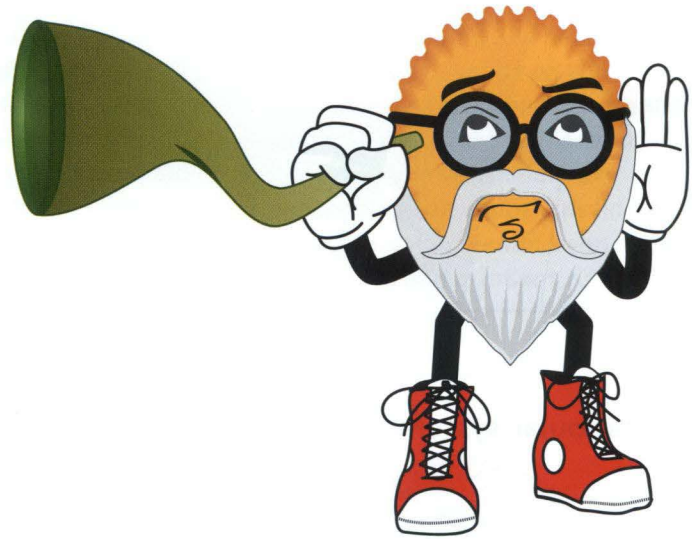
The *auricle* or *pinna* is the flap of skin and cartilage that is commonly called the ear. The auricle directs the sound wave into the *external auditory canal*, which then carries the wave to the *tympanic membrane* or *eardrum*. The tympanic membrane begins the middle ear.

The middle ear contains three small bones: the *malleus*, the *incus*, and the *stapes*. These three bones act as a lever system translating the wave into a physical vibration that is conveyed to the *oval window*. Like any lever system, these bones change the combination of force and displacement from the inforce to the outforce. In this case the displacement is lessened, which causes an increase in force. In addition, the oval window is smaller than the tympanic membrane, acting to increase the pressure. (See the Energy and Equilibrium Lecture in the *Physics Manual* for more on machines and mechanical advantage.) This increase in force is necessary because the wave is being transferred from the air in the outer ear to a more resistant fluid within the inner ear.

The wave in the inner ear moves through the *scala vestibuli* of the **cochlea** to the center of the spiral, and then spirals back out along the *scala tympani* to the *round window*. As the wave moves through the cochlea, the alternating increase and decrease in pressure causes vibration of the **organ of Corti**, which is located on the cochlea's basilar membrane. This, in turn, causes movement of the specialized microvilli, called *stereocilia*, on the **hair cells** of the organ of Corti. The movement of these hair cells is transduced into neural signals that are sent to the brain, as will be described.

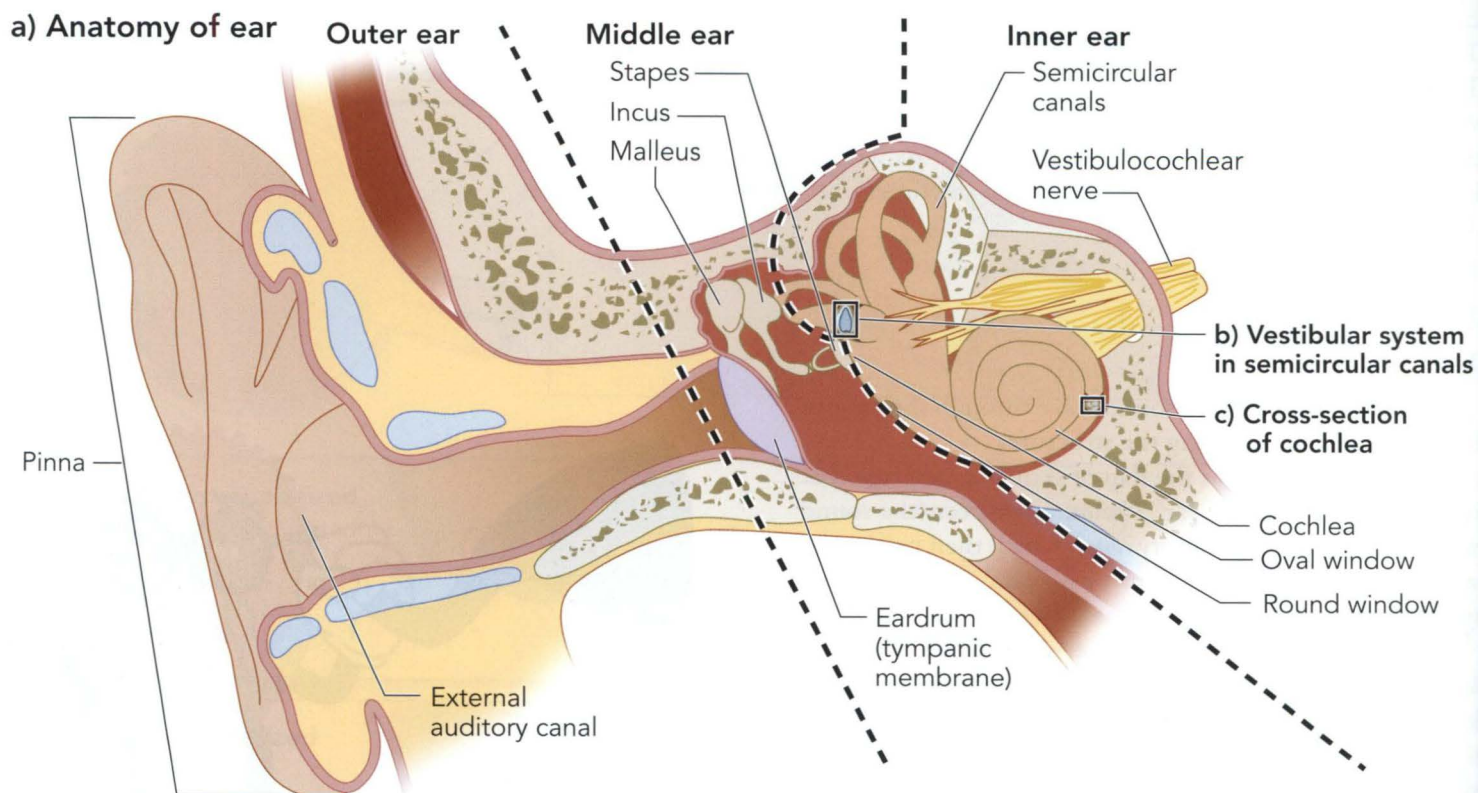
Also in the inner ear are the **semicircular canals** and the adjacent **otolith organs**, which are involved in the **vestibular system**. This system is responsible for detecting changes in position and signaling the body to make necessary adjustments to maintain balance. The semicircular canals are primarily responsible for detecting twisting of the head, while the otolith organs detect tilting and linear acceleration. Both structures contain fluid and hair cells. When the body moves or the head position changes with respect to gravity, the momentum of the fluid impacting on the hair cells is changed, and the body senses motion. The canals are oriented at right angles to each other, allowing the detection of movement in all directions. Damage to the vestibular system can be devastating, as the vestibular sense is crucial for everyday functioning.

The vestibular sense works together with the **kinesthetic sense**, which contributes to the awareness of the body's location and movement, to give the individual an overall sensation of the body.

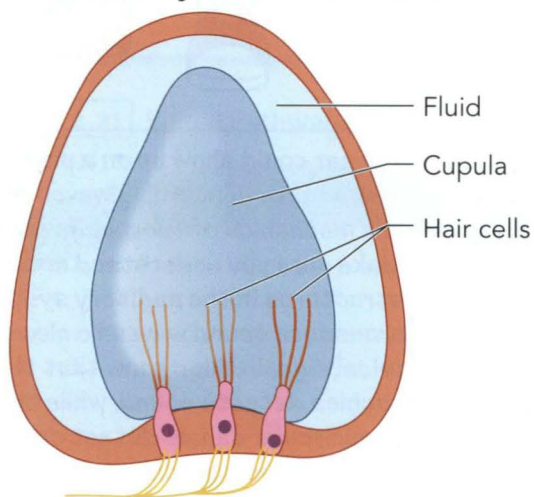


The ear could show up on a physics passage concerning waves or the mechanics of the middle ear. Make sure you understand how structures in the auditory system transduce sound waves to electrical signals. Also know that the cochlea detects sound, while the semicircular canals detect orientation and movement of the head.

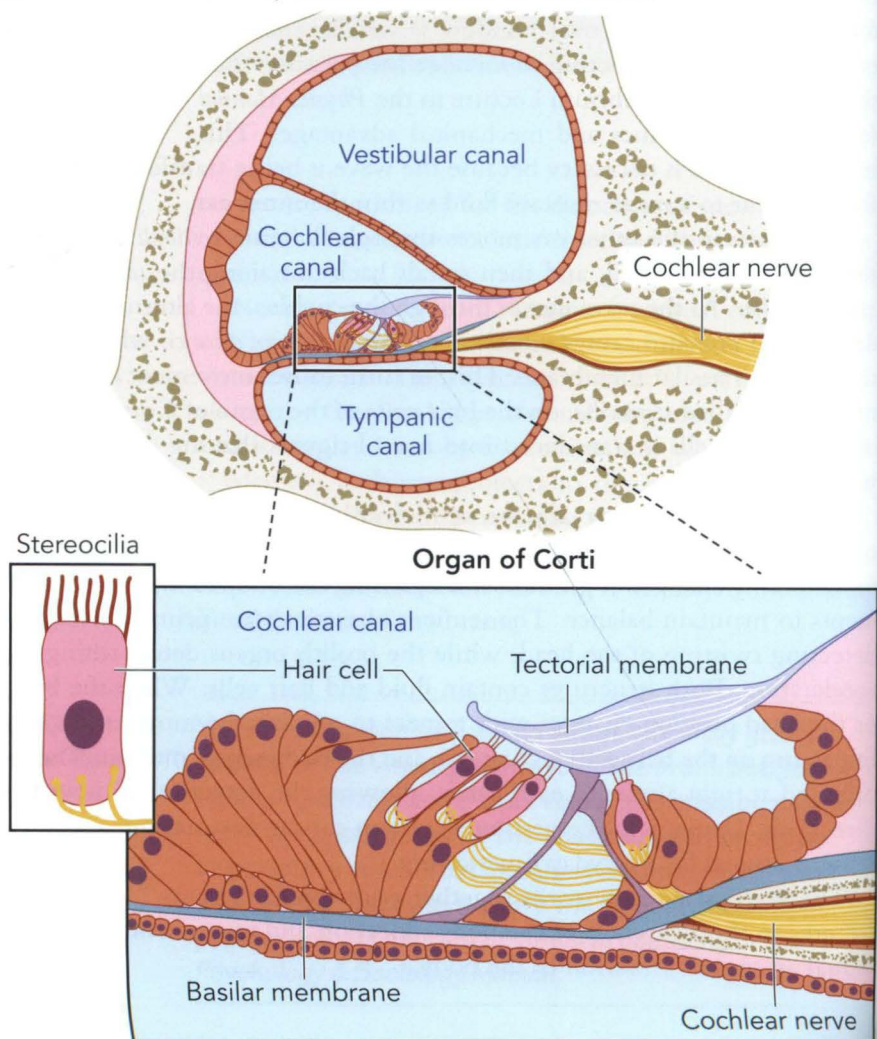
FIGURE 2.22 Anatomy of the Ear



b) Vestibular system in semicircular canals



c) Cross-section of cochlea



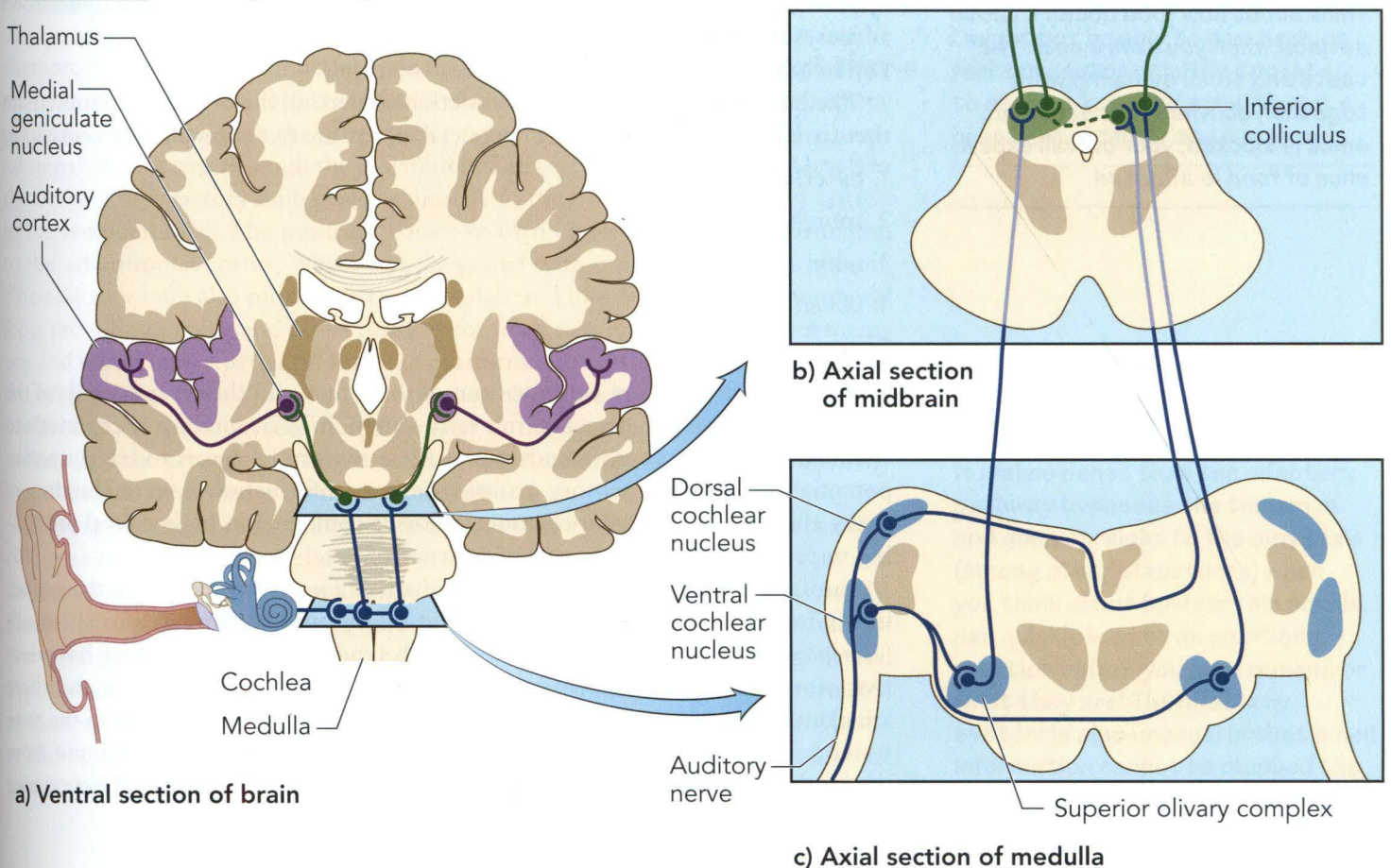
Processing of Auditory Information

As with all of the sensory systems, the next step after exploring the physical structures that receive stimuli in the auditory system is the consideration of how these stimuli are converted into neural signals. Recall that the hair cells of the organ of Corti are mechanoreceptors. As described above, they sense the bending of microvilli that results when the organ of Corti vibrates under the influence of sound waves in the fluid. Hyperpolarization or depolarization occurs depending on the direction in which the microvilli bend. When hair cells experience depolarization, they release a neurotransmitter into their synapses with neurons of the auditory nerve, which can then convey an electrical signal to higher levels of the nervous system.

As auditory information travels through the nervous system, it undergoes processing and integration at each stage. Neural signals encoding sound information primarily travel along a pathway that starts with the auditory nerve and then proceeds to the *cochlear nuclei* within the medulla. Next, axons of the cochlear nuclei synapse with neurons within the *inferior colliculus*. (On the way to the inferior colliculus, some crossover occurs such that auditory information from each ear is sent to the opposite hemisphere.) From there, the electrical signals are passed on to the **medial geniculate nucleus** of the thalamus. (Recall that visual information similarly passes through an area of the thalamus, the lateral geniculate nucleus, on its way to a higher cortical area.) Finally, the **auditory cortex** in the temporal lobe receives information from the thalamus. The auditory cortex is where the detection of complex features of auditory information, such as patterns, takes place.

Senses like vision and hearing depend just as much on the brain as they do on the sensory organs involved. Damage to an area of the brain involved in sensory processing can cause a deficit in the associated sense, even if the sensory organ is intact.

FIGURE 2.23 Auditory Pathways in the Brain





Hair cells (in yellow) in the organ of Corti, shown in an electron micrograph.

Consider the most important features of the experience of sound. Loudness, which is the psychological perception of the intensity of the sound wave, is one. Another is the frequency of the sound wave, experienced as pitch. How are these pieces of information transferred from the level of sensory receptors to the areas of the brain that process and interpret auditory information?

The answer for frequency lies with the spatial organization of hair cells along the organ of Corti. Hair cells in the part of the basilar membrane that is closest to the stapes, and thus most stiff, respond best to higher frequencies. (It is difficult to move these hair cells embedded in a stiff substance, so only higher frequencies will do the trick!) The opposite is true for hair cells that are further from the entrance to the inner ear, in the more flexible portion of the basilar membrane. Thus a spatial map of frequencies is created that is preserved at each level of auditory processing, all the way to the auditory cortex.

As for intensity, think about how the intensity of physical stimuli is usually communicated by sensory receptors. Just like in other areas of the sensory system, a stimulus of higher intensity causes higher firing rates of the associated sensory neurons. In addition, some sensory neurons of the auditory nerve only respond to sounds that pass a certain threshold of intensity, much as nociceptors only respond to extreme stimuli.

Think about how food doesn't taste as good when you have a cold. The taste and smell systems work together, so when your sense of smell is blocked, your overall experience of food is affected.

2.11

Smell, Taste, and Pain

The highly linked senses of **smell** and **taste** are called **olfactory** and **gustatory**, respectively. The mechanisms of both of these systems are not as well understood as those of the auditory and visual systems. Both senses involve chemoreceptors. Different chemoreceptors sense different chemicals.

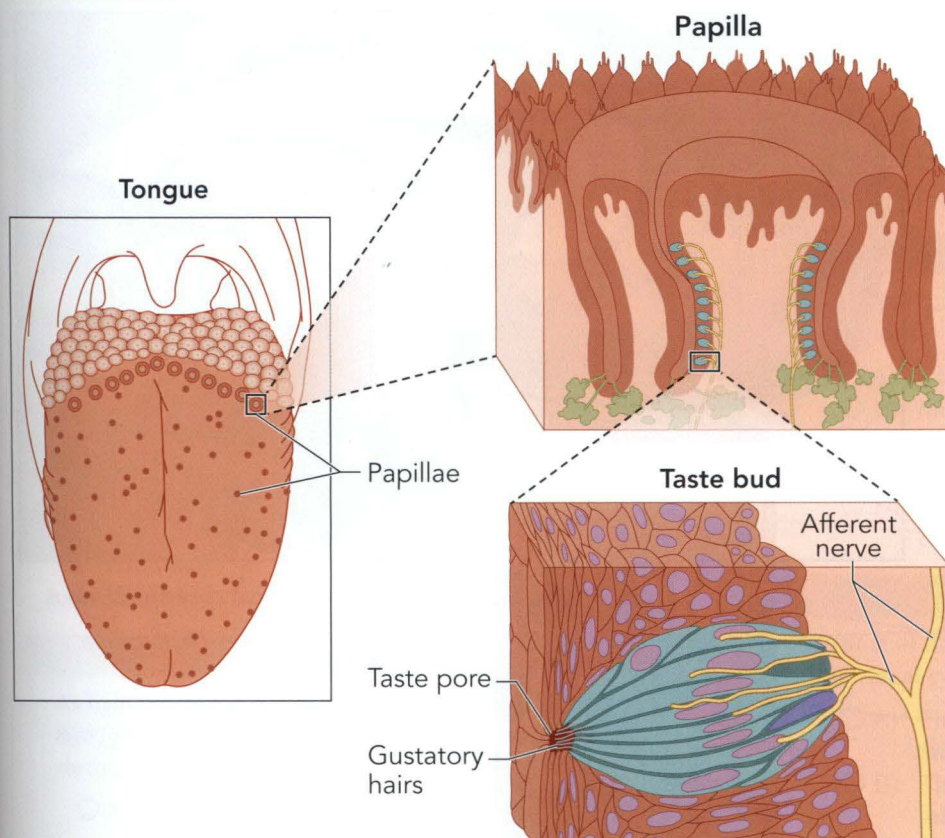
The taste system evolved for the function of alerting the organism to substances that are harmful or nutritionally beneficial. There are five primary taste sensations:

1. bitter;
2. sour;
3. salty;
4. sweet; and
5. umami (savory).

All taste sensations are combinations of these five, and the receptor cells of the taste system are able to detect all five taste sensations. The binding of chemicals to chemoreceptors in the taste buds causes these sensory receptors to trigger action potentials in associated sensory neurons. Sensory information from the binding of many chemicals to different chemoreceptors is combined in higher-level processing to produce the psychological experience of taste.

Similarly to taste, the olfactory sense evolved for the protection of the organism. Chemoreceptors located in the nasal cavity bind certain gaseous chemicals (**odorants**) that enter during inspiration. Each type of olfactory receptor has selectivity for a certain set of chemicals, rather than just one type. Furthermore, there are a multitude of types of olfactory chemoreceptors (many more than in the taste system) and, as in the taste system, processing in the brain combines input from the binding of many different receptors. This allows for the perceived experience of a wide variety of complex smells.

FIGURE 2.24 Taste Structures



Unlike chemoreceptors in the gustatory system, olfactory chemoreceptors are themselves sensory neurons. The axons of the olfactory chemoreceptors form the **olfactory nerve**. The binding of chemicals to G-protein coupled receptors on the chemoreceptors triggers an action potential that is transmitted by the olfactory nerve to neurons of the **olfactory bulb**. An important feature of the **olfactory pathways** is that unlike in the other sensory systems described in this lecture, neural signals do not pass through the thalamus before reaching higher cortical levels in the brain. The olfactory bulb projects directly to the **piriform (olfactory) cortex** in the temporal lobe. The piriform cortex in turn conveys olfactory information to the orbitofrontal cortex, where it is integrated with other sensory information. The olfactory bulb also projects to the amygdala and hippocampus in the temporal lobe, providing a quick and direct pathway for smell to influence processes of memory and emotional experience. Like the piriform cortex, the amygdala projects to the orbitofrontal cortex, allowing information about the emotional significance of smells to reach consciousness. It also projects to the hypothalamus; thus, olfactory stimuli (and the emotional interpretation of these stimuli) can influence the many functions that are linked with the hypothalamus.

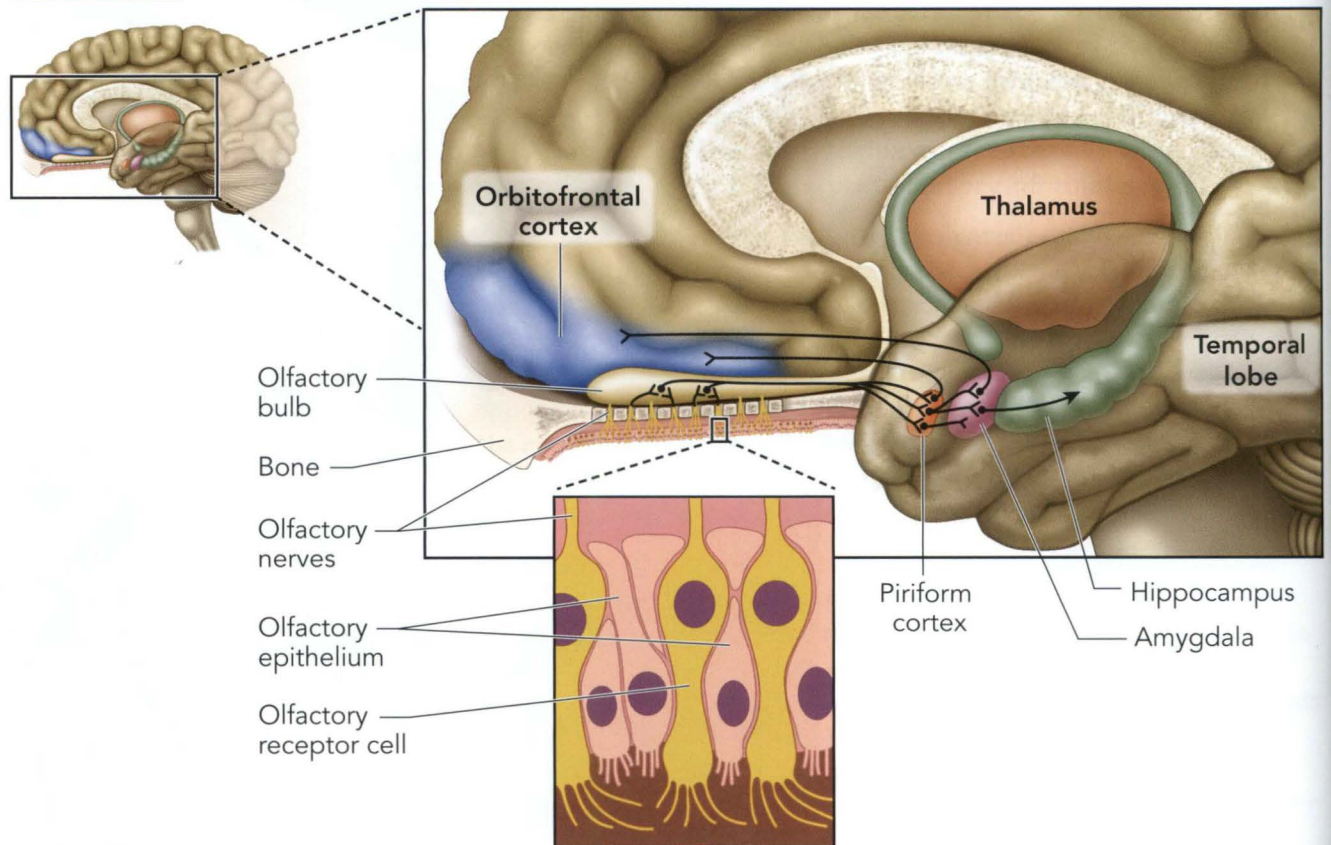
Some species have a related but separate set of sensory receptors that detect a specific type of odorant called **pheromones**. The key feature that makes pheromones different from other types of smell stimuli is that they are not perceived consciously. Pheromones play a much greater (and better understood) role in the behavior of non-primate species. Information about pheromones travels to the amygdala and hypothalamus and is thought to exert a subconscious influence on behaviors related to these structures, particularly aggression and sexual behavior. It is unclear whether pheromones affect human behavior, but they may have some influence on social interaction and the timing of menstrual cycles.



I might not be able to see, hear, or feel a predator until it's too late to escape, but I can smell that it's been here recently and run away!

It makes sense that the olfactory pathway bypasses the thalamus and goes straight to the amygdala (among other structures) when you think about how certain smells can quickly lead to an emotional reaction before you even remember what they are! The olfactory system is also unusual in that smell information cannot be mapped the way visual, auditory, and tactile stimuli can be.

FIGURE 2.25 Olfactory Pathways



Finally, the way that the experience of **pain** is produced by the somatosensory system is representative of the type of complex processing that allows higher areas of the central nervous system to both interpret and influence the organism's experience of the environment. The perception of potentially damaging stimuli conforms to the general pattern seen in most of the other sensory systems: nociceptors transduce the physical stimulus to an electrical signal that is conveyed through the spinal cord, ultimately reaching the thalamus and then a higher cortical area for processing (in this case, the somatosensory cortex). However, the perception of pain is far from being just a bottom-up process. The brain can exert top-down influence to enhance or diminish the experience of pain. Both types of influence have evolutionary advantages, depending on the situation: pain is adaptive in that it alerts the organism to a dangerous stimulus, but it can also be maladaptive if it presents a distraction when attention to other factors is necessary for survival.

MCAT® THINK

If you have any doubts that pain and other sensory processing can be a top-down process, consider the phenomenon of phantom limb pain. This occurs when people experience the feeling of pain in a limb that they no longer have, such as after an amputation. They feel pain as though signals were being sent from sensory receptors that no longer exist! Phantom limb pain and other sensations associated with the missing limb occur because the neurons that were previously devoted to sensing that limb reassign themselves to structures that are adjacent in the map of the somatosensory cortex. However, the brain still interprets these neural representations as coming from the missing limb, resulting in the subjective experience of phantom limb sensations.

These questions are NOT related to a passage.

Item 41

Pressure waves in the air are converted to neural signals at the:

- ☐ A) retina.
- ☐ B) tympanic membrane.
- ☐ C) cochlea.
- ☐ D) semicircular canals.

Item 42

Which of the following physical stimuli cannot be converted to electrical signals by the chemoreceptors of the human body?

- ☐ A) Light
- ☐ B) Taste
- ☐ C) Smell
- ☐ D) Blood chemistry

Item 43

As light enters the eye, what is the correct order of the layers through which it passes before being converted into an electrical signal?

- ☐ A) Lens → retina → cornea → aqueous humor → vitreous humor
- ☐ B) Cornea → aqueous humor → lens → vitreous humor → retina
- ☐ C) Cornea → vitreous humor → lens → retina → aqueous humor
- ☐ D) Lens → aqueous humor → cornea → vitreous humor → retina

Item 44

Which of the following is NOT true of the olfactory system?

- ☐ A) The olfactory system makes use of chemoreceptors that bind odorants.
- ☐ B) Olfactory information does not reach the amygdala and hippocampus until after it undergoes processing in the cortex.
- ☐ C) Unlike other sensory systems, the olfactory system does not create a “map” of olfactory information in the environment.
- ☐ D) Olfactory information does not pass through the thalamus before reaching cortical areas for higher-level processing.

Item 45

Which type of sensory receptor is primarily associated with the sensation of pain?

- ☐ A) Chemoreceptors
- ☐ B) Mechanoreceptors
- ☐ C) Photoreceptors
- ☐ D) Nociceptors

Item 46

The vestibular system carries out which of the following functions?

- ☐ A) Converting sound waves into auditory signals
- ☐ B) Maintaining balance and detecting changes in body position
- ☐ C) Detecting and interpreting touch sensations
- ☐ D) Conveying information about pheromones in the environment to the amygdala

Item 47

Which of the following correctly describes a component of the visual system and its function?

- ☐ A) The optic nerve carries out “what” and “where” processing of visual stimuli.
- ☐ B) The lateral geniculate nucleus conveys visual information to the brain for processing.
- ☐ C) Photoreceptors respond to the stimulus of photons by triggering signaling in the eye that ultimately causes visual information to be conveyed to the brain.
- ☐ D) Hair cells distinguish between colors by responding differently to different wavelengths of light.

Item 48

The process of sensory adaptation can be described as:

- ☐ A) the adaptation of sensory receptors to become most sensitive to a single type of stimulus.
- ☐ B) the temporal and spatial combination of multiple inputs.
- ☐ C) the experience of a decreased response to a repetitive stimulus.
- ☐ D) the adaptation of physical stimuli into electrical stimuli.

TERMS YOU NEED TO KNOW

Acetylcholine	Inhibitory	Pons
Action potential	Inner ear	Primary visual cortex
All-or-none	Interneuron	Pupil
Antagonistic control	Ion channels	Pyramidal (olfactory) cortex
Auditory cortex	Iris	Receptors
Autonomic nervous system (ANS)	Kinesthetic sense	Reflex
Axon	Lateral geniculate nucleus (LGN)	Reflex arc
Axon hillock	Lateralization of cortical functions	Repolarization
Brainstem	Lens	Resting potential
Cell body	Limbic system	Retina
Central nervous system (CNS)	Mechanoreceptors	Rods
Cerebellum	Medial geniculate nucleus	Saltatory conduction
Cerebral cortex	Medulla	Schwann cells
Cerebrum	Methods of studying the brain	Second messenger system
Chemical synapse	Middle ear	Semicircular canals
Chemoreceptors	Motor cortex	Sensory adaptation
Ciliary muscle	Motor end plate	Sensory (afferent) neuron
Cochlea	Motor (effector/efferent) neuron	Sensory receptors
Concentration cell	Myelin	Smell
Cones	Negative feedback loop	Sodium potassium pump (Na ⁺ /K ⁺ pump)
Cornea	Nernst equation	Somatic nervous system
Dendrites	Nerves	Somatosensory cortex
Depolarization	Neuroglia	Somatosensory system
Diencephalon	Neuron	Summation
Dorsal ("where") pathway	Neurotransmitter	Supraspinal circuit
Ear	Nociceptors	Sympathetic nervous system
Effector	Nodes of Ranvier	Synapse
Electrical synapse	Norepinephrine (noradrenaline)	Taste
Electrochemical gradient	Occipital lobe	Temporal lobe
Electromagnetic receptors	Olfactory	Thalamus
Epinephrine (adrenaline)	Olfactory bulb	Thermoreceptors
Equilibrium potential	Olfactory nerve	Threshold stimulus
Eye	Olfactory pathways	Unidirectional
Excitatory	Optic nerve	Ventral ("what") pathway
Feedback control	Organ of Corti	Vestibular system
Frequency of firing	Otolith organs	Visual processing
Frontal lobe	Outer ear	Voltage gated potassium channels
Glial cells	Pain	Voltage gated sodium channels
Grey matter	Parasympathetic nervous system	White matter
Hair cells	Parietal lobe	
Hyperpolarization	Peripheral nervous system (PNS)	
Hypothalamus	Pheromones	
Information processing model	Photoreceptors	



DON'T FORGET YOUR KEYS

1. The nervous system senses the environment, processes information, and responds.
2. Neural signals are fast, fleeting, and specific; endocrine signals are slow, sustained, and general.
3. Receptors and channels are the hidden players.

The Endocrine System

3.1 Introduction

The endocrine system, like the nervous system, allows communication within the organism and regulation in response to stimuli in the internal and external environment. While the nervous system has fast, fleeting, and specific signals, the endocrine system acts more slowly but exerts effects that are more general and sustained. The neurotransmitters and local mediators discussed in the Nervous System Lecture are often referred to as local hormones. They are secreted by neurons and cause action potentials. By contrast, the hormones released by the endocrine system are called general hormones. They are referred to as 'general' because they are released into the body fluids, often the blood, and may affect many cell types in a tissue, as well as multiple tissues in the body. Although this lecture concentrates on general hormones, the chemistry described is accurate for local hormones as well.

Hormones can be placed into one of three major categories according to how they are synthesized. Each type has different chemical and physical characteristics that determine the mechanisms by which the hormones act and the effects that they can produce, as will be discussed.

FIGURE 3.1 Communication via the Endocrine and Nervous Systems



Hormones are released by endocrine glands, which differ from exocrine glands in the following manner. **Exocrine glands** release enzymes to the external environment through ducts. Types of exocrine glands include sudoriferous (sweat), sebaceous (oil), mucous, and digestive glands. **Endocrine glands** release hormones directly into the bloodstream. For instance, the pancreas acts as both an exocrine gland, releasing digestive enzymes through the pancreatic duct, and an endocrine gland releasing insulin and glucagon (described further in this lecture) directly into the blood.

After their release from endocrine glands, hormones may take anywhere from seconds to days to produce their effects. They do not move directly to their target tissue, but are released into the general circulation. All hormones act by binding to protein **receptors**. Each receptor is highly specific to a particular hormone. One method of hormone regulation is the reduction or increase of a receptor type in the presence of high or low concentrations of its hormone. Some hormones have receptors on virtually all cells, while other hormones have receptors only on specific tissues. Very low concentrations of hormones in the blood can have significant effects on the body.

3.1 Introduction

3.2 The Chemistry of Hormones

3.3 Organizing the Endocrine System

3.4 Regulation of Hormones

3.5 Endocrine Glands and their Hormones

3.6 Homeostasis and Hormones

3.7 Reproduction and Development

THE 3 KEYS

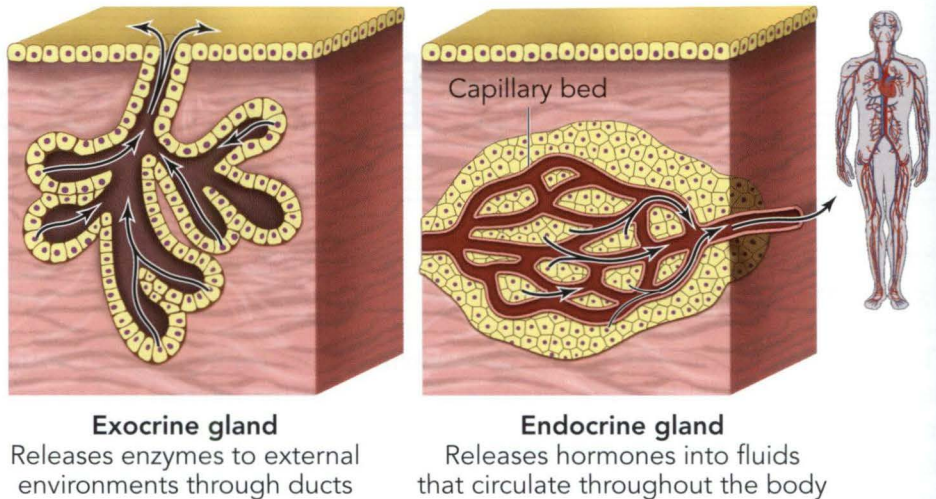


1. See a hormone, think of its gland, function, polarity, and target(s).
2. Hormones respond to imbalance in the body to restore homeostasis. Normally functioning hormones do not create imbalance.
3. Reproductive hormones and cells in male and females are similar in both structure and process but act along different timelines.

Digestive System
BIOLOGY 2

FIGURE 3.2 Exocrine and Endocrine Glands

Remember that hormones need a receptor, either on the membrane or inside the cell. Also, when comparing the endocrine system to the nervous system, remember that the endocrine system is slower, less direct, and longer lasting.



In general, the effects of the endocrine system are to alter metabolic activities, regulate growth and development, and guide reproduction. The endocrine system works in conjunction with the nervous system. Many endocrine glands are stimulated by neurons to secrete their hormones. Thus, even though the endocrine system acts via generalized communication with multiple parts of the body, it can be tightly regulated by specific neural control.

Communication via the endocrine system can seem disorganized and nonspecific when compared to the nervous system. The brain has fine control of the body's musculature via the nervous system. What evolutionary advantage would there be in the brain not having precise control over all aspects of physiology?

The endocrine system controls body states. For example, after eating a meal, the body absorbs the consumed food over approximately two hours, causing a temporary elevation in blood glucose. Various hormones coordinate the metabolic activity of the liver, the musculature, and the adipose tissue to match the influx of glucose at that moment. If the nervous system were to assume these functions, separate nerves communicating with each organ would have to fire action potentials in accordance with the state of the body at that moment. Action potentials are metabolically expensive, so this setup would waste valuable energy.

3.2 The Chemistry of Hormones

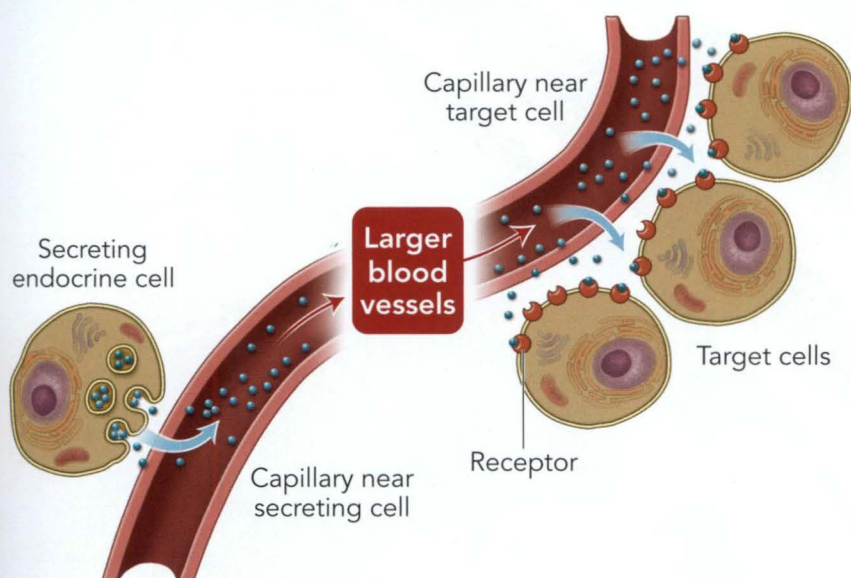
Hormones exist in three basic chemistry types:

1. **peptide hormones**;
2. **steroid hormones**; and
3. **tyrosine derivatives**.

The hormones of each type can be categorized according to solubility, which has implications for their physical characteristics, mechanisms of action, and ultimate effects on their targets.

Peptide hormones are derived from peptides. As discussed in the Cell Lecture, since peptide hormones are water soluble, they can move freely through the blood but have difficulty diffusing through the cell membrane of the **effector**. (The

FIGURE 3.3 Transport of Hormones in the Blood



The endocrine system delivers hormones to target cells throughout the body via the circulatory system.

effector is the **target cell** of the hormone, the cell that the hormone is meant to affect.) Instead of diffusing through the membrane, peptide hormones attach to a membrane bound receptor. Once bound by a hormone, the common mechanisms of the receptor include activating an enzyme and activating a second messenger system such as cAMP, cGMP, or calmodulin.

Peptide hormones may be large or small, and often include carbohydrate portions. All peptide hormones are manufactured in the rough ER, typically as *preprohormones* that are larger than the active hormones. The preprohormone is cleaved in the ER lumen to become a *prohormone* and then transported to the Golgi apparatus. In the Golgi, the prohormone is cleaved and sometimes modified with carbohydrates to produce the hormone's final form. The Golgi packages the hormone into secretory vesicles, and, upon stimulation by another hormone or a nervous signal, the cell releases the vesicles via exocytosis.

The peptide hormones that must be known for the MCAT® are:

1. the anterior pituitary hormones: FSH, LH, ACTH, HGH, TSH, and prolactin;
2. the posterior pituitary hormones: ADH and oxytocin;
3. the parathyroid hormone PTH;
4. the pancreatic hormones: glucagon and insulin; and
5. the thyroid C cell hormone: calcitonin.

The specifics of these hormones will be discussed later in this lecture.

Steroid hormones are derived from and are often chemically similar to cholesterol. They are formed in a series of steps taking place mainly in the smooth endoplasmic reticulum and the mitochondria. Since they are lipids and thus hydrophobic, steroids typically require a protein transport molecule (carrier protein) in order to dissolve into the bloodstream. (Usually, a fraction of the steroid concentration is bound to a transport molecule and a fraction is free in the blood.) Steroids are able to diffuse through the cell membrane of their effectors. Once inside the cell, they combine with a receptor in the cytosol or the nucleus and act at the

MCAT® THINK

cAMP stands for cyclic adenosine monophosphate. It is very similar to ATP, adenosine triphosphate, except that it only has one phosphate group, which attaches to the ribose sugar in two places to make a ring.

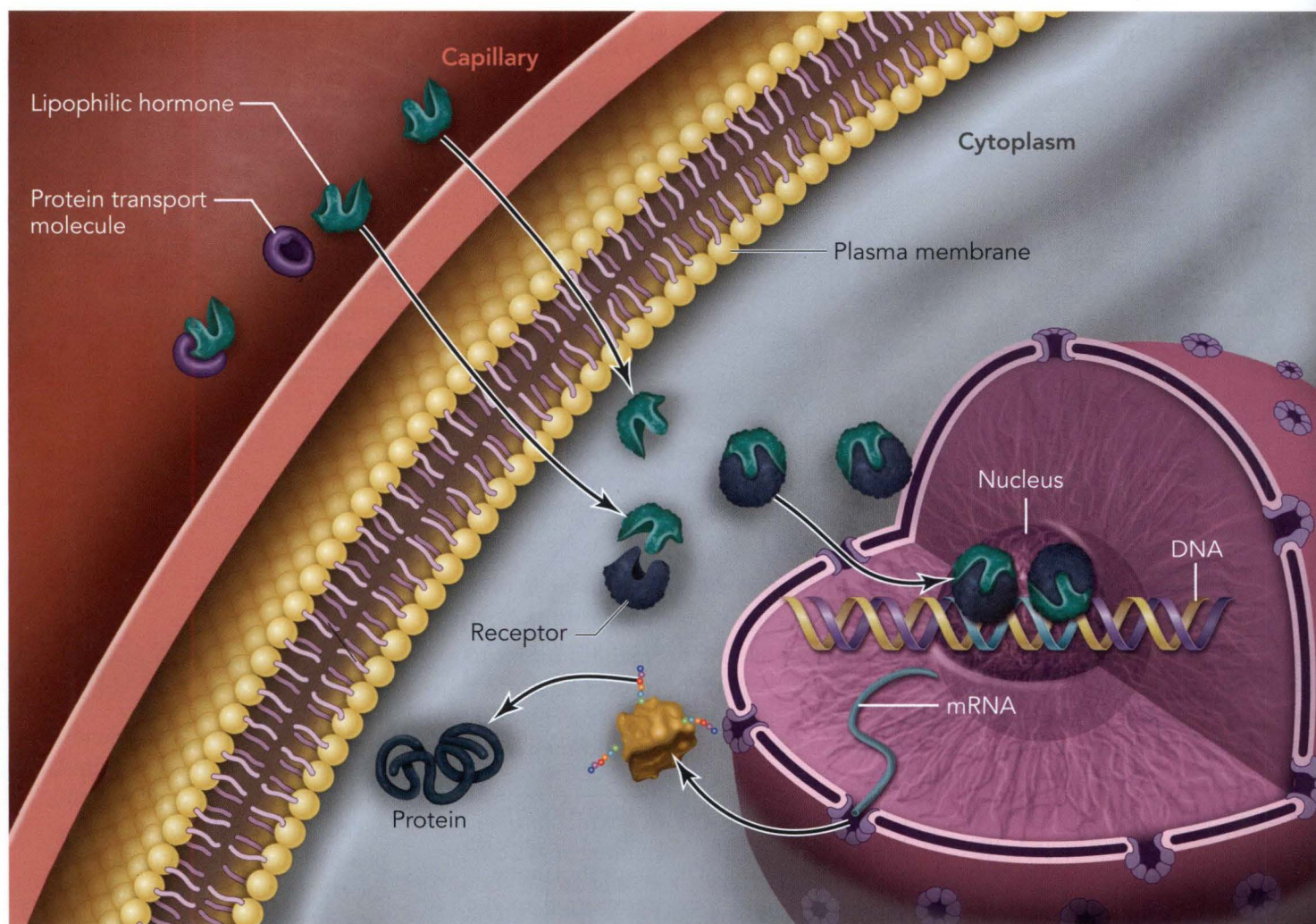


FIGURE 3.4 Mechanism of Nonpolar Hormones

Nonpolar hormones such as steroids and some tyrosine derivatives are transported in the blood by carrier proteins. Once they reach their target cell, they freely diffuse across the membrane and attach to receptors. The receptor-hormone complex then moves to the nucleus, where it regulates transcription of certain genes or gene families.

level of transcription. Thus, the typical effect of a steroid hormone is to increase certain membrane or cellular proteins within the effector. The important steroid hormones for the MCAT® are:

1. the glucocorticoids and mineral corticoids of the adrenal cortex: cortisol and aldosterone; and
2. the gonadal hormones: estrogen, progesterone, testosterone. (Estrogen and progesterone are also produced by the placenta.)

The specifics of these steroids will be discussed later in this lecture.

The tyrosine derivatives include the thyroid hormones: T_3 (triiodothyronine, containing 3 iodine atoms) and T_4 (thyroxine, containing 4 iodine atoms), as well as the catecholamines formed in the adrenal medulla: epinephrine and norepinephrine. Tyrosine derivative hormones are formed by enzymes in the cytosol or on the rough ER. Unlike the peptide and steroid hormones, tyrosine derivatives do not all have either water or lipid solubility in common.

Thyroid hormones are lipid soluble and therefore must be carried in the blood by plasma protein carriers. They are slowly released to their target tissues and bind to receptors inside the nucleus. Thyroid hormones have a strong affinity to their binding proteins in the plasma and in the nucleus, creating a latent period in the response produced and increasing the duration of the effects. Thyroid hormones increase the transcription of large numbers of genes in nearly all cells of the body.

Epinephrine and norepinephrine are water soluble, so they dissolve in the blood. They bind to receptors on the target tissue and act mainly through the second messenger cAMP.

The specifics of the tyrosine derivative hormones will be discussed later in this lecture.

3.3 Organizing the Endocrine System

Because of their different physical properties, hydrophilic and hydrophobic hormones necessarily play different roles in the body. Just as the nervous system has a faster, more specific and a less fast, more diffuse portion, the endocrine system has faster and slower acting hormones. This spectrum is illustrated in Figure 3.5.

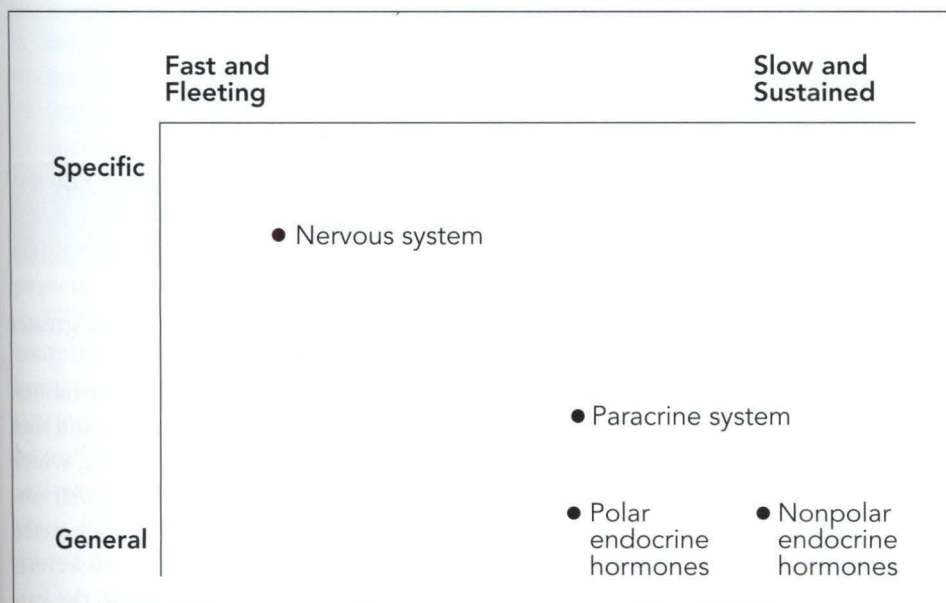


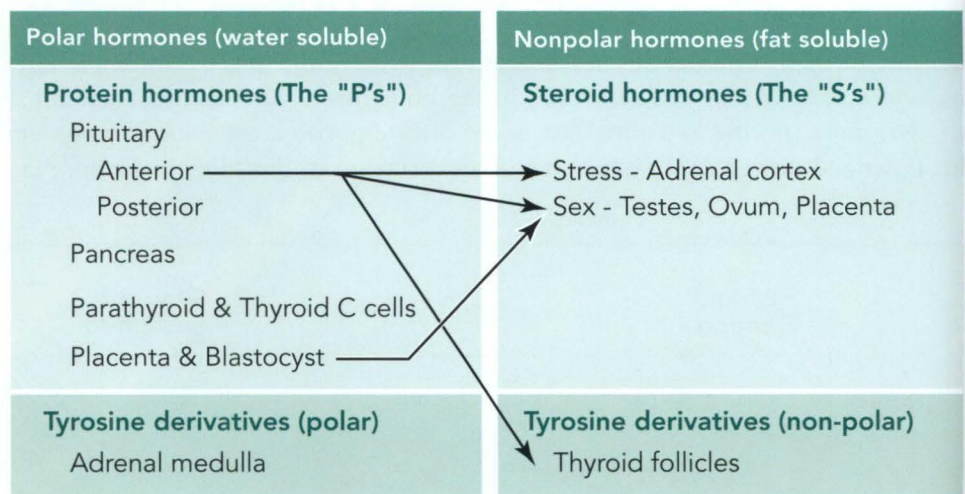
FIGURE 3.5 Comparison of Communication Systems: Polar and Nonpolar Hormones

Overall, the effects of the endocrine system are far more general, slow, and sustained than those of the nervous system. However, different types of endocrine hormones have different qualities: the effects of nonpolar hormones are more slow and sustained than those of polar hormones.

Hydrophilic hormones are the fast and fleeting players of the endocrine system. They are fast because they are readily soluble in water and thus do not need a carrier protein to travel in the plasma. Because they are free in the plasma, they can also be cleared quickly from the blood and have a relatively short half-life. As a result, the concentration of hydrophilic hormones can be adjusted on a minute to minute basis. The nature of their receptors also allows them to enact changes within their target cells quickly. Activating an enzyme or opening a channel is a relatively fast cellular event.

Hydrophobic hormones have effects that are slower and more sustained. They are slower to arrive at their targets because they are not readily soluble in water; in fact, only a small amount of these hormones are free floating in the blood at any given time. Carrier proteins in the blood both transport hydrophobic hormones around the body and protect them from breakdown. Because they are hydrophobic, these hormones also have a tendency to dissolve in the fatty tissues of the body, where they can hide indefinitely from enzymes that would degrade them. These hormones thus have a relatively long half-life, and their concentrations can only be adjusted on an hour to hour basis. Furthermore, because nonpolar hormones operate at the level of transcription, the response by target cells is slow. However, the effect that these hormones produce is sustained because it involves the production of new proteins for the cell's use. Unlike polar hormones, which cause quick but short-lasting effects, nonpolar hormones stimulate long-lasting changes in the infrastructure and functioning of their target cells.

The endocrine system can be understood by organizing glands in terms of the solubility of the hormones that they secrete. The rest of this section will introduce this framework, as demonstrated in Figure 3.6. Each major hormone will be briefly introduced in terms of its secreting gland, target, and major function. This introductory section provides a basis from which to understand the rest of the

FIGURE 3.6 Polar Hormones vs. Nonpolar Hormones

lecture, which will describe the characteristics of glands and hormones in greater detail.

Almost all glands only secrete either hydrophilic or hydrophobic hormones. The glands can be organized along a spectrum according to the polarity, and thus solubility, of the hormones that they secrete. Tyrosine derivative hormones, which can be either polar or nonpolar, lie between the polar peptides and nonpolar steroids. There are two major types of tyrosine derivative hormones: those secreted by the thyroid and those secreted by the adrenal medulla. The thyroid secretes tyrosine derivatives that are nonpolar, like the steroid hormones, while the catecholamines of the adrenal medulla are polar, like the peptide hormones.

Notice that regulatory hormones, indicated by arrows extending to the glands that they influence, are all peptides. Their targets are glands that secrete hydrophobic hormones. In fact, every hydrophobic hormone has a correlating hydrophilic control hormone. This makes sense because the effects of hydrophilic hormones are faster and more fleeting than those of hydrophobic hormones, making them well-suited for a regulatory function.

Peptide-Secreting Glands

The pituitary gland is an important site of interaction between the nervous and endocrine systems, as discussed in the Nervous System Lecture. The connection between the hypothalamus and pituitary gland allows fine nervous control over the levels of hormones released by the pituitary. Because many of these hormones have a regulatory effect on other endocrine glands, the interface between the hypothalamus and pituitary gland has a widespread impact on the functioning of the endocrine system.

The posterior pituitary gland is essentially a continuation of the nervous system. In fact, it is a bundle of axons of neurons whose cell bodies lie in the hypothalamus. Rather than producing hormones itself, it is a storage site for hormones that are synthesized by the hypothalamus. Two major types of hormones are released by the posterior pituitary: anti-diuretic hormone (ADH) and oxytocin. ADH plays a critical role in the regulation of plasma volume by stimulating receptors on cells of the kidneys' collecting ducts to facilitate reabsorption of water. The direct nervous control of ADH afforded by the fact that it is released from the posterior pituitary allows changes in ADH levels to occur rapidly in response to the body's needs, as described later in this lecture. Oxytocin is involved in the stimulation of labor and milk ejection for nursing, so receptors for oxytocin are present in the uterus and the milk ducts of the breasts. In the case of milk ejection, the benefit of close nervous control is that oxytocin can be quickly released by the posterior

Almost all of the glands that secrete Peptide hormones start with P. The exception is the adrenal medulla. Think of it as the P-Med (rhymes with premed!) to remember that the adrenal medulla also secretes Peptide hormones. Also, the glands that secrete Steroid hormones can be grouped into functions that start with S. Use these memory tools to keep your hormones and glands straight!

Since the peptide hormones are fast and fleeting (more similar to nervous system signals) compared to the steroid hormones, it makes sense that the hormones released by the pituitary gland under nervous system control are peptides.

pituitary in response to suckling or other stimuli that indicate the infant's need for milk.

The anterior pituitary gland is the higher regulatory gland of the endocrine system, releasing hormones that in turn affect the release of hormones by other glands. Like the posterior pituitary, it is subject to nervous control; however, it is a group of endocrine cells rather than an extension of the nervous system. The hypothalamus communicates with the anterior pituitary by releasing hormones into shared blood vessels. Because the anterior pituitary gland is located such a short distance from the hypothalamus, signaling between these structures is faster and more direct than most endocrine communication. As a result, the hypothalamus can closely regulate the release of hormones produced by the anterior pituitary.

The anterior pituitary exerts its regulatory effects by releasing hormones that regulate the secretion of steroid hormones by other glands, as illustrated in Figure 3.6. Thus, polar hormones control the slower nonpolar hormones, under the direction of the nervous system. The individual hormones secreted by the anterior pituitary gland will be considered later in this lecture.

The parathyroid glands and the thyroid are physically adjacent glands that have complementary roles in the regulation of calcium levels in the bloodstream and bone. Calcium must be closely regulated because it is both necessary for the functioning of the body and potentially harmful at high levels. Although calcium must be readily available for muscles and neurons to function, it has low water solubility and must be prevented from precipitating in the plasma. Both the parathyroid and the C cells of the thyroid secrete polar hormones that act in opposition to each other to regulate calcium.

The parathyroid glands release parathyroid hormone (PTH) in response to lowered levels of calcium in the bloodstream. Although PTH receptors are present on osteoblasts rather than osteoclasts, intercellular signaling ultimately causes increased osteoclast activity and thus increased bone breakdown. The breakdown of bone releases calcium, thus causing the level of blood calcium to rise.

Calcitonin is released by the C cells of the thyroid in response to rising calcium levels. Like parathyroid hormone, calcitonin functions by affecting the action of osteoclasts. However, while PTH causes osteoclasts to increase their activity, calcitonin has an inhibitory effect. As a result, the breakdown of bone decreases while the rate of bone formation is unchanged, and the level of calcium in the bloodstream decreases.

The pancreas secretes two hormones, insulin and glucagon, that act antagonistically to regulate cellular metabolism. One of the most significant effects of these hormones is the tight regulation of glucose. (See the Metabolism Lecture in *Biology 1: Molecules* for a more in-depth consideration of the multiple hormones that contribute to glucose regulation). Glucose must be maintained at a certain level for use by cells, but abnormally high glucose levels in the bloodstream can have significant negative effects.

Insulin is released when the level of glucose in the bloodstream increases (such as after a meal) and is higher than the amount needed by the body's cells. Insulin reduces the amount of glucose in the blood by inducing cells to take it up for storage; most cells in the body have receptors for insulin. The net effect of rising insulin levels is that excess nutrients are stored for later use.

In contrast to insulin, glucagon release by the pancreas is triggered by a drop in the level of blood glucose, indicating a deficit of nutrients. The purpose of glucagon is opposite to that of insulin: mobilizing the release of nutrients from storage. Glucagon acts on the liver to stimulate the release of glucose into the bloodstream.

Much like the anterior pituitary gland, the placenta secretes a peptide hormone that regulates the secretion of steroid hormones. In this case, the result is that the uterus is prepared to support a pregnancy. The developing blastocyst has a layer of cells that ultimately contributes to the formation of the placenta. These cells start secreting human chorionic gonadotropin (HCG) after implantation, and the

To remember that the posterior pituitary is the part of the pituitary that is really just an extension of the hypothalamus used for storage, think of the name: the posterior pituitary is like any posterior—it just sits there!



For now, think of osteoclasts as cells that eat up bone and osteoblasts as cells that bring bone its lunch. The Muscle, Bone and Skin Lecture will discuss the different types of cells that build up and break down bone. When you reach that lecture, review the hormones involved in calcium regulation and make sure you understand how they interact with bone.

It is crucial to know that the pairs of hormones that act antagonistically to regulate calcium and glucose levels are all peptides. This is easy to remember if you keep in mind that polar hormones are faster than non-polar ones. Compared to steroid hormones, peptide hormones are better able to respond quickly to changing bloodstream levels of calcium and glucose.

HCG is the developing blastocyst's way of asking the mother for room and board! You can think of the ovaries as the bosses of the uterus. They give the uterus commands based on information from both the blastocyst (if present) and the anterior pituitary gland.

The Steroid hormones are involved in Stress and Sex (reproduction).

The major hormones secreted by the Adrenal Cortex are Aldosterone and Cortisol. Also, know that the GLUCOCorticoids regulate glucose mobilization (and other aspects of the stress response), while MINERALocorticoids regulate levels of minerals in the plasma.

placenta then takes over the task of HCG secretion. HCG travels to the ovaries, which exert control over the uterus. In response to HCG, the ovaries signal the continuing synthesis and secretion of the steroid hormones progesterone and estrogen. These hormones suppress menstruation (as described below), allowing the buildup of the uterine wall in preparation for implantation. The placenta continues to secrete HCG at a low level throughout pregnancy.

The placenta is a specialized organ that exists only in pregnancy, and it is unusual in that it secretes both a polar and nonpolar hormone (although the secretion of HCG is greatly diminished when the secretion of steroid hormones begins). The only other glands that likewise secrete polar and nonpolar hormones are the thyroid gland and adrenal gland. One of the hormones secreted by each of these glands is a tyrosine; unlike the placenta, neither gland secretes both a peptide and a steroid. The adrenal gland is actually two glands, while the thyroid is truly a single gland that secretes a polar and nonpolar hormone.

The adrenal medulla, one of the glands contained in the adrenal gland, is involved in the stress response. It secretes the polar tyrosines epinephrine and norepinephrine. They are also called adrenaline, after the adrenal gland, and are catecholamines (amine derivatives). Note that these are the same chemicals that are used by the sympathetic nervous system to facilitate a fight-or-flight response. Rather than being secreted into the synapse as part of a nervous system response, adrenaline from the adrenal medulla is secreted into the bloodstream in response to SNS input, supplementing nervous system activity by sending signals that are slower but more sustained and generalized.

In addition to helping regulate blood and bone calcium, the thyroid gland is largely responsible for basal metabolic rate through secretion of the thyroid hormones, T_3 and T_4 . These hormones are nonpolar and are the other type of tyrosine derivative. While the polar hormone calcitonin is secreted by the C cells of the thyroid, the thyroid hormones are instead secreted by follicular cells. The release of thyroid hormones is regulated by one of the hormones released by the anterior pituitary. Thyroid hormones have a widespread effect due to the presence of receptors for these hormones on cells in almost all parts of the body. Heightened levels of thyroid hormones cause the basal metabolic rate to rise, while the opposite is true of low levels.

Besides the thyroid hormones, the major nonpolar hormones are all steroids. The main functions of the steroid hormones fall under the categories of stress and reproduction.

The testes and ovaries release hormones that stimulate reproductive development and functions. These glands secrete their hormones in response to regulation by the anterior pituitary, another example of a peptide hormone regulating a steroid hormone. Testosterone, secreted by the testes, facilitates male puberty and spermatogenesis. The ovaries secrete estrogen and progesterone, which determine female pubertal development and the progression of menstruation and pregnancy. As discussed earlier in this section, the secretion of hormones by the ovaries is affected by HCG when pregnancy occurs. Later in pregnancy, the production of these hormones occurs in the placenta.

The adrenal cortex is the other gland that secretes steroid hormones. It is involved in blood pressure regulation and the production of the body's stress response. The adrenal cortex secretes two categories of hormones: glucocorticoids and mineralocorticoids. For the purposes of the MCAT®, it is necessary to know the actions of cortisol (the major glucocorticoid) and aldosterone (the major mineralocorticoid).

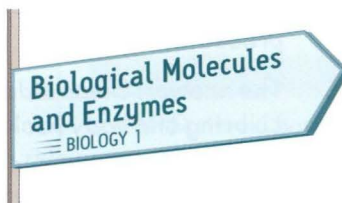
The adrenal cortex influences stress response, much like the adrenal medulla, in this case via the secretion of cortisol. However, cortisol produces a more long-term stress response, as when the organism is under some type of chronic stress.

The adrenal cortex also secretes the mineralocorticoid aldosterone, which affects blood pressure by altering processes in the kidney. As will be described in this lecture and in later lectures, aldosterone stimulates increased reabsorption of the mineral Na^+ , which in turn causes increased water reabsorption and plasma volume.

The endocrine system may seem overwhelming at first, with all of its glands, hormones, targets, and functions. Don't make the mistake of focusing so much on memorizing that you forget to learn the bigger picture! Using the framework of solubility to organize the properties of different hormone types will help you keep things straight. As you read the rest of the lecture, refer back to this section as necessary to put all the pieces in place.

3.4 Regulation of Hormones

Endocrine glands tend to over-secrete their hormones. Typically, some aspect of their effect on the target tissue will inhibit this secretion. This is an example of negative feedback. A critical aspect of negative feedback in endocrine glands is that hormones act to bring the body back to normal, not to cause abnormalities. For example, insulin, a hormone that lowers blood glucose, would be expected to be released when blood glucose is high. If the body had low blood glucose, insulin would be expected to be low. Notice that the control point of the feedback is the behavior of the effector, not the concentration of hormone. In other words, the gland lags behind the effector. So if an MCAT[®] question indicates that a person has high blood sugar and asks whether insulin levels would be high or low, the correct response is that insulin will try to correct this abnormality, and therefore a high concentration will be present.



Epinephrine explains why I still feel nervous and jittery a few minutes after I'm done running from a bear. If I have to run from bears several times a day for a month, my cortisol level will rise and I will have an even more prolonged stress response. You can remember that cortisol contributes to a long-term stress response because it is a non-polar steroid hormone, whereas epinephrine is a polar tyrosine hormone and has a more short-term effect.

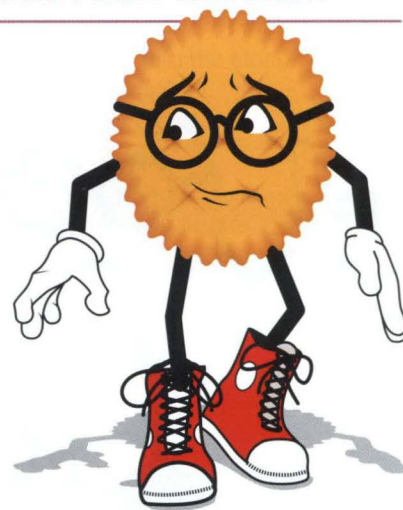
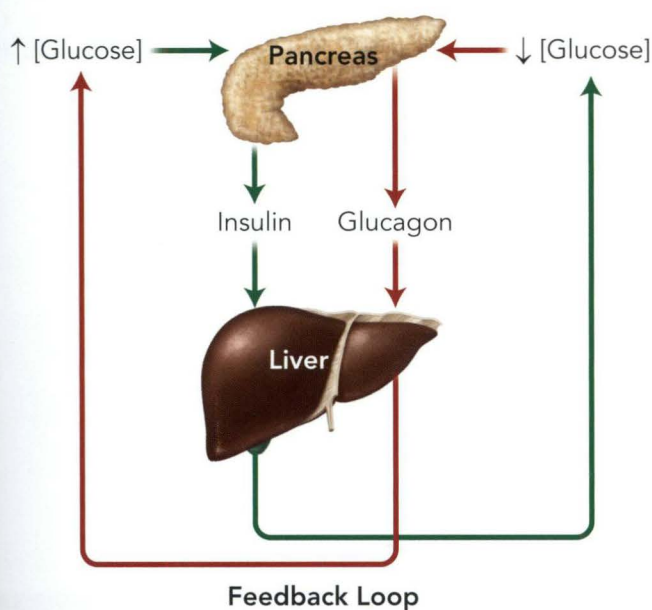


FIGURE 3.7 Negative Feedback Mechanism



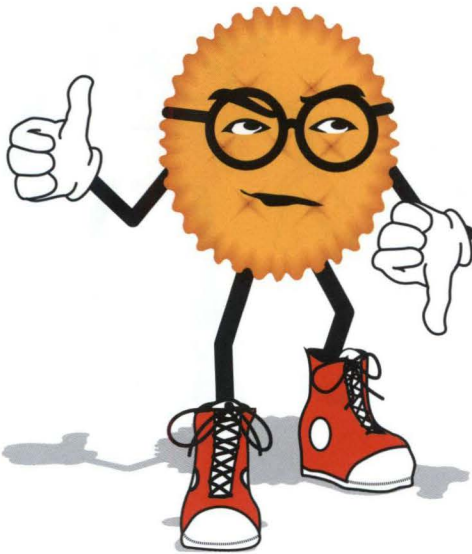
There will be a negative feedback question on the MCAT®. An air conditioner provides a good analogy. You might set your air conditioner to 78 °F during the summer. If your house were 65 °F, would you expect your air conditioner to be on or off? You would expect it to be off, because it should only come on when your house warms up to 78 °F. If your air conditioner had simply stayed on and caused your house to get so cold, you would say it is broken. The MCAT® does not test broken physiology.

See if you get the idea. Calcitonin is a hormone that decreases blood calcium levels. If blood calcium levels are low, would that person have a high or a low level of calcitonin?

If you said high, then you reasoned that the calcitonin created the low calcium level. **WRONG!** On the MCAT®, hormones act to correct problems, not to cause problems. If you said low, then you reasoned that the body decreased output to respond to the low calcium state. **CORRECT!**

How about another? One effect of aldosterone is to increase blood pressure. Would expected aldosterone levels be high or low in a person with low blood pressure?

The answer: Since aldosterone increases blood pressure, and hormones act to bring the body back to its normal state, the adrenal cortex should release more aldosterone into the blood to increase blood pressure. Expected aldosterone levels would be higher than normal.



These questions are NOT related to a passage.

Item 49

Aldosterone exerts its effects on target cells by:

- ☐ A) binding to a receptor at the cell surface, setting off a second-messenger cascade.
- ☐ B) diffusing into adrenal cortical cells, where it influences transcription of certain DNA sequences.
- ☐ C) flowing across the synapse, where it binds and initiates an action potential.
- ☐ D) entering into target cells, where it increases the rate of production of sodium-potassium pump proteins.

Item 50

A patient develops an abdominal tumor resulting in the secretion of large quantities of aldosterone into the bloodstream. Which of the following will most likely occur?

- ☐ A) Levels of renin secreted by the kidney will increase.
- ☐ B) Levels of oxytocin secreted by the pituitary will increase.
- ☐ C) Levels of aldosterone secreted by the adrenal cortex will decrease.
- ☐ D) Levels of aldosterone secreted by the tumor will decrease.

Item 51

Which of the following is true for all endocrine hormones?

- ☐ A) They act through a second messenger system.
- ☐ B) They bind to a protein receptor.
- ☐ C) They dissolve in the blood.
- ☐ D) They are derived from a protein precursor.

Item 52

All of the following act as second messengers for hormones EXCEPT:

- ☐ A) cyclic AMP.
- ☐ B) calmodulin.
- ☐ C) acetylcholine.
- ☐ D) cyclic GMP.

Item 53

Which of the following is true of all steroids?

- ☐ A) The target cells of any steroid include every cell in the body.
- ☐ B) Steroids bind to receptor proteins on the membrane of their target cells.
- ☐ C) Steroids are synthesized on the rough endoplasmic reticulum.
- ☐ D) Steroids are lipid soluble.

Item 54

The pancreas is a unique organ because it has both exocrine and endocrine function. The exocrine portion of the pancreas releases:

- ☐ A) digestive enzymes directly into the blood.
- ☐ B) digestive enzymes through a duct.
- ☐ C) hormones straight into the blood.
- ☐ D) hormones through a duct.

Item 55

Most steroid hormones regulate enzymatic activity at the level of:

- ☐ A) replication.
- ☐ B) transcription.
- ☐ C) translation.
- ☐ D) the reaction.

Item 56

Which of the following side effects might be experienced by a patient who is administered a dose of thyroxine?

- ☐ A) An increase in endogenous TSH production
- ☐ B) A decrease in endogenous TSH production
- ☐ C) An increase in endogenous thyroxine production
- ☐ D) A decrease in endogenous parathyroid hormone production

Endocrine Glands and their Hormones

Memorization of several major hormones, their glands, and their target tissues is required for the MCAT®. As a memory aid, group hormones according to the gland that secretes them and remember that a given gland produces either steroids, peptides, or tyrosine derivatives, but not two categories of hormones. (The adrenal glands are really two glands. The cortex produces steroids; the medulla produces catecholamines. The thyroid is a true exception. The thyroid secretes T_3 and T_4 , which are tyrosine derivatives, and calcitonin, which is a peptide. Calcitonin and the thyroid hormones are produced by different types of cells within the thyroid.) This section will start by discussing the hormones of the anterior pituitary.

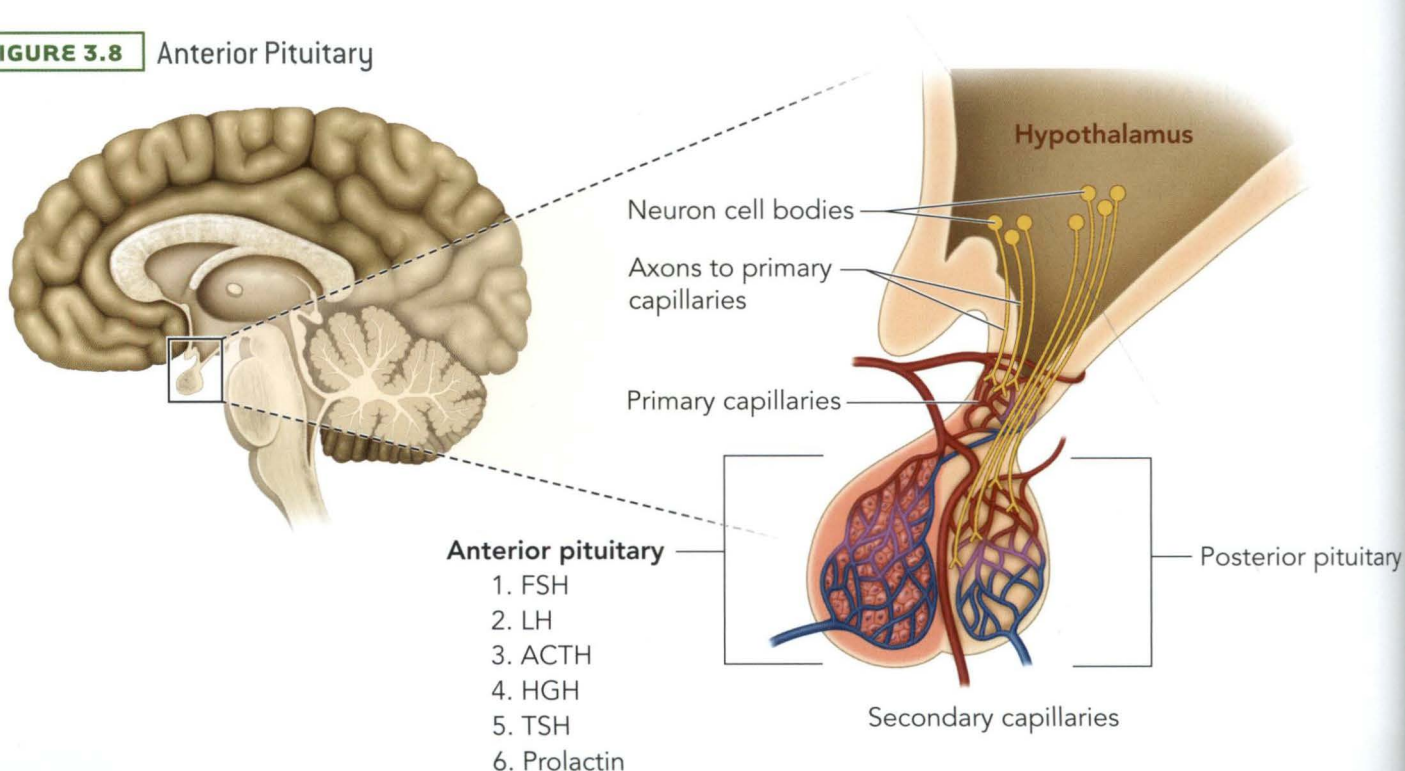
Anterior Pituitary

The **anterior pituitary** (Figure 3.8) (also called the *adenohypophysis*), which functions to regulate much of the endocrine system, is located in the brain beneath the **hypothalamus**. The hypothalamus controls the release of the anterior pituitary hormones with *releasing* and *inhibitory hormones* of its own. These releasing and inhibitory hormones are carried to the capillary bed of the anterior pituitary by small blood vessels. The release of the releasing and inhibitory hormones is, in turn, controlled by nervous signals.

The anterior pituitary releases six major hormones and several minor hormones. All of these are peptide hormones. The MCAT® requires familiarity with the six major hormones, their target tissues, and their functions. The hormones are:

1. Thyroid-stimulating hormone (TSH);
2. Adrenocorticotropin (ACTH);
3. Follicle-stimulating hormone (FSH);
4. Luteinizing hormone (LH);
5. Human growth hormone (HGH); and
6. Prolactin.

FIGURE 3.8 Anterior Pituitary



Human growth hormone (HGH) (also called *somatotropin*), a peptide, stimulates growth in almost all cells of the body. All other hormones of the anterior pituitary have specific target tissues. HGH stimulates growth by increasing episodes of mitosis, increasing cell size, increasing the rate of protein synthesis, mobilizing fat stores, increasing the use of fatty acids for energy, and decreasing the use of glucose. The effect of HGH on proteins is accomplished by increasing amino acid transport across the cell membrane, increasing translation and transcription, and decreasing the breakdown of protein and amino acids.

Adrenocorticotrophic hormone (ACTH), a peptide, stimulates the adrenal cortex to release glucocorticoids via the second messenger system using cAMP. Release of ACTH is stimulated by many types of stress. Glucocorticoids are stress hormones. (See below for the effects of the adrenal cortical hormones.)

Thyroid-stimulating hormone (TSH) (also called thyrotropin), a peptide, stimulates the thyroid to release T_3 and T_4 via the second messenger system using cAMP. Among other effects on the thyroid, TSH increases thyroid cell size, number, and the rate of secretion of T_3 and T_4 . It is important to note that T_3 and T_4 concentrations have a negative feedback effect on TSH release, both at the anterior pituitary and the hypothalamus. (See below for effects of T_3 and T_4 .)

FSH and LH are discussed later in this lecture in the context of reproduction.

Prolactin, a peptide, promotes lactation (milk production) by the breasts. Milk is not normally produced before birth due to the inhibitory effects of progesterone and estrogen on milk production. Although the hypothalamus has a stimulatory effect on the release of all other anterior pituitary hormones, it mainly inhibits the release of prolactin. The act of suckling, which stimulates the hypothalamus to stimulate the anterior pituitary to release prolactin, inhibits the menstrual cycle. It is not known whether this is directly due to prolactin. The milk production effect of prolactin should be distinguished from the milk ejection effect of oxytocin, which is secreted by the posterior pituitary.

Posterior Pituitary

The **posterior pituitary** is also called the *neurohypophysis* because it is composed mainly of support tissue for nerve endings extending from the hypothalamus. The hormones oxytocin and ADH are synthesized in the neural cell bodies of the hypothalamus, and transported down axons to the posterior pituitary, where they are released into the blood. Both oxytocin and ADH are small polypeptides.

Antidiuretic hormone (ADH) (also called **vasopressin**) is a small peptide hormone which causes the collecting ducts of the kidney to become permeable to water, reducing the volume of urine and concentrating the urine. When water is reabsorbed from the collecting tubule, the osmolarity of the blood plasma increases. Conversely, when excretion of water in the urine is permitted, the osmolarity of the blood plasma increases. In this way, ADH is the primary hormonal determinant of blood osmolarity. Since fluid is reabsorbed, ADH also secondarily increases blood pressure. Throughout the evolution of mammals, ADH secretion has always been under tight neural control. As a peptide hormone, it has a fast action and is therefore able to finely control plasma osmolarity and quickly respond to blood loss.

Oxytocin is a small peptide hormone that increases uterine contractions during pregnancy and causes milk to be ejected from the breasts. Notice that both of these effects are associated with the periodic contraction of smooth muscle, although they are on different scales.

The hormones released by the anterior pituitary can be remembered by the acronym **HALF PiT**:

H- Human growth hormone

A- Adrenocorticotropin

L- Luteinizing hormone

F- Follicle-stimulating hormone

P- Prolactin

i- ignore

T- Thyroid stimulating hormone



Coffee and beer are ADH blockers that increase urine volume. I am going to have to pee later!



Adrenal Glands

The **adrenal glands** (Figure 3.9) are located on top of the kidneys. They are separated into the adrenal cortex and the adrenal medulla. The **adrenal cortex** is the outside portion of the gland. The cortex secretes only steroid hormones. There are two types of steroids secreted by the cortex: **mineral corticoids** and **glucocorticoids**. (The cortex also secretes a small amount of sex hormones, significant in the female but not the male.) Mineral corticoids affect the electrolyte balance in the bloodstream; glucocorticoids increase blood glucose concentration and have an even greater effect on fat and protein metabolism. Approximately 30 corticoids have been isolated from the cortex, but the major mineral corticoid is aldosterone, and the major glucocorticoid is cortisol.

Aldosterone, a steroid, is a mineral corticoid that acts in the distal convoluted tubule and the collecting duct to increase Na^+ and Cl^- reabsorption and K^+ and H^+ secretion. Each NaCl is reabsorbed with a corresponding water molecule, so while the total amount of salt in the body increases, the concentration of salt in the bloodstream remains the same. This reabsorption results in an eventual increase in blood pressure. Aldosterone has the same effect, but to a lesser extent, on the sweat glands, salivary glands, and intestines.

For the MCAT®, the main effect of aldosterone is to increase plasma volume without affecting plasma osmolarity. It accomplishes this via the reabsorption of Na^+ and Cl^- .

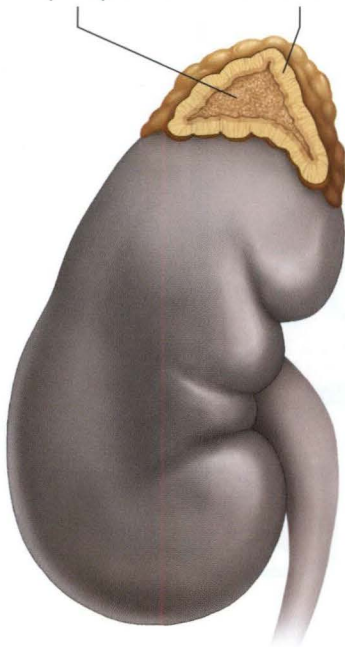
Cortisol, a steroid, is a glucocorticoid that increases blood glucose levels by stimulating **gluconeogenesis** in the liver. (See the Metabolism Lecture in *Biology 1: Molecules* for more on gluconeogenesis.) Cortisol also liberates fatty acids from adipose cells to be used for cellular energy. In addition, cortisol causes a moderate decrease in the use of glucose by the cells. Cortisol causes the degradation of nonhepatic proteins, a decrease of nonhepatic amino acids, and a corresponding increase in liver and plasma proteins and amino acids.

Cortisol is a stress hormone. The benefit of excess cortisol under stressful situations is not fully understood. One factor may be anti-inflammatory properties possessed by cortisol. Cortisol also diminishes the capacity of the immune system to fight infection.

The **catecholamines** are the tyrosine derivatives synthesized in the adrenal medulla: **epinephrine** and **norepinephrine** (also called **adrenaline** and **noradrenaline**). The effects of epinephrine and norepinephrine on the target tissues are similar to their effects in the sympathetic nervous system, but they last much longer. Epinephrine and norepinephrine are vasoconstrictors (they constrict blood vessels) of most internal organs and skin, but are vasodilators of skeletal muscle (they increase blood flow); this is consistent with the 'fight-or-flight' response of these hormones. Because of their 'fight or flight' response, the catecholamines are also considered stress hormones.

FIGURE 3.9 Adrenal Glands

- | Adrenal medulla | Adrenal cortex |
|-------------------|----------------|
| 1. Epinephrine | 1. Aldosterone |
| 2. Norepinephrine | 2. Cortisol |



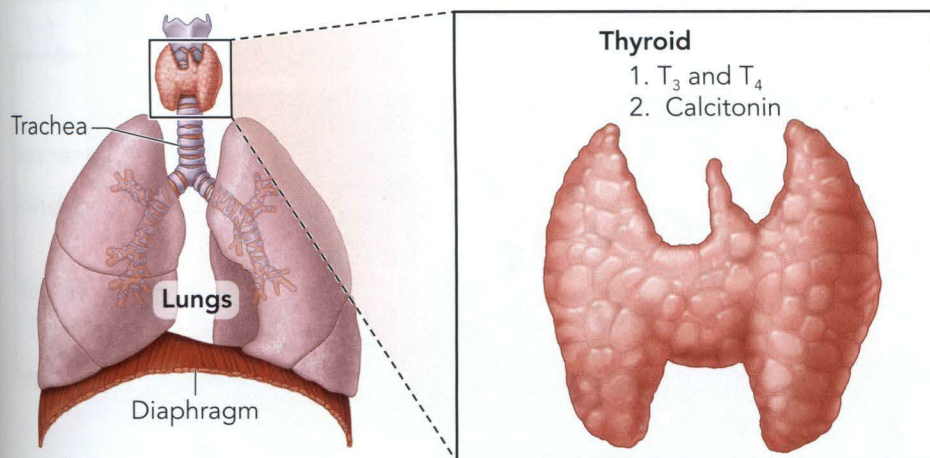
Nervous System
BIOLOGY 2

Thyroid

The thyroid hormones are *triiodothyronine* (T_3), *thyroxine* (T_4), and *calcitonin*. The thyroid (Figure 3.10) is located along the trachea just in front of the larynx.

The general effect of the thyroid hormones is to increase the **basal metabolic rate** (the resting metabolic rate). The basal metabolic rate is the amount of energy expended at rest in one day and is commonly measured as rate of oxygen consumption. The determinants of basal metabolic rate include heart rate and muscle mass.

FIGURE 3.10 Thyroid



T_3 and T_4 are very similar in their effects, and no distinction will be made by an MCAT[®] question unless it is thoroughly explained in a passage. T_3 contains three iodine atoms, and T_4 contains four. Both hormones are lipid soluble tyrosine derivatives that diffuse through the lipid bilayer and act in the nuclei of the cells of their effectors. Thyroid hormone secretion is regulated by TSH.

Calcitonin is a large peptide hormone released by the thyroid gland. Calcitonin slightly decreases blood calcium by decreasing osteoclast activity and number. Calcium levels can be effectively controlled in humans in the absence of calcitonin.

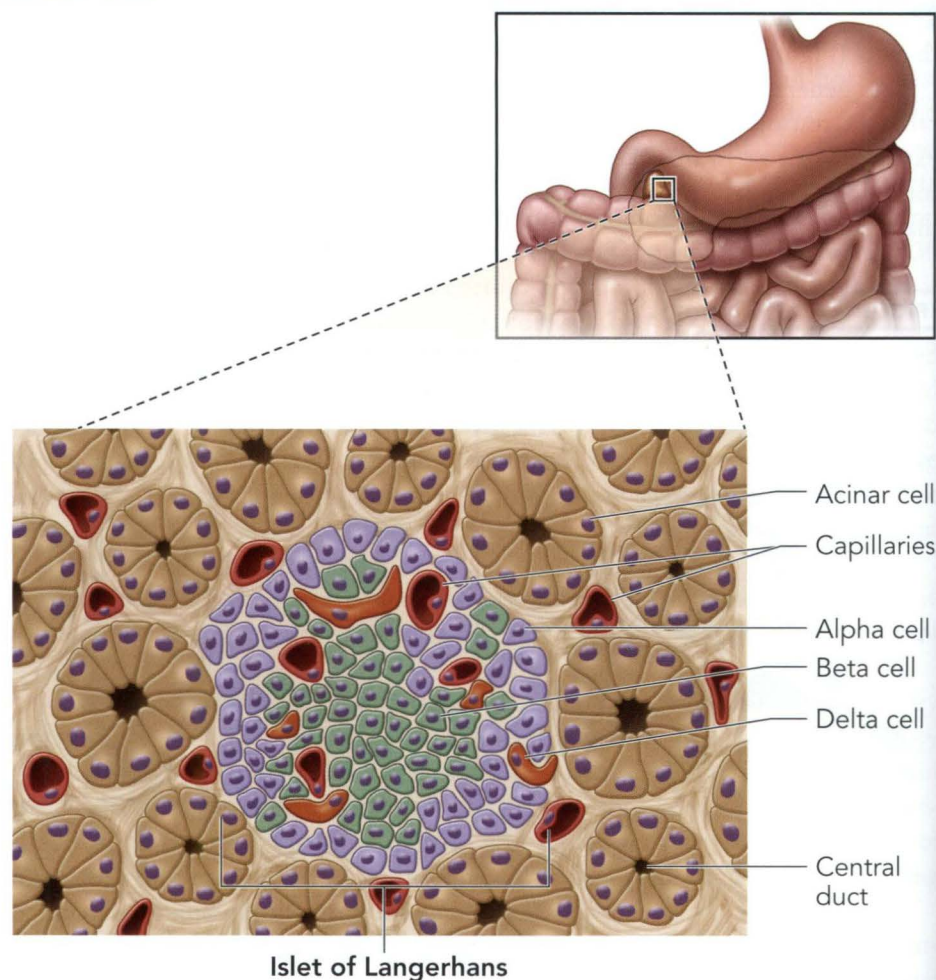
Some people say calcitonin “tones down calcium” in the bloodstream. Other people say calcitonin moves “calcium into bones.” Both are correct and are good memory aids.

T_3 and T_4 help determine the basal metabolic rate but are not the sole determinants of it. Why some people have higher or lower basal metabolic rates is largely unknown.

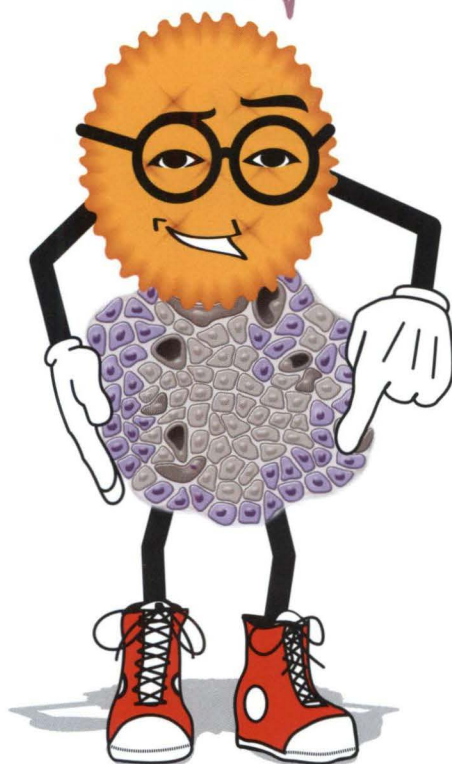
Pancreas (Islets of Langerhans)

The pancreas (Figure 3.11) acts as both an endocrine and an exocrine gland. For the MCAT[®], the two important endocrine hormones released into the blood by the pancreas are the peptide hormones insulin and glucagon. *Somatostatin*, not likely to be seen on the MCAT[®], is released by the δ -cells of the pancreas. Somatostatin inhibits both insulin and glucagon. The role of somatostatin may be to extend the period of time over which nutrients are absorbed.

FIGURE 3.11 Pancreas and Islets of Langerhans



Glucagon has an A, and it is made by alpha cells.

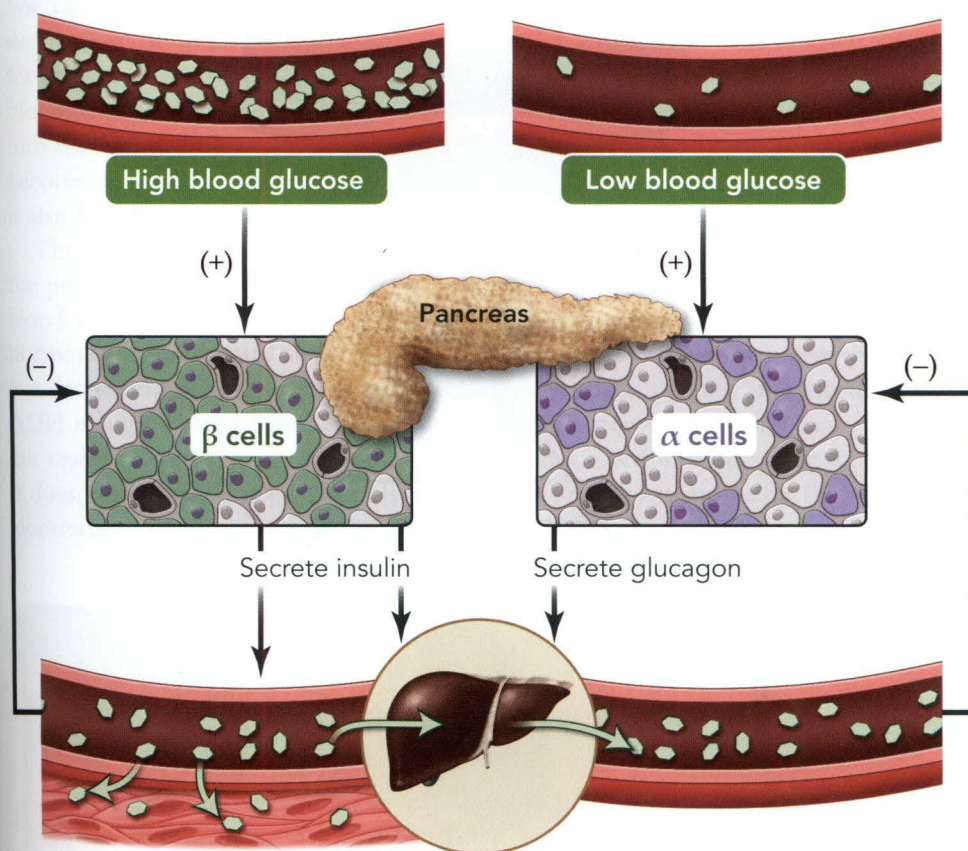


Insulin is associated with energy abundance in the form of high energy nutrients in the blood. Insulin is released by the β -cells of the pancreas when blood levels of carbohydrates or proteins are high. It affects carbohydrate, fat, and protein metabolism. In the presence of insulin, carbohydrates are stored as glycogen in the liver and muscles, fat is stored in adipose tissue, and amino acids are taken up by the cells of the body and made into proteins. The net effect of insulin is to lower blood glucose levels.

When insulin binds to a membrane receptor, a cascade of reactions is triggered inside the cell. Except for neurons in the brain and a few other cell types that are not affected by insulin, the cells of the body become highly permeable to glucose upon the binding of insulin. The binding of insulin causes the insulin receptor to activate the opening of a membrane bound glucose transporter. The permeability of the membrane to amino acids is also increased. In addition, intracellular metabolic enzymes are activated and, much more slowly, even translation and transcription rates are affected.

The effects of **glucagon** are nearly opposite to those of insulin. Glucagon is released by the α -cells of the pancreas. Glucagon stimulates glycogenolysis (the breakdown of glycogen), and gluconeogenesis in the liver. It acts via the second messenger system of cAMP. In higher concentrations, glucagon breaks down adipose tissue, increasing the fatty acid level in the blood. The net effect of glucagon is to raise blood glucose levels.

FIGURE 3.12 The Antagonistic Effects of Insulin and Glucagon



Parathyroid

Parathyroid hormone (PTH), a peptide, increases blood calcium. It increases osteocyte absorption of calcium and phosphate from the bone and stimulates proliferation of osteoclasts. PTH increases renal calcium reabsorption and renal phosphate excretion. It increases calcium and phosphate uptake from the gut by increasing renal production of a steroid derived from vitamin D. PTH secretion is regulated by the calcium ion plasma concentration, and the parathyroid glands shrink or grow accordingly.

As with other hormones, PTH has multiple effectors, and its effects may vary between different effectors.

FIGURE 3.13 Parathyroid

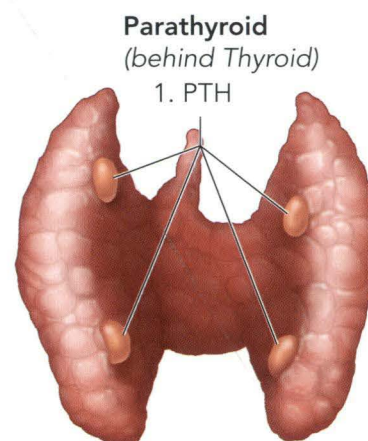
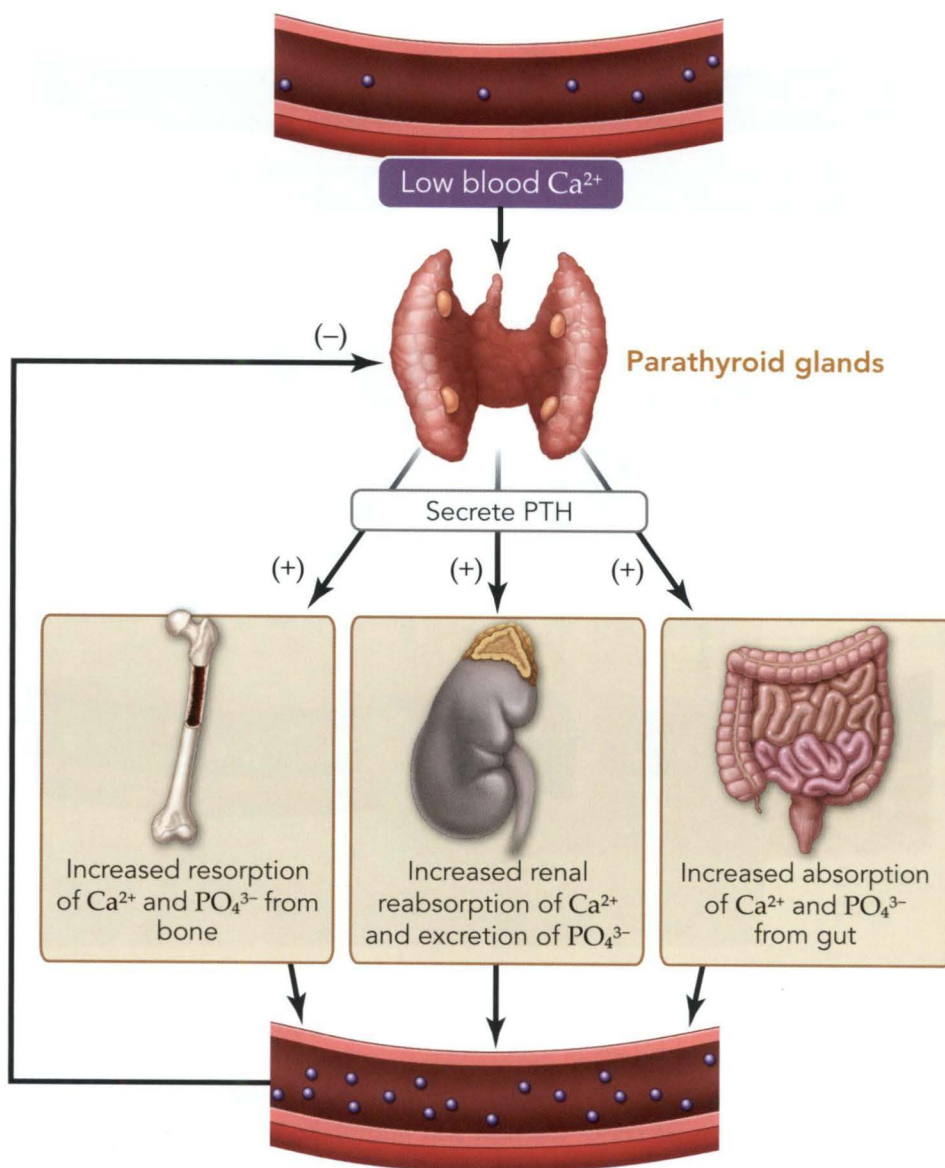


FIGURE 3.14 PTH Control of Blood Calcium Level



3.6

Homeostasis and Hormones

The hormones that have been discussed in this lecture can be grouped into five categories according to their functions in maintaining homeostasis in the body.

Tropic Hormones

Tropic hormones are hormones that have other endocrine glands as their targets. They include TSH, ACTH, LH, and FSH. They are all peptide hormones and are all released from the anterior pituitary.

Blood Chemistry Hormones

The **blood chemistry hormones** control the concentrations of sodium, glucose, and calcium in the bloodstream. They are peptide hormones released from the posterior pituitary, pancreas, parathyroid, and thyroid.

Osmolarity

For the purposes of the MCAT®, **osmolarity** in the bloodstream is primarily determined by sodium concentrations. The control of blood osmolarity is critical for the survival of each and every cell. Recall from the Cell Lecture that if the blood plasma were to become significantly hypotonic, it could cause water to rush into the cell, leading to lysis and death. Conversely, if the blood plasma were to become significantly hypertonic, it could cause water to rush out of the cell; this is also fatal for the cell.

The two hormones that act on blood volume and osmolarity are ADH, from the posterior pituitary, and aldosterone, from the adrenal medulla. Both increase blood volume, but they do so through different mechanisms. ADH is a peptide hormone that increases free water absorption, thereby increasing blood volume but decreasing plasma osmolarity. In fact, the primary stimulus for the release of ADH is high plasma osmolarity. Aldosterone is a steroid hormone that increases salt reabsorption, thereby increasing blood volume without affecting osmolarity. It does, however, increase total blood salt. The primary stimulus for the release of aldosterone is low blood volume.

MCAT® THINK

Try these questions to see if you understand the difference between ADH and aldosterone.

1. A person eats a bag of potato chips for lunch and now has a high concentration of sodium in the bloodstream. What will be the primary hormonal response?
2. A person enters a water-drinking contest on the local radio station. She drinks two gallons of water over the course of two hours, and now has a low concentration of sodium in the bloodstream. What will be the primary hormonal response?
3. A person has studied hard for four hours without anything to drink. His blood volume is now low. What will be the primary hormonal response?
4. A person has been in the desert for two days and ran out of water 10 hours ago. He now feels like he will pass out. What will be the primary hormonal response?

Answers:

1. ADH would be high, to absorb free water and decrease plasma osmolarity.
2. ADH would be low, to promote the excretion of water in the urine.
3. Aldosterone would initially be high, to promote the increase of blood volume without affecting blood osmolarity.
4. This is a tricky question. Blood volume is low, so levels of aldosterone will increase. However, this question is different from question three because it involves more extended and severe dehydration. Since the body is desperate to maintain its intravascular volume, ADH will be high. In emergency situations, the body will sacrifice blood sodium levels for volume. An MCAT® question will always make it clear that blood volume is very low (here, words like “desert” and “feels like he will pass out”), and it will not require you to choose between high levels of aldosterone and ADH.

Blood Glucose

The two principal hormones involved in **blood glucose regulation** are insulin and glucagon, both of which are produced by the endocrine pancreas.

Other hormones also affect blood glucose. Notably, human growth hormone, cortisol, and epinephrine will all increase blood glucose. For the purposes of the MCAT®, insulin is the only hormone that will decrease blood glucose.

Calcium Regulation

Calcium has a number of important functions in the body, and it is discussed in many contexts in this manual. In relatively low concentrations and in the absence of phosphorus, it is soluble and is generally associated with the movement of intracellular proteins. For example, its release from the sarcoplasmic reticulum causes tropomyosin to uncover myosin binding sites on actin, allowing for muscle contraction. Another example is the entrance of calcium into a neuron at the terminal axon, which causes vesicles filled with neurotransmitter to undergo exocytosis and release their contents into the synapse. By contrast, higher concentrations of calcium in the presence of phosphorus will cause calcium phosphate to precipitate from solution. The primary physiological example of this in the body is hydroxyapatite, the principle mineral of bone.

On the MCAT®, calcium is regulated by parathyroid hormone and calcitonin. Parathyroid hormone will increase blood calcium, and calcitonin will decrease it.

Stress Hormones

The **stress hormones** control how the body reacts to stress, including the short-term and long-term response. They cause increased blood pressure and raised levels of glucose in the bloodstream, among other effects. Epinephrine, a hydrophilic hormone released by the adrenal medulla, acts as a stress hormone in response to sudden emergencies. Cortisol, a hydrophobic hormone from the adrenal cortex, acts as a stress hormone that is released in response to more chronic stresses.

Determinants of Metabolic Rate

The **determinants of metabolic rate** control the body's use of energy on a day to day basis. While many hormones affect the metabolic rate, the major hormones are T_3 and T_4 , produced by the thyroid follicles.

Reproduction and Development

The **reproduction and development** hormones control the body's ability to reproduce effectively. They include both hydrophobic and hydrophilic hormones from the anterior pituitary, posterior pituitary, gonads, and placenta. These hormones will be discussed with reproductive physiology in the last section of this lecture.

Remember that oxytocin is responsible for ejecting milk and babies. Prolactin is PRO-lactation, that is, for the promotion of milk formation.

These questions are NOT related to a passage.

Item 57

Sympathetic stimulation results in responses most similar to the effects of which of the following hormones?

- ☐ A) Insulin
- ☐ B) Acetylcholine
- ☐ C) Epinephrine
- ☐ D) Aldosterone

Item 58

When compared with the actions of the nervous system, those of the endocrine system are:

- ☐ A) quicker in responding to changes, and longer-lasting.
- ☐ B) quicker in responding to changes, and shorter-lasting.
- ☐ C) slower in responding to changes, and longer-lasting.
- ☐ D) slower in responding to changes, and shorter-lasting.

Item 59

Insulin shock occurs when a patient with diabetes self-administers too much insulin. Typical symptoms are extreme nervousness, trembling, sweating, and ultimately loss of consciousness. The physiological effects of insulin shock most likely include:

- ☐ A) a pronounced increase in gluconeogenesis by the liver.
- ☐ B) a rise in blood fatty acid levels, leading to atherosclerosis.
- ☐ C) a dramatic rise in blood pressure.
- ☐ D) dangerously low blood glucose levels.

Item 60

Vasopressin, a hormone involved in water balance, is produced in the:

- ☐ A) hypothalamus.
- ☐ B) posterior pituitary.
- ☐ C) anterior pituitary.
- ☐ D) kidney.

Item 61

Osteoporosis is an absolute decrease in bone tissue mass, especially trabecular bone. All of the following might be contributory factors to the disease EXCEPT:

- ☐ A) increased sensitivity to endogenous parathyroid hormone.
- ☐ B) defective intestinal calcium absorption.
- ☐ C) menopause.
- ☐ D) abnormally high blood levels of calcitonin.

Item 62

All of the following hormones are produced by the anterior pituitary EXCEPT:

- ☐ A) thyroxine.
- ☐ B) growth hormone.
- ☐ C) prolactin.
- ☐ D) luteinizing hormone.

Item 63

Which of the following hormonal and physiological effects of stress would NOT be expected in a marathoner in the last mile of a marathon?

- ☐ A) Increased glucagon secretion
- ☐ B) Increased heart rate
- ☐ C) Decreased ACTH secretion
- ☐ D) Decreased blood flow to the small intestine

Item 64

Parathyroid hormone is an important hormone in the control of blood calcium ion levels. Parathyroid hormone directly impacts:

- I. bone density.
- II. renal calcium reabsorption.
- III. blood calcium concentration.

- ☐ A) I only
- ☐ B) I and II only
- ☐ C) I and III only
- ☐ D) I, II and III

Be aware of basic male anatomy but don't stress too much about it.

Except for FSH, LH, HCG, and *inhibin*, which are peptides, the reproductive hormones discussed in this section are steroids released from the testes, ovaries, and placenta.

The Male Reproductive System

The MCAT® requires knowledge of the basic anatomy of the male and female reproductive systems (Figures 3.15 and 3.18). The male **gonads**, meaning organs involved in the production of gametes, are called the **testes**. Production of sperm (Figure 3.16 and 3.17) occurs in the **seminiferous tubules**, a set of long, twisted tubes in the testes that are lined by Sertoli cells and spermatogonia. Spermatogonia located in the seminiferous tubules arise from epithelial tissue to become spermatocytes, spermatids, and then spermatozoa. Sertoli cells stimulated by **follicle-stimulating hormone (FSH)** surround and nurture the spermatocyte and spermatids. *Leydig cells*, located in the interstitium between the tubules, release **testosterone** when stimulated by **luteinizing hormone (LH)**. Testosterone is the primary **androgen** (male sex hormone), and stimulates the germ cells to differentiate into sperm. Testosterone is also responsible for the development of secondary sex characteristics such as pubic hair, enlargement of the larynx, and growth of the penis and seminal vesicles. While testosterone helps to initiate the growth spurt at puberty, it also stimulates closure of the epiphyses of the long bones, ending growth in height. Sertoli cells secrete *inhibin*, a peptide hormone (actually a glycoprotein) that acts on the pituitary gland to inhibit FSH secretion.

A **spermatogonium** is a sperm stem cell before it undergoes meiosis. Once the cell enters meiosis, it is referred to as a *spermatocyte*. At the end of meiosis, it is known as a *spermatid*. The spermatid loses its cytoplasm and forms the *head*, *mid-piece*, and *tail*, as shown in Figure 3.17, to become a spermatozoon (**sperm**). The

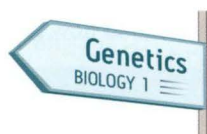


FIGURE 3.15 Male Reproductive Anatomy

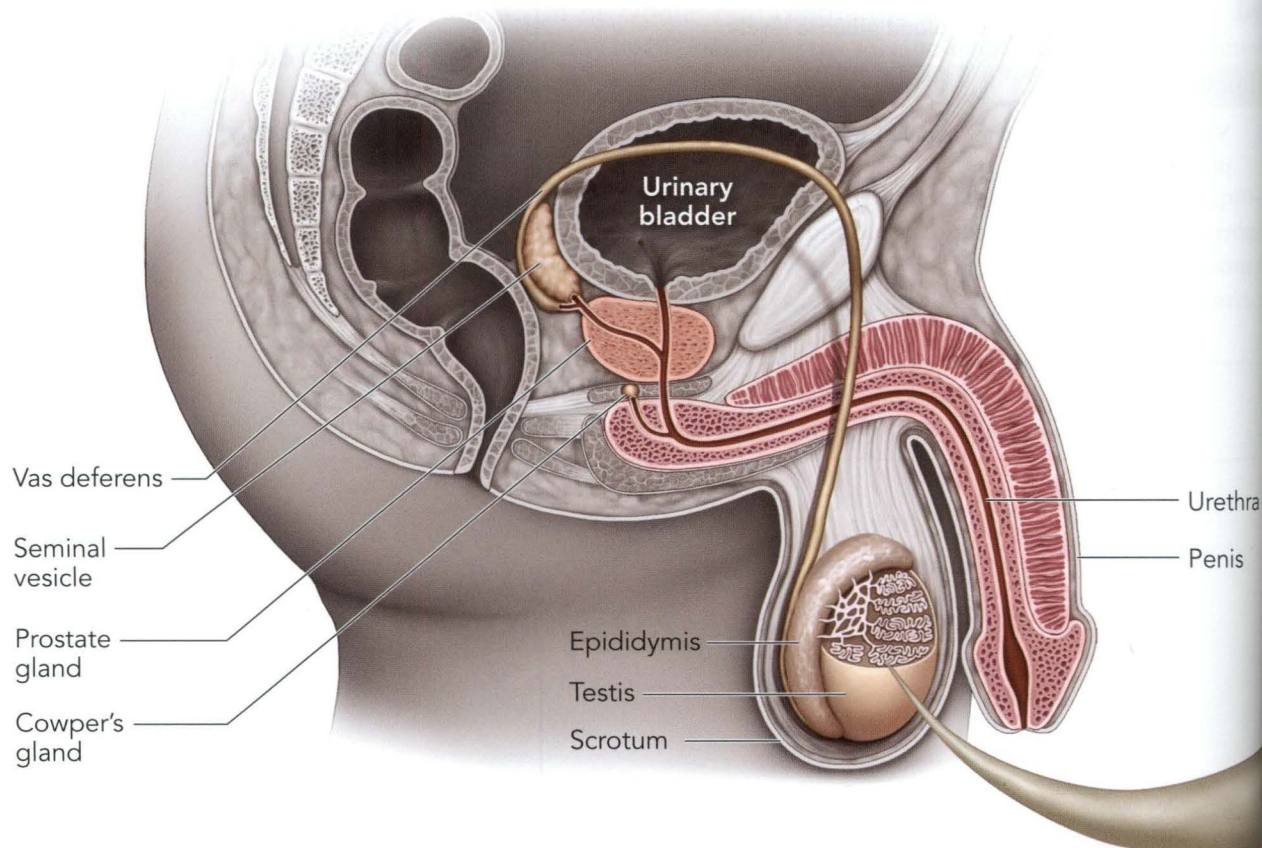
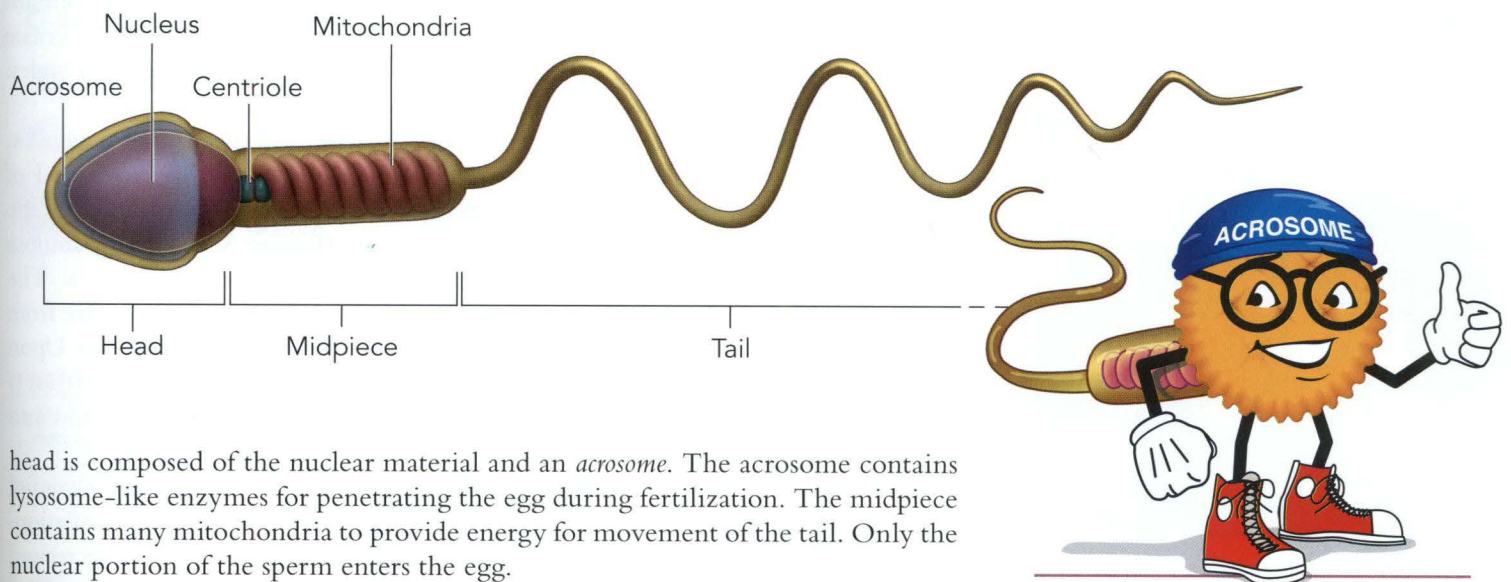


FIGURE 3.16 Spermatozoon

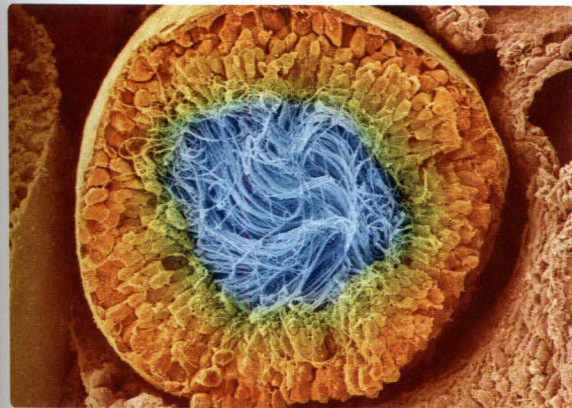


head is composed of the nuclear material and an *acrosome*. The acrosome contains lysosome-like enzymes for penetrating the egg during fertilization. The midpiece contains many mitochondria to provide energy for movement of the tail. Only the nuclear portion of the sperm enters the egg.

Once freed into the tubule lumen, the spermatozoon is carried to the **epididymis** to mature. Upon ejaculation, spermatozoa are propelled through the **vas deferens** into the **urethra** and out of the penis. **Semen** is the complete mixture of spermatozoa and fluid that leaves the penis upon ejaculation. Semen is composed of fluid from the **seminal vesicles**, the **prostate**, and the **bulbourethral glands** (also called **Cowper's glands**). Spermatozoa become activated for fertilization in a process called *capacitation*, which takes place in the vagina.

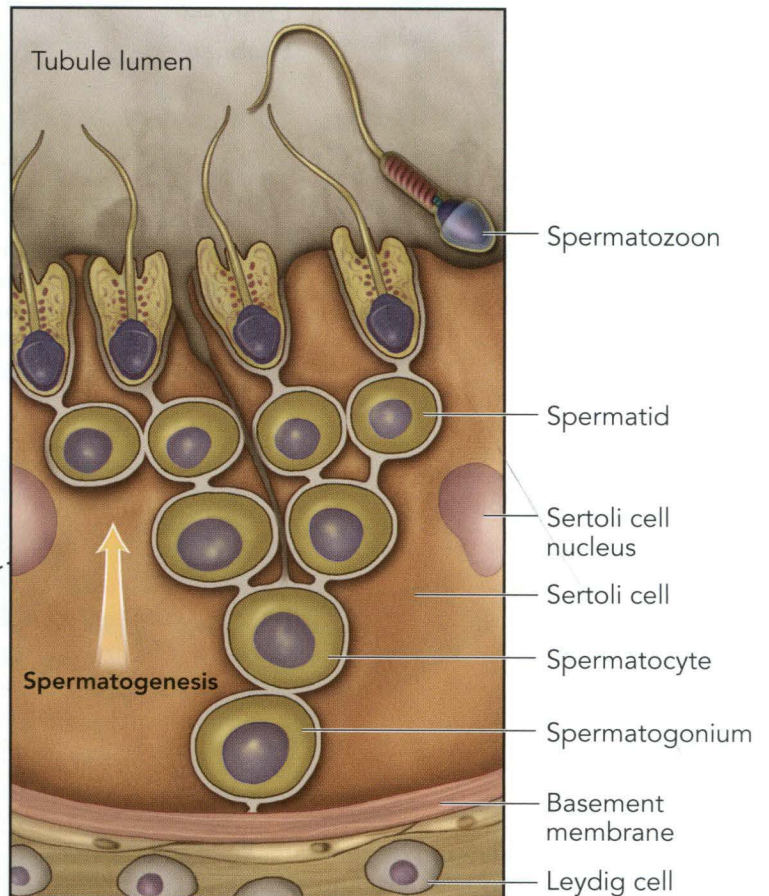
I am ready to go on my trip! I have only the things I need. I have my tail to swim. I have my mitochondria to give me lots of energy. And I have my acrosome to let me get inside an egg. Anything else would just slow me down!

FIGURE 3.17 Spermatogenesis



The seminiferous tubules are the site of spermatogenesis (sperm production). Each sperm cell consists of a head (green) and a tail (blue). The heads of the sperm are buried in Sertoli cells (yellow and orange), which nourish the developing sperm.

Cross-section of seminiferous tubule



The Female Reproductive System

The male reproductive cycle is relatively linear. Sperm are produced at a constant rate every day, and hormones have no true monthly cycle. By contrast, the female reproductive cycle is indeed a cycle. In fact, there are two intricately related cycles: one in the ovaries and one in the uterus.

The foundations of the ovarian cycle begin at birth with the start of oogenesis. All of the eggs of the female are arrested as primary oocytes, in prophase I of meiosis, at birth. At puberty, the ovarian cycle truly begins. FSH stimulates the growth of *granulosa cells* around the primary oocyte (Figure 3.18). The granulosa cells secrete a viscous substance around the egg called the **zona pellucida**. The structure at this stage is called a *primary follicle*. Next, theca cells differentiate from the interstitial tissue and grow around the follicle to form a *secondary follicle*. Upon stimulation by LH, theca cells secrete androgen, which is converted to **estradiol** (a type of **estrogen**) by the granulosa cells in the presence of FSH and secreted into the blood.

Eventually, the follicle grows and bulges from the ovary. Typically, estradiol inhibits LH secretion by the anterior pituitary. However, just before ovulation, the estradiol level rises rapidly and causes a dramatic increase in LH secretion. This increase is called the **luteal surge**. The luteal surge results from a positive feedback loop, where rising estrogen levels increase LH levels, which increase estrogen. The luteal surge causes

ovulation, the bursting of the follicle and release of the egg (now a secondary oocyte, having just completed meiosis I) into the body cavity. The egg is swept into the **Fallopian (uterine) tube** by the **fimbriae**. The remaining portion of the follicle is left behind to become the **corpus luteum**. The corpus luteum secretes estradiol and **progesterone** throughout pregnancy, or, in the case of no pregnancy, for about 2 weeks until the corpus luteum degrades into the **corpus albicans**.

FIGURE 3.18 Female Reproductive Anatomy and Ovulation

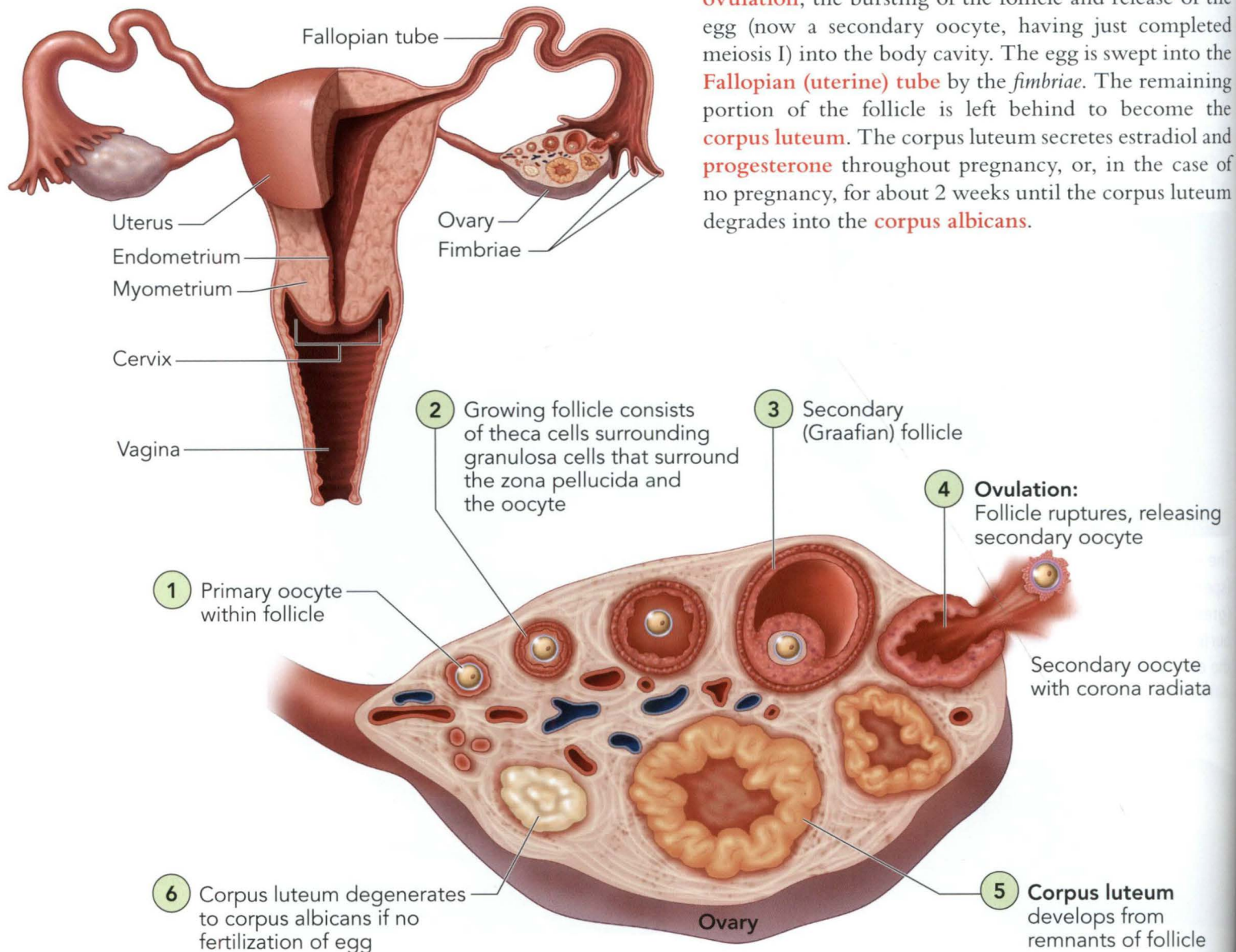
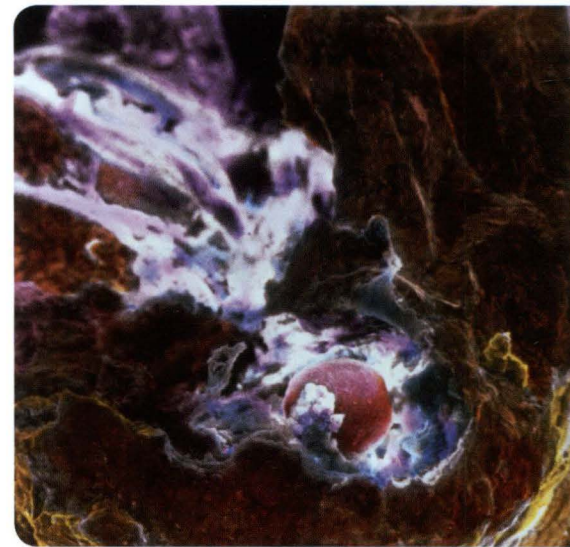
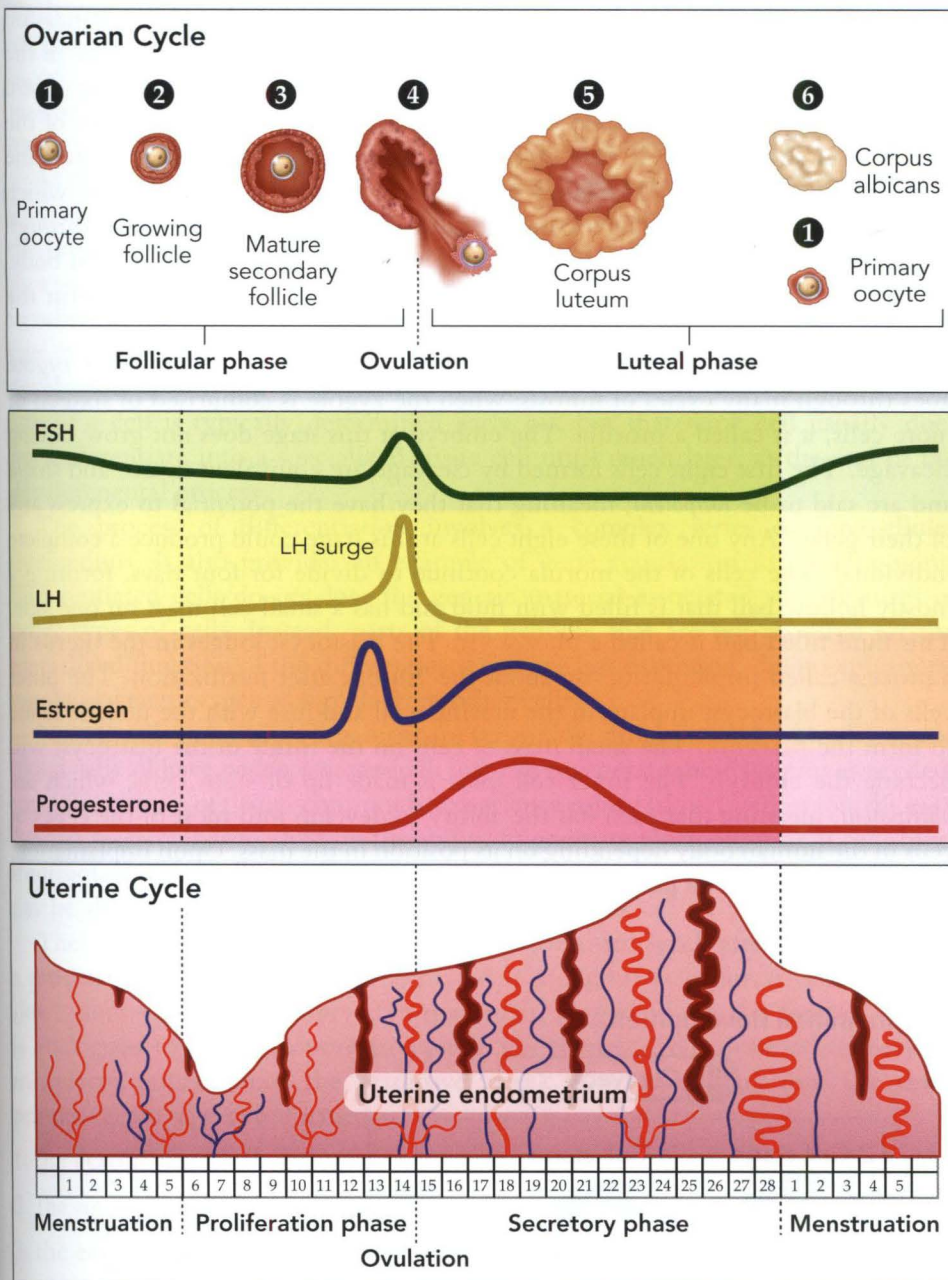


FIGURE 3.19 The Menstrual Cycle



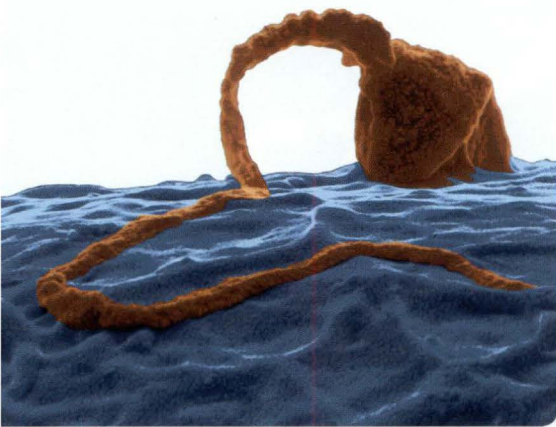
Shown above is a mature ovum (Graafian follicle) at ovulation. The ovum (red) is surrounded by remnants of corona cells and liquid from the ruptured ovarian follicle.

Notice that both menstruation and the proliferation phase of the uterus occur during the follicular phase of the ovarian cycle.

The ovarian cycle is thus divided into two parts separated by ovulation:

1. The *follicular phase*, which begins with the development of the follicle and ends at ovulation; and
2. The *luteal phase*, which begins with ovulation and ends with the degeneration of the corpus luteum into the corpus albicans.

The hormones produced during the ovarian cycle set the course of the cycle that takes place in the uterus. The uterine cycle begins on day 0, which marks the first day of *menstruation*. The first day of the uterine cycle corresponds is also the first day of the follicular phase in the ovary. As the follicle matures and begins to release more estradiol, menstruation stops, and the uterine wall enters the *proliferation phase*. The proliferative phase is the building phase, and lasts until ovulation. After ovulation, the corpus luteum begins to secrete progesterone, which acts as a maintenance hormone for the uterus. The uterine wall is held intact in the event of pregnancy. As the corpus luteum degrades into the corpus albicans, it is no longer able to secrete progesterone to maintain the uterine wall. The uterine wall sloughs off and produces menstruation, starting a new cycle.



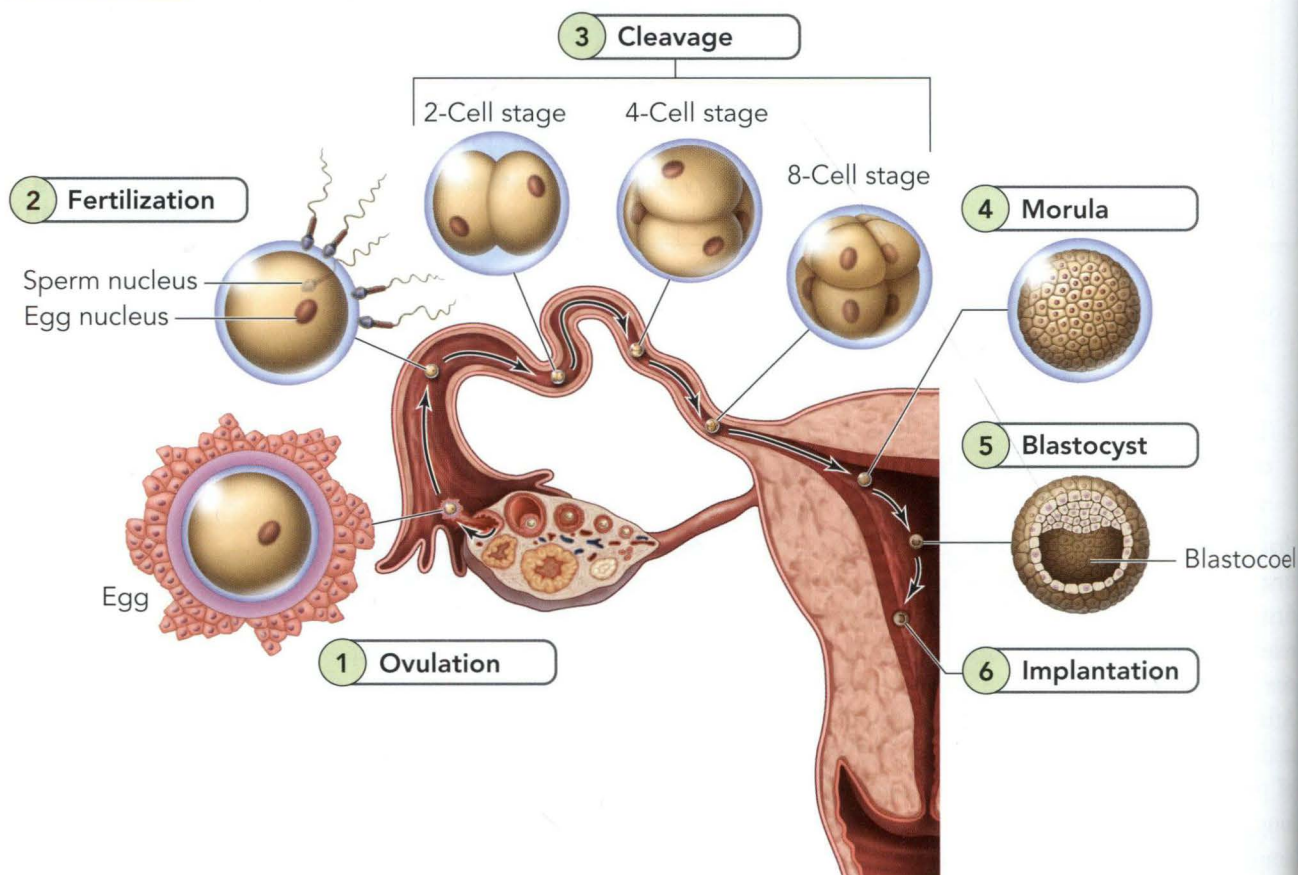
Sperm cell fertilizing an egg cell. The sperm cell (brown) is trying to penetrate the surface of the egg cell (blue). Once a sperm has fertilized the egg, rapid chemical changes make the outer layer (zona pellucida) of the egg cell thicken, preventing other sperm cells from entering. The head of the successful sperm cell releases genetic material that mixes with the genetic material in the egg cell.

Pregnancy and Embryology

Once in the Fallopian tube, the egg is swept toward the uterus by cilia. Fertilization normally takes place in the Fallopian tubes. The enzymes of the acrosome in the sperm are released upon contact with the egg, and digest a path for the sperm through the granulosa cells and the zona pellucida. The cell membranes of the sperm head and the oocyte fuse upon contact, and the sperm nucleus enters the cytoplasm of the oocyte. The entry of the sperm causes the *cortical reaction*, which prevents other sperm from fertilizing the same egg. Now the oocyte goes through the second meiotic division to become an **ovum** and releases a second polar body. Fertilization occurs when the nuclei of the ovum and sperm fuse to form the **zygote**.

Cleavage begins while the zygote is still in the Fallopian tube. The zygote goes through many cycles of mitosis; when the zygote is comprised of sixteen or more cells, it is called a **morula**. The embryo at this stage does not grow during cleavage. The first eight cells formed by cleavage are equivalent in size and shape and are said to be *totipotent*, meaning that they have the potential to express any of their genes. Any one of these eight cells at this stage could produce a complete individual. The cells of the morula continue to divide for four days, forming a mostly hollow ball that is filled with fluid and has a small cell mass on one side. This fluid filled ball is called a **blastocyst**. The blastocyst lodges in the uterus in a process called **implantation** on about the 7th day after fertilization. The outer cells of the blastocyst implant in the uterine wall and fuse with the uterine tissue to form the **placenta**. The small mass of cells on the inside of the blastocyst will become the embryo. The inner cell mass is made up of **stem cells**, which are *pluripotent*, meaning that each has the ability to develop into most of the types of cells in the human body depending on its position in the mass. Upon implantation, the female is said to be pregnant.

FIGURE 3.20 Early Cleavages in Animal Development



After implantation, the placenta begins secreting the peptide hormone **human chorionic gonadotropin (HCG)**. HCG prevents the degeneration of the corpus luteum and maintains its secretion of estrogen and progesterone. HCG in the blood and urine of the mother is the first outward sign of pregnancy. The placenta reaches full development by the end of the first trimester and begins secreting its own estrogen and progesterone while lowering its secretion of HCG.

As the embryo develops past the eight cell stage, the cells become different from each other due to **cell-cell communication**. In the blastocyst, for example, the inner cells become the embryo and the outer cells become the placenta. This process where a cell becomes committed to a specialized developmental path is called **determination**. Cells undergo determination such that they will give rise to a particular tissue early on. The specialization that occurs at the end of development, forming a specialized tissue cell, is called **differentiation**. The fate of a cell is typically determined early on, but that same cell usually does not differentiate into a specialized tissue cell until much later, at the end of the developmental process.

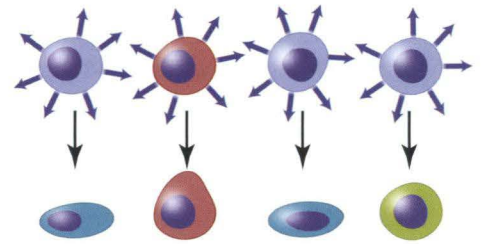
The process of differentiation involves a complex series of intercellular interactions. It also provides an example of **gene regulation in development**. Differentiated cells do not lose the genetic material associated with features of other types of cells. Instead, parts of the genome that are not required for the specialized function of the differentiated cell are not expressed, due to epigenetic regulatory factors such as signals from other cells.

Not all cells in an adult organism are terminally differentiated. Skin, liver, and blood cells all have *multipotent stem cells* that can regenerate these systems as needed, since these types of tissues commonly experience injury (skin, liver) or loss (blood). Recent research has focused on the ability to generate pluripotent stem cells from multipotent stem cells, so that organs without **regenerative capacity** might one day be able to regenerate following injury or removal.

The formation of the **gastrula** occurs in the third week after fertilization in a process called **gastrulation**. The **first cell movements** occur as cells begin to slowly move about the embryo. In mammals, a *primitive streak* is formed, which is analogous to the blastopore in aquatic vertebrates. Cells destined to become mesoderm migrate into the primitive streak. During gastrulation, the three primary germ layers are formed:

1. the **ectoderm**;
2. the **mesoderm**; and
3. the **endoderm**.

FIGURE 3.21 Influence of Neighboring Cells



Genetics
BIOLOGY 1

Totipotent stem cells can become any cell, placenta or embryo. Pluripotent stem cells can become any one of the initial three germ layers, all of which are a part of the embryo. Multipotent stem cells can replace cells of a particular lineage, such as skin, liver, and blood.

FIGURE 3.22 Gastrulation

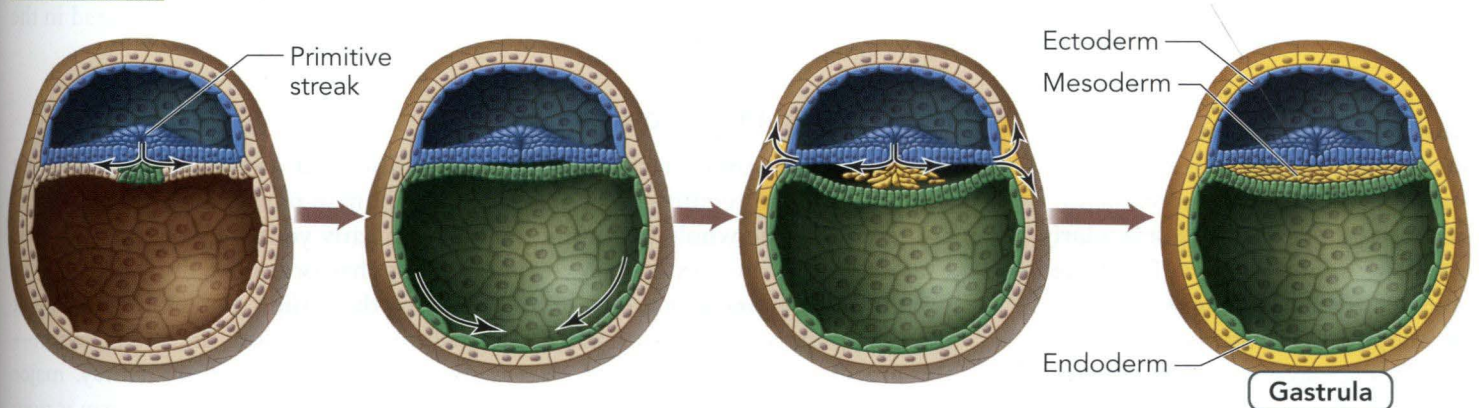


TABLE 3.1 > Fates of the Primary Germ Layers

Ectoderm	Epidermis of skin, nervous system, sense organs
Mesoderm	Skeleton, muscles, blood vessels, heart, blood, gonads, kidneys, dermis of skin
Endoderm	Lining of digestive and respiratory tracts, liver, pancreas, thymus, thyroid

Although there are no absolute rules for memorizing which tissues arise from which germ layer, certain guidelines can be followed for the MCAT®. The ectodermal cells develop into the outer coverings of the body, such as the outer layers of skin, nails, and tooth enamel, and into the cells of the nervous system and sense organs. The endodermal cells develop into the lining of the digestive tract, and into much of the liver and pancreas. The mesoderm develops into the structures that lie between the inner and outer coverings of the body: the muscle, bone, and the rest.

In the third week, the gastrula develops into a **neurula** in a process called **neurulation**. Through **induction**, the **notochord** (made from mesoderm) causes overlying ectoderm to thicken and form the *neural plate*. The notochord eventually degenerates, while a *neural tube* forms from the neural plate to become the spinal cord, brain, and most of the nervous system. The cells of the ectoderm that are close to the neural tube are known as the **neural crest**. The cells of the neural crest function mostly as accessory cells to the nervous system, such as Schwann cells. They form the second order neurons of the autonomic nervous system. They also give rise to parts of the endocrine organs discussed in this lecture, including the adrenal medulla and the C cells of the thyroid. In order to travel to various locations in the body, neural crest cells undergo **cell migration**. Throughout embryological development, this regulated process of cell movement ensures that cells end up in the correct locations of the structures to which they contribute.

Part of normal cell development is **programmed cell death** or **apoptosis**. Apoptosis is essential for development of the nervous system, operation of the immune system, and destruction of tissue between fingers and toes to create hands and feet in humans. Damaged cells may undergo apoptosis as well. Failure to do so may result in cancer. Apoptosis is a complicated process in humans, but it is essentially regulated by protein activity as opposed to regulation at the level of transcription or translation. The proteins involved in apoptosis are present but inactive in a normal healthy cell. In mammals, mitochondria play an important role in apoptosis.

Senescence is the process by which cells stop proliferating in response to environmental stressors and are ultimately cleared away by immune cells. It is another developmental mechanism that allows the shaping of tissues. Senescence is necessary for normal embryological development, but it is also implicated in the **aging** process later in life.

Physiological Development

So far developmental mechanisms have been discussed on the cellular level, but the MCAT® also requires an understanding of human physiological development at the level of the whole organism prenatally, in early youth, and during puberty. **Prenatal development**, which is development that occurs before birth, begins with the development of the embryo. Following the earliest stages of development described above—cleavage, blastula formation, gastrulation, and neurulation—the process of organ formation begins. By the ninth week of pregnancy, major organs are developing in their final locations, and the developing organism is now considered to be a fetus. Development continues throughout the second trimester, but the fetus is not yet capable of independent survival. The third trimester is

For the MCAT®, know that induction occurs when one cell type affects the direction of differentiation of another cell type. It is also important to know that the neural tube becomes the nervous system and is derived from ectoderm.

Throughout the process of prenatal development, the fast growth of multiple structures means that harmful substances (teratogens) can have particularly negative consequences. Teratogens and some other aspects of development will be discussed in the *Psychology & Sociology Manual*. Much of the information in this section could appear on the Psychosocial section of the MCAT®.

characterized by continued growth, particularly in the brain. The brain is not yet fully developed at the time of **parturition** (birth); a completely developed brain would be too large to pass through the human pelvis.

Development in childhood and adolescence, like prenatal development, follows a predictable sequence. Consider **motor development**, which takes the infant from the earliest stage—the immobility of a newborn—to independent walking. Although children progress at different rates, the basic milestones of progress are generally the same. The direction of development is from head to toe (a *cephalocaudal pattern*) and from the midline of the body to the periphery (a *proximodistal pattern*). In other words, progress starts with the head, moves down to the trunk, and then moves down and out as limb movement is mastered. More specifically, lifting of the head is followed by lifting of the chest. Next the child is able to sit with support, and then without support. Then the ability to stand with support is developed, followed by crawling. The last three steps are walking with support, standing independently, and finally walking independently.

Another important period of rapid and dramatic physical development is puberty. **Puberty** refers to the biological changes that ultimately lead to sexual maturity. **Adolescent development** includes the psychosocial processes that accompany puberty. Thus adolescence is a socially designated period of rapid psychological and social change that is intertwined with pubertal development. Like prenatal development, adolescent development involves rapid physical growth. At the same time, sexual maturation occurs in the context of primary sex characteristics (i.e. development of the reproductive organs) and the secondary sex characteristics.

In addition to influencing physiological development, reproductive hormones influence behavior during pubertal development. This is just one of the many ways that the endocrine system affects behavior.



Prenatal development can be roughly categorized by trimester. The 1st semester is mostly development; the 2nd trimester is growth and development; and the 3rd trimester is mostly growth.

To remember how motor development progresses, think “head to toe and in to out.”

It is less important to know each step than it is to understand that motor development is predictable. You can't skip straight from sitting up to walking!

TABLE 3.2 > Major Hormones of the Endocrine System

Gland	Hormone	Solubility	Effect
Anterior pituitary	HGH	Water soluble	Growth of nearly all cells
	ACTH	Water soluble	Stimulates adrenal cortex
	FSH	Water soluble	Growth of follicles in female; Sperm production in male
	LH	Water soluble	Causes ovulation; stimulates estrogen and testosterone secretion
	TSH	Water soluble	Stimulates release of T_3 and T_4 in the thyroid
	Prolactin	Water soluble	Promotes milk production
Posterior pituitary	Oxytocin	Water soluble	Milk ejection and uterine contraction
	ADH	Water soluble	Water absorption by the kidney; increases blood pressure
Adrenal cortex	Aldosterone	Lipid soluble	Reduces Na^+ excretion; increases K^+ excretion; raises blood pressure
	Cortisol	Lipid soluble	Increases blood levels of carbohydrates, proteins, and fats
Adrenal medulla	Epinephrine	Water soluble	Stimulates sympathetic actions
	Norepinephrine	Water soluble	Stimulates sympathetic actions
Thyroid	T_3, T_4	Lipid soluble	Increase basal metabolic rate
	Calcitonin	Water soluble	Lowers blood calcium
Parathyroid	PH	Water soluble	Raises blood calcium
Pancreas	Insulin	Water soluble	Promotes glucose entry into cells, decreasing blood glucose levels
	Glucagon	Water soluble	Increases gluconeogenesis, increasing blood glucose levels
Ovaries	Estrogen	Lipid soluble	Growth of female sex organs; causes LH surge
	Progesterone	Lipid soluble	Prepares and maintains uterus for pregnancy
Testes	Testosterone	Lipid soluble	Secondary sex characteristics; closing of epiphyseal plate
Placenta	HCG	Water soluble	Stimulates corpus luteum to grow and release estrogen and progesterone
	Estrogen	Lipid soluble	Enlargement of mother's sex organs; stimulates prolactin secretion
	Progesterone	Lipid soluble	Maintains uterus for pregnancy

These questions are NOT related to a passage.

Item 65

A drug that causes increased secretion of testosterone from the interstitial cells of a physically mature male would most likely:

- ☐ A) cause the testes to descend prematurely.
- ☐ B) delay the onset of puberty.
- ☐ C) cause enhanced secondary sex characteristics.
- ☐ D) decrease core body temperature.

Item 66

During the female menstrual cycle, increasing levels of estrogen cause:

- ☐ A) a positive feedback response, stimulating LH secretion by the anterior pituitary.
- ☐ B) a positive feedback response, stimulating FSH secretion by the anterior pituitary.
- ☐ C) a negative feedback response, stimulating a sloughing off of the uterine lining.
- ☐ D) a negative feedback response, stimulating decreased progesterone secretion by the anterior pituitary.

Item 67

The function of the epididymis is to:

- ☐ A) store sperm until they are released during ejaculation.
- ☐ B) produce and secrete testosterone.
- ☐ C) conduct the ovum from the ovary into the uterus.
- ☐ D) secrete FSH and LH to begin the menstrual cycle.

Item 68

Decreasing progesterone levels during the luteal phase of the menstrual cycle are associated with:

- ☐ A) thickening of the endometrial lining in preparation for implantation of the zygote.
- ☐ B) increased secretion of LH, leading to the luteal surge and ovulation.
- ☐ C) degeneration of the corpus luteum in the ovary.
- ☐ D) increased secretion of estrogen in the follicle, leading to the flow phase of the menstrual cycle.

Item 69

The inner linings of the Fallopian tubes are covered with a layer of cilia. The purpose of this layer is to:

- ☐ A) remove particulate matter that becomes trapped in the mucus layer covering the Fallopian tubes.
- ☐ B) maintain a layer of warm air close to the inner lining, protecting the ovum from temperature changes occurring in the external environment.
- ☐ C) kill incoming sperm, thus preventing fertilization.
- ☐ D) facilitate movement of the ovum towards the uterus.

Item 70

Which of the following endocrine glands produces testosterone?

- ☐ A) The anterior pituitary
- ☐ B) The pancreas
- ☐ C) The adrenal cortex
- ☐ D) The adrenal medulla

Item 71

Which of the following does NOT accurately describe cleavage in human embryos?

- ☐ A) The solid ball of cells produced during cleavage is called a morula.
- ☐ B) The size of the embryo remains constant throughout the cell divisions of cleavage.
- ☐ C) Cell division occurs in one portion of the egg in meroblastic cleavage.
- ☐ D) Daughter cells are genetically identical to parent cells.

Item 72

The heart, bone and skeletal muscle most likely arise from which of the following primary germ layers?

- ☐ A) The ectoderm
- ☐ B) The endoderm
- ☐ C) The gastrula
- ☐ D) The mesoderm

TERMS YOU NEED TO KNOW

Adolescent development	Estrogen	Parathyroid hormone (PTH)
Adrenal cortex	Exocrine glands	Parturition
Adrenal glands	Fallopian (uterine) tube	Peptide hormones
Adrenaline	First cell movement	Placenta
Adrenocorticotrophic hormone (ACTH)	Follicle-stimulating hormone (FSH)	Posterior pituitary
Aging	Gastrula	Prenatal development
Aldosterone	Gastrulation	Progesterone
Androgen	Gene regulation in development	Programmed cell death
Anterior pituitary	Glucagon	Prolactin
Antidiuretic hormone (ADH or vasopressin)	Glucocorticoids	Prostate
Apoptosis	Gluconeogenesis	Puberty
Basal metabolic rate	Gonads	Receptors
Blastocyst	Human chorionic gonadotropin (HCG)	Regenerative capacity
Blood chemistry hormones	Human growth hormone (HGH)	Reproduction and development
Blood glucose regulation	Hypothalamus	Semen
Bulbourethral glands (Cowper's glands)	Implantation	Seminal vesicles
Calcitonin	Induction	Seminiferous tubules
Cell-cell communication	Insulin	Senescence
Cell migration	Luteal surge	Sperm
Cleavage	Luteinizing hormone (LH)	Spermatogonium
Corpus albicans	Mesoderm	Stem cells
Corpus luteum	Mineral corticoids	Steroid hormones
Cortisol	Morula	Stress hormones
Determinants of metabolic rate	Motor development	Target cell
Determination	Neural crest	Testes
Differentiation	Neurula	Testosterone
Ectoderm	Neurulation	Thyroid hormones: T ₃ , T ₄
Effector	Noradrenaline	Thyroid-stimulating hormone (TSH)
Endocrine glands	Norepinephrine	Tropic hormones
Endoderm	Notochord	Tyrosine derivatives
Epididymis	Osmolarity	Urethra
Epinephrine	Ovulation	Vas deferens
Estradiol	Ovum	Zona pellucida
	Oxytocin	Zygote



DON'T FORGET YOUR KEYS

1. See a hormone, think of its gland, function, polarity, and target(s).
2. Hormones respond to imbalance in the body to restore homeostasis. Normally functioning hormones do not create imbalance.
3. Reproductive hormones and cells in male and females are similar in both structure and process but act along different timelines.

The Circulatory, Respiratory, and Immune Systems

4

LECTURE

4.1 Introduction

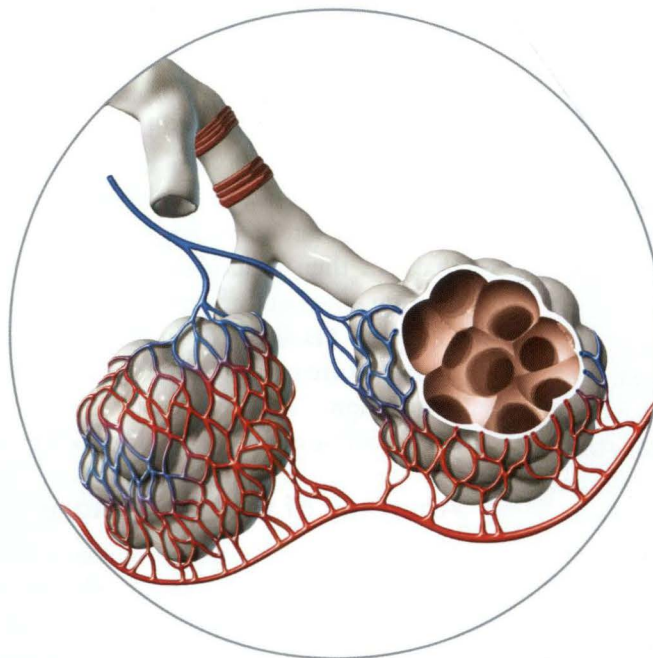
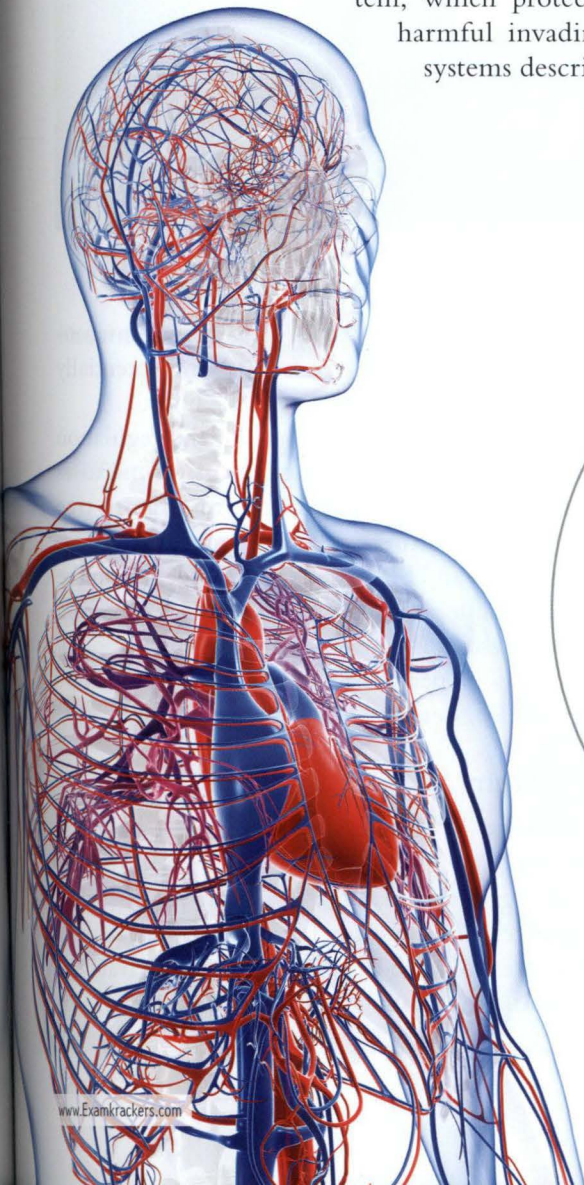
This lecture covers multiple systems with interrelated functions that all concern the transport and delivery of important substances throughout the body. The unique features that allow each system to carry out its function will be considered. The respiratory and cardiovascular systems work together to deliver oxygen to the tissues, allowing cells to carry out metabolism and gain energy to perform their necessary functions. Both of these systems make use of branching structures that generate a huge surface area for the exchange of materials. Furthermore, differential pressures drive the movement of substances in both of these systems, as will be described throughout the lecture.

The blood is the link between the respiratory and cardiovascular systems. Oxygen diffuses into the bloodstream, binds to a carrier molecule, and is then carried throughout the body for delivery to the tissues according to their metabolic needs. The cardiovascular system routinely deposits excess fluid into the tissues, which is transported away by the lymphatic system. The immune system, which protects the organism from potentially harmful invading substances, involves all of the systems described above.

- 4.1 Introduction
- 4.2 The Respiratory System and Gas Exchange
- 4.3 The Blood
- 4.4 The Cardiovascular System and Blood Pressure
- 4.5 The Lymphatic System as Drainage
- 4.6 The Immune System: Components and Communication

THE 3 KEYS

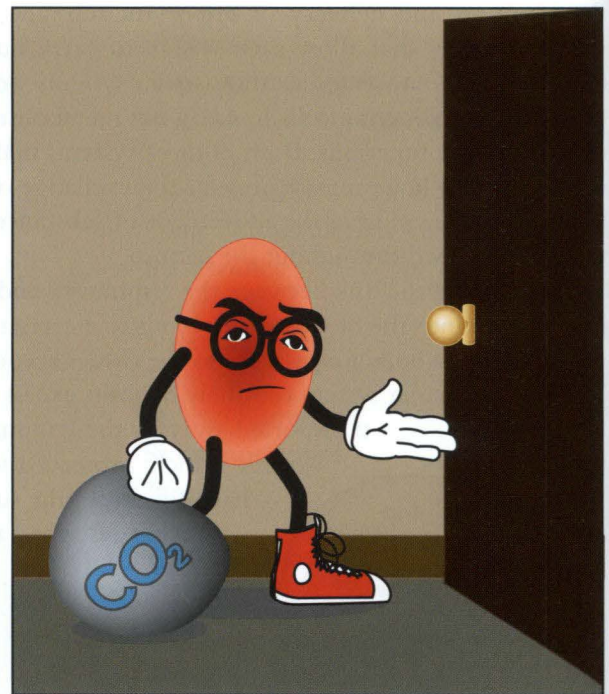
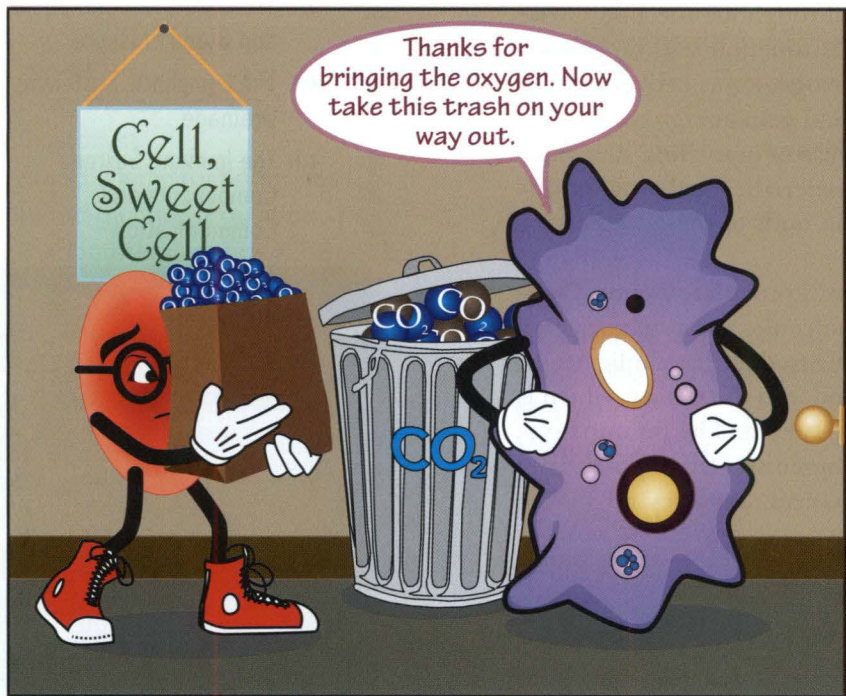
1. The goal of respiration and circulation is to meet metabolic needs.
2. Differential pressures and concentrations drive fluid flow and reactions.
3. Increasing surface area facilitates exchange of materials.



The Respiratory System and Gas Exchange

Metabolism BIOLOGY 1

The respiratory system is used by the body to ensure that the cells have a constant supply of oxygen and are able to get rid of the waste product carbon dioxide. Both oxygen and carbon dioxide are involved in aerobic respiration: oxygen is necessary for the last step in chemiosmotic synthesis of ATP, while carbon dioxide is produced by the Krebs cycle. Cells need a constant supply of oxygen, and they also need a way to prevent the buildup of carbon dioxide and other waste products. The respiratory system is key to both of these cellular requirements.



You need to know that the primary job of the respiratory system is to deliver oxygen to the blood and expel carbon dioxide. It is also important to know the basic anatomy of the respiratory system given here. Another part of the respiratory tract's function is to prepare the air by warming, moistening, and cleaning it. Ciliated cells in the respiratory tract play a role in filtering the air by trapping foreign particles. Since microtubules are found in cilia, and ciliated cells are found in the respiratory tract (and the Fallopian tubes and ependymal cells of the spinal cord), a defect in microtubule production might result in a problem with breathing (or fertility or circulation of cerebrospinal fluid).

Because the respiratory system is a site of exchange between the external environment and the body, it plays a role in protection against disease by trapping potentially harmful incoming **particulate matter** and ushering it back out of the body.

The respiratory system is also important for **thermoregulation**, the regulation of body temperature such that it stays within a narrow range. **Panting** increases respiration rate, bringing more water into the upper part of the respiratory tree that can then evaporate. **Evaporation** is an exothermic process and thus has a cooling effect on the body. (See the Solutions and Electrochemistry Lecture in the *Chemistry Manual* to learn about evaporation in general, and the Muscle, Bone and Skin Lecture in this manual to learn more about how evaporation cools the body). In addition, **nasal and tracheal capillary beds** participate in a method of thermoregulation used by the cardiovascular system, described later in this lecture.

Anatomy of the Respiratory System

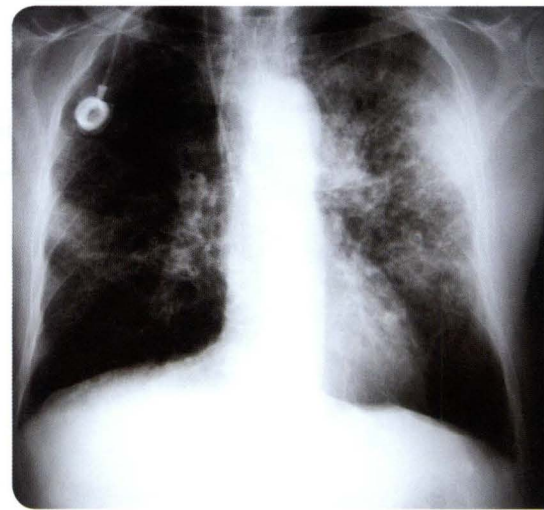
The respiratory system provides a path for gas exchange between the external environment and the blood (Figure 4.1). The movement of oxygen and carbon dioxide through the respiratory system is governed by changes in the pressure differential between the chest cavity and external environment, as will be described. Air enters through the nose and then moves through the pharynx, larynx, trachea, bronchi, bronchioles, and into the alveoli, where oxygen is exchanged for carbon dioxide from the blood.

The *nasal cavity* is the space inside the nose. Various structures and substances within the nasal cavity act to filter, moisten, and warm incoming air. **Nasal hairs** at the front of the cavity trap large dust particles. **Mucus** secreted by goblet cells traps smaller dust particles that were able to bypass the coarse nasal hair and also moistens the air. Capillaries within the nasal cavity warm the air. **Cilia** move mucus and dust back toward the pharynx to be removed by spitting or swallowing. Thus, the nasal cavity participates in the immune function of the respiratory system, preventing some potentially harmful substances from entering the body.

The *pharynx* (or throat) functions as a passageway for food and air.

The *larynx* contains the vocal cords. It sits behind the *epiglottis*, which is the cartilaginous structure that rises to block the opening of the trachea during swallowing, preventing the entry of food into the airway. Any nongaseous material that enters the larynx triggers a coughing reflex and is forced back out.

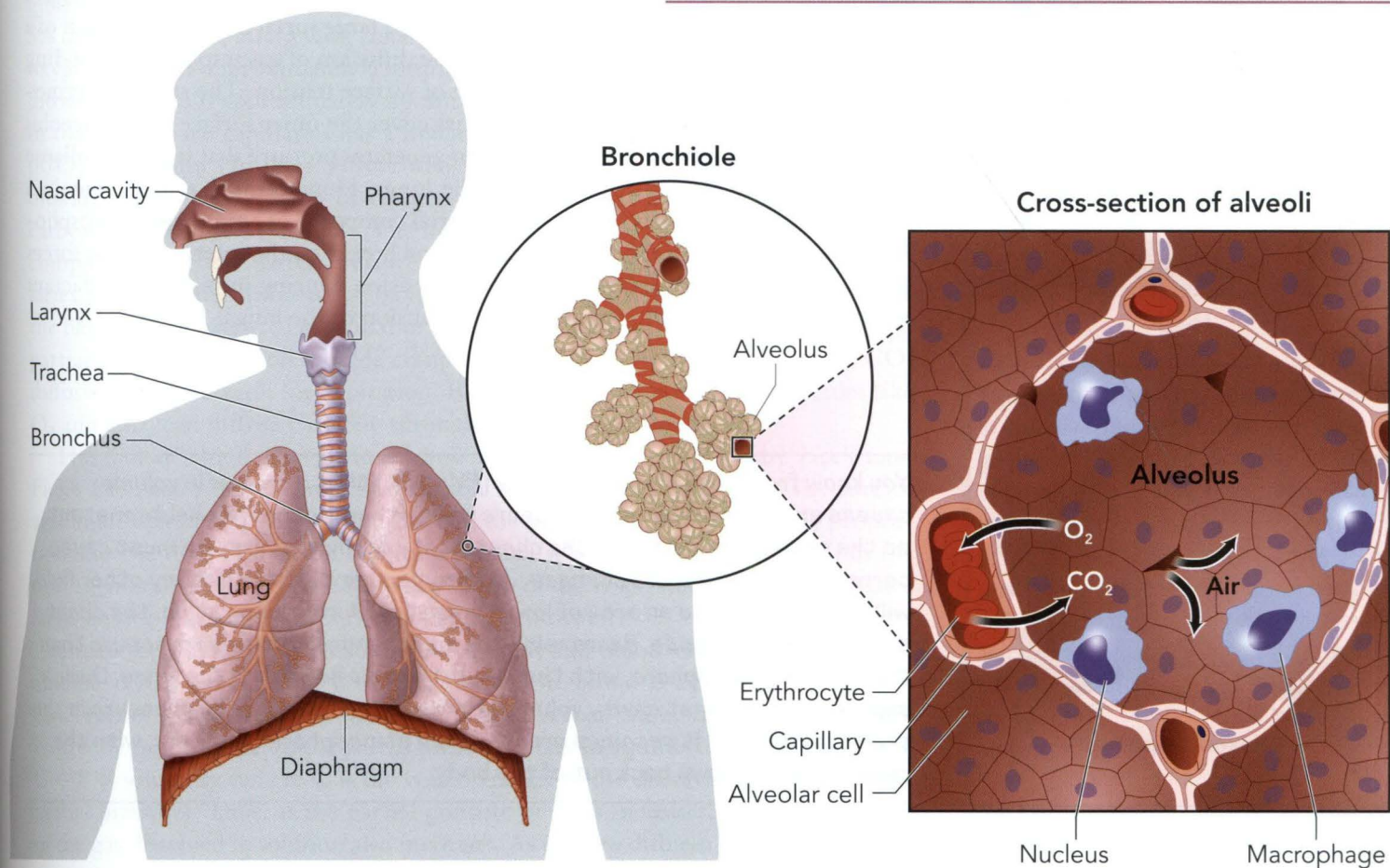
The **trachea** (or windpipe) lies in front of the esophagus. It is composed of ringed cartilage covered by ciliated mucous cells. Like in the nasal cavity, mucus and cilia in the trachea collect particulate matter and usher it back out, in this case toward the pharynx. Before entering the lungs, the trachea splits into the right and left **bronchi**. Each bronchus branches many more times to become tiny **bronchioles**. Bronchioles terminate in grape-like clusters called *alveolar sacs*, composed of tiny **alveoli**. Oxygen diffuses from each alveolus into an adjacent capillary, where it is picked up by red blood cells. The red blood cells release carbon dioxide, which diffuses into the alveolus and is expelled upon exhalation.



X-ray of a lung cancer.

Why does the airway undergo so much branching into smaller structures? The answer is that branching creates a huge amount of surface area for gas exchange. The cardiovascular system branches into capillaries for similar reasons.

FIGURE 4.1 Respiratory System



Mechanics of Respiration

Inspiration and expiration of air is governed by changing **differential pressures** in the chest cavity and airway. Air flows from the external environment into the body and back out again according to changes in the pressure of the airway relative to atmospheric pressure. When the airway and alveoli are at a negative gauge pressure, air flows inwards; when the airway and alveolar pressure become greater than atmospheric pressure, air flows back out to the environment.

To understand the mechanisms of inspiration and expiration, it is first necessary to examine the pressures in the respiratory system at rest. The lungs have a natural tendency to collapse inward due to their elasticity, while the **rib cage** tends to expand outwards, in the opposite direction. The combination of these effects causes the pressure of the chest cavity at rest to be negative compared to atmospheric pressure. However, alveolar pressure is equal to atmospheric pressure, so air does not flow inwards.

Inspiration occurs when the **medulla oblongata** of the midbrain signals the **diaphragm** to contract. The diaphragm is a thin sheet of skeletal muscle that is innervated by the phrenic nerve. The diaphragm is dome-shaped in a relaxed state, but it flattens upon contraction, expanding the chest cavity. *Intercostal muscles* (rib muscles) also help to expand the chest cavity. As a result, pressure in the air cavity becomes even more negative than it is at rest, and pressures in the airway and alveoli also become negative. Atmospheric pressure forces air into the lower-pressure area of the lungs.

When the medulla stops signaling the diaphragm to contract, it relaxes, causing the chest cavity to shrink. The **elasticity** (also called **resiliency**) of the lungs, along with the increased pressure in the chest cavity, forces air out of the body. Note that expiration as described here is a passive process. When forced expiration is needed, such as during exercise, the shrinking of the chest cavity is aided by the abdominal muscles and a set of intercostal muscles distinct from those involved in inspiration.

During inspiration, the ability of the lungs to expand in response to changing pressure is counteracted by **surface tension** in the alveoli. Each tiny alveolus has a high ratio of surface area to volume, providing a large surface for the diffusion of a small amount of gas. This ratio facilitates the diffusion of gas into the surrounding capillaries, but it also leads to the problem of surface tension. The strong intermolecular forces of the thin layer of water that cover the inner surface of the alveolus create high surface tension, which in turn generates pressure that tends to collapse the alveolus and opposes expansion of the lungs. However, the alveoli contain a type of cell that produces *surfactant*, a material composed of amphipathic phospholipids. Surfactant coats the alveolar surface and breaks up the intermolecular forces between water molecules, reducing surface tension. During inspiration, surfactant decreases surface tension and assists the expansion of the lungs.

You know from the universal gas law ($PV = nRT$) that a change in volume causes an inverse change in pressure when other factors are held constant, so the changes in volume of the chest cavity during respiration must cause corresponding pressure changes. Just remember that air, like any other fluid, will generally flow to an area of lower pressure. During inspiration, the chest cavity volume expands, decreasing the air pressure to a lower pressure than that of the atmosphere, with the result that air flows into the lungs. During expiration, the chest cavity volume decreases, increasing the pressure in the chest cavity until it becomes greater than atmospheric pressure, with the result that air flows back out of the body.

FIGURE 4.2 Respiration and the Diaphragm

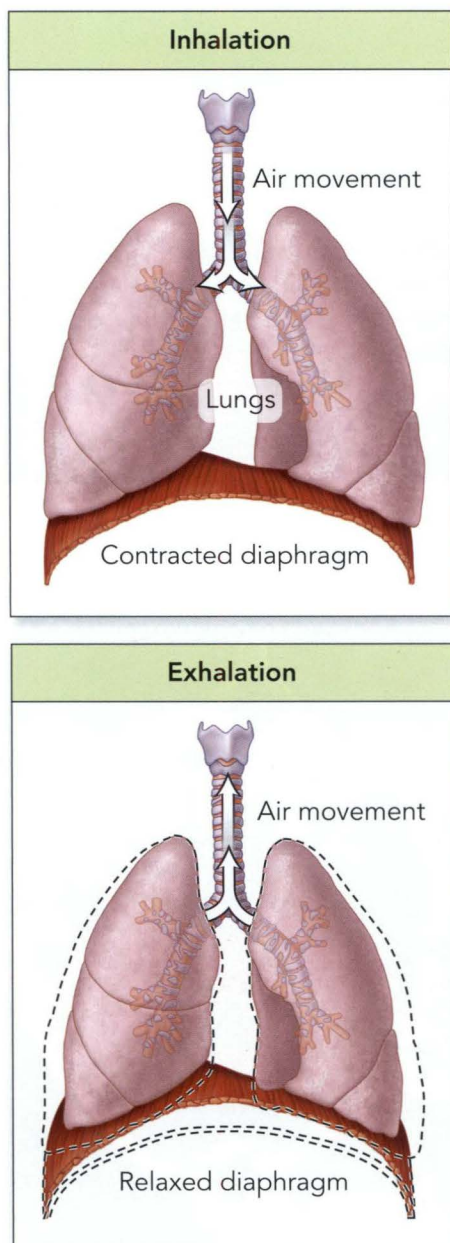
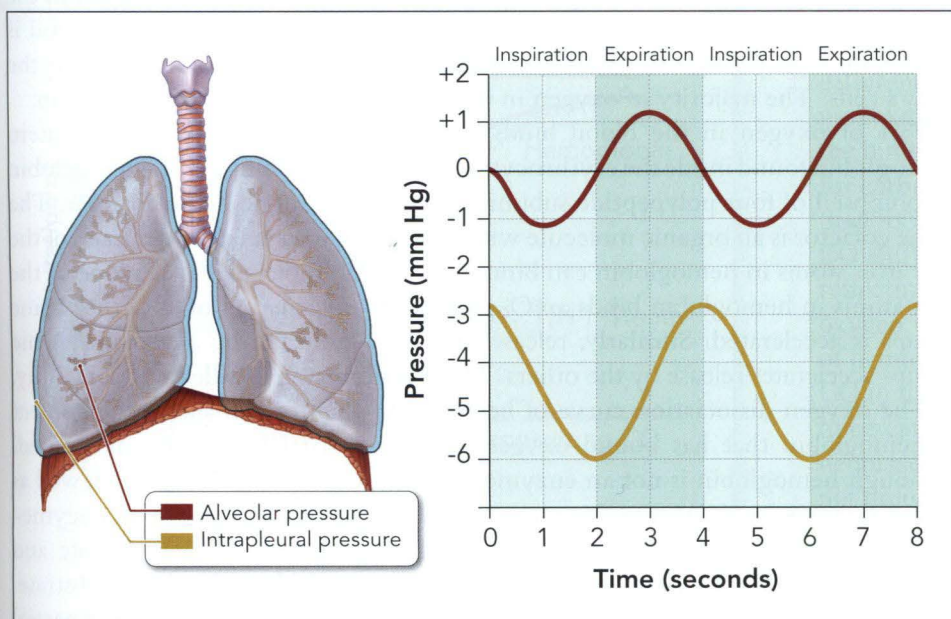


FIGURE 4.3 Alveolar and Intrapleural Pressure



The Chemistry of Gas Exchange

Alveolar gas exchange is governed by principles of gas and solution chemistry. It occurs passively, through **diffusion**, the tendency of a gas to travel towards an area of lower concentration or pressure. This section will describe how differing partial pressures of oxygen and carbon dioxide ensure their movement in the correct direction. In addition, given the fact that these gases must be transported in the liquid substance of the blood, gas solubility and transport will be considered.

Typically, the air we breathe in is 79% nitrogen and 21% oxygen, with negligible amounts of other trace gases. Exhaled air is 79% nitrogen, 16% oxygen, and 5% carbon dioxide, along with trace gases. Inside the lungs, the partial pressure of oxygen (pO_2) is approximately 110 mm Hg, while the partial pressure of carbon dioxide (pCO_2) is approximately 40 mm Hg. The deoxygenated blood contained in the pulmonary capillaries has a much lower pO_2 , at 40 mm Hg, and a higher pCO_2 of 46 mm Hg. The **differential partial pressures** of oxygen and carbon dioxide cause the diffusion of oxygen into the capillaries and the diffusion of carbon dioxide into the alveoli. The high partial pressure of oxygen in the alveoli compared to the low partial pressure in the deoxygenated blood in adjacent capillaries promotes the diffusion of oxygen into the capillaries. Meanwhile, because the blood has transported carbon dioxide away from the cells as waste, it has a high partial pressure of carbon dioxide compared to that of the alveoli; as a result, CO_2 diffuses into the alveoli for expiration. Remember, small nonpolar molecules like O_2 and CO_2 can diffuse passively through a cellular membrane.

The rate at which gases diffuse across a membrane is governed by *Fick's Law*. Fick's Law states that the rate of diffusion is directly proportional to the surface area and differential partial pressure across the membrane, and is inversely proportional to the thickness of the membrane across which diffusion occurs. Thus the thin membranes of alveoli and the branching of the respiratory system to create a large surface area are features that encourage diffusion.

Once oxygen has diffused across the alveolar and blood vessel membranes, the amount of the gas that can be dissolved into the blood is described by **Henry's Law**. Henry's Law states that the amount of a gas that can be dissolved in solution is directly proportional to the partial pressure of gas in equilibrium with the liquid: $C = P \times \text{solubility}$ (where C is the concentration of the dissolved gas, and P is the partial pressure). Thus, as the partial pressure of a gas increases, the concentration of the gas dissolved in solution also increases. As oxygen diffuses into the capillaries

Solutions
CHEMISTRY

To understand how gases diffuse in the alveoli, just remember that gases will diffuse to an area of lower pressure. You can even think of this in terms of Le Châtelier's Principle, where dissolved gas in solution is on one side of the reaction and the gas vapor is on the other. When pressure increases on one side, more of the gas shifts in the reverse direction.

It is easy to remember that increases in CO_2 , hydrogen ion concentration, and temperature all cause the oxygen dissociation curve to shift to the right if you realize that they all reflect the body's increased need for oxygen. When metabolic demands are high, such as during exercise, more oxygen is needed for aerobic respiration. At the same time, CO_2 builds up as a byproduct of metabolism (causing hydrogen ion concentration to increase). Finally, heat is released during the process of metabolism, so increased temperature also signals the need for increased oxygen delivery.

from the alveoli, the pO_2 of the blood rises until it reaches the high partial pressure of O_2 found in the alveoli. This process facilitates the dissolution of oxygen in the blood, as described by Henry's Law. Still, the solubility of oxygen in the blood is not nearly high enough for sufficient oxygen to be dissolved for transport to the body's cells. The majority of oxygen in the blood is transported by hemoglobin.

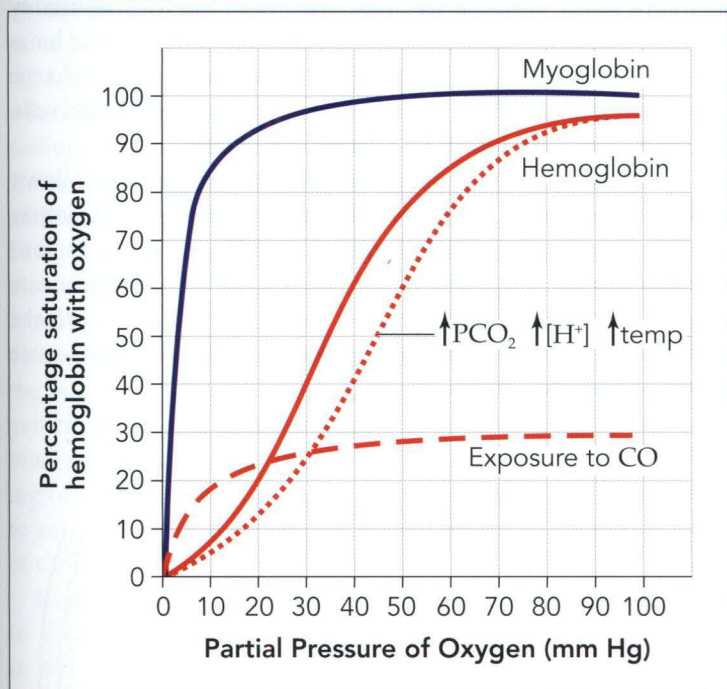
98% of oxygen in the blood binds rapidly and reversibly with the protein **hemoglobin** found inside the erythrocytes, forming **oxyhemoglobin**. Hemoglobin is composed of four polypeptide subunits, each with a single heme cofactor. The heme cofactor is an organic molecule with an atom of iron at its center. Each of the four iron atoms in hemoglobin can bind with one O_2 molecule. When one of the iron atoms in hemoglobin binds an O_2 molecule, oxygenation of the other heme groups is accelerated. Similarly, release of an O_2 molecule by any of the heme groups accelerates release by the others. This phenomenon is called **cooperativity**.

The oxygen dissociation curve of hemoglobin (Figure 4.4) shows the percent of hemoglobin that has bound oxygen at various partial pressures of oxygen. Although hemoglobin is not an enzyme, the dissociation curve can be viewed as a modified Michaelis-Menten enzyme curve. Recall that the rate of an enzyme-catalyzed reaction increases with increasing concentration of the substrate and then levels off, due to a lack of enzymes that are available to bind the substrate. In a similar fashion, the percent saturation of hemoglobin increases as the partial pressure of oxygen increases and then levels off when all of the subunits have bound oxygen. (In the arteries of a typical person breathing room air, the oxygen saturation is 97%; the flat portion of the curve in this region shows that small fluctuations in oxygen pressure have little effect.) The dissociation curve demonstrates the **oxygen affinity** of hemoglobin by showing the percentage bound at a given partial pressure, just as the slope of a Michaelis-Menten curve indicates the enzymatic affinity for the substrate. However, the shape of the oxygen dissociation curve is impacted by the cooperativity effect, which causes the affinity of hemoglobin to increase as the subunits bind O_2 . As a result, the O_2 saturation of hemoglobin increases sigmoidally (in an S-shape) rather than linearly.

In addition to the cooperativity effect, environmental conditions affect the affinity of hemoglobin for oxygen, just as the presence of competitors and other types of environmental influences can change the affinity of an enzyme for its substrate. The oxygen saturation of hemoglobin depends on the carbon dioxide pressure, pH, and temperature of the blood. A **rightward shift of the oxygen dissociation curve** occurs in response to an increase in carbon dioxide pressure, hydrogen ion concentration, or temperature. In each case, the rightward shift reflects hemoglobin's lowered affinity for oxygen and can also be viewed as a downward shift. An increased demand for oxygen leads to a shift that allows for a lower affinity of hemoglobin for oxygen, which leads to the release of oxygen for increased delivery to the tissues. When the shift is due to increasing hydrogen ion concentration (i.e. decreased pH), it is called the *Bohr shift*. As will be described, increasing CO_2 concentration causes lowered pH in the bloodstream, so the Bohr shift encompasses both increasing CO_2 and increasing hydrogen ion concentration. CO_2 and hydrogen ions affect the oxygen dissociation curve through allosteric effects: they bind to deoxygenated hemoglobin and cause a change in shape that then discourages the binding of oxygen.

2,3-DPG, a chemical found in red blood cells, also shifts the curve to the right/downwards by binding to deoxygenated hemoglobin and decreasing its affinity for oxygen. 2,3-DPG increases in response to low-oxygen environments, such as high altitudes, to ensure that the tissues still receive sufficient oxygen. Note that by lowering the affinity of hemoglobin for oxygen when oxygen is scarce, 2,3-DPG contributes to the flattened slope of the oxygen dissociation curve at low pO_2 .

FIGURE 4.4 Oxygen Dissociation Curve



Oxygen pressure is typically 40 mm Hg in body tissues, lower than in the lungs because oxygen has been used up by aerobic respiration. Carbon dioxide, however, is built up as a waste product and is at a higher partial pressure in the tissues than in the blood. As the blood moves through the systemic capillaries, oxygen diffuses into the tissues, and carbon dioxide diffuses into the blood. Carbon dioxide is carried by the blood in three forms:

1. dissolved in solution;
2. as bicarbonate ion; and
3. in carbamino compounds (combined with hemoglobin and other proteins).

Ten times as much carbon dioxide is carried as bicarbonate as in either of the other forms. The formation of bicarbonate ion is catalyzed by the enzyme **carbonic anhydrase** in the reversible reaction:



For the MCAT®, memorize this equation and understand how it proceeds in the forward and reverse directions!

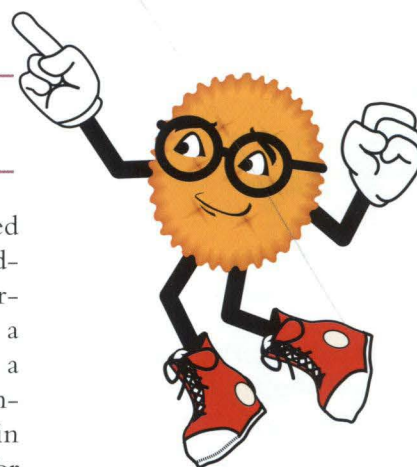
As with any reversible reaction, the predominant direction can be predicted according to Le Châtelier's Principle, where an increased ratio of reactant to product favors the forward direction and vice versa. The reaction above is best understood by considering the amount of CO_2 present. In the tissues, where there is a high concentration of CO_2 created as a metabolic waste product (and thus also a high partial pressure of CO_2), the forward reaction dominates, forming bicarbonate ion. The low partial pressure of CO_2 in the lungs then shifts the reaction in the reverse direction, allowing the conversion of the bicarbonate ion to CO_2 for expiration.

Carbonic anhydrase is present inside the red blood cells but not in the plasma. When carbon dioxide is absorbed from the tissue by erythrocytes, bicarbonate ion builds up in the red blood cells. As a result, bicarbonate diffuses out of the erythrocytes and into the plasma. To prevent a buildup of negative charge in the plasma, chloride ions move into the red blood cell in exchange for bicarbonate ions in a

MCAT® THINK

In contrast to carbon dioxide, which binds to a different site on hemoglobin from oxygen, carbon monoxide acts as a competitive inhibitor and prevents the binding of oxygen. The affinity of hemoglobin for carbon monoxide is more than 200 times greater than its affinity for oxygen. However, the presence of CO shifts the oxygen-dissociation curve to the left, reflecting the remaining sites' heightened affinity for oxygen while the maximum saturation percentage of hemoglobin is reduced relative to the amount of CO in the blood. Thus the overall ability of oxygen to be carried bound to hemoglobin in the blood is decreased, while the oxygen that is able to bind does not unload at the tissues as it should, with the net result that oxygen delivery to the tissues is severely limited. In cases of carbon monoxide poisoning, pure oxygen can be administered to displace the CO from hemoglobin.

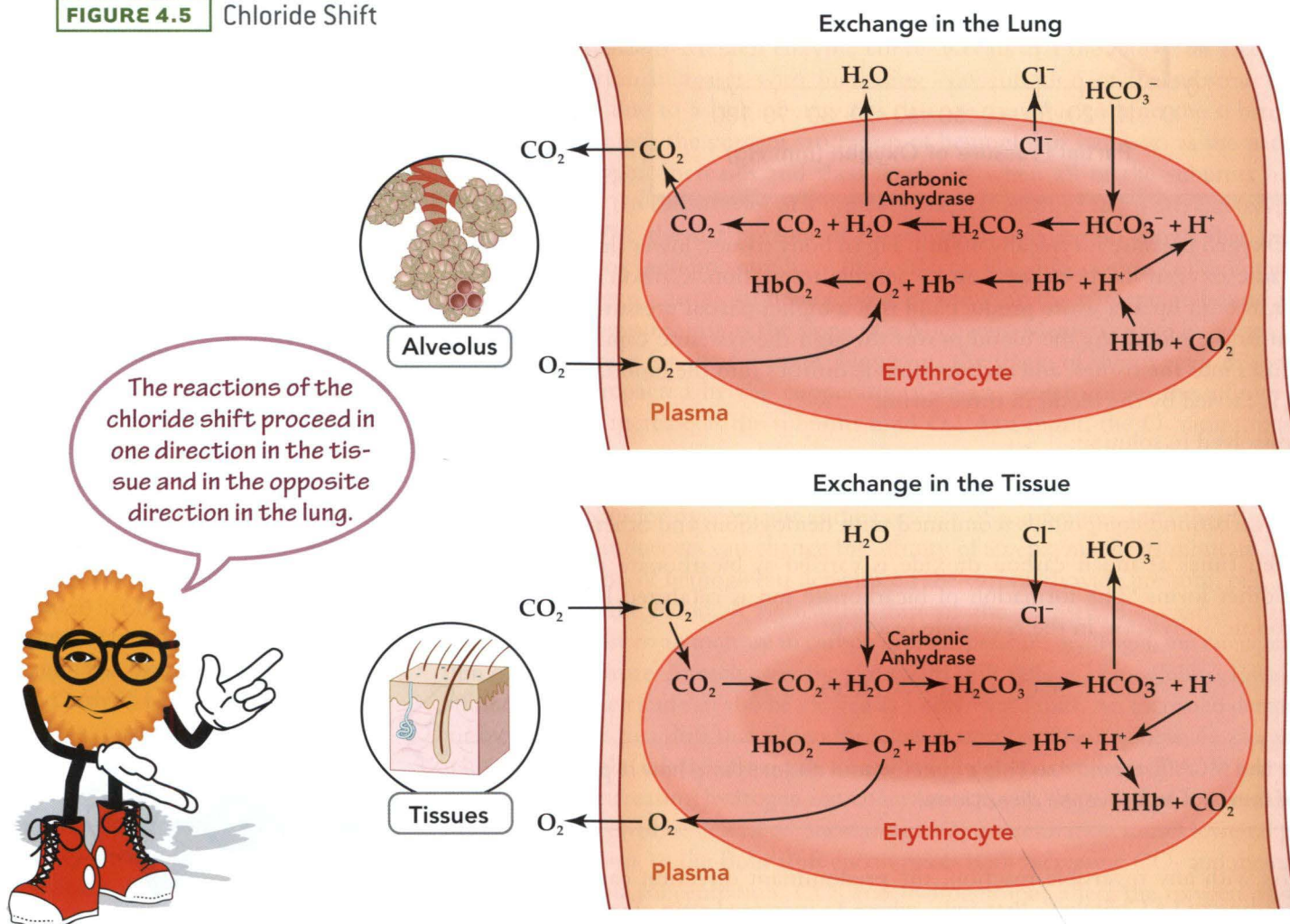
Use your understanding of enzyme inhibition to remember how the oxygen dissociation curve shifts. Just as inhibitors that lower enzyme affinity for the substrate cause a downward shift, environmental conditions that decrease the affinity of hemoglobin for oxygen cause a rightward/downward shift in the oxygen dissociation curve.



phenomenon called the *chloride shift* (Figure 4.5). The entry of chloride ions offsets the buildup of hydrogen ions in the erythrocyte, contributing to electrical neutrality and helping to prevent the buildup of acidity. The chloride shift occurs in the lungs as well, but in the opposite direction. Chloride ions flow into the plasma in exchange for bicarbonate ions, which diffuse out of the plasma and back into the red blood cells. Bicarbonate ion is then converted back into CO_2 that can be expired.

The overall process of carbon dioxide transport can be summarized as follows: once CO_2 has diffused into red blood cells from the tissues, carbonic anhydrase catalyzes its conversion to bicarbonate. Bicarbonate then diffuses down its concentration gradient into the plasma. Once the blood reaches the lungs, bicarbonate diffuses back into the erythrocytes and is converted back into CO_2 . In both the lungs and the tissues, chloride ions diffuse in the opposite direction of bicarbonate ions to prevent a buildup of negative charge.

FIGURE 4.5 Chloride Shift



You don't need to memorize too many of the details of gas exchange; however, it is crucial to understand the mechanisms. Know the effects that temperature, pH, and carbon dioxide pressure have on hemoglobin. Be sure that you can read a dissociation curve and predict shifts.

Now that you have a greater understanding of how hemoglobin interacts with oxygen and carbon dioxide, let's revisit the shifts of the oxygen dissociation curve discussed earlier in this section. Recognize that the

Bohr shift is associated with both pH and CO_2 , since the hydrolysis of carbon dioxide leads to an increased concentration of hydrogen ions. Also note that the decreased affinity of hemoglobin for oxygen at the high carbon dioxide level found in the tissues assists in the release of oxygen that then diffuses into the cells. In a similar effect, 2,3-DPG increases when the body is at a high altitude, shifting the curve to the right and facilitating increased oxygen delivery to the tissues when oxygen is low.

Carbon dioxide has its own dissociation curve, which relates blood content of carbon dioxide to carbon dioxide pressure. The greater the partial pressure of carbon dioxide, the greater the concentration of carbon dioxide dissolved in the blood, increasing the amount capable of binding to hemoglobin. However, when hemoglobin becomes saturated with oxygen, it has a lowered affinity for carbon dioxide. In other words, just as the binding of carbon dioxide to hemoglobin reduces its affinity for oxygen, the oxygenation of hemoglobin lowers its affinity for carbon dioxide. This is called the *Haldane effect*. The Haldane effect facilitates the transfer of carbon dioxide from the blood to the lungs, and from the tissues to the blood. Recall that oxygen pressure, and thus the percent of hemoglobin saturated with oxygen, is higher in the lungs. As a result, carbon dioxide is released from hemoglobin in the lungs, facilitating its exhalation from the body. On the other hand, hemoglobin will have a lower oxygen saturation percentage at the lower oxygen pressure found in the tissues, facilitating the binding of carbon dioxide for transport to the lungs. Furthermore, the off-loading of oxygen allows reduced hemoglobin (that is, hemoglobin without oxygen) to act as a blood buffer by accepting excess protons produced by the conversion of carbon dioxide to bicarbonate ion.

Respiratory centers in the medulla regulate breathing rate and can respond to changes in the chemical composition of the blood, particularly changes in the partial pressure of CO_2 . An inspiratory center stimulates inspiration by signaling the diaphragm to contract. When necessary due to exercise or other causes of active breathing, an expiratory center signals muscles that assist in forced exhalation. Control of breathing rate by the medulla is affected by the input of **central chemoreceptors** located in the medulla and **peripheral chemoreceptors** in the carotid arteries and aorta. (Chemoreceptors are a type of sensory receptor that bind chemicals and signal higher centers in the nervous system to produce a response.) Central and peripheral chemoreceptors monitor carbon dioxide concentration in the blood and increase the breathing rate when the level is too high. Nervous system regulation of respiration rate has high **CO_2 sensitivity**; a small increase in the partial pressure of CO_2 quickly triggers an increased respiration rate to allow more carbon dioxide to be expired. Since increased CO_2 and decreased pH go hand in hand, CO_2 levels must be tightly controlled to avoid a dangerous decrease in the pH of the blood. By contrast, the partial pressure of oxygen dissolved in the bloodstream must drop significantly in order to change respiration rate.

Oxygen concentration is monitored mainly by peripheral chemoreceptors, while CO_2 concentration is monitored by central chemoreceptors. Both peripheral and central chemoreceptors respond to pH changes. The respiratory system exerts **pH control** by adjusting breathing rate, and thus the partial pressure of CO_2 in the body, in response to potentially dangerous disturbances to the pH of the bloodstream. In the case of acidosis (too much acid in the blood), the body compensates by increasing the breathing rate, thereby expelling carbon dioxide and raising the pH of the blood.

What about all that nitrogen? What effect does nitrogen have on the body?

Remember your chemistry. Nitrogen is extremely stable due to its strong triple bond. Thus, nitrogen diffuses into the blood, but doesn't react with the chemicals in the blood. However, people that go diving must be careful. As the pressure increases with depth, more nitrogen diffuses into the blood. When divers come back up, the pressure decreases and the gas volume increases. If they don't allow enough time for the nitrogen to diffuse out of the blood and into the lungs, the nitrogen will form bubbles. Among other problems, these bubbles may occlude (block) vessels, causing decompression sickness, also known as 'the bends.'

Nervous System

BIOLOGY 2

Understand the connection between rate of breathing and carbon dioxide, pH, and oxygen levels in the blood. When you see carbon dioxide in the biological environment, always think of increased acidity due to the hydrogen ions that are produced by the hydration of CO_2 .



These questions are NOT related to a passage.

Item 73

Alkalosis is increased blood pH resulting in a leftward shift of the oxyhemoglobin dissociation curve. Which of the following might cause alkalosis?

- ☐ A) Hypoventilation
- ☐ B) Hyperventilation
- ☐ C) Breathing into a paper bag
- ☐ D) Adrenal steroid insufficiency

Item 74

Which of the following would most likely occur in the presence of a carbonic anhydrase inhibitor?

- ☐ A) The blood pH would increase.
- ☐ B) The carbamino hemoglobin concentration inside erythrocytes would decrease.
- ☐ C) The rate of gas exchange in the lungs would decrease.
- ☐ D) The oxyhemoglobin concentration inside erythrocytes would increase.

Item 75

Which of the following will most likely occur during heavy exercise?

- ☐ A) Blood pH will decrease in the active tissues.
- ☐ B) Less oxygen will be delivered to the tissues due to increased cardiac contractions that result in increased blood velocity.
- ☐ C) Capillaries surrounding contracting skeletal muscles will constrict to allow increased freedom of movement.
- ☐ D) The respiratory system will deliver less nitrogen to the blood.

Item 76

An athlete can engage in blood doping by having blood drawn several weeks before an event, removing the blood cells, and having them reinjected into her body a few days before an athletic activity. Blood doping is most likely an advantage to athletes because:

- ☐ A) the increased concentration of immune cells in the blood after reinjection can decrease the chances of becoming ill just before the competition.
- ☐ B) the increased red blood cell count in the blood after reinjection can facilitate greater gas exchange with the tissues.
- ☐ C) the increased blood volume after reinjection can ensure that the athlete maintains adequate hydration during the event.
- ☐ D) the decreased red blood cell count of the blood in the weeks before the competition can facilitate training by decreasing the viscosity of the blood.

Item 77

Carbon dioxide partial pressure:

- ☐ A) increases in the blood as it travels from the systemic venules to the inferior vena cava.
- ☐ B) increases in the blood as it travels from the pulmonary arteries to the pulmonary veins.
- ☐ C) is greater in the blood in the systemic capillary beds than in the alveoli of the lungs.
- ☐ D) is greater in the blood in the systemic capillary beds than in the systemic tissues.

Item 78

At high altitude, water vapor pressure in the lungs remains the same and carbon dioxide pressure falls slightly. Oxygen pressure falls. The body of a person remaining at high altitudes for days, weeks, and even years will acclimatize. All of the following changes assist the body in coping with low oxygen EXCEPT:

- ☐ A) increased red blood cells.
- ☐ B) decreased vascularity of the tissues.
- ☐ C) increased pulmonary ventilation.
- ☐ D) increased diffusion capacity of the lungs.

Item 79

In an asthma attack, a patient suffers from difficulty breathing due to constricted air passages. The major causative agent is a mixture of leukotrienes called slow-reacting substance of anaphylaxis. During an asthma attack, slow reacting substance of anaphylaxis most likely causes:

- ☐ A) smooth muscle spasms of the bronchioles.
- ☐ B) cartilaginous constriction of the trachea.
- ☐ C) edema in the alveoli.
- ☐ D) skeletal muscle spasms in the thorax.

Item 80

Sustained heavy exercise results in all of the following changes to blood chemistry except:

- ☐ A) lowered pH.
- ☐ B) raised CO₂ tension.
- ☐ C) increased temperature.
- ☐ D) decreased carboxyhemoglobin.

4.3 The Blood

Blood has many important functions in the body. It plays a crucial role in the respiratory system by transporting oxygen to the tissues and carrying away carbon dioxide. It also regulates the extracellular environment of the body by transporting nutrients, waste products, and hormones. Additionally, it is important for the thermoregulation of the body. The blood is **connective tissue**, so like any connective tissue, it contains cells and a matrix. It travels throughout the body via the cardiovascular system, as will be described in the following section.

Blood contains three main components, which separate when a blood sample is placed in a centrifuge (Figure 4.6): 1. the plasma; 2. red blood cells; and 3. the buffy coat (white blood cells).

Think of the blood as the body's highway for the transport of various substances. It is a solution that exists for the purpose of carrying cells and molecules to their destinations.

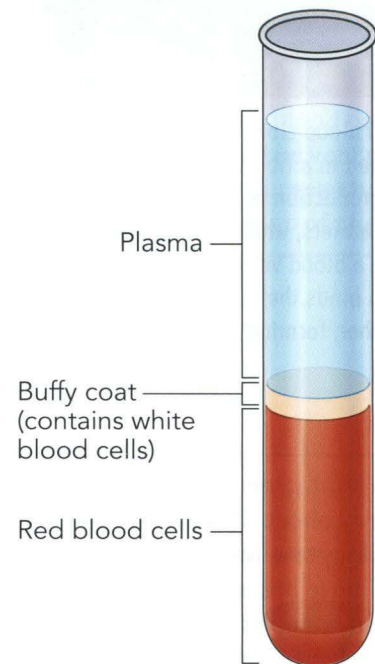
Plasma contains the matrix of the blood, which includes water, ions, urea, ammonia, proteins, and other organic and inorganic compounds. The body regulates the overall volume of blood by altering the amount of water in the plasma. This regulation of blood volume contributes to the control of blood pressure. Important proteins contained in the plasma are albumin, immunoglobulins, and clotting factors. **Albumins** transport fatty acids and steroids. They also help regulate the osmotic pressure of the blood, facilitating transfer of substances across capillary walls. Immunoglobulins (also called antibodies) are a major component of the immune system and are discussed later in this lecture. Plasma from which the clotting protein fibrinogen has been removed is called **serum**. Albumin, fibrinogen, and most other plasma proteins are formed in the liver. Gamma globulins that constitute antibodies are made in the lymph tissue. An important function of plasma proteins is to act as a source of amino acids for tissue protein replacement.

Erythrocytes (red blood cells) are essentially bags of hemoglobin. They have no organelles, not even nuclei, which means they do not undergo mitosis. They are disk-shaped vesicles whose main function is to transport O_2 and CO_2 . Squeezing through capillaries wears out their plasma membranes in about 120 days. Most worn out red blood cells are removed from circulation and destroyed as they squeeze through channels in the spleen or, to a lesser extent, in the liver. The percentage by volume of red blood cells is called the **hematocrit**. The hematocrit is typically 35–50% and is greater in men than women.

Unlike erythrocytes, **leukocytes** (white blood cells) do contain organelles, but do not contain hemoglobin. Their function is to protect the body from foreign invaders.

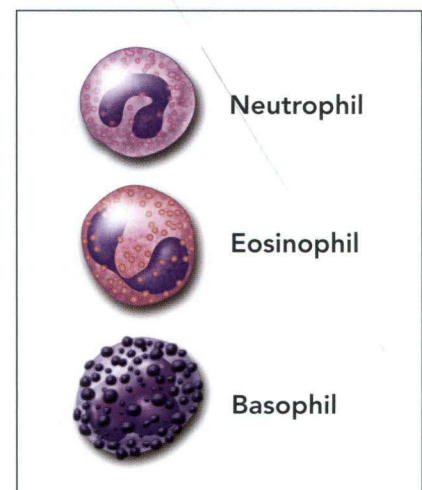
All blood cells differentiate from the same type of precursor, a **stem cell** residing in the bone marrow. Erythrocytes lose their nuclei while still in the marrow. After entering the bloodstream as reticulocytes, they lose the rest of their organelles within 1 or 2 days. Leukocyte formation is more complex due to the existence of many different types. The *granular leukocytes* (*granulocytes*) are neutrophils, eosinophils, and basophils. With respect to dyeing techniques, neutrophils are neutral to acidic and basic dyes, eosinophils stain in acidic dyes, and basophils stain in basic dyes. Generally, granulocytes remain in the blood for only 4 to 8 hours before they are deposited in the tissues, where they live for 4 to 5 days. *Agranular leukocytes* (*agranulocytes*) include monocytes, lymphocytes, and megakaryocytes. Once deposited in the tissues, monocytes become macrophages and may live for months to years. Lymphocytes may also live for years.

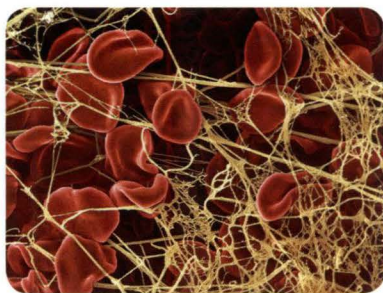
FIGURE 4.6 Blood Composition



Know that the job of erythrocytes is to deliver oxygen to the tissues and to remove carbon dioxide. Also, remember that red blood cells do not have nuclei.

FIGURE 4.7 Granulocytes





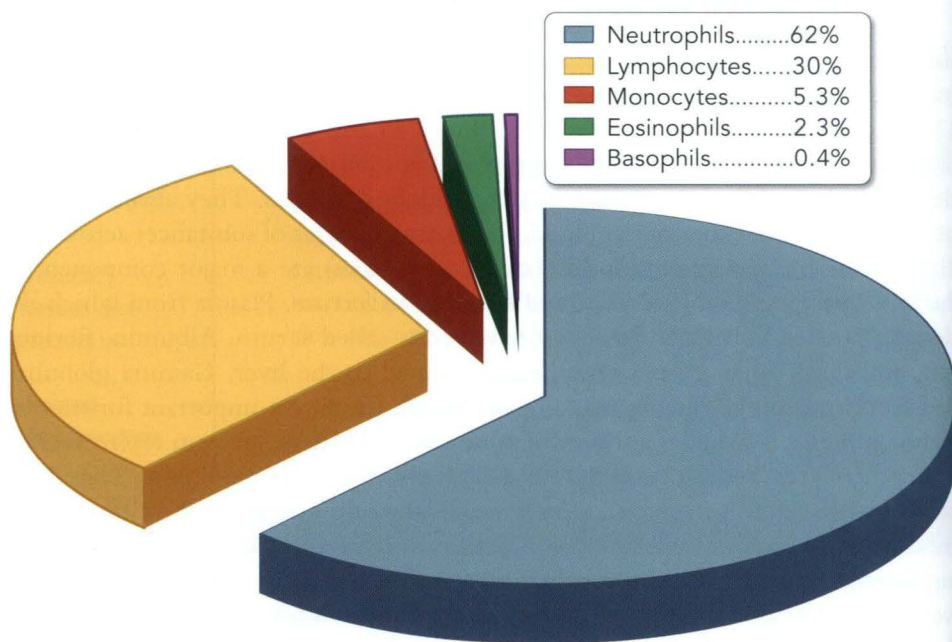
When blood clots, erythrocytes are trapped in a fibrin mesh (yellow). The production of fibrin is triggered by platelets, which are activated when a blood vessel is damaged. The fibrin binds the various blood cells together, forming a solid blood clot.

Notice that granulocytes live for a very short time, whereas agranulocytes live for a very long time. This is because granulocytes function nonspecifically against all infective agents, whereas most agranulocytes work against specific agents of infection. Agranulocytes need to hang around in case the same infective agent returns; granulocytes multiply quickly against any infection, and then die once the infection is gone. Make sure you understand this distinction, but don't worry too much about the other details.

Platelets are small portions of membrane-bound cytoplasm torn from megakaryocytes. Like red blood cells, platelets do not have nuclei. However, they do contain actin and myosin, mitochondria, and residual pieces of the Golgi body and endoplasmic reticulum. Platelets are capable of making prostaglandins and some important enzymes. Healthy individuals have many platelets in their blood. Platelets have a half-life of 8-12 days in the blood.

Platelets have an important function in **coagulation**, which functions to minimize blood loss and facilitate healing when blood vessels are damaged. When platelets come into contact with injured endothelium, they become sticky and begin to swell, releasing various chemicals. They also activate other platelets. The platelets stick to the endothelium and to each other, forming a loose *platelet plug*. The accumulated platelets assist in triggering an enzymatic cascade that ultimately results in the formation of a **blood clot**. The most important step in coagulation is the polymerization of the plasma protein **fibrinogen** to form fibrin threads that attach to the platelets and form a tight plug. Coagulation begins to appear in seconds in small injuries and 1 to 2 minutes in larger injuries.

The leukocyte composition in the blood is shown below:



4.4

The Cardiovascular System and Blood Pressure

The cardiovascular system consists of the heart, blood, and blood vessels. It is a transport system that pumps blood throughout the body, thus carrying out the functions of extracellular environment regulation and the delivery of nutrients, oxygen, hormones, and immune cells to the tissues. Furthermore, the cardiovascular system transports metabolic waste such as carbon dioxide away from the cells. Thus, as described in the previous section, the cardiovascular system works closely with the respiratory system to meet cells' metabolic needs by delivering oxygen and preventing a buildup of metabolic byproducts.

A significant feature of the cardiovascular system is its ability to react to internal and external conditions by directing the flow of blood in response to **nervous and endocrine control**. Epinephrine and norepinephrine, released by neurons of the sympathetic nervous system and by the adrenal medulla of the endocrine system, can direct blood by causing the constriction of blood vessels. Furthermore, the division of the cardiovascular system into ever smaller branches allows strict regu-

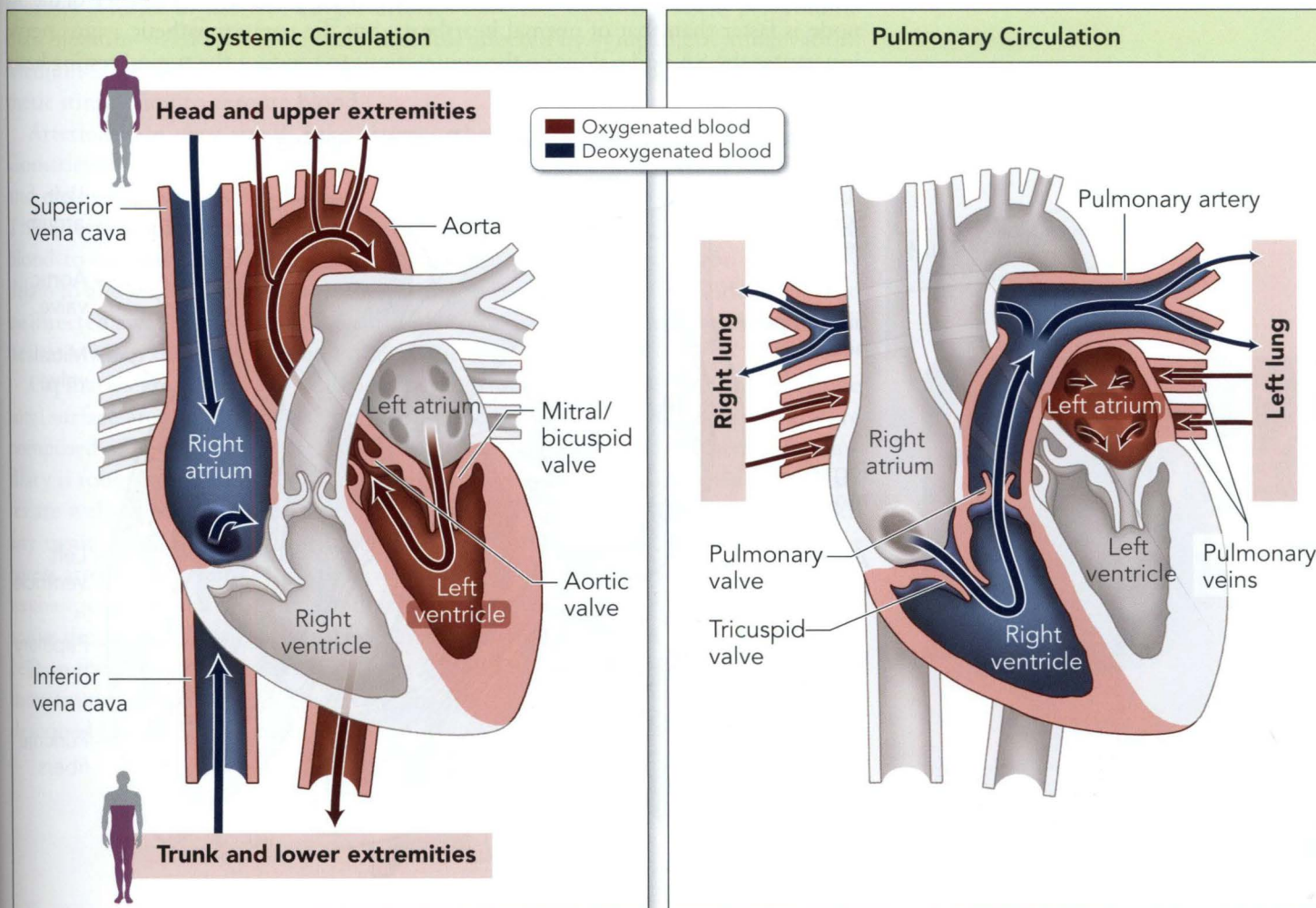
lation of the flow of blood according to the metabolic needs of the tissues. The physical structures of the blood vessels of each section of the cardiovascular system are particularly suited to specific functions, as will be described.

The cardiovascular system is said to be a **closed circulatory system** because it contains no openings for the blood to leave the vessels. For the MCAT®, it is important to be able to trace the circulatory path of the blood through two distinct sections of the cardiovascular system that are separated by the heart. The first half of the circulation, called the **systemic circulation**, directs oxygenated blood to the tissues and then returns deoxygenated blood to the heart. Beginning with the **left ventricle**, blood is pumped through the **aorta**. From the aorta branch many smaller **arteries**, which themselves branch into still smaller **arterioles**, which branch into still smaller **capillaries**. Blood from the capillaries is collected into **venules**, which collect into larger **veins** that collect again into the **superior** and **inferior venae cavae**. The venae cavae empty into the **right atrium** of the heart.

The second half of the circulation is called the **pulmonary system** because it transports blood to the lungs for oxygenation. From the right atrium, blood is squeezed into the **right ventricle**. The right ventricle pumps blood through the **pulmonary arteries** to the arterioles and then to the capillaries of the lungs. From the capillaries of the lungs, blood collects in venules, then in veins, and finally in the **pulmonary veins** leading to the heart. (True capillaries branch off arterioles, and do not represent the only route between an arteriole and venule.) The pulmonary veins empty into the **left atrium**, which leads to the left ventricle.

Use the names of the atria and ventricles to help you remember their functions. An atrium is a big room that could be used as a waiting area; the atria of the heart are like waiting rooms where blood collects before moving on to the ventricles. The VENTricles are pumps that VENT blood to the rest of the body.

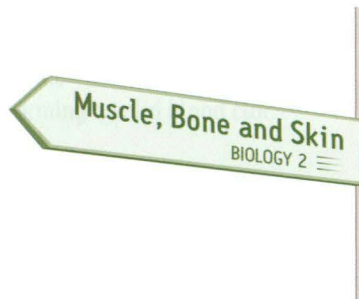
FIGURE 4.8 Circulation of Blood



It is crucial to know that the heart has four chambers and to know the **bolded** names of the different parts of the heart and types of blood vessels, but *don't be too concerned with memorization. Instead, concentrate on function. You can think of the ventricles as two neighboring pumps with differing functions and corresponding physical features. Each pump serves one of the sections of the circulatory system. The*

*left ventricle has to propel the blood through the systemic circulation, so it contracts with more force; its muscular wall is thicker and stronger than that of the right ventricle. The **RIGHT** ventricle pumps blood to the pulmonary circulation to send waste **RIGHT** out of the body! The pulmonary circulation also functions to oxygenate blood that has transferred oxygen to the tissues, as described earlier in this lecture.*

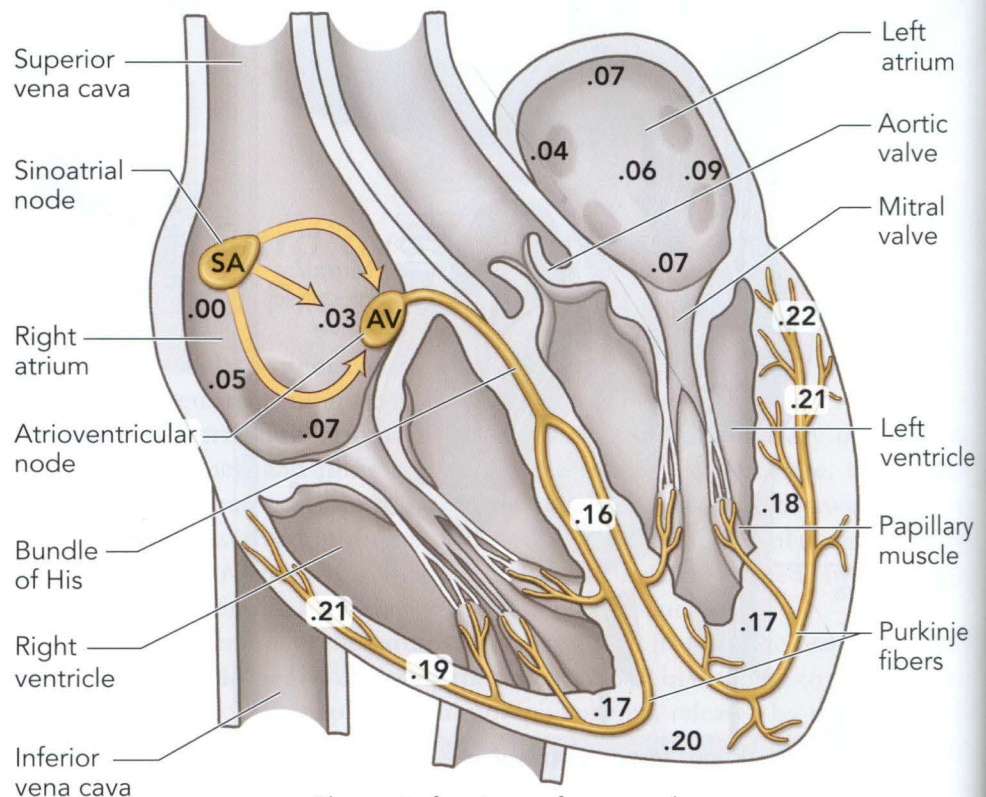
The Cardiac Impulse



The heart is a large muscle with regular contractions that are stimulated by electrical activity, i.e. action potentials. Specialized groups of cells in the heart initiate the cardiac impulse. Nervous system regulation of these cells can slow down or speed up the heart rate according to the body's needs. Conducting cells gather into fibers that ensure the coordinated spread of the action potential throughout the heart. Unlike skeletal muscle, cardiac muscle is not attached to bone. Instead, its fibers form a net that contracts upon itself, squeezing blood into the arteries. Systole occurs when the ventricles contract; diastole occurs during relaxation of the entire heart and then contraction of the atria.

The blood is propelled by hydrostatic pressure created by the contractions of the heart. The rate of these contractions is controlled by the autonomic nervous system, but the autonomic nervous system does not initiate the contractions. Instead the heart contracts according to the pace set by the **sinoatrial (SA) node**, a group of specialized cardiac muscle cells located in the right atrium. The SA node is *autorhythmic* (meaning it contracts by itself at regular intervals), spreading its contractions to the surrounding cardiac muscles via **electrical synapses** formed by **gap junctions**. The pace of the SA node is faster than that of normal heartbeats, but the parasympathetic **vagus nerve** innervates the SA node, slowing the contractions to produce the typical resting heart

FIGURE 4.9 Transmission of the Cardiac Impulse



Shown in fractions of a second

rate. Increased or decreased parasympathetic input can trigger quick changes in heart rate in response to the organism's internal and external environment.

The action potential generated by the SA node spreads around both atria, causing them to contract. While the atria are contracting, the action potential spreads to the **atrioventricular (AV) node** located in the interatrial septum (the wall of cardiac muscle between the atria). The AV node is slower to depolarize than the SA node, creating a delay which allows the atria to finish their contraction and squeeze their contents into the ventricles before the ventricles begin to contract. From the AV node, the action potential moves down conductive fibers called the **bundle of His**, located in the wall separating the ventricles. The action potential then branches out through the ventricular walls via conductive fibers called **Purkinje fibers**. From the Purkinje fibers, the action potential spreads through gap junctions from one cardiac muscle cell to the next. The Purkinje fibers in the ventricles allow for a more unified, and stronger, contraction.

The Blood Vessels: Specialization of Function

The three major types of blood vessels in the cardiovascular system are arteries, capillaries, and veins. This section describes the unique function and corresponding physical features of each type. Arteries act as a pressure store; capillaries are the site of the exchange of materials with the tissues; and veins act as a volume store for blood travelling back towards the heart.

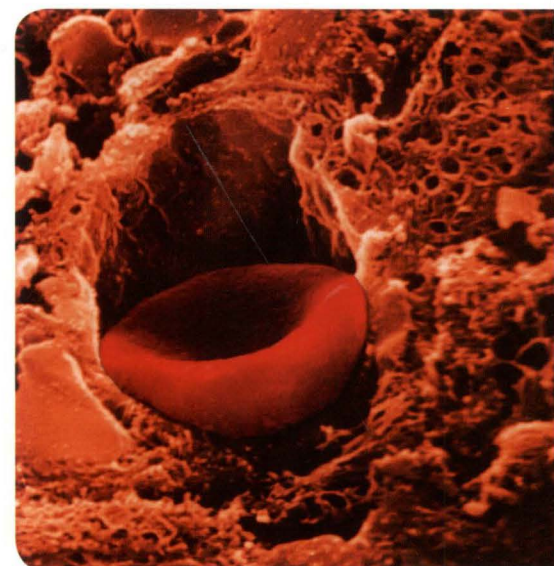
The structure of arteries allows them to maintain a high pressure, facilitating the travel of blood to the lower-pressure venous system. Arteries have thick elastic walls that stretch as they fill with blood during systole. When the ventricles finish their contraction, the stretched arteries recoil, keeping the blood moving smoothly. Arteries are wrapped in smooth muscle that is typically innervated by the sympathetic nervous system. Epinephrine is a powerful vasoconstrictor, meaning that it causes arteries to narrow. Larger arteries have less smooth muscle per volume than medium-sized arteries and are thus less affected by sympathetic innervation. Medium-sized arteries, on the other hand, can constrict enough under sympathetic stimulation to reroute blood.

Arterioles are very small. Like arteries, they are wrapped by smooth muscle. Constriction and dilation of arterioles in response to stimulation from the nervous and endocrine systems can be used to regulate blood pressure and reroute blood. The arterioles participate in thermoregulation by controlling the flow of warm blood to capillary beds in the skin. When body temperature is too high, they dilate to allow blood flow to increase so that heat can dissipate. Blood can instead be directed away from the surface through constriction of the arterioles to prevent heat loss when the body's temperature is too low.

Capillaries are microscopic blood vessels. Much like alveoli, they have a huge total surface area created by the branching of larger structures. Capillary walls are composed of **endothelial cells** and are only one cell thick. The diameter of a capillary is roughly equal to that of a single red blood cell. The thin walls of capillaries are well-suited for the transport of materials. Nutrient and gas exchange with any tissue other than vascular tissue takes place only across capillary walls, not across arterioles or venules. As described in the context of thermoregulation, **heat exchange** across the walls of capillaries can also occur. When substances travel across the capillary wall, they enter the *interstitium*, which is the fluid surrounding cells in the cellular networks known as *tissues*. Differential pressures between the interstitium and blood in the adjacent capillary guide the transfer of materials, as described later in this lecture.

The only nerve necessary to know is the vagus nerve, which is part of the parasympathetic nervous system. It innervates the heart and the intestines. The vagus nerve slows the rate of heart contractions and increases digestive activity in the intestines, consistent with the overall "rest and digest" function of the parasympathetic nervous system. Know the role and location of the Purkinje fibers as well.

Muscle, Bone and Skin
BIOLOGY 2



A red blood cell enters a capillary.

FIGURE 4.10 Types of Blood Vessels

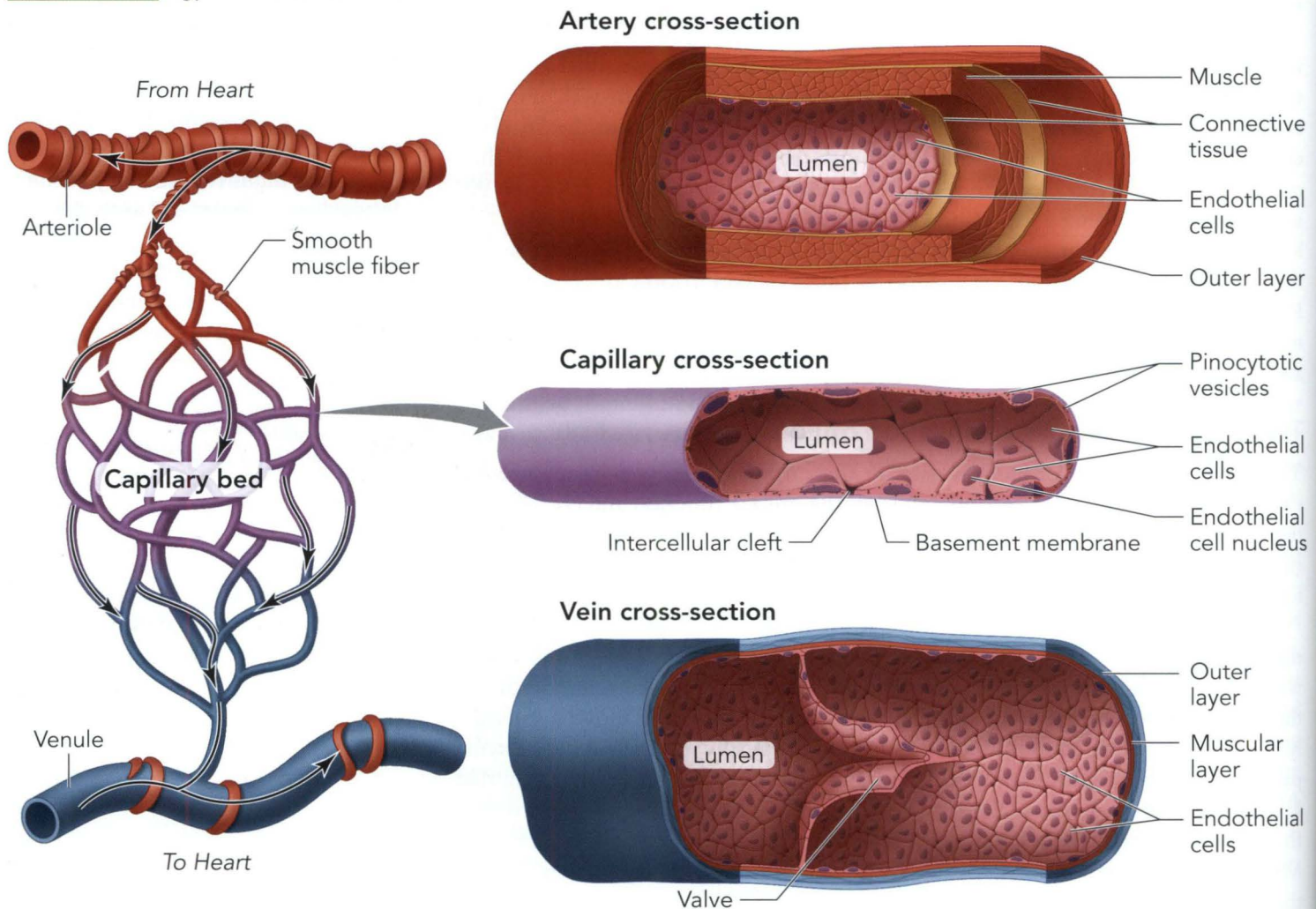
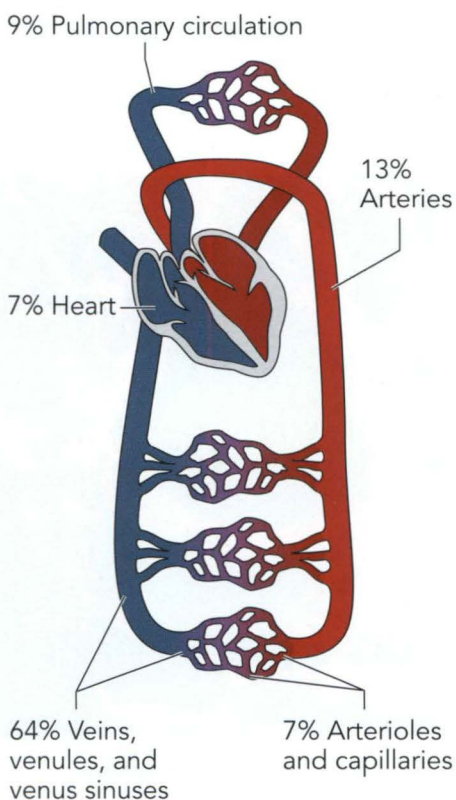


FIGURE 4.11 Blood Volume



For the MCAT®, you need to know the methods by which substances cross the walls of capillaries. The thin walls of capillaries are particularly important for gas exchange within the respiratory system, since the rate of diffusion across a membrane is inversely proportional to the thickness of the membrane.

There are four methods by which materials cross capillary walls:

1. pinocytosis;
2. diffusion or transport through capillary cell membranes;
3. movement through pores in the cells called fenestrations; and
4. movement through the spaces between the cells.

Substances use different methods to cross capillary walls according to their chemical and physical characteristics. Small lipid-soluble molecules, such as oxygen and carbon dioxide, can easily diffuse through the membranes of the endothelial cells. Water-soluble substances are forced to pass through gaps between the cells rather than travelling through the cell membranes. Proteins are even more restricted in their passage in or out of capillaries, since they are large and charged. When they are able to cross capillary walls, they do so via pinocytosis or fenestrations.

Venules and veins are similar in structure to arterioles and arteries, with a few key differences relating to their role of providing volume storage. The lumen of

veins is larger than the lumen of comparable arteries, and the walls are much thinner and have less elasticity. Veins can stretch to hold a far greater volume of blood. Veins, venules, and venous sinuses in the systemic circulation hold about 64% of the blood in a body at rest, acting as a reservoir. By contrast, arteries, arterioles, and capillaries in the systemic circulation contain about 20% of the blood.

An artery carries blood away from the heart; a vein carries blood toward the heart. Don't make the mistake of defining arteries as blood vessels that carry oxygenated blood. The pulmonary arteries contain blood that has already traveled through the entire systemic circulation and is thus the most deoxygenated blood in the body.

Blood Pressure and Flow

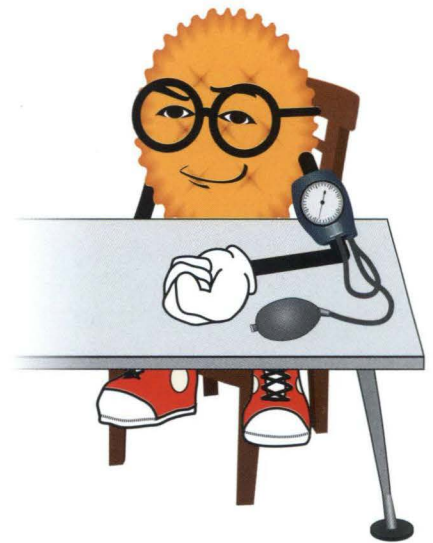
The physical characteristics of the different types of blood vessels described in the previous section impact flow and pressure within the cardiovascular system. The relationship between pressure difference and fluid flow (described in the Fluids Lecture of the *Physics Manual*) is analogous to the relationship between voltage and current flow. Pressure encourages flow throughout the system, while resistance in the blood vessels affects pressure and flow.

At the level of the heart, pressure is generated to pump blood to the body. Recall that the pumping of the heart can be considered in two phases: systole and diastole. The pressure of blood in the arteries can be measured during these two periods, providing measures of the highest and lowest pressures throughout the cardiac cycle. Systole refers to the period in which the ventricles are contracting to eject blood. **Systolic pressure** is the highest pressure, and is measured in the arteries during systole. **Diastolic pressure** is the pressure during the relaxation of the ventricles and filling of the atria and is the lowest pressure in the cardiac cycle.

The relationship between pressure and flow in the cardiovascular system can be roughly described by the following equation: $Q = \frac{\Delta P}{R}$. This is analogous to the equation for current in an electric circuit, $I = \frac{V}{R}$. Pressure difference and voltage follow the same basic principles. Just as current flows from higher to lower voltage, fluids flow from higher to lower pressure. This equation demonstrates the inversely proportional relationship between pressure and resistance, which has implications for the regulation of blood pressure.

As in other systems of the body, the smooth functioning of the cardiovascular system requires homeostatic mechanisms. Blood pressure in the arteries must be kept at a constant high level, about 100 mm Hg, to provide a sufficient driving pressure for blood to travel through the systemic circulation and back to the heart. The maintenance of high pressure in the arteries is also important because blood pressure drops as it travels through the cardiovascular system (as described below). If blood pressure were too low at the first set of blood vessels, the arteries, the lower pressure at the level of the capillaries would be insufficient for the exchange of nutrients and waste.

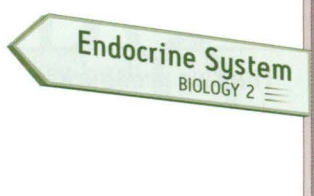
The two main methods used by the body to regulate blood pressure are the baroreceptor reflex (involving quick nervous system control) and the renin-angiotensin-aldosterone system (involving slower hormonal control). Both systems involve the detection of changes in blood pressure by mechanoreceptors, and they both alter blood pressure by changing the output of blood from the heart. Furthermore, both systems can affect blood pressure by changing the **total peripheral resistance**, meaning the overall resistance of the entire systemic circulatory system. Changes in total peripheral resistance are primarily achieved through constriction or dilation of smooth muscle surrounding arterioles, which are the blood vessels that contribute the most to peripheral resistance. Just as resistance in a wire increases when cross-sectional area decreases, smaller blood vessels have greater



The two pressures, systolic and diastolic, correspond to the two numbers that represent your blood pressure at the doctor's office. The systolic pressure is always the greater number and goes on top, while the lower number, the diastolic pressure, goes on the bottom.

Electricity
PHYSICS

To understand regulation of blood pressure, remember that the cardiovascular system as a whole is being considered. The inverse relationship between pressure and resistance assumes that flow remains constant. This is true in the cardiovascular system because it is a closed circulatory system. Even though flow through various blood vessels can be altered according to the metabolic needs of the surrounding tissues, the total flow through the system is relatively constant.



resistance than larger ones. It might seem counter-intuitive that the arterioles have a greater resistance than the capillaries, since they are not as small, but resistance in the capillaries is offset by the fact that they are arranged in parallel.

The *baroreceptor reflex* regulates blood pressure by altering both cardiac output and blood vessel resistance to flow. Baroreceptors (a type of mechanoreceptor) located within arteries detect changes in blood pressure. They respond by signaling centers in the brainstem to alter sympathetic and parasympathetic nervous system (SNS and PNS) output to the heart and blood vessels. Increased PNS activation counteracts an increase in blood pressure by slowing the heart's rate of contraction, whereas increased SNS output counteracts a decrease in blood pressure by causing heart rate to increase. SNS signals also cause blood vessels to constrict, thus increasing their resistance. Both of these effects of SNS activation increase blood pressure.

The *renin-angiotensin-aldosterone system* regulates blood pressure through the **regulation of plasma volume**. This system is activated when mechanoreceptors in arteries leading to the kidneys detect a decrease in blood pressure. A cascade of enzymatic effects triggered by the secretion of renin (itself an enzyme) leads to increased intake and retention of water, which in turn increases plasma volume. The increase in the volume of blood flowing through the cardiovascular system causes an increase in blood pressure. Two hormones, aldosterone and antidiuretic hormone, are involved in the mechanism of this effect.

As described above, the flow of blood through the cardiovascular system is greatly affected by changes in blood pressure. The characteristics of different blood vessels also cause variations in blood flow in different areas of circulation. Cross-sectional area is a particularly significant factor. The total cross-sectional area of the veins is about four times that of the arteries, but the total cross-sectional area of the capillaries is far greater than the cross-sectional area of either the arteries or veins. Since the blood volume flow rate is approximately constant, the blood velocity is inversely proportional to the cross-sectional area. Therefore, the movement of blood is slowest in the capillaries. This allows more time for exchange of oxygen and waste products with the tissues.

The flow rate of blood can be more precisely described using *Poiseuille's Law*, as discussed in the Fluids Lecture of the *Physics Manual*:

$$Q = \Delta P \frac{\pi r^4}{8\eta L}$$

This equation can be used to calculate the flow of a real fluid. Poiseuille's Law again demonstrates that flow is directly proportional to pressure difference. The equation also shows how significantly radius affects flow rate, since radius is raised to the fourth power. Note that this equation, like the continuity equation, predicts a low blood flow rate in the capillaries. (In this case it is the influence of the small radii of individual capillaries, rather than their large total cross-sectional area, that is considered.) Poiseuille's Law also demonstrates how significantly nervous input to smooth muscle around vessels can affect blood flow by inducing even tiny changes in radius.

To understand the movement of blood through the cardiovascular system, it is necessary to understand how pressure changes throughout the different types of blood vessels. Pressure is highest in the aorta, right next to the ventricular pump, and continues decreasing to reach the lowest level in the veins. The pumping force of the heart is the major contributor to pressure in the blood vessels. To compensate for their lower pressure, veins have a valve system that prevents back flow of blood. Contraction of skeletal muscle helps blood move through veins; however, the major propulsive force moving blood through the veins is the pumping of the heart.

Remember that while each individual capillary is tiny, the total cross-sectional area of all of the capillaries is much greater than that of any of the other types of blood vessels.

It is easy to remember that pressure is highest in the aorta, lower in the capillaries, and lowest in the veins if you remember the principle that fluid travels from high to low pressure. Since blood travels from the heart to the aorta, through the capillaries, and back to the heart via the veins, pressure must be dropping at each subsequent set of blood vessels to encourage flow. You can also remember that the arteries are a pressure store, while the veins are a volume store. This is partly because the lower pressure allows blood to pool in the veins.

According to Bernoulli's equation, the sum of potential energy, kinetic energy, and pressure of a flowing fluid is equal to a constant. In other words, a decrease in the velocity of blood should correspond to an increase in pressure. This would imply that blood pressure should be higher in the capillaries than in the aorta, since blood travels much more slowly in the capillaries. This is not the case because Bernoulli's equation only applies to ideal fluid flow, where energy is conserved. Blood is not an ideal fluid; energy (and thus pressure) is lost due to friction against the walls of the blood vessels.

In addition to the important role that pressure plays in the flow of blood through the vessels and back to the heart, a counterbalance of pressures governs the exchange of materials at the level of the capillaries. Even though pressure is very low in the capillaries, there is still sufficient hydrostatic pressure against the walls to facilitate the transfer of materials from capillaries to the tissues, as described below.

Capillaries are found close to all cells of the body. *Precapillary sphincters* regulate the flow of blood into capillary beds according to the metabolic needs of the tissues. There are two types of pressure across the wall of the capillary: osmotic pressure and hydrostatic pressure. **Osmotic pressure**, as discussed in the Cell Lecture, is the "pulling" pressure of solutes in solution that leads to the diffusion of solvent across a membrane. In the case of the capillaries, osmotic pressure encourages the flow of fluid from the tissues into the capillaries. Because the fluid is moving so slowly in the capillaries, it exerts a high hydrostatic pressure on the walls (in the opposite direction of the osmotic pressure), encouraging the flow of fluid into the interstitium. When blood first enters a capillary (Figure 4.12), hydrostatic pressure is greater than osmotic pressure, so net fluid flow is out of the capillary and into the interstitium. Osmotic pressure remains relatively constant throughout the capillary because it is set by proteins in the blood that are too large to move out of the capillaries. However, hydrostatic pressure drops from the arteriole end to the venule end as fluid flows out of the capillary. Thus, osmotic pressure overcomes hydrostatic pressure near the venule end of a capillary, and net fluid flow is out of the interstitium and into the capillary. The net result of fluid exchange by the capillaries is a 10% loss of fluid from the capillaries to the interstitium. The next section of this lecture will describe how the lymphatic system acts to prevent excess fluid buildup in the tissues.

The discussion of how pressure contributes to the exchange of fluids across capillary walls should sound familiar: it's the same principle as the differential partial pressures that drive gas exchange in the respiratory system! Just as O_2 and CO_2 each diffuse to areas of lower partial pressure, in the circulatory system fluid travels to the area of lowest pressure.

FIGURE 4.12 Fluid Exchange in the Capillaries

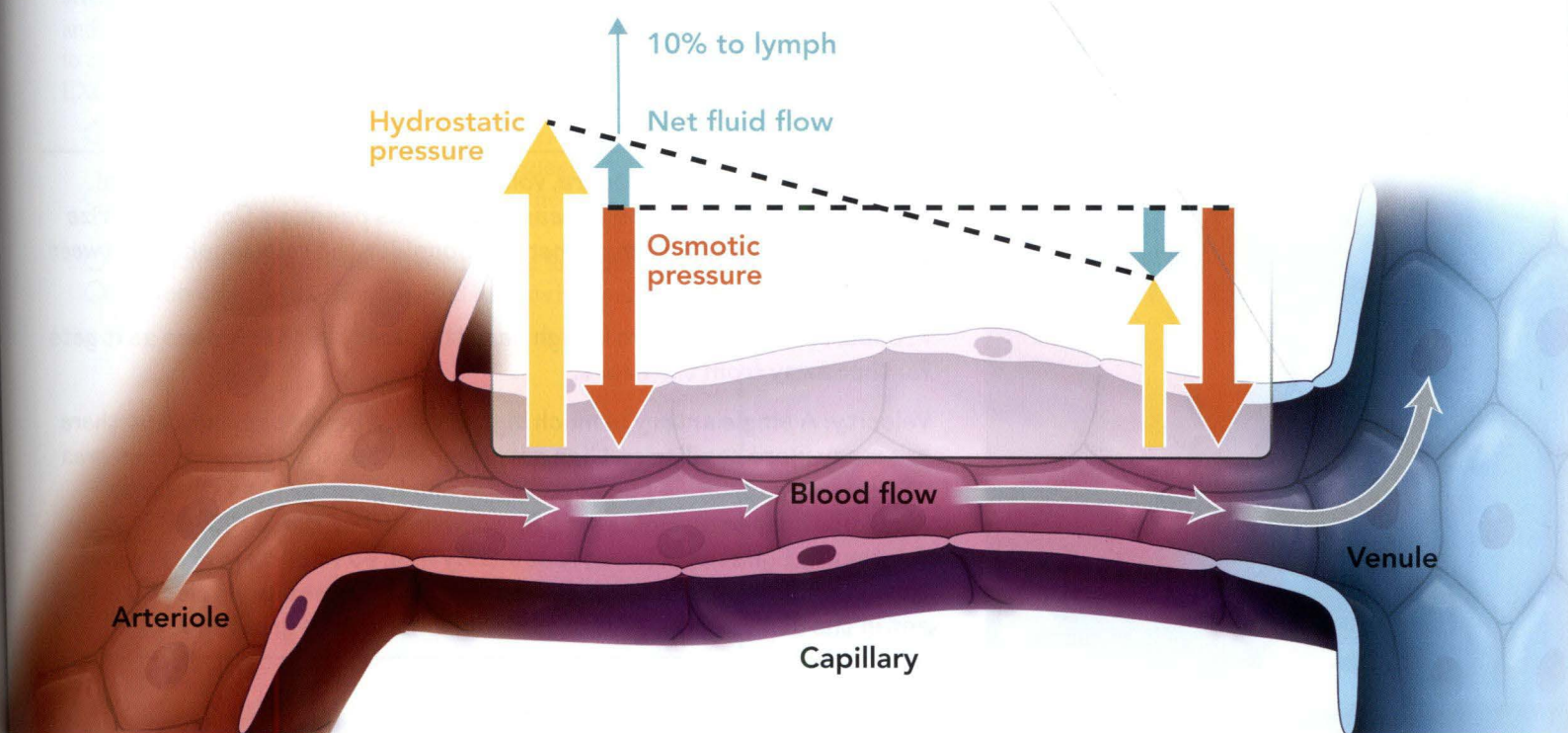


FIGURE 4.13 Cross-sectional Area vs. Velocity

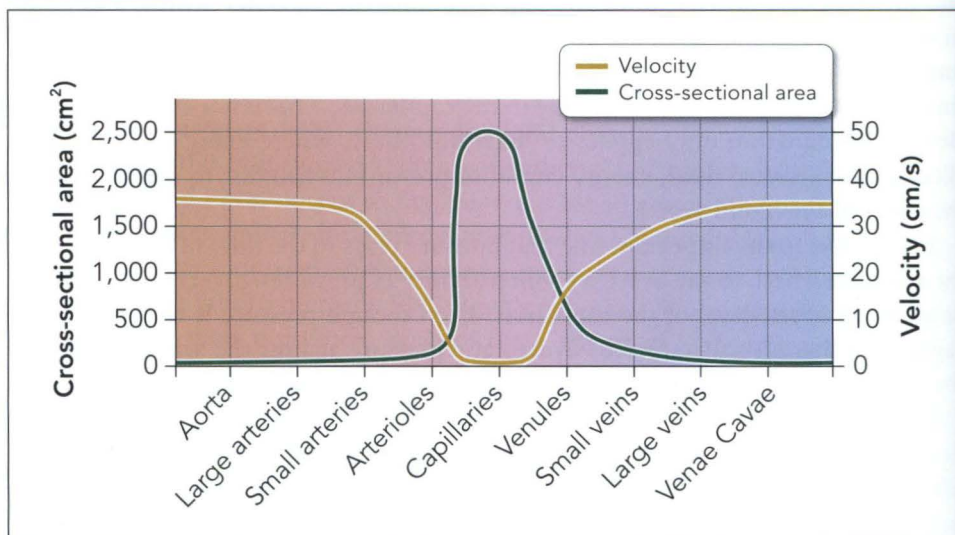
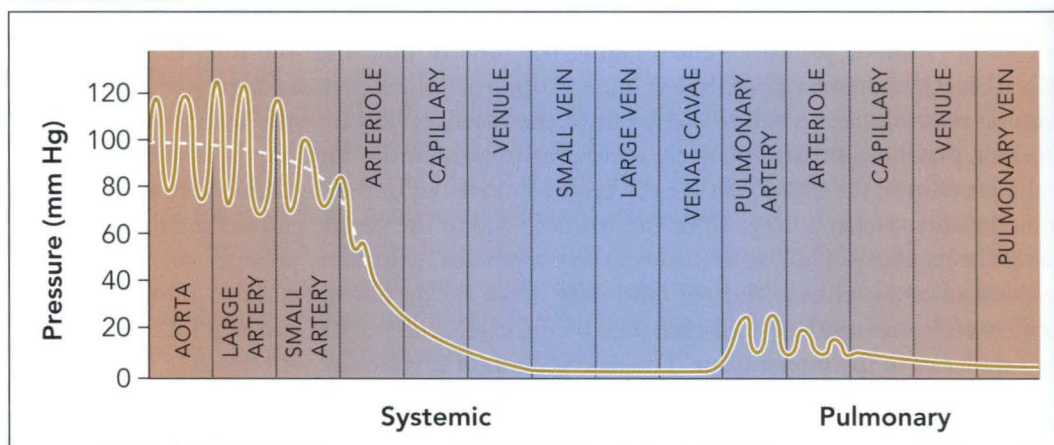


FIGURE 4.14 Blood Pressure



Information on blood pressure, volume, velocity, and cross-sectional area of vessels is likely to appear in a physics passage. Don't memorize anything, but take a moment here to consider the relationships between variables.

Pressure: Blood pressure is high near the heart and decreases as it gets farther away from the heart.

Velocity: A single artery is much bigger than a single capillary, but there are many more capillaries than arteries. The total cross-sectional area of all those capillaries put together is much greater than the cross-sectional area of a single aorta or a few arteries. Blood flow follows the Continuity Equation, $Q = Av$, reasonably well, so velocity is greatest in the arteries, where cross-sectional area is smallest, and velocity is lowest in the capillaries, where cross-sectional area is greatest.

These questions are NOT related to a passage.

Item 81

The atrioventricular node:

- ☐ A) is a parasympathetic ganglion located in the right atrium of the heart.
- ☐ B) conducts an action potential from the vagus nerve to the heart.
- ☐ C) sets the rhythm of cardiac contractions.
- ☐ D) delays the contraction of the ventricles of the heart.

Item 82

Cardiac output, which is the product of the heart rate and the stroke volume (the amount of blood pumped per contraction by either the left or the right ventricle), would most likely be:

- ☐ A) greater if measured using the stroke volume of the left ventricle.
- ☐ B) greater if measured using the stroke volume of the right ventricle.
- ☐ C) the same regardless of which stroke volume is measured.
- ☐ D) dependent on the viscosity of the blood.

Item 83

Which of the following is responsible for the spread of the cardiac action potential from one cardiac muscle cell to the next?

- ☐ A) Gap junctions
- ☐ B) Desmosomes
- ☐ C) Tight junctions
- ☐ D) Acetylcholine

Item 84

In the congenital heart defect known as patent ductus arteriosus, the ductus arteriosus, which connects the aorta and the pulmonary artery during fetal development, fails to close at birth. This will likely lead to all of the following EXCEPT:

- ☐ A) equal, or increased, oxygen concentration in the blood that reaches the systemic tissues.
- ☐ B) increased oxygen concentration in the blood that reaches the lungs.
- ☐ C) increased work load imposed on the left ventricle.
- ☐ D) increased work load imposed on the right ventricle.

Item 85

Which chambers of the heart pump oxygenated blood?

- ☐ A) The right and left atria
- ☐ B) The right and left ventricles
- ☐ C) The right atria and the left ventricle
- ☐ D) The left atria and the left ventricle

Item 86

Hypovolemic shock represents a set of symptoms that occur when a patient's blood volume falls abruptly. Hypovolemic shock is most likely to occur during:

- ☐ A) arterial bleeding.
- ☐ B) venous bleeding.
- ☐ C) low oxygen intake.
- ☐ D) excess sodium consumption.

Item 87

The capillary network comprises the greatest cross-sectional area of blood vessels in the body with high resistance to blood flow. In a healthy individual, the highest blood pressure would most likely be found in:

- ☐ A) the aorta.
- ☐ B) the venae cavae.
- ☐ C) the systemic capillaries.
- ☐ D) the pulmonary capillaries.

Item 88

Gas exchange between the blood and tissues occurs:

- ☐ A) throughout the circulatory system.
- ☐ B) in the arteries, arterioles, and capillaries.
- ☐ C) in the systemic arteries only.
- ☐ D) in the capillaries only.

Digestive System
BIOLOGY 2

One of the primary functions of the lymphatic system is to collect excess interstitial fluid that results from fluid exchange in the capillary beds, as described in the previous section, and return it to the blood. The lymphatic system also removes proteins and other particles that are too large to be taken up by the capillaries, including **glycerides**. The pathway back to the blood takes the excess fluid through lymph nodes, which are well prepared to elicit an immune response if necessary. Thus, the lymph system recycles interstitial fluid while also monitoring it for infection. In addition, the lymph system reroutes low soluble fat digestates around the small capillaries of the intestine and into the large veins of the neck. (As discussed in the Digestive and Excretory Systems Lecture, fats, unlike other biological molecules, enter the lymphatic system rather than traveling into the capillaries.) Most tissues are drained by lymphatic channels. A notable exception is the central nervous system.

Lymph circulates one way through the lymphatic vessels, eventually dumping into the thoracic duct and the vena cava.

The lymphatic system is an **open system**. In other words, fluid enters at one end and leaves at the other. This is in contrast to the closed circulatory system. Lymph capillaries are like tiny fingers protruding into the tissues. To enter the lymph system, interstitial fluid flows between overlapping endothelial cells (Figure 4.15c). Large particles literally push their way between the cells into the lymph. The cells overlap in such a fashion that, once inside, large particles cannot push their way out.

Fluids
PHYSICS

Typically, the interstitial fluid has a slightly negative gauge pressure. As the interstitial pressure rises toward zero, lymph flow increases. Factors that affect interstitial pressure include: blood pressure; plasma osmotic pressure; interstitial osmotic pressure (e.g. from proteins and infection response); and permeability of capillaries. Like veins, lymph vessels contain intermittent valves, which allow fluid to flow in only one direction.

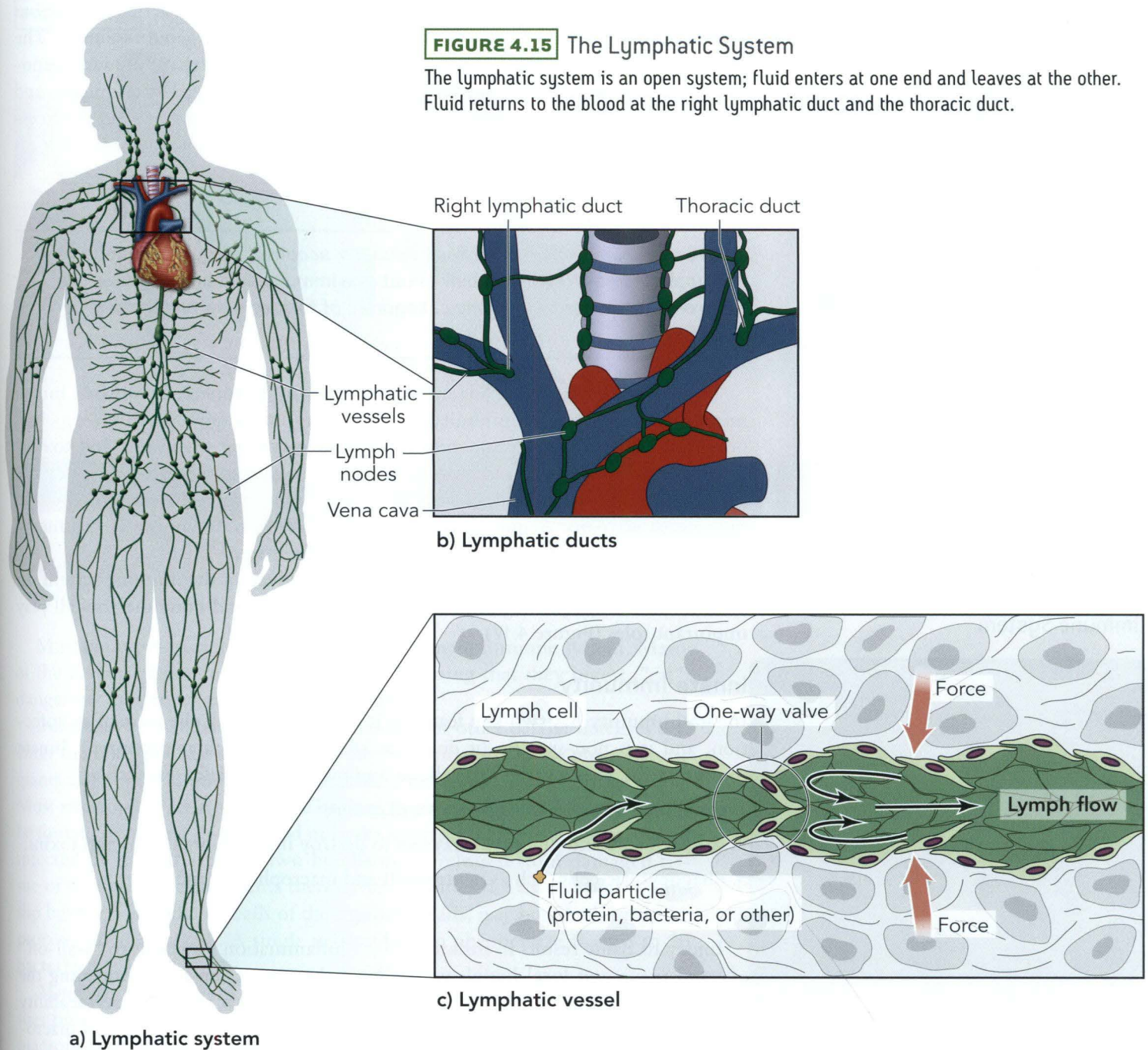
Fluid is propelled through these valves in two ways. First, smooth muscle in the walls of larger lymph vessels contracts when stretched. Second, the lymph vessels may be squeezed by adjacent skeletal muscles, body movements, arterial pulsations, and compression from objects outside the body. Lymph flow in an active individual is considerably greater than in an individual at rest.

The lymph system empties into large veins at the *thoracic duct* and the *right lymphatic duct*. Lymph from the right arm and head enters the blood through the right lymphatic duct. The rest of the body is drained by the thoracic duct. Thus, fluid is returned back into the cardiovascular system.

Throughout the lymphatic system there are many lymph nodes, containing large quantities of lymphocytes. Lymph nodes filter and trap particles; they are also where lymphocytes are stimulated to respond to pathogens, as will be discussed in the following section.

FIGURE 4.15 The Lymphatic System

The lymphatic system is an open system; fluid enters at one end and leaves at the other. Fluid returns to the blood at the right lymphatic duct and the thoracic duct.



4.6

The Immune System: Components and Communication

The purpose of the immune system is to protect the human body from toxins and from invasion by other organisms, including bacteria, viruses, fungi, and parasites. The immune system involves many cell types and is present in nearly all tissues of the body. Each of the systems described previously plays a role in the immune system. Generally speaking, immune cells use one of two strategies to accomplish the primary goals of the immune system. They either phagocytose ("eat") dangerous material or secrete effector molecules that have downstream functions.

Immune cells either eat or secrete.

FIGURE 4.16 Innate and Acquired Immunity

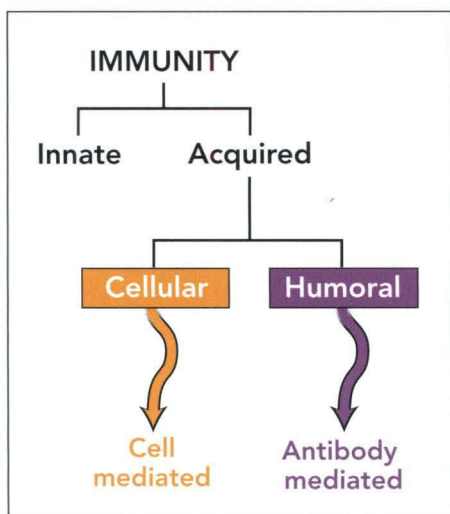
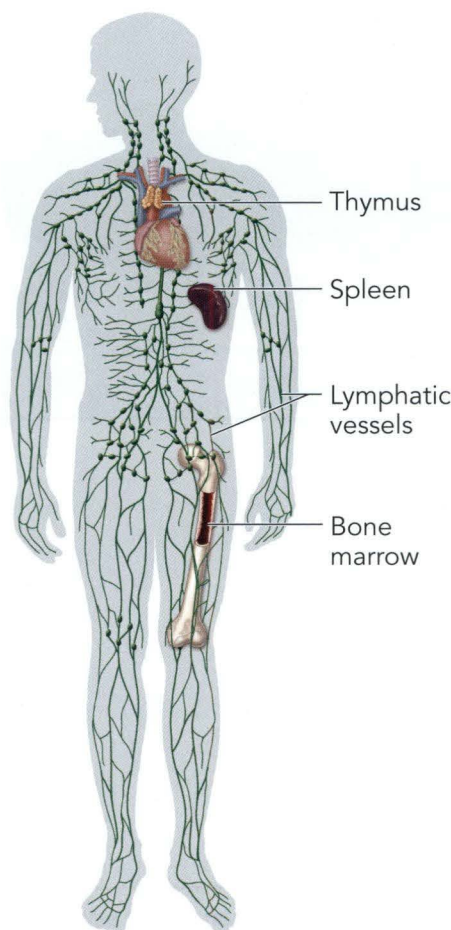


FIGURE 4.17 Organs of the Immune System



Some parts of the immune system are front line defenders, acting swiftly but non-specifically. Others act more slowly, but with strong targeted responses. The immune system also learns over time (has “memory”) such that following exposure to a particular pathogen, subsequent exposures will lead to a quicker and stronger response. Furthermore, the immune system is tightly regulated. Excessive regulation causes susceptibility to infection, while insufficient regulation leads to autoimmune destruction of the organism’s own cells.

Innate immunity includes our foot soldiers; acquired immunity includes our tactical strikes! When you think about the immune system, organize the different components into the categories of fast or slow and general or specific.

The immune system is made up of two major interconnected branches: innate immunity and acquired immunity. **Innate immunity** is quick and **non-specific**, providing a generalized protection from most intruding organisms and toxins. **Acquired (adaptive) immunity** develops more slowly and only after the body has experienced the initial attack. This branch provides protection against **specific** organisms or toxins. Acquired immunity can be broken down into B-cell mediated and T-cell mediated immunity, as will be discussed.

Many different cells, tissues, and organs are involved in the immune system. In addition to the lymphatic system, the spleen, thymus, and bone marrow all play important roles (Figure 4.17).

Innate Immunity

Innate immunity has two key features: it occurs quickly at the start of an infection, and it is non-specific (it does not adapt to a particular pathogen). Innate immunity includes a variety of cellular and non-cellular defenses, such as:

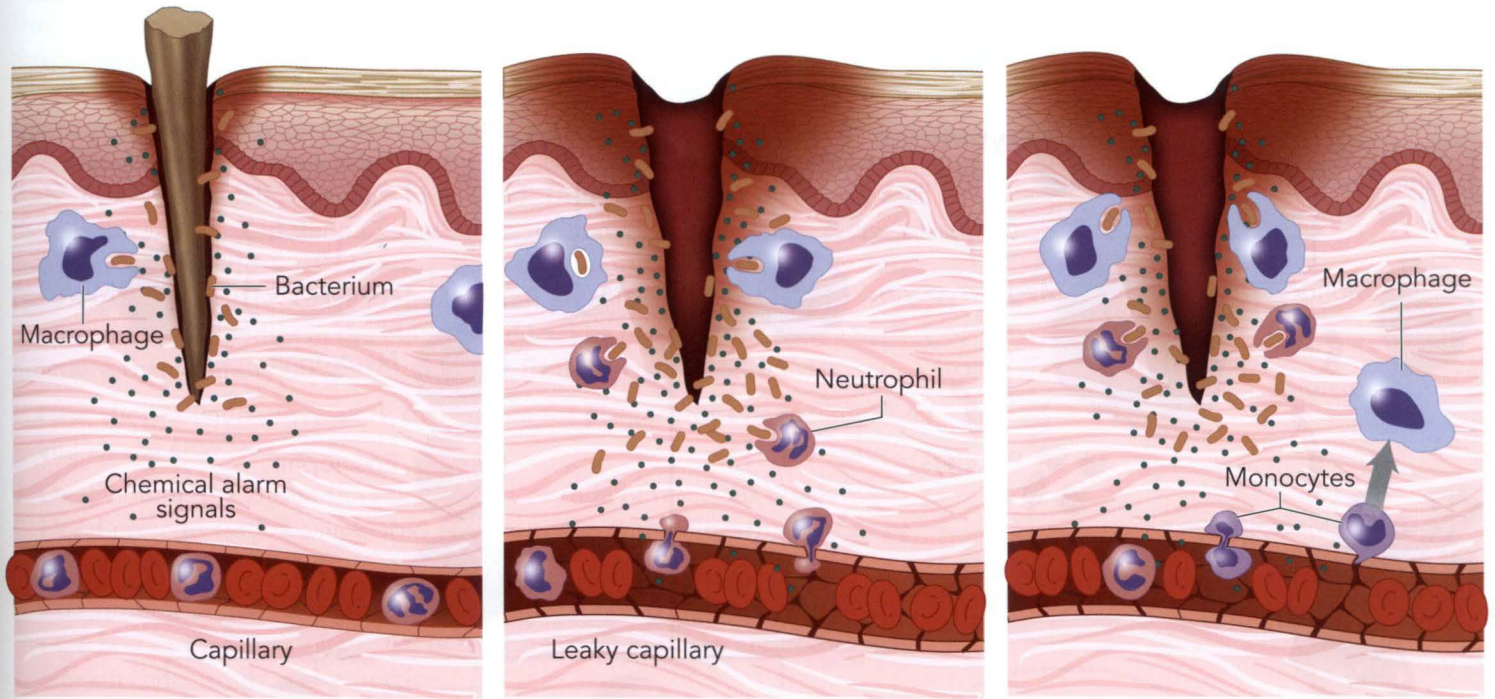
1. the skin as a barrier to organisms and toxins;
2. stomach acid and digestive enzymes to destroy ingested organisms and toxins;
3. phagocytotic cells such as neutrophils and macrophages; and
4. chemicals in the blood.

Injury to tissue results in **inflammation**. Inflammation functions to “wall-off” affected tissue and local lymph vessels from the rest of the body, impeding the spread of the infection. It includes dilation of blood vessels, increased permeability of capillaries, swelling of tissue cells, and migration of granulocytes and macrophages to the inflamed area (Figure 4.18). *Histamine, prostaglandins, and lymphokines* are just some of the causative agents of inflammation that are released by the tissues.

MCAT® THINK

How can innate immune cells recognize that there is a foreign invader? One way is by sensing Pathogen-Associated Molecular Patterns, or PAMPs. In this mechanism, innate immune cells look for molecules that are expressed by pathogens but not by humans. For example, many gram-negative bacteria express a carbohydrate called lipopolysaccharide, or LPS. The human body does not produce LPS, and certain innate immune cells recognize LPS as foreign. In fact, purified LPS alone, in the absence of bacteria, could send a person into septic shock due to the innate immune response.

FIGURE 4.18 The Inflammatory Response



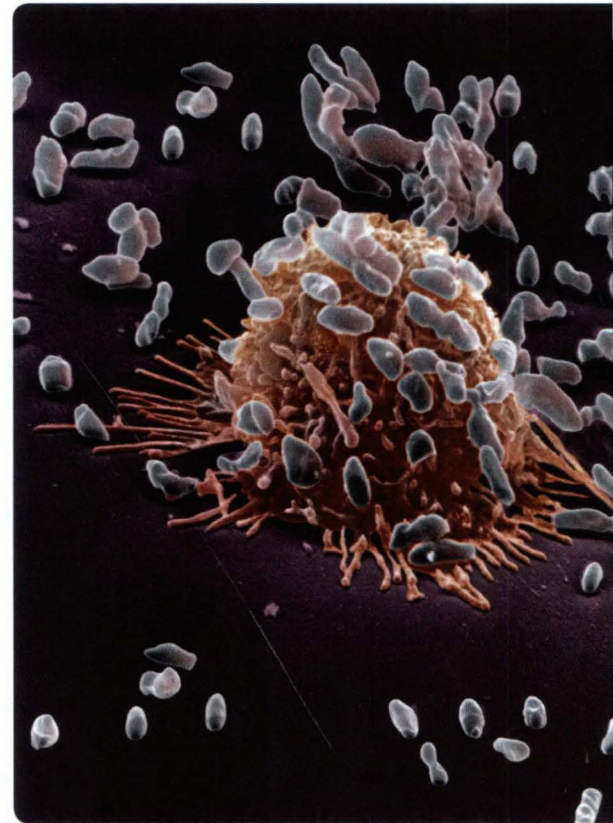
Multiple types of cells are involved in the innate immune system. Many of the earliest responders are **phagocytes**, meaning that they ingest ("eat") dangerous substances and then destroy them.

Infectious agents that pass through the skin or other barrier defenses and enter the body are first attacked by local **macrophages**. These phagocytotic giants can engulf as many as 100 bacteria. *Neutrophils* are next on the scene. Most neutrophils are stored in the bone marrow until needed, but some can be found circulating in the blood or in the tissues. Neutrophils move toward infected or injured areas, drawn by chemicals released from damaged tissue or by the infectious agents themselves. To enter the tissues, neutrophils slip between endothelial cells of the capillary walls, using an amoeboid like process called *diapedesis*. A single neutrophil can phagocytize from 5 to 20 bacteria.

Monocytes circulate in the blood until they, too, move into the tissues by diapedesis. Once inside the tissues, monocytes mature to become macrophages.

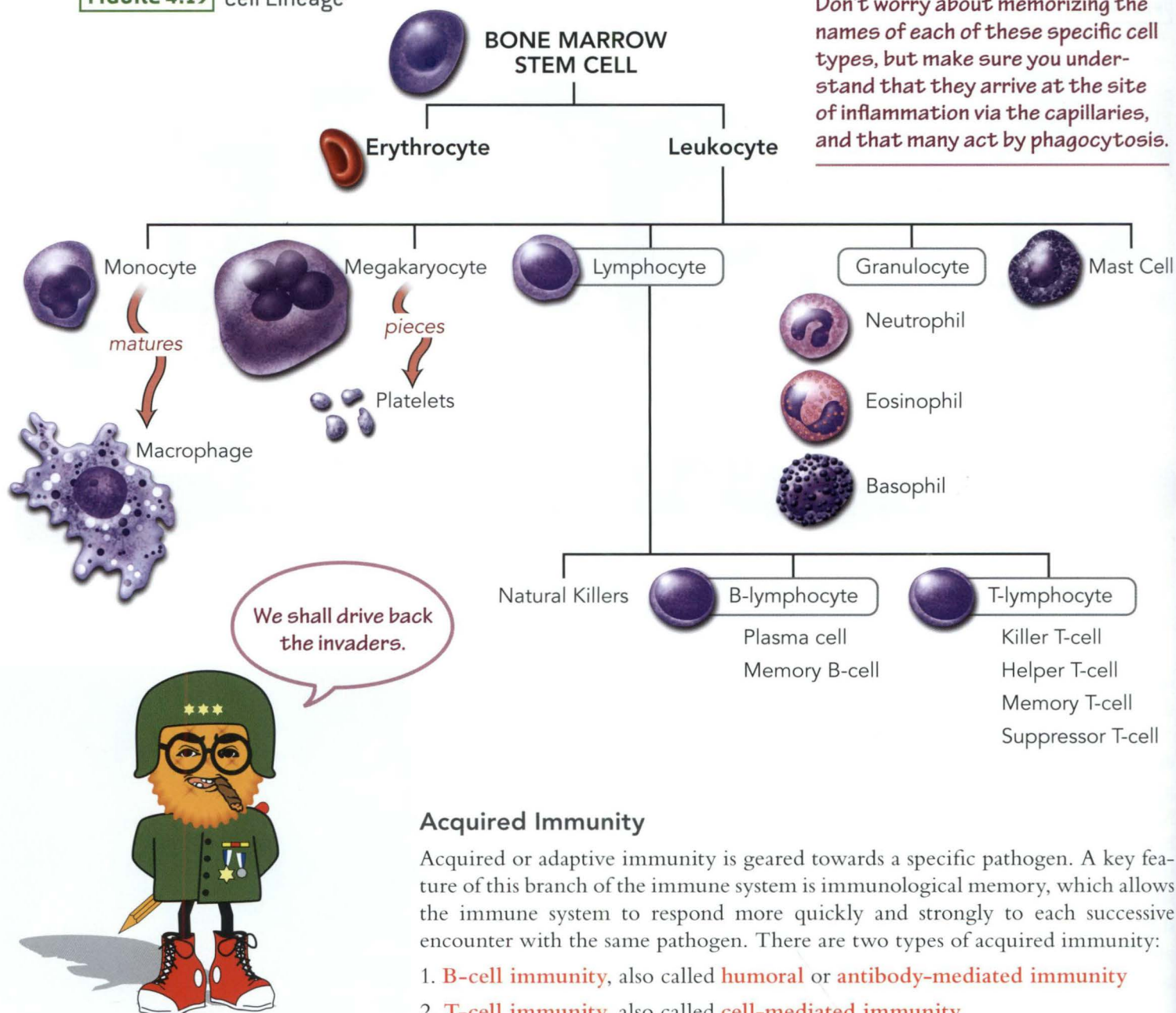
Neutrophils and macrophages die after engulfing bacteria and dead tissue. These dead leukocytes, along with tissue fluid and dead tissue, make up the substance known as *pus*. These first responders are expendable because they are non-specific and thus can be easily replaced.

Eosinophils and *basophils* are two additional innate immune cells related to neutrophils. Eosinophils work mainly against parasitic infections, while basophils release many of the chemicals of the inflammation reaction.



Macrophages ingest bacteria as part of the innate immune response to infection.

FIGURE 4.19 Cell Lineage



Don't worry about memorizing the names of each of these specific cell types, but make sure you understand that they arrive at the site of inflammation via the capillaries, and that many act by phagocytosis.

Acquired Immunity

Acquired or adaptive immunity is geared towards a specific pathogen. A key feature of this branch of the immune system is immunological memory, which allows the immune system to respond more quickly and strongly to each successive encounter with the same pathogen. There are two types of acquired immunity:

1. **B-cell immunity**, also called **humoral** or **antibody-mediated immunity**
2. **T-cell immunity**, also called **cell-mediated immunity**

T-cell Immunity

Humoral or antibody-mediated immunity is effective against bacteria, fungi, parasitic protozoans, viruses, and blood toxins. However, it cannot act against invading substances that have already made their way into cells.

Antibody-mediated immunity is promoted by **B-lymphocytes**, which differentiate and mature in the adult bone marrow and the fetal liver. Each B-lymphocyte makes a single type of **antibody** or **immunoglobulin**, which can recognize and bind to a particular potentially harmful foreign particle (an **antigen**). Initially, a B-lymphocyte displays this antibody on its membrane, and the antibody is called a **B-cell receptor (BCR)**. Later, many antibodies are produced as secreted proteins. The process by which an antibody (or BCR) recognizes a foreign particle is called **antigen-antibody recognition**. The portion of the antibody that binds to an antigen is highly specific for that antigen and is called an **antigenic determinant**.

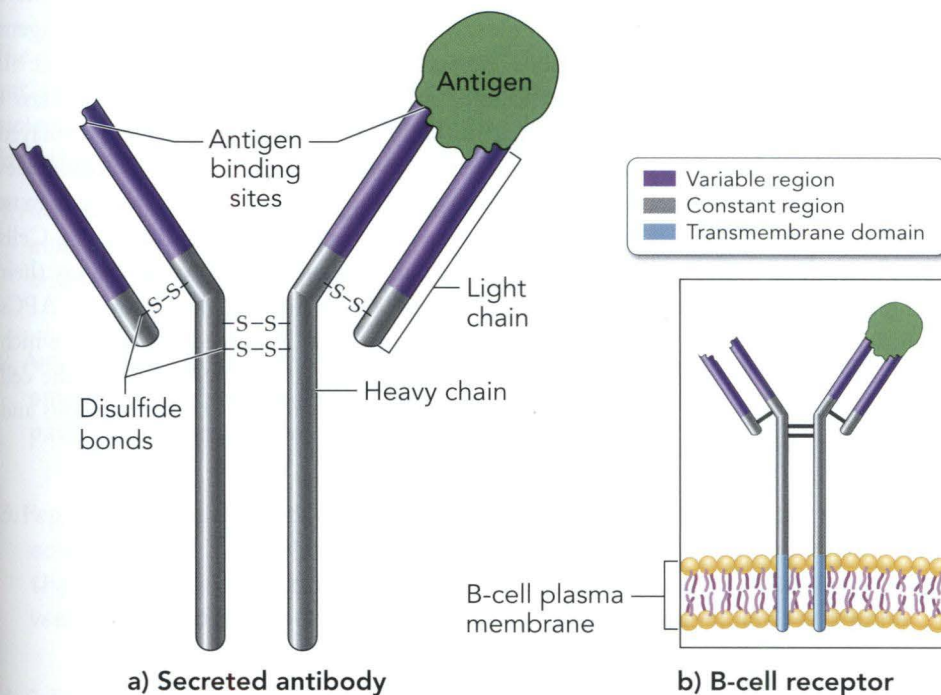
The immune response that results from the first exposure to an antigen is known as the **primary response**, which requires 20 days to reach its full potential. During the primary response, the BCR recognizes the appropriate antigen under the right conditions. When this happens, the B-lymphocyte, assisted by a helper T-cell, differentiates into plasma cells and memory B-cells. **Plasma cells**, which can survive for decades or even a lifetime, begin synthesizing free antibodies and releasing them into the blood. **Memory B-cells** proliferate and remain in the body. Like plasma cells, they are long-lived. In the case of re-infection, each of these cells can be called upon to synthesize antibodies, resulting in a faster acting and more potent effect called the **secondary response**. The secondary response requires approximately 5 days to reach its full potential.

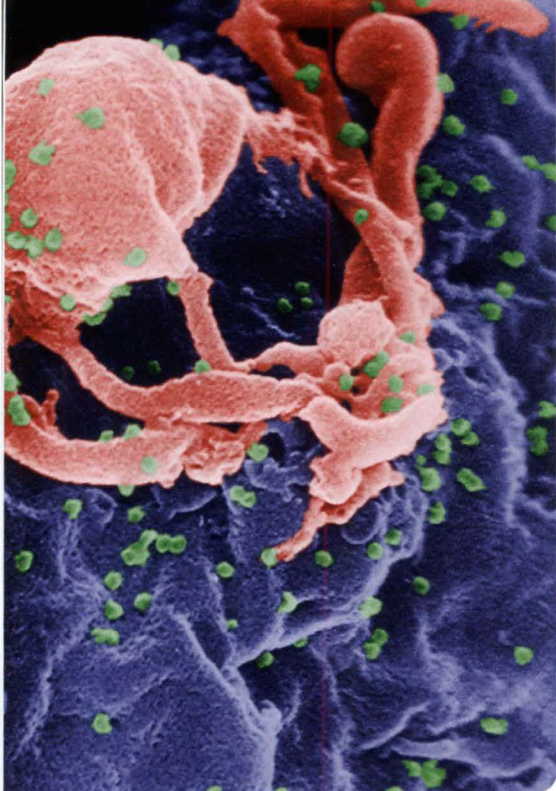
Circulating antibodies in the blood, produced by plasma cells, have a variety of functions that promote the destruction of harmful invading substances:

1. First, the antibodies may mark the antigen for phagocytosis by macrophages and *natural killer cells*.
2. Once bound, the antibodies may begin a cascade of reactions involving blood proteins (called *complement*) that cause the antigen bearing cell to be perforated.
3. The antibodies may cause the antigenic substances to *agglutinate* (stick together) or even precipitate, or, in the case of a toxin, the antibodies may block its chemically active portion.
4. Finally, free antibodies may attach their bases to *mast cells*. When an antibody whose base is bound to a mast cell also binds to an antigen, the mast cell releases histamine and other chemicals. This mechanism plays a role in allergies and in anaphylactic shock.

The potency of the secondary response explains how vaccines, which allow exposure to a non-active version of a particular infectious agent, protect the body from future infection. It also explains why it's said that some diseases, like chicken pox, "can't be caught twice."

FIGURE 4.20 Antibody Structure





This scanning electron micrograph shows HIV particles budding from an infected T-lymphocyte.

T-cell Immunity

Cell-mediated immunity is effective against cells that have already been infected because it is not restricted to free-floating substances, unlike antibody-mediated immunity. It involves **T-lymphocytes**, which mature in the thymus. Similar to a B-lymphocyte, a T-lymphocyte has an antibody-like protein at its surface that recognizes antigens, termed the *T-cell receptor (TCR)*. However, T-lymphocytes never make free antibodies.

During a primary immune response, when a TCR recognizes the appropriate antigen under the right conditions, T-lymphocytes differentiate into *helper T-cells*, *memory T-cells*, *suppressor T-cells*, and *killer T-cells* (also called *cytotoxic T-cells*). As discussed previously, helper T-cells assist in activating B-lymphocytes. They also activate other types of T-lymphocytes, including killer and suppressor T-cells. Long-lived memory T-cells have a similar function to memory B-cells in the secondary immune response. Suppressor T-cells play a negative feedback and regulatory role in the immune system. Killer T-cells bind to the antigen-carrying cell and release *perforin*, a protein that punctures the antigen-carrying cell. Killer T-cells can attack many cells because they do not phagocytize their victims; thus, unlike macrophages and neutrophils, they are not themselves destroyed when they kill invading pathogens. Killer T-cells are responsible for fighting some forms of cancer and for attacking transplanted tissue.

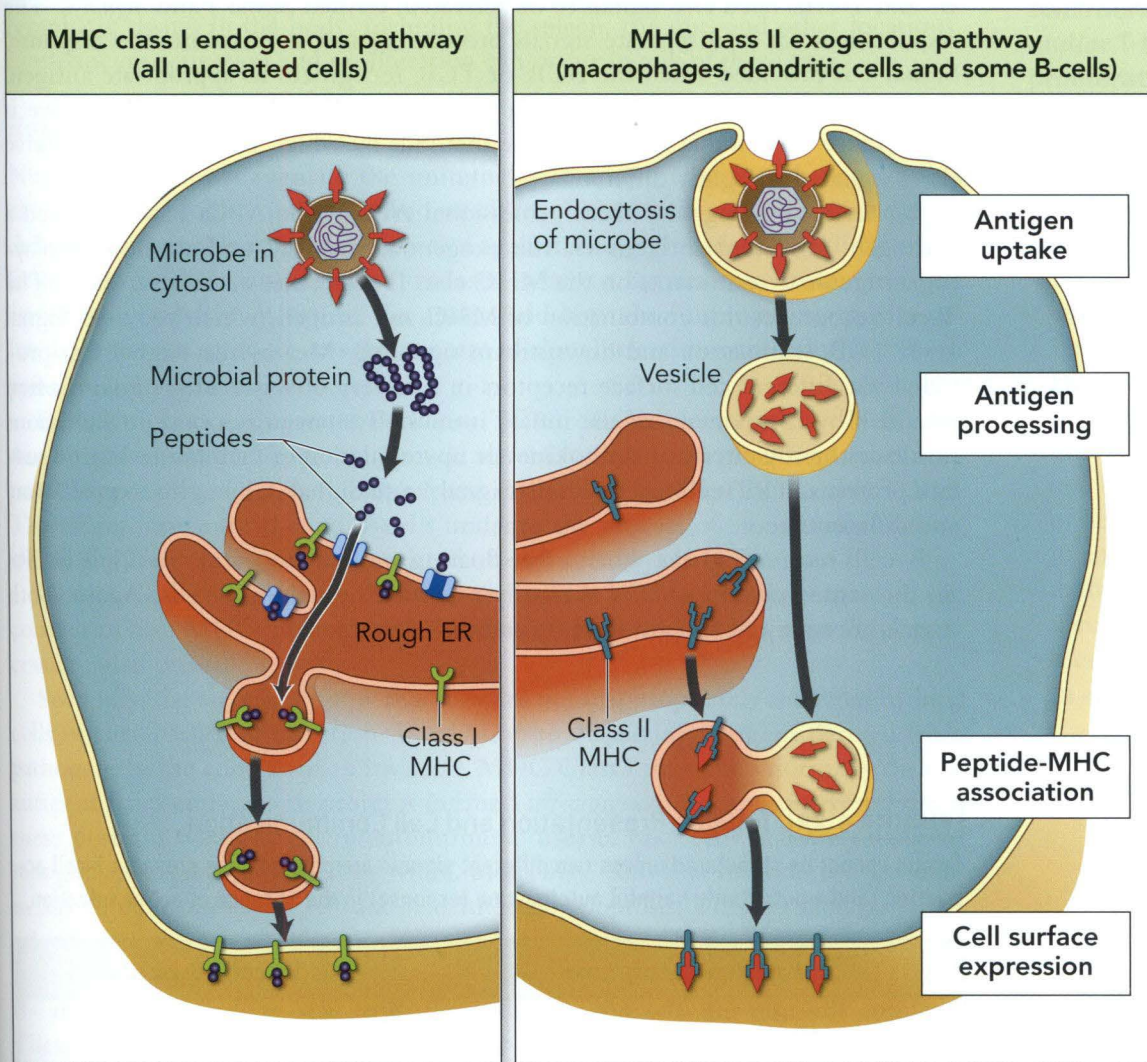
Helper T-cells are the cells attacked by HIV. This is why the virus is so devastating to the body's ability to produce an effective immune response.

Antigen Recognition by B-cells and T-cells

The complex process by which B-cells and T-cells recognize antigens and are activated (stimulated to multiply and differentiate) has great importance for the functioning of the immune response. Errors in this process can cause immunodeficiencies or autoimmune disease.

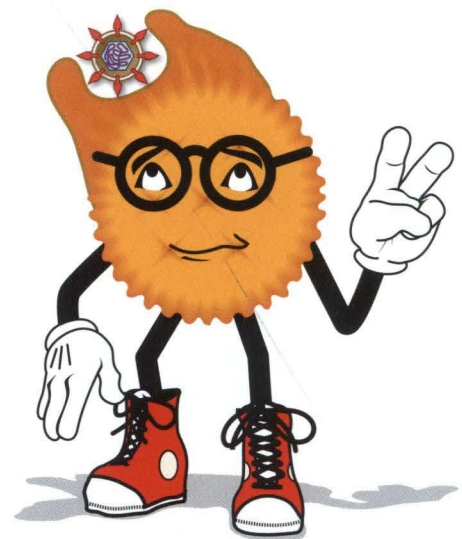
All human cells, except for those that do not contain nuclei, express **major histocompatibility complex (MHC)** molecules on their cell surface. The function of these membrane bound proteins is to display antigens for recognition. There are two major types of MHC molecules. **MHC class I** molecules display antigens derived from intracellular pathogens such as viruses and some bacteria. Since all cells can be infected by these pathogens, all nucleated cells have MHC class I molecules. The process by which intracellular antigens are processed and displayed on the cell surface is termed the *endogenous pathway*. **MHC class II** molecules display antigens derived from extracellular pathogens. Since these pathogens must be phagocytosed, MHC class II molecules are displayed by phagocytic cells. Cells that phagocytose extracellular bacteria or other pathogens in order to display their antigens are termed *professional antigen presenting cells (APCs)*. Professional APCs include macrophages, dendritic cells, and some B-cells. The process by which these antigens are processed and displayed by MHC class II molecules on the cell surface is termed the *exogenous pathway*. Figure 4.21 compares the exogenous and endogenous pathways.

FIGURE 4.21 Endogenous vs. Exogenous Pathways



The goal of both the endogenous and exogenous pathways is to process an antigen from a pathogen or molecule and display that antigen on an MHC molecule on the cell surface. Generally speaking, both pathways have the same four steps:

1. **Antigen uptake:** In the case of the endogenous pathway, the pathogen or molecule is already inside the cell. In the case of the exogenous pathway, the antigen is extracellular and must be phagocytosed.
2. **Antigen processing:** The pathogen or molecule must be processed into smaller peptides (antigens). This occurs in the cytosol in the endogenous pathway, and in vesicles in the exogenous pathway.
3. **Peptide-MHC association:** The antigens then associate with the MHC molecules, which have undergone folding in the ER. In the endogenous pathway, the antigens are transported into the ER. In the exogenous pathway, a vesicle containing MHC Class II fuses with a vesicle containing antigens.
4. **Cell surface expression:** The end result of both pathways is that the antigen-MHC complex is expressed on the cell surface and can interact with the appropriate immune cells.



B-cell and T-cell activation

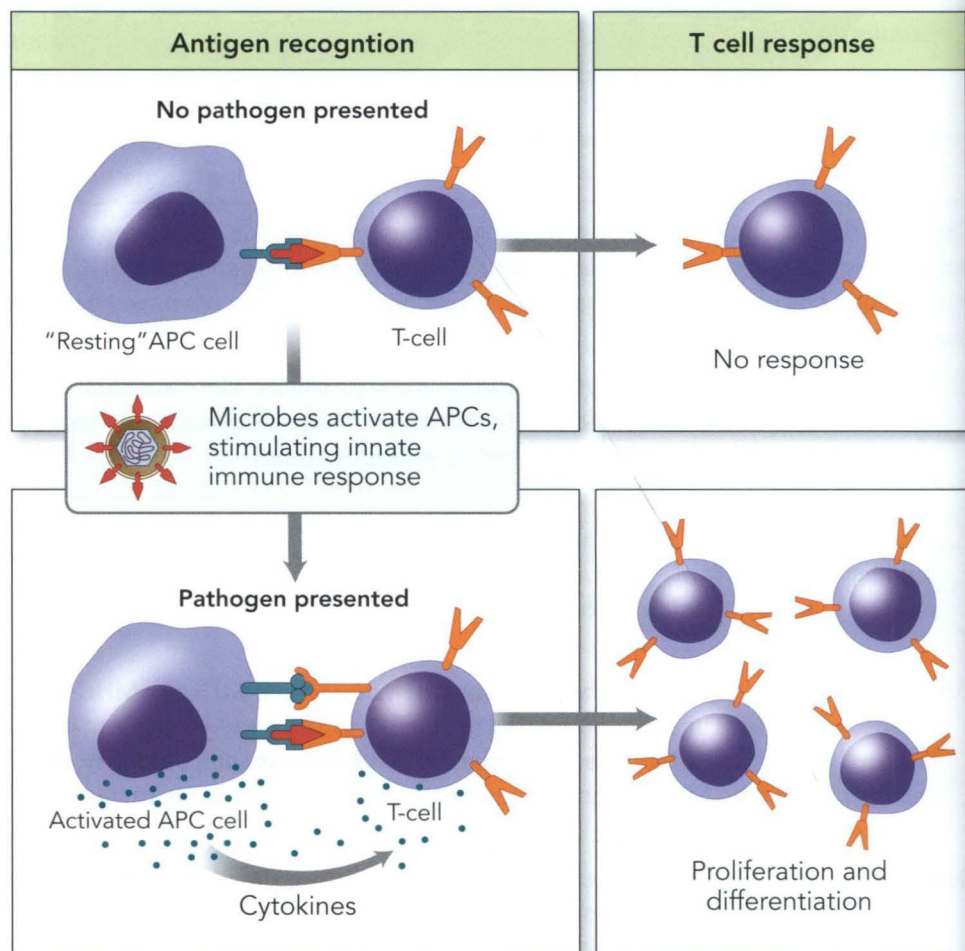
B- and T-cells need two signals to be activated, termed *Signal 1* and *Signal 2*. The requirement for two separate signals protects against an autoimmune response. Signal 1 is provided when the BCR or TCR recognizes its appropriate antigen. Signal 2 is often called a “danger signal” because B-cells and T-cells receive it when there is an active infection. The methods by which B- and T-cells receive these signals are slightly different.

T-cells receive Signal 1 from professional APCs. The APCs have engulfed a pathogen, processed antigens via the exogenous pathway, and are now displaying antigenic determinants on the MHC class II molecules on their surfaces. The T-cell recognizes this combination of MHC and antigen, which provides Signal 1 via TCR stimulation and downstream signaling. Meanwhile, Signal 2 is provided via different cell surface receptors in a variety of ways. This signal is often provided by components of the innate immune system in response to infectious insults, either by circulating cytokines or up-regulation of membrane-bound surface proteins. If a T-cell receives both Signal 1 and Signal 2, it begins to proliferate and differentiate.

B-cells receive Signal 1 when a free floating antigen cross-links multiple BCRs on the same cell. Signal 2 is normally provided by helper T-cells. Again, both signals are required for proliferation and differentiation.

FIGURE 4.22 Antigen Presentation and Cell Communication

T-cells cannot be stimulated unless two different signals are present. This prevents T-cell activation (and a potentially harmful autoimmune response) in the absence of active infection.



Infection often occurs in connective tissues, so B- and T-cell activation often takes place in the nearest lymph node. However, there are numerous sites with lymphatic tissues in the body, including the spleen, the gut, and other locations. Lymphocyte activation and proliferation can occur in any of these sites.

Regulation of the Immune System

Numerous processes regulate the immune system, and errors in these processes can cause pathologic conditions. Too much regulation renders the immune system deficient and unable to properly protect against foreign invaders. Too little regulation can result in **autoimmune diseases**, where a hyperactive immune system attacks the body's own tissues. To understand how the immune system is regulated, it is necessary to discuss the concept of clonal selection, which includes both positive and negative selection.

Each lymphocyte expresses BCRs or TCRs of a single specificity. However, due to processes that generate genetic diversity during development, the total population of B- and T-cells can express millions of different BCRs and TCRs. Therefore, immature B- and T-cells undergo the process of **clonal selection**, in which only certain types are permitted to mature and proliferate.

First of all, cells must show that they are capable of recognizing antigens in the context of host MHC molecules. Those that cannot undergo apoptosis. This process is called **positive selection**.

Secondly, the cells must show that they are not inappropriately activated by host cells in the absence of infection. In addition to displaying antigens derived from pathogens in the context of an invasion, MHC Class I molecules normally display antigens from endogenous proteins (termed *self-antigens*). An immune response to these proteins would result in autoimmune disease. Like cells that are unable to recognize antigens presented by MHC molecules, cells that respond too strongly to MHC molecules with self-antigens undergo apoptosis. This is called **negative selection**.

Collectively, positive and negative selection allow for the survival of only those B- and T-cells that are able to distinguish between self and non-self antigens. These opposing processes eliminate both lymphocytes that are ineffective in the production of an immune response and those that present the danger of overreacting and attacking the organism's own cells. T-cells undergo clonal selection in the thymus, while B-cells undergo selection in the bone marrow. Cells that survive the selection process are released to lodge in lymphoid tissue or to circulate between the blood and the lymph fluid. Once these surviving cells recognize the appropriate foreign antigen, they undergo differentiation and proliferation, thus completing the process of clonal selection.

Let's imagine a bacterial infection. First we have inflammation. Macrophages, then neutrophils, engulf the bacteria. Interstitial fluid is flushed into the lymphatic system, where lymphocytes wait in the lymph nodes. Macrophages process and present the bacterial antigens on MHC molecules to T-lymphocytes. With the assistance of helper T-cells, B-cells differentiate into memory cells and plasma cells. The memory cells are preparation in the event that the same bacteria attacks again (the secondary response). The plasma cells produce antibodies, which are released into the blood to attack the bacteria. It is important to know that a single antibody is specific for a single antigen, and that a single B-lymphocyte produces only one antibody type.

The reason your lymph nodes may swell during infection is that B- and/or T-lymphocytes are rapidly proliferating in response to the pathogen.

MCAT® THINK

Some autoimmune diseases are among the most common reasons for seeking medical intervention. For example, Type I diabetes results from autoimmune destruction of insulin-producing pancreatic beta cells. Although failure of negative selection can result in autoimmune disease, there are many other immunoregulatory mechanisms in place. Failure of these mechanisms can also result in autoimmunity.

In clonal selection, the appropriate B- or T-cell is positively and negatively selected, and then it is cloned in response to a pathogen.

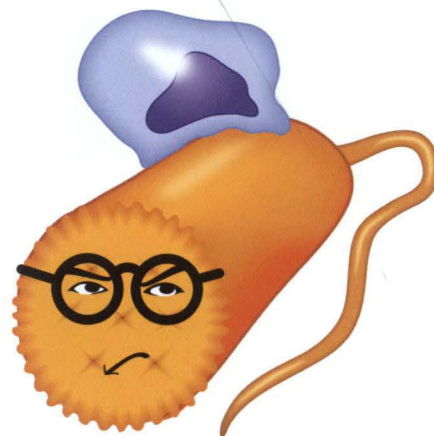
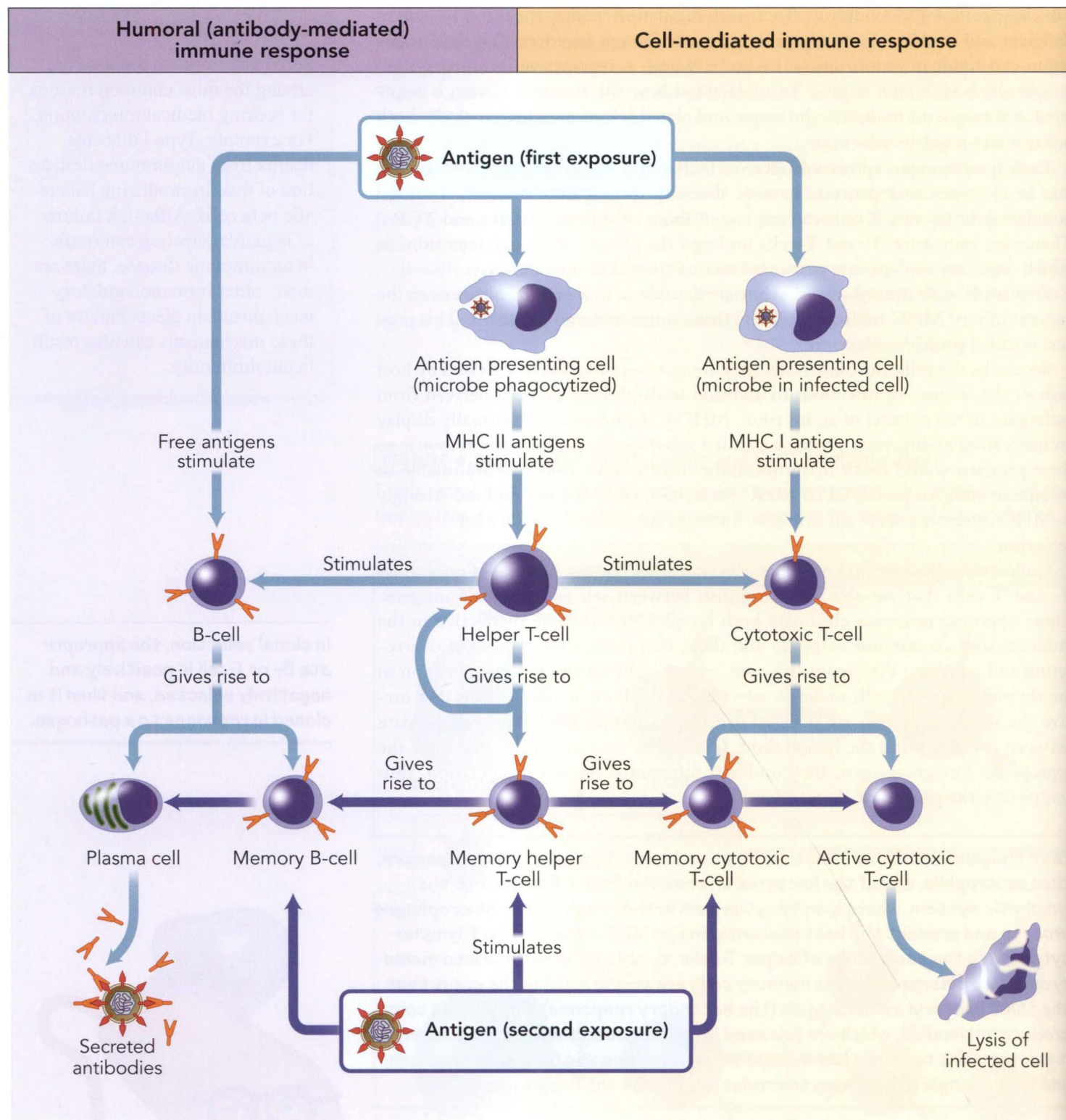


FIGURE 4.23 Humoral vs. Cell-Mediated Immunity

This figure provides a summary of adaptive immunity. Note the many ways in which cells from both branches of the adaptive immune system interact with each other. When a cell is stimulated, either by a molecule or by another cell, it undergoes proliferation and/or differentiation. Also note the difference between the primary antigen exposure (top) and the secondary antigen exposure (bottom). Remember that the secondary exposure will generate a much quicker adaptive immune response.



Blood Types

Blood can be categorized into different types according to the presence of certain types of antigens on the surfaces of red blood cells. Because heredity determines an individual's blood type, a full understanding of blood types requires knowledge of both genetics and immunology. Blood types are identified by A and B surface antigens. For instance, in type A blood, the red blood cell membrane has A antigens and does not have B antigens. Of course, if the erythrocytes have A antigens, the immune system does not make A antibodies. Type O blood has neither A nor B antigens, and thus the immune system makes both A and B antibodies. A blood donor can donate blood only to an individual that does not make antibodies against the donor blood. Table 1.1 shows a '+' sign for donor/recipient combinations where blood agglutinates (is rejected), and a '-' sign for combinations where no agglutination occurs. Notice that an individual with type O blood is a "universal donor" who can donate to anyone (all minuses in the donor column), because type O blood does not contain any antigens that could trigger an immune response in a recipient. Meanwhile, an individual with type AB blood is a "universal recipient" who can receive blood from anyone (all minuses in the recipient row) because no antibodies for A or B antigens will be produced.

The genes that produce the A and B antigens are co-dominant. Thus, an individual having type A or B blood can be heterozygous or homozygous. An individual with type O blood has two recessive alleles.

Rh factors are surface proteins on red blood cells, first identified in Rhesus monkeys. Individuals with genotypes that code for nonfunctional products of the Rh gene are said to be *Rh-negative*. All others are *Rh-positive*. Transfusion reactions involving the Rh factor, if they occur at all, are usually mild. Rh factor is more of a concern during the pregnancy of an Rh-negative mother with an Rh-positive fetus. In the first pregnancy, the mother is not exposed to fetal blood until giving birth, and problems are rare. Upon exposure, the mother develops an immune response against the Rh-positive blood. In a second pregnancy, the fetus, if Rh-positive, may be attacked by the antibodies of the mother, which are small enough to pass through the placental barrier. This problem can be life threatening.



TABLE 4.1 > Blood Types

Recipient	Donor				
		A	B	AB	O
	A	-	+	+	-
	B	+	-	+	-
	AB	-	-	-	-
	O	+	+	+	-

Blood type	Genotype
A	I ^A I ^A or I ^A i
B	I ^B I ^B or I ^B i
AB	I ^A I ^B
O	ii



These questions are NOT related to a passage.

Item 89

"Swollen glands" are often observed in the neck of a person with a cold. The most likely explanation is that:

- ☐ A) blood pools in the neck in an attempt to keep it warm.
- ☐ B) lymph nodes swell as white blood cells proliferate within them to fight the infection.
- ☐ C) the infection sets off an inflammatory response in the neck, causing fluid to be drained from the area.
- ☐ D) fever causes a general expansion of the tissues of the head and neck.

Item 90

Humoral immunity involves the action of:

- ☐ A) cytotoxic T-lymphocytes.
- ☐ B) stomach acid.
- ☐ C) pancreatic enzymes.
- ☐ D) immunoglobulins.

Item 91

Antibodies function by:

- ☐ A) phagocytizing invading antigens.
- ☐ B) adhering to circulating plasma cells and marking them for destruction by phagocytizing cells.
- ☐ C) preventing the production of stem cells in the bone marrow.
- ☐ D) attaching to antigens via their variable portions.

Item 92

Lymphatic vessels absorb fluid from the interstitial spaces and carry it to the:

- ☐ A) kidneys, where it is excreted.
- ☐ B) large intestine, where it is absorbed and returned to the bloodstream.
- ☐ C) lungs, where the fluid is vaporized and exhaled.
- ☐ D) lymphatic ducts, which return it to the circulation.

Item 93

Which of the following would not normally be found in a lymph node?

- ☐ A) B-lymphocytes
- ☐ B) Proteins discarded by tissue cells
- ☐ C) Invading bacteria
- ☐ D) Old erythrocytes

Item 94

An organism exposed to a pathogen for the first time will exhibit an innate immune response involving:

- ☐ A) B-lymphocytes.
- ☐ B) T-lymphocytes.
- ☐ C) granulocytes.
- ☐ D) An organism exposed to a pathogen for the first time must acquire immunity before it can respond.

Item 95

Influenza is an intracellular virus. Antigens derived from influenza are mainly processed by the _____ pathway and displayed on MHC Class ____.

- ☐ A) endogenous, I
- ☐ B) endogenous, II
- ☐ C) exogenous, I
- ☐ D) exogenous, II

Item 96

In type I diabetes, self-reactive T-cells erroneously attack and destroy pancreatic beta cells that display self-antigens. This autoimmune process can be most precisely described as a failure of:

- ☐ A) antigen processing.
- ☐ B) B-cell activation.
- ☐ C) positive selection.
- ☐ D) negative selection.

TERMS YOU NEED TO KNOW

Acquired (adaptive) immunity	Electrical synapses	Phagocytes
Albumin	Endothelial cells	pH control
Alveolar gas exchange	Erythrocytes	Plasma
Alveoli	Evaporation	Plasma cells
Antibody	Fibrinogen	Platelets
Antigen	Gap junctions	Positive selection
Antigen-antibody recognition	Glycerides	Primary response
Aorta	Heat exchange	Pulmonary arteries
Arteries	Hematocrit	Pulmonary system
Arterioles	Hemoglobin	Pulmonary veins
Atrioventricular (AV) node	Henry's Law	Purkinje fibers
Autoimmune diseases	Inflammation	Regulation of plasma volume
B-cell immunity (humoral/antibody-mediated immunity)	Innate immunity	Rib cage
B-lymphocytes	Left atrium	Right atrium
Blood clot	Left ventricle	Right ventricle
Bronchi	Leukocytes	Rightward shift of oxygen dissociation curve
Bronchioles	Macrophage	Secondary response
Bundle of His	Major histocompatibility (MHC)	Serum
Capillaries	Medulla oblongata	Sinoatrial (SA) node
Carbonic anhydrase	Memory B-cells	Specific
Central chemoreceptors	MHC Class I	Stem cell
Cilia	MHC Class II	Superior and inferior venae cavae
Clonal selection	Mucus	Surface tension
Closed circulatory system	Nasal and tracheal capillary beds	Systemic circulation
CO ₂ sensitivity	Nasal hairs	Systolic pressure
Coagulation	Negative selection	T-cell immunity (cell-mediated immunity)
Connective tissue	Nervous and endocrine control	T-lymphocytes
Cooperativity	Non-specific	Thermoregulation
Diaphragm	Open system	Total peripheral resistance
Diastolic pressure	Osmotic pressure	Trachea
Differential partial pressures	Oxygen affinity	Vagus nerve
Differential pressures	Oxyhemoglobin	Veins
Diffusion	Panting	Venules
Elasticity (resiliency)	Particulate matter	
	Peripheral chemoreceptors	



DON'T FORGET YOUR KEYS

1. The goal of respiration and circulation is to meet metabolic needs.
2. Differential pressures and concentrations drive fluid flow and reactions.
3. Increasing surface area facilitates exchange of materials.

The Digestive and Excretory Systems

5

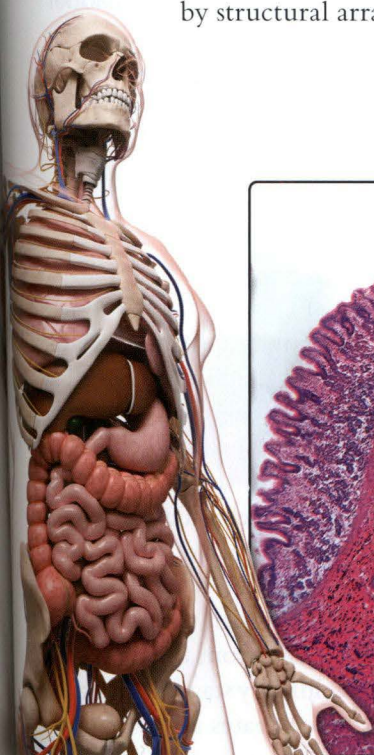
LECTURE

5.1 Introduction

This lecture discusses the structure and function of the human digestive and excretory systems. Humans use the macromolecules that make up food to power the body through the metabolic processes of glycolysis and cellular respiration. The body's ability to extract useful nutrition from food is central in sustaining life.

Digestion, the process by which the body extracts nutrition, allows macromolecules to enter the body by passing through the membranes lining the digestive tract. Digestion consists of three main processes: macromolecule breakdown, absorption, and excretion. Once food is broken down into its smaller constituent parts, nutrients can be absorbed into the bloodstream and made available for metabolic processes. Following digestion and absorption, the excretory system serves to process toxins and eliminate the waste products of metabolism and other bodily functions from the body. Although excretion involves the liver, which processes toxins, the excretory system primarily involves the kidney and the smallest operating unit of the kidney, the nephron. The manipulation of permeability and concentration gradients at the level of the nephron ensures that waste products are properly eliminated. All of these processes are mediated by enzyme activity.

When studying digestion for the MCAT®, keep the following organizing principles in mind: location, pH, and surface area. Within the digestive tract, each location has a specific function. The environments of different locations have different pH values, which help facilitate their various functions. Also, remember that digestion is primarily a system of exchange between the external and internal environments of the body. As in other systems of exchange, such as the respiratory and circulatory systems, surface area is critical. Surface area is increased by structural arrangements in different regions of the digestive tract.



The small intestines have multiple small projections, called villi, that increase the surface area through which absorption of nutrients can occur.

- 5.1 Introduction
- 5.2 Anatomy of the Digestive System
- 5.3 Gastrointestinal Hormones
- 5.4 Molecular Digestion and Absorption
- 5.5 The Liver: Storage, Distribution, and Detox
- 5.6 The Kidney: Excretion, Blood Pressure & Composition

THE 3 KEYS



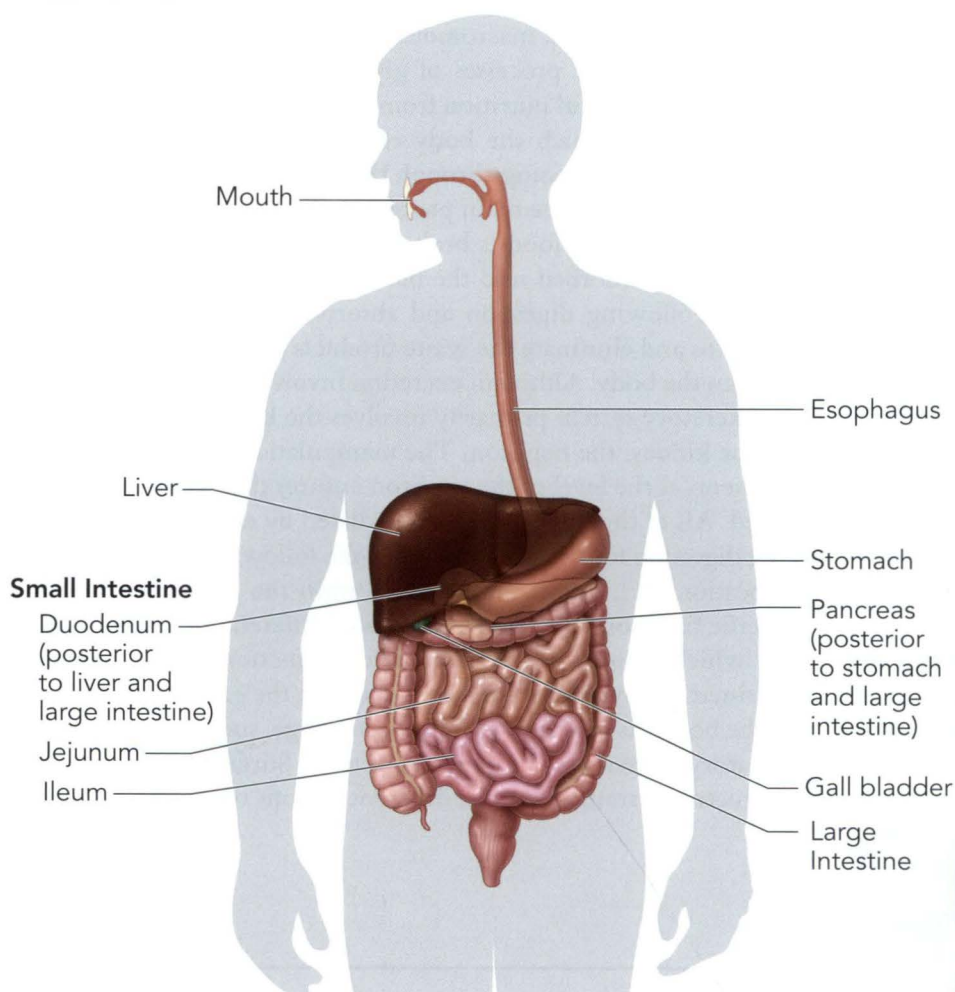
1. The three processes of the digestive system are digestion, absorption, and excretion. Surface area and length promote absorption.
2. From the kidney, substances travel in one of only two directions: "into the toilet" (filtration, secretion) and "back to the body" (reabsorption).
3. The nephron works by diffusion across membranes and active pumps in the ascending loop of Henle.

Anatomy of the Digestive System

Be familiar with the basic anatomy of the digestive system and consider how location is related to function.

It is important to know the basic anatomy of the digestive tract (Figure 5.1). In the order in which food passes, the main components of the digestive tract are the **mouth**, **esophagus**, **stomach**, **small intestine**, **large intestine**, and **anus**. The entire digestive tract is considered to be outside the body because it is open to the environment at the mouth and the anus. Nutrients passing through the digestive tract do not enter into the body until they pass through the membrane of one of the digestive organs and are absorbed into the bloodstream.

FIGURE 5.1 Anatomy of the Digestive System

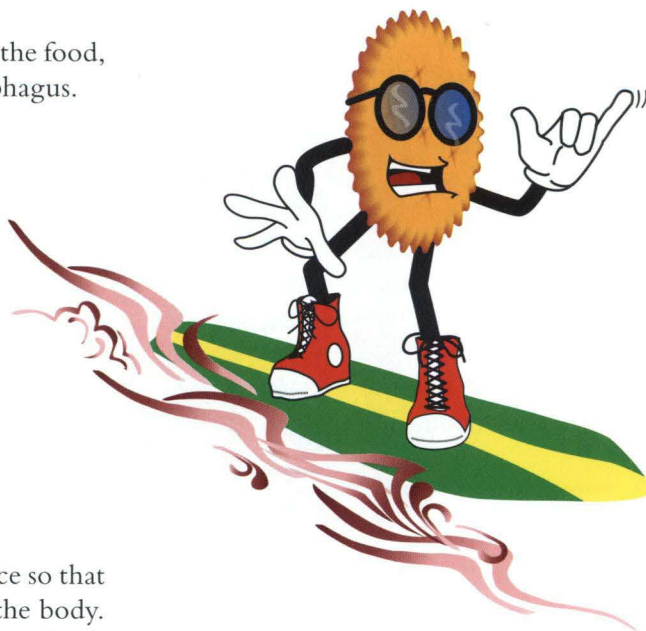


The Mouth and Esophagus

The first step in digestion is **ingestion**, the process of taking in food through the mouth. Two kinds of digestion begin in the mouth: physical and chemical. The physical breakdown of food occurs through the process of chewing, while the chemical breakdown of food is initiated by the enzyme **α -amylase**, contained in saliva. Starch is the major carbohydrate in the human diet. α -amylase begins to break down the long straight chains of starch into polysaccharides. Chewing increases the surface area of food, enabling more enzymes to act on the food at any one time. Chewed food forms a clump in the mouth called a **bolus**. The bolus is pushed into the esophagus by swallowing and then moves down the esophagus. (Technically, swallowing includes the movement of the bolus from the esophagus into the stomach, and is composed of a voluntary and involuntary stage.) **Peristalsis**, a contraction of the smooth muscle in the digestive tract, creates a wave motion

that pushes along the partially digested food. Saliva acts as **lubrication** for the food, helping it to move down the esophagus. No digestion occurs in the esophagus.

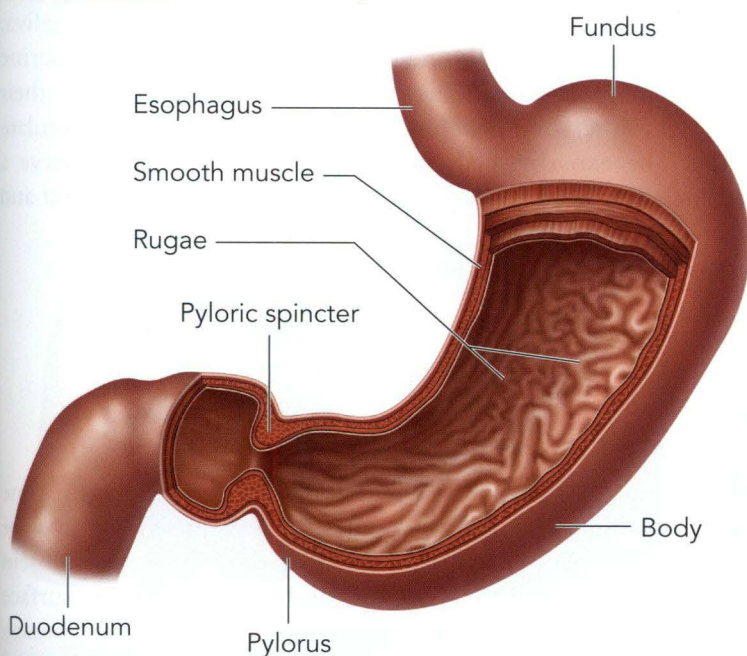
Remember that digestion begins with carbohydrates in the mouth via α -amylase, and that there is no digestion in the esophagus. Also understand peristalsis, the wavelike motion of smooth muscle that moves food through the digestive tract. It is similar to squeezing a tube of toothpaste at the bottom and sliding your fingers toward the top to expel the toothpaste.



The Stomach

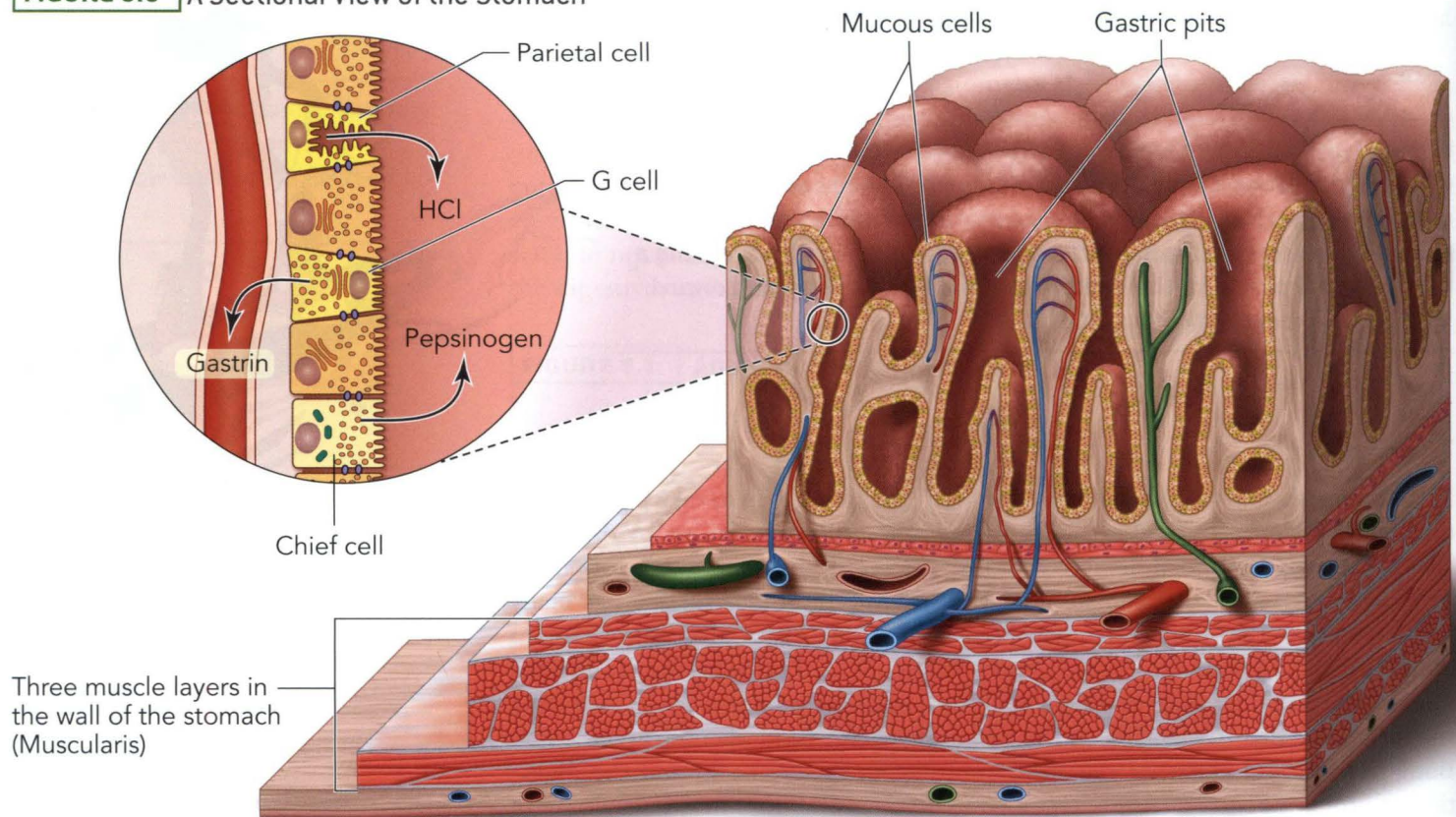
In the stomach, some of the major processes of digestion begin to take place so that the macromolecules in food can be broken down sufficiently for use by the body. The stomach is a rounded flexible pouch that serves to both mix and store food. The outer surface of the stomach is smooth, while the inner surface has many folds that allow the stomach to expand as it fills. The major anatomical regions of the stomach include the **fundus**, **body**, and **pylorus**. The bolus moves into the stomach through the *lower esophageal sphincter* (or *cardiac sphincter*). A **sphincter** is a ring of muscle that is normally contracted so that there is no opening at its center. Both physical and chemical digestion continue in the stomach, and the digestion of proteins begins. The enzyme pepsin catalyzes the chemical breakdown of proteins in the stomach. The stomach also breaks food into smaller pieces using physical means. It is composed of several layers of smooth muscle that powerfully churn the contents of the stomach and reduce food to a semi-fluid mass called *chyme*. Chyme leaves the stomach through the *pyloric sphincter*, which leads into the small intestine.

FIGURE 5.2 Gross Anatomy of the Stomach



The lining of the stomach is called the mucosa.

FIGURE 5.3 A Sectional View of the Stomach



The inside of the stomach is highly acidic. The acidic environment is maintained by **gastric juice**, a combination of acid, enzymes, and hormones released by cells in the lining of the stomach. A full stomach has a pH of 2. The low pH of the stomach contributes to protein digestion by denaturing proteins. It also helps to kill ingested bacteria.

The stomach contains **exocrine glands** in recesses called *gastric pits*, as shown in Figure 5.3. Exocrine glands use ducts to deliver their secretions to specific locations in the external environment; in this case, to the lumen of the digestive tract. Other examples of exocrine glands are those that produce sweat, saliva, milk, and earwax. The exocrine system is understood in contrast to the endocrine system, which is a system of glands that do not have ducts and instead secrete their products directly into the internal environment of the bloodstream to circulate throughout the body. The exocrine cells in the lining of the stomach serve a variety of purposes, including maintenance of the acidity of the environment and aiding in digestion.

There are four major cell types in the stomach (Figure 5.4):

1. **mucous cells**;
2. **chief (peptic) cells**;
3. **parietal (oxyntic) cells**; and
4. **G cells**.

There are multiple types of mucous cells, but all of them perform the same basic function of secreting mucus. The mucous cells line the stomach wall and the necks of the exocrine glands. Mucus, composed mainly of a sticky glycoprotein and electrolytes, lubricates the stomach wall so that food can slide along its surface without causing damage. Mucus also protects the epithelial lining of the stomach wall from the acidic environment inside the stomach. Some mucous cells secrete a small amount of pepsinogen.

Chief cells are found deep in the exocrine glands. They secrete **pepsinogen**, the zymogen precursor to **pepsin**. Zymogens (also called proenzymes) are inactive

precursors to enzymes that can be activated to become functional enzymes. The low pH in the stomach activates pepsinogen to become pepsin. Once activated, pepsin begins protein digestion.

Parietal cells are also found in the exocrine glands of the stomach. Parietal cells secrete **hydrochloric acid (HCl)** into the lumen of the stomach through active transport, which requires a large input of energy. Carbon dioxide is involved in the process, making carbonic acid inside the cell. The hydrogen from the carbonic acid is expelled to the lumen side of the cell, while the bicarbonate ion is expelled to the interstitial fluid side. The net result is that the pH of the stomach is lowered and the pH of the blood is raised. Parietal cells also secrete *intrinsic factor*, which, further into the digestive process, helps the ileum absorb the vitamin B12.

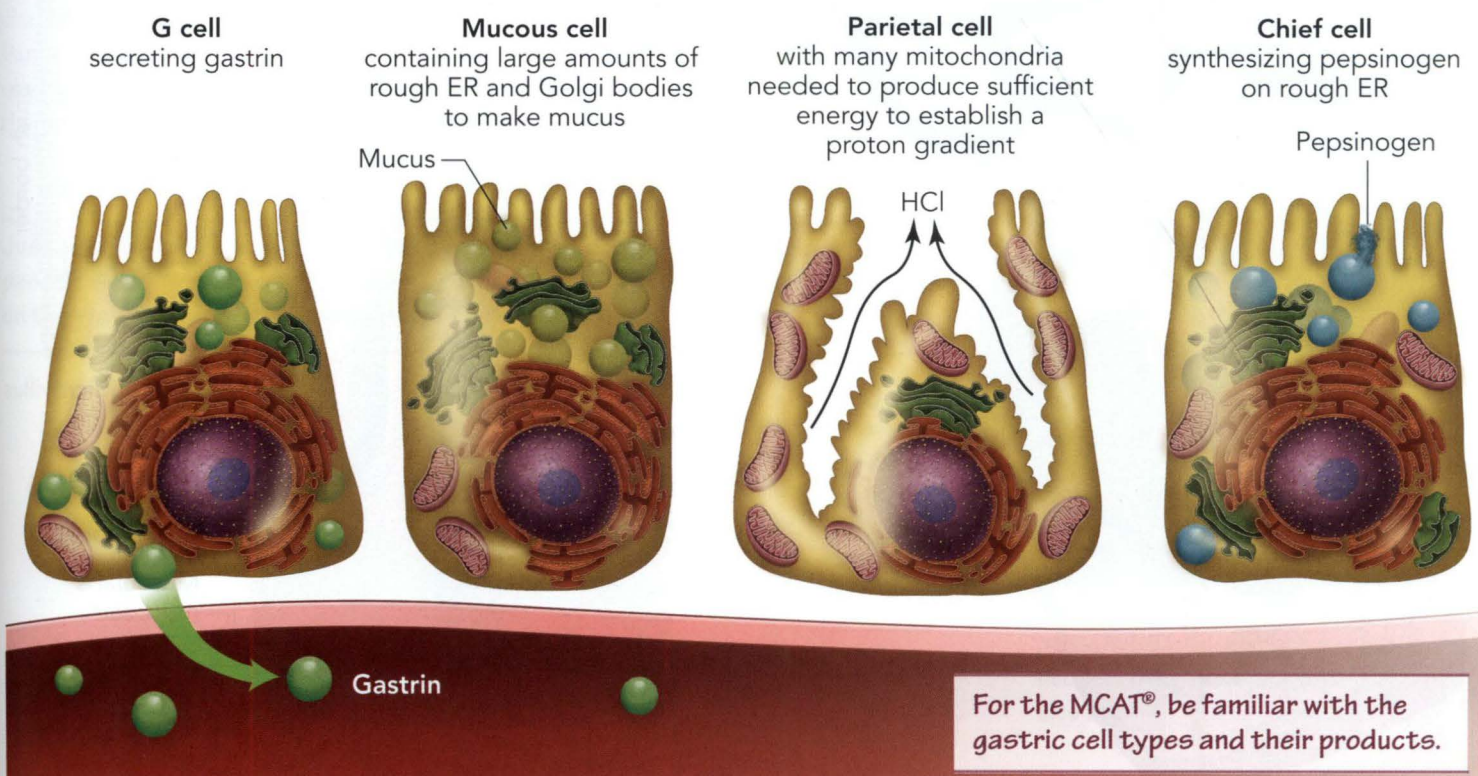
G cells secrete **gastrin**, a large peptide hormone that stimulates parietal cells to secrete HCl. G cells communicate with both the outside (the stomach lumen) and the inside (the bloodstream) of the body. The G cells in the stomach wall are activated through a variety of methods, including the presence of polypeptides in the stomach, stomach distension, and input from the parasympathetic nervous system through the vagus nerve. When an activated G cell releases gastrin into the bloodstream, the signal causes increased HCl production in stomach parietal cells. The major hormones that affect the secretion of the stomach juices are acetylcholine, gastrin, and *histamine*. Acetylcholine increases the secretion of all cell types. Gastrin and histamine mainly increase HCl secretion.

The function of pepsin is to break down proteins. The body, which is made out of proteins, has to be careful about where pepsin is secreted to avoid digesting its own cells! The pepsin precursor, pepsinogen, is inactive and therefore doesn't harm the cells of the stomach as it is released. It only becomes active in response to the acidic environment of the stomach.

MCAT® THINK

The cell types in the stomach wall are a good example of how form follows function. Parietal cells use a lot of energy to create HCl for digestion, so these cells contain large numbers of mitochondria. Cells specializing in secretion, such as mucous cells, chief cells, and G cells, contain larger amounts of rough endoplasmic reticulum and Golgi bodies.

FIGURE 5.4 Gastric Gland Cell Types



For the MCAT®, be familiar with the gastric cell types and their products.



False-color scanning electron micrograph of a section through the wall of the human duodenum, showing the villi, which project 0.5 to 1 mm out into the intestinal lumen. Villi greatly increase the effective absorptive and secretory surface of the mucosa (mucus membrane) lining the small intestine. Each villus contains a central core of connective tissue (yellowish orange). This tissue contains large blood vessels, capillaries, some smooth muscle cells, and a lymph vessel known as a lacteal.

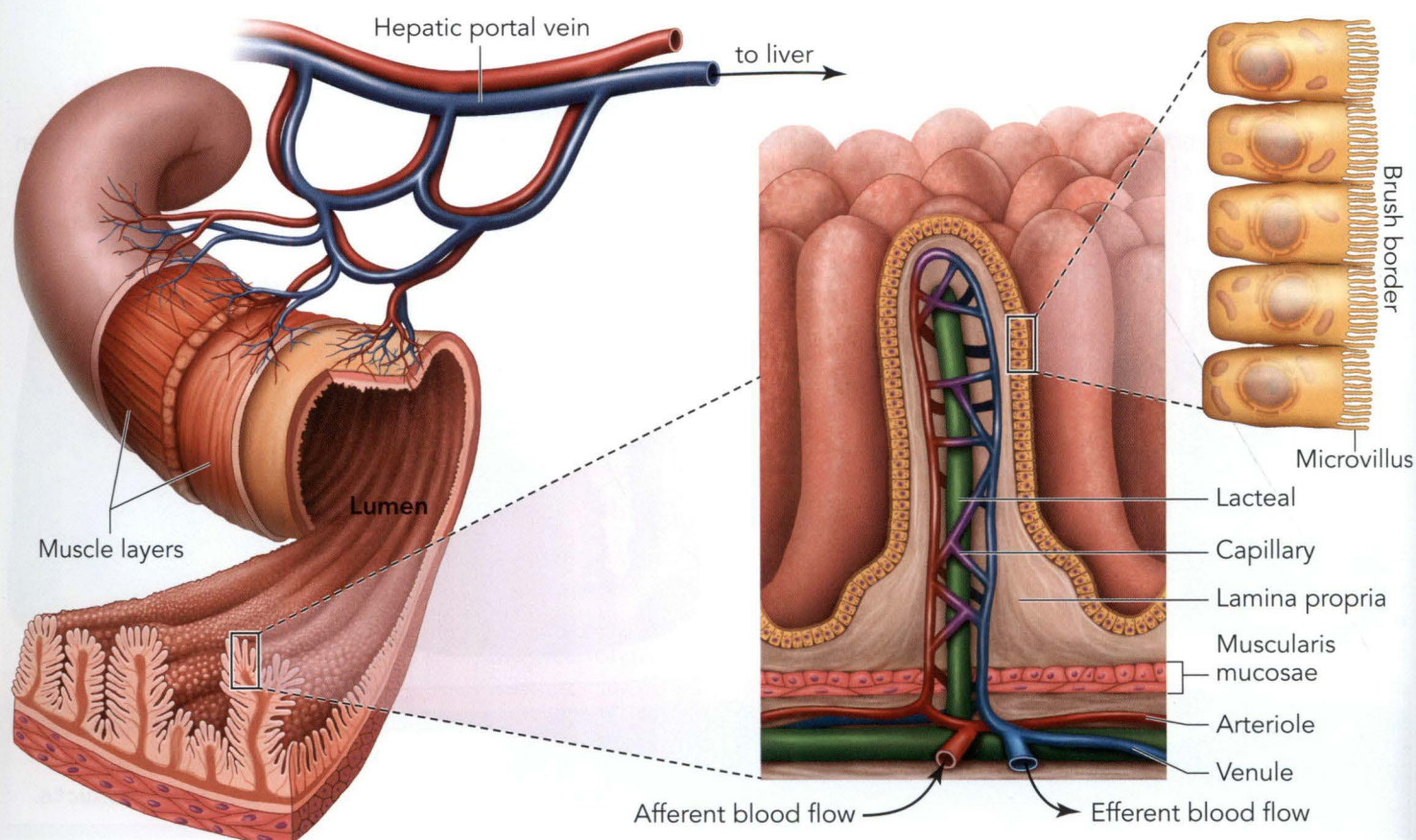
The Small Intestine

About 90% of digestion and absorption occurs in the small intestine. In a living human, the small intestine is about 3 meters in length. As food is digested, it passes through the three parts of the small intestine: the **duodenum**, the **jejunum**, and then the **ileum**. Most digestion occurs in the duodenum, and most absorption occurs in the jejunum and ileum. The wall of the small intestine is similar to the wall of the stomach except that the outermost layer contains finger-like projections called **villi** (Figure 5.5). The villi increase the surface area of the intestinal wall, allowing for greater digestion and absorption. Within each villus are a capillary network and a lymph vessel, called a **lacteal**. Nutrients absorbed through the wall of the small intestine pass into the capillary network or the lacteal, depending on the type of macromolecule.

On the apical (lumen side) surface of the cells of each villus (cells called *enterocytes*) are much smaller finger-like projections called **microvilli**. The microvilli increase the surface area of the intestinal wall still further. Ample surface area is essential to facilitate the absorption of nutrients through the wall of the digestive tract and into the body. Under a light microscope, the microvilli appear as a fuzzy covering, called the brush border. The **brush border** contains membrane bound digestive enzymes, such as carbohydrate digesting enzymes (*dextrinase*, *maltase*, *sucrase*, and *lactase*), protein-digesting enzymes called peptidases, and nucleotide-digesting enzymes called *nucleosidases*. Some of the epithelial cells are **goblet cells** that secrete mucus to lubricate the intestine and help protect the brush border from mechanical and chemical damage. Dead cells regularly slough off into the lumen of the intestine and are replaced by new cells.

Digestion occurs in the small intestine on both a small and large scale. The breakdown of macromolecules into smaller pieces takes place within the lumen of the small intestine. These pieces are then broken down ever further within the brush border. Micro-digestion within the brush border is an example of how the

FIGURE 5.5 Small Intestine and Villus



size of a structure matches the task that it carries out. The microvilli of the brush border are very small and are located directly adjacent to the channels through which nutrients will be transported. Microvilli are ideally sized to capture the pieces of macromolecules that have been broken down in the lumen. Enzymes in the microvilli further break down these pieces into their smallest constituent parts (e.g. amino acids, dipeptides, or tripeptides, in the case of proteins). The constituent parts are then transported through the membrane and into the body.

Located deep between the villi are the intestinal exocrine glands, called *crypts of Lieberkuhn*. These glands secrete an intestinal juice with a pH of 7.6 and *lysozyme*. Lysozyme contributes to regulation of bacteria within the intestine.

As discussed throughout this section, the cells lining the small intestine are highly specialized for absorption. As a tradeoff, these cells are not as well suited to the secretion of digestive enzymes. Digestion within the small intestine is therefore aided by digestive enzymes from the pancreas.

The Pancreas

The **pancreas** aids the digestive process in a number of ways. The fluid inside the duodenum has a pH of 6 because the acid from the stomach is neutralized by **bicarbonate ion** secreted by the pancreas. The pancreas is an endocrine gland that secretes insulin and glucagon, regulators of carbohydrate and fat metabolism. The pancreas also acts as an exocrine gland, creating enzymes that aid the digestive processes in the small intestine. The *acinar cells* of the pancreas release digestive enzymes into the *main pancreatic duct*, which carries the enzymes to the duodenum. The major enzymes released by the pancreas are trypsin, chymotrypsin, pancreatic amylase, lipase, ribonuclease, and deoxyribonuclease. All pancreatic enzymes are released as zymogens. Trypsin is activated by the enzyme *enterokinase* located in the brush border. Activated trypsin then activates the other enzymes.

Trypsin and **chymotrypsin** degrade proteins into small polypeptides. Another pancreatic enzyme, *carboxypolypeptidase*, cleaves amino acids from the sides of these peptides. Most proteins reach the brush border as small polypeptides. Here they are reduced to amino acids, dipeptides, and tripeptides before they are absorbed into the enterocytes. Enzymes within the enterocytes reduce the dipeptides and tripeptides to amino acids.

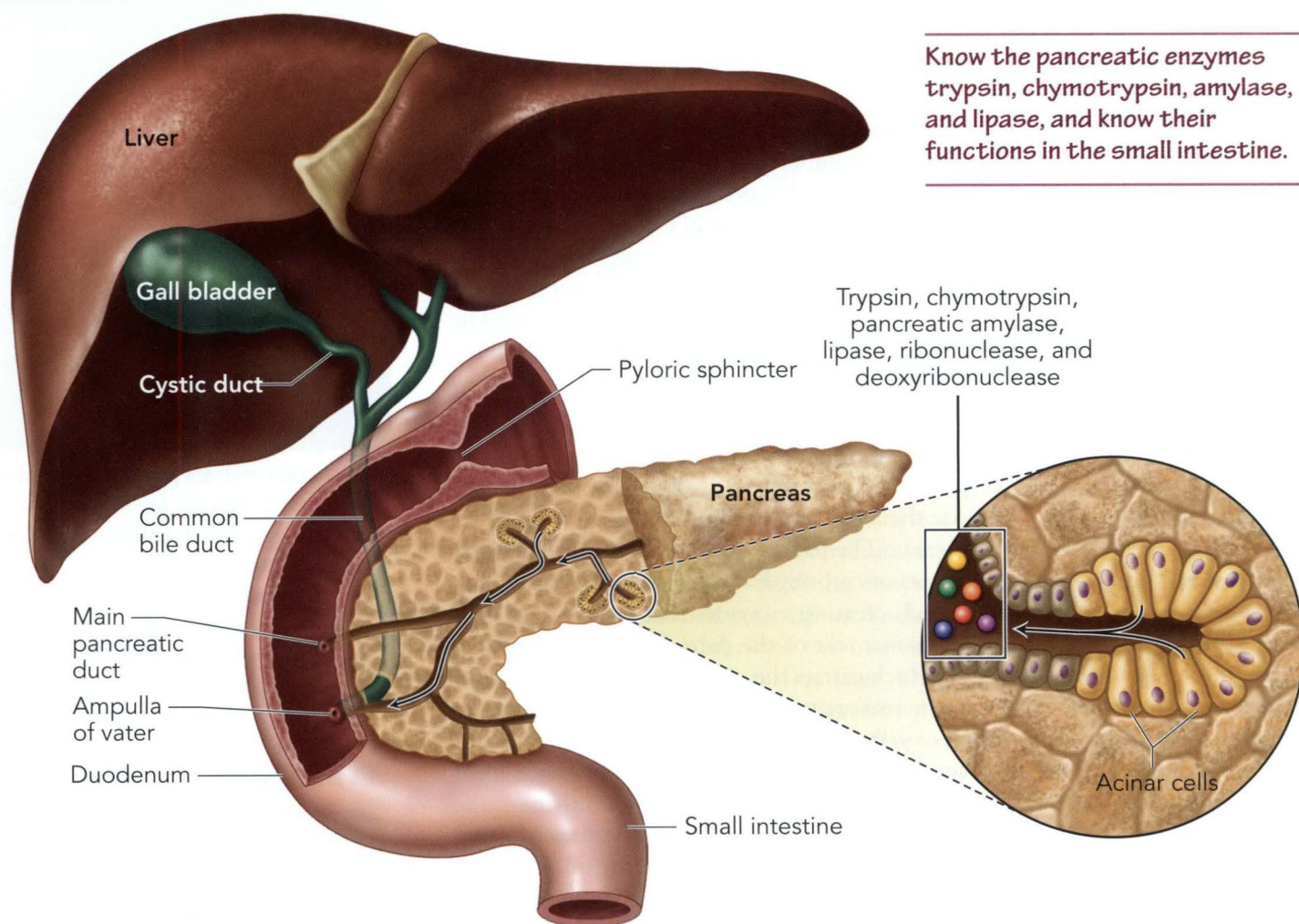
Like salivary amylase, **pancreatic amylase** hydrolyzes polysaccharides to disaccharides and trisaccharides; however, pancreatic amylase is much more powerful. Pancreatic amylase degrades nearly all of the carbohydrates from the chyme into oligosaccharides. The brush border enzymes finish degrading these polymers to their respective monosaccharides before they are absorbed.

Just as zymogens are released in the stomach, digestive enzymes from the pancreas are released as zymogens so that they do not digest the pancreas on the way to their destination – the food in the small intestine.



Several lobes of the pancreas are seen here, separated by fissures. The smaller sections seen on each lobe are clusters of acinar cells. The enzymes secreted by acinar cells drain into a highly branched system of ducts of increasing size, terminating in the main pancreatic duct, which feeds into the duodenum. The other function of the pancreas is the endocrine secretion of hormones, particularly insulin. Fragments of connective tissue and blood vessels are also seen.

FIGURE 5.6 The Pancreas



Know the pancreatic enzymes trypsin, chymotrypsin, amylase, and lipase, and know their functions in the small intestine.

Bile is necessary to increase the surface area of fat, but it does not digest the fat. In other words, bile physically separates fat molecules, but does not break them down chemically.

Lipase degrades fat, specifically **triglycerides**. However, since the intestinal fluid is an aqueous solution, the fat clumps together, reducing the surface area upon which lipase can act. This problem is solved by the addition of **bile**. Bile is produced in the liver and stored in the **gall bladder**. The gall bladder releases bile through the *cystic duct*, which empties into the *common bile duct* shared with the liver. The common bile duct empties into the *pancreatic duct* before connecting to the duodenum. In the small intestine, bile emulsifies the fat, breaking it up into small particles without changing it chemically. Emulsification increases the surface area of the fat so that lipase can degrade it into mainly fatty acids and monoglycerides. These products are shuttled to the brush border in bile micelles and then absorbed by the enterocytes. Much of the bile is reabsorbed by the small intestine and transported back to the liver.

Even though the pancreas is located right next to the small intestine, the communication between them is not direct, instead taking place through hormones. Recall that hormones circulate throughout the bloodstream. They travel to all parts of the body, including the pancreas. When the small intestine secretes hormones to communicate with its neighbor, the pancreas, it is much like using a cell phone to call your friend who is in the next room!

The Large Intestine

The large intestine has five parts:

1. **ascending colon**;
2. **transverse colon**;
3. **descending colon**;
4. **sigmoid colon**; and
5. **rectum**.

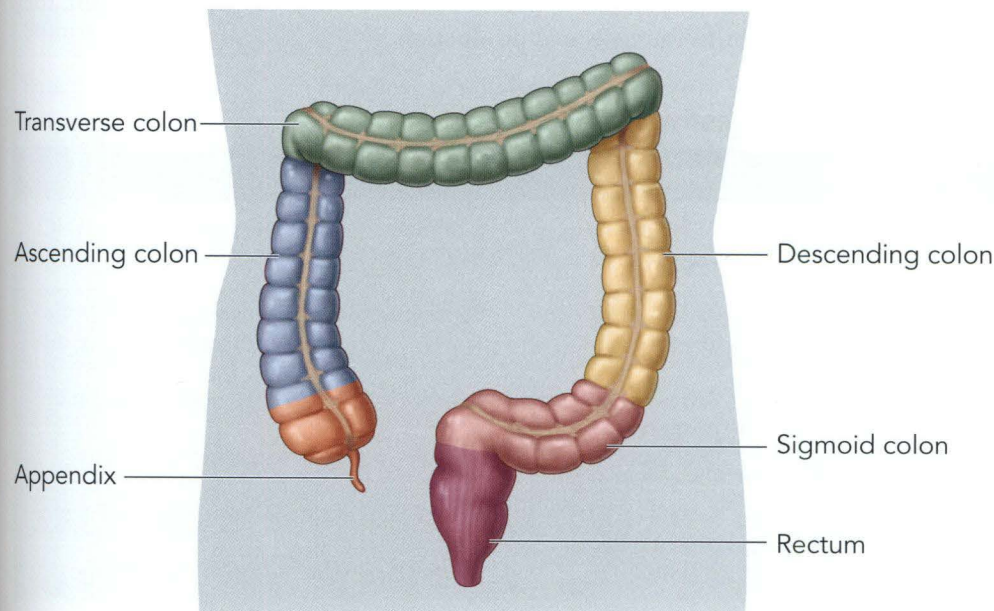
The large intestine is involved in excretion, absorption, and some digestion. The major functions of the large intestine are **water absorption** and **electrolyte absorption**. When these functions fail, diarrhea results. The large intestine also contains a variety of **bacterial flora**. The bacteria are in a symbiotic relationship with the human that they inhabit. They live off of partially digested food within the digestive tract and, in turn, produce vitamin K, B12, thiamin, and riboflavin that can be used by the body.

Healthy **feces** are composed of 75% water. The remaining solid mass is 30% dead bacteria, 10–20% fat (mainly from bacteria and sloughed enterocytes), 10–20% inorganic matter, 2–3% protein, and 30% roughage (i.e. cellulose) and undigested matter. The rectum acts as a storage receptacle for feces until the waste is eliminated through the anus.



The folded structure of the large intestine is shown above.

FIGURE 5.7 Large Intestine



Whenever you get an MCAT® question involving the large intestine, think of water absorption. Profuse water loss in the form of diarrhea often results when there is a problem with the large intestine. Be aware that there is a symbiotic relationship between humans and bacteria in the large intestine. Bacteria get our leftovers, and we get certain vitamins from them. We have more bacteria in our gut than we have cells. Bacteria can sometimes cause disease, but in the large intestine they are necessary for our survival. See the Cell Lecture for more about symbiotic relationships and bacteria.

The hormones involved in digestion are part of the **endocrine** (not exocrine) system and are a means of communication between organs of the digestive system. **Hormones** circulate within the bloodstream, so this kind of communication takes place within, rather than outside, the body.

Although there is inter-communication between the organs of digestion and the brain, the hormonal regulation in digestion tends to function according to an orderly chain of command. The brain stimulates the stomach to begin the digestive process; the stomach signals the small intestine; and the small intestine releases hormones that act on the pancreas. All of these processes promote normal digestion and also provide feedback to the brain on how digestion is progressing in the body.

Much of the nervous input to the digestive system takes place through the enteric nervous system. The **enteric nervous system** consists of a large network of neurons surrounding the digestive organs, helping to regulate processes such as smooth muscle contraction (peristalsis), fluid exchange, blood flow to the digestive organs, and hormone release. Nervous input from the brain also helps start the production of hormones. Parasympathetic input via the vagus nerve helps prepare the stomach and small intestine for digestion. As described in the context of the stomach, parasympathetic nervous stimulation causes the stomach to produce gastrin in anticipation of digestion. (For detailed information on the parasympathetic system, see the Nervous System Lecture.) Gastrin is one of the major hormones of digestion because of its action in causing increased HCl production. The stomach can also use gastrin to send signals to itself. The fuller the stomach becomes, the more acid it needs for digestion. When G cells sense that the stomach is full, they release more gastrin to increase acid production.

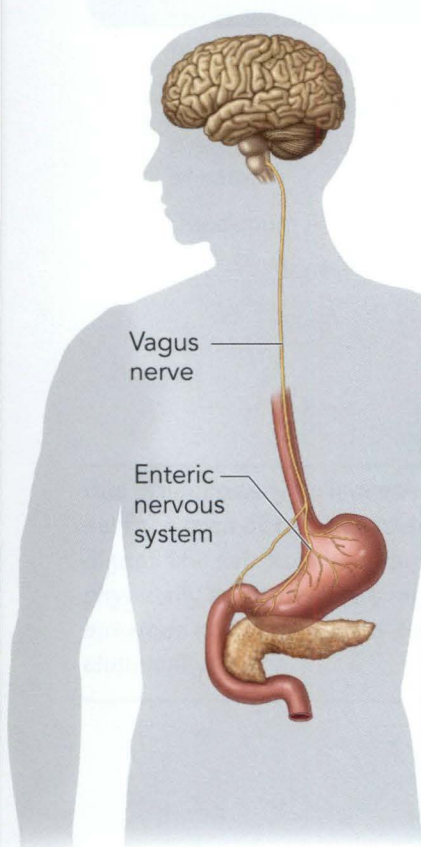


TABLE 5.1 > Vagus Nerve and Digestive Hormones

Site	Hormone	Stimulus	Target	Effects
Stomach	Gastrin	ACh release from vagus nerve	Stomach	Stimulates production of HCl
Duodenum	Secretin	Arrival of HCl in chyme	Pancreas	Stimulates secretion of sodium bicarbonate and enzymes
	Gastric inhibitory peptide	Arrival of fat and protein digestates in chyme	Pancreas	Stimulates enzyme secretion
			Stomach	Decreases motor activity
	Cholecystikinin (CCK)	Arrival of fat digestates in chyme	Pancreas	Stimulates enzyme secretion
			Stomach	Decreases motor activity

Signals from the stomach to the small intestine usually take the form of the release of chyme. The presence of chyme in the duodenum is both the message and the messenger telling the duodenum to start digestion.

Other important digestive hormones include *secretin*, *cholecystikinin*, and *gastric inhibitory peptide*, local peptide hormones secreted by the small intestine after a meal that act on the pancreas. Each of these hormones increases blood insulin levels, especially in the presence of glucose.

Secretin acts as a messenger from the small intestine to the pancreas. It lets the pancreas know that chyme has reached the small intestine and that pancreatic enzymes are needed for digestion. Hydrochloric acid in the duodenum causes secretin release. When it reaches the pancreas, secretin stimulates the release of sodium bicarbonate, which helps control pH, along with the pancreatic enzymes that aid in the digestive processes of the duodenum.

The contents of the duodenum may also influence what type of hormones are released. *Gastric inhibitory polypeptide* is released in response to fat and protein digests in the duodenum, and to a lesser extent, in response to carbohydrates. It has a mild effect in decreasing the motor activity of the stomach. Similarly, food in the upper duodenum, especially fat digests, causes the release of *cholecystokinin* (CCK). Cholecystokinin causes gallbladder contraction and pancreatic enzyme secretion. It also decreases the motor activity of the stomach. These changes occur because fats are more difficult to digest than carbohydrates, due to the fact that they are hydrophobic and the digestive tract is an aqueous environment. The decreased motility of the stomach resulting from the action of both of these hormones causes the stomach to release chyme into the duodenum at a slowed pace, giving the pancreatic enzymes in the duodenum more time to emulsify fats.

TABLE 5.2 > Major Digestive Enzymes in Humans

Source/Enzyme	Action
Salivary Glands	
Salivary amylase	Starch → Maltose
Stomach	
Pepsin	Proteins → Peptides; autocatalysis
Pancreas	
Pancreatic amylase	Starch → Maltose
Lipase	Fats → Fatty acid and glycerol
Nuclease	Nucleic acids → Nucleotides
Trypsin	Proteins → Peptides; Zymogen activation
Chymotrypsin	Proteins → Peptides
Carboxypeptidase	Peptides → Shorter peptides and amino acids
Small intestine	
Aminopeptidase	Peptides → Shorter peptides and amino acids
Dipeptidase	Dipeptides → Amino acids
Enterokinase	Trypsinogen → Trypsin
Nuclease	Nucleic acids → Nucleotides
Maltase	Maltose → Glucose
Lactase	Lactose → Galactose and glucose
Sucrase	Sucrose → Fructose and glucose

You don't have to remember all of these gastrointestinal hormones, although they may appear in a passage. Instead, study the major ideas of digestion. The body eats in order to gain energy from food. The digestive system breaks down the food so it can be absorbed into the body. If the food moved too fast through the digestive tract, it could come out undigested. The stomach stores food and releases small amounts at a time to be digested and absorbed by the intestine. This way, the body can take in (eat) a large amount of food at a single time and take a long time to digest it. Some of the gastrointestinal hormones described in this section help regulate this process.

Digestion is the breakdown of food. The next section will discuss absorption, the process by which byproducts of digestion enter the body.

These questions are NOT related to a passage.

Item 97

As chyme is passed from the stomach to the small intestine, the catalytic activity of pepsin:

- ☐ A) increases because pepsin works synergistically with trypsin.
- ☐ B) increases because pepsin is activated from its zymogen form.
- ☐ C) decreases in response to the change in pH.
- ☐ D) decreases because pepsin is digested by pancreatic amylase in the small intestine.

Item 98

Which of the following is the best explanation for why pancreatic enzymes are secreted in zymogen form?

- ☐ A) A delay in digestion is required in order for bile to increase the surface area of chyme.
- ☐ B) Enzymes are most active in zymogen form.
- ☐ C) Zymogens will not digest bile in the pancreatic duct.
- ☐ D) Pancreatic cells are not as easily replaced as intestinal epithelium.

Item 99

Omeprazole is used to treat duodenal ulcers that result from gastric acid hyper-secretion. Omeprazole blocks the secretion of HCl from the parietal cells of the stomach. Which of the following is LEAST likely to occur in a patient taking omeprazole?

- ☐ A) An increase in microbial activity in the stomach
- ☐ B) A decrease in the activity of pepsin
- ☐ C) An increase in stomach pH
- ☐ D) A decrease in carbohydrate digestion in the stomach

Item 100

Which of the following reaction types is common to the digestion of all macronutrients?

- ☐ A) Hydrolysis
- ☐ B) Reduction
- ☐ C) Glycolysis
- ☐ D) Phosphorylation

Item 101

One function of the large intestine is:

- ☐ A) to absorb water.
- ☐ B) to secrete excess water.
- ☐ C) to digest fat.
- ☐ D) to secrete urea.

Item 102

Salivary α -amylase begins the digestion of:

- ☐ A) lipids.
- ☐ B) nucleic acids.
- ☐ C) proteins.
- ☐ D) carbohydrates.

Item 103

All of the following enzymes are part of pancreatic exocrine function EXCEPT:

- ☐ A) bile.
- ☐ B) chymotrypsin.
- ☐ C) pancreatic amylase.
- ☐ D) lipase.

Item 104

In humans, most chemical digestion of food occurs in the:

- ☐ A) mouth.
- ☐ B) stomach.
- ☐ C) duodenum.
- ☐ D) ileum.

Molecular Digestion and Absorption

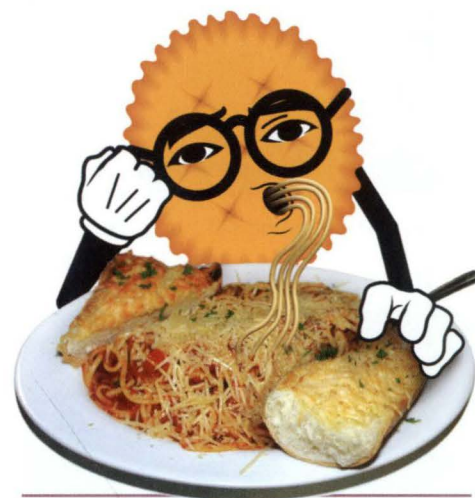
The function of the entire digestive tract is to convert ingested food into basic nutrients that can be absorbed by the small intestine. Once absorbed into the enterocytes, nutrients are processed and carried to individual cells throughout the body for use. The following section describes the process of absorption and the fates of the major nutrients: carbohydrates, proteins, and fats. The polarity of nutrients is an important factor when considering how nutrients pass through digestive membranes and how they travel once inside the body. This section is mainly background knowledge to provide the bigger picture of the digestive system; very little of this information will be tested directly on the MCAT®.

It is not necessary to memorize all of the details of the mechanisms for digestion of carbohydrates, proteins, and fats. Instead, understand the general principles. Recall that what substances are able to pass through plasma membranes is highly dependent on size and polarity. The inside of a plasma membrane is non-polar. In order to pass through a membrane, polar molecules must be broken down into smaller pieces. Non-polar molecules can pass through the membrane even if they are large. In the aqueous, polar environment of the cytoplasm or bloodstream, the opposite is true. Larger polar molecules travel freely, while non-polar molecules require assistance to travel through these polar environments. Use these principles to guide your understanding of digestion and absorption of macromolecules.

Carbohydrates

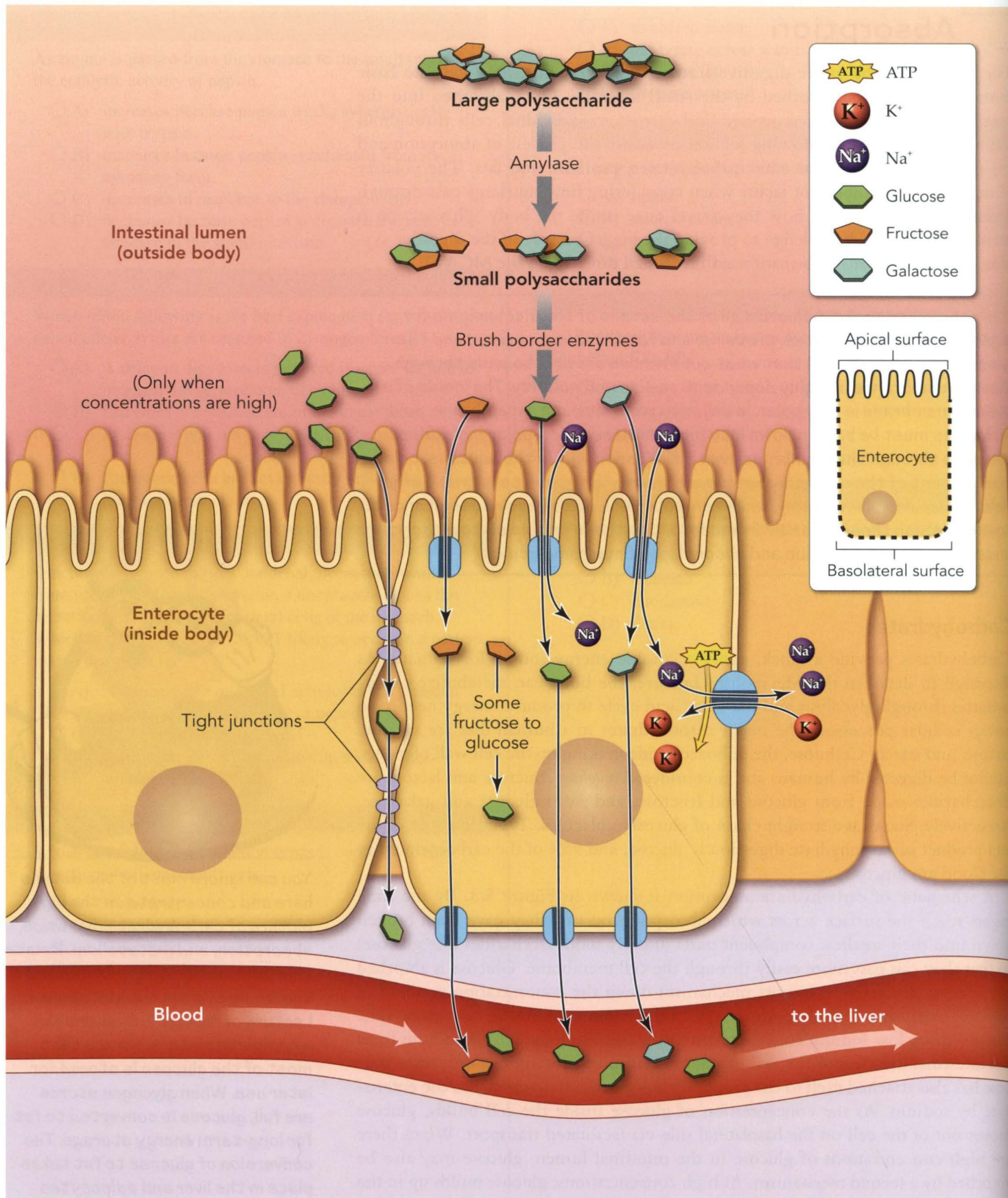
Carbohydrates provide a quick, easily accessible energy source for humans. As discussed in detail in the Metabolism Lecture, the body can metabolize carbohydrates through glycolysis and the citric acid cycle to produce energy needed to power cellular processes. The major carbohydrates in a human diet are sucrose, lactose, and starch. Cellulose, the polysaccharide making up the cell wall of plants, cannot be digested by humans and is considered *roughage*. Sucrose and lactose are disaccharides made from glucose and fructose, and from glucose and galactose, respectively. Starch is a straight chain of glucose molecules. Typically, 80% of the end product of carbohydrate digestion is glucose, and 95% of the carbohydrates in the blood are glucose.

A schematic of carbohydrate absorption is shown in Figure 5.8. By the time sugars reach the surface across which absorption occurs, they have been broken down into their smallest component parts (usually monosaccharides like glucose) so that they can pass more easily through the cell membrane. Glucose is absorbed via a secondary active transport mechanism down the concentration gradient of sodium. Sodium is actively pumped out of the enterocyte on the basolateral side. The resulting low sodium concentration inside the enterocyte drags sodium from the intestinal lumen into the cell through a transport protein, but only after glucose has also attached itself to the protein. Thus glucose is dragged into the enterocyte by sodium. As the concentration of glucose inside the cell builds, glucose moves out of the cell on the basolateral side via facilitated transport. When there are high concentrations of glucose in the intestinal lumen, glucose may also be absorbed by a second mechanism. At high concentrations, glucose builds up in the space around the cells and raises the osmotic pressure there. The aqueous solution of the lumen is dragged into the space, pulling glucose along with it.



You can ignore most of the details here and concentrate on the big picture of carbohydrate digestion, absorption, and metabolism. Relate this information to glycolysis and the Krebs cycle in the Metabolism Lecture of Biology 1: Systems for a complete picture. Notice that most of the glucose is stored for later use. When glycogen stores are full, glucose is converted to fat for long-term energy storage. The conversion of glucose to fat takes place in the liver and adipocytes and is stored in the adipocytes. Keep in mind the role of the liver in processing carbohydrates.

FIGURE 5.8 Carbohydrate Digestion and Absorption



Galactose follows a similar absorption path to glucose. Fructose is absorbed via facilitated diffusion, and much of it is converted to glucose inside the enterocyte. All carbohydrates are absorbed into the bloodstream and carried by the portal vein to the liver. One of the functions of the liver is to maintain a fairly constant blood glucose level by releasing and storing glucose. The liver absorbs the carbohydrates and converts nearly all the galactose and fructose into glucose. If blood glucose levels are sufficient, the liver converts excess glucose into glycogen for storage. The formation of glycogen is called **glycogenesis**. When the blood glucose level decreases, the reverse process, **glycogenolysis**, takes place in the liver and glucose is returned to the blood.

In all cells except enterocytes and the cells of the renal tubule, glucose is transported from high concentration to low concentration through facilitated diffusion. Nearly all cells are capable of producing and storing some glycogen, but only muscle cells and especially liver cells store large amounts. When the cells have reached their saturation point with glycogen, carbohydrates are converted to fatty acids and then triglycerides in a process requiring a small amount of energy.

Proteins

Like carbohydrates, proteins tend to be hydrophilic and cannot easily pass through the cell membrane. They are also broken down into small pieces during absorption. Protein digestion results in amino acids, dipeptides, and tripeptides. Absorption of many of these products occurs via a co-transport mechanism down the concentration gradient of sodium, similar to the mechanism used by glucose. A few amino acids are transported by facilitated diffusion. Because the chemistry of amino acids varies greatly, each transport mechanism is specific to a few amino acids or polypeptides.

Nearly all polypeptides that are absorbed into an enterocyte are hydrolyzed to their amino acid constituents by enzymes. From the enterocytes, amino acids are absorbed directly into the blood and then are taken up by all cells of the body, especially the liver. Transport into the cells may be facilitated or active, but is never passive, since amino acids are too large and polar to diffuse through the membrane. The cells immediately create proteins from the amino acids so that the intracellular amino acid concentration remains low, preserving the concentration gradient. Most proteins are easily broken down and returned to the blood when needed. When cells reach their upper limit for protein storage, amino acids can be burned for energy or converted into fat for storage. Approximately 4 Calories of energy can be gained per gram of protein. By contrast, carbohydrates produce about 4.5 Calories per gram, and fats produce about 9 Calories per gram. Ammonia, a nitrogen containing compound, is a byproduct of gluconeogenesis from proteins. Nearly all ammonia is converted to **urea** by the liver and then excreted in the urine.

Again, concentrate on the big picture. Remember that virtually all dietary protein is completely broken down into its amino acids before being absorbed into the blood. In fact, any protein that is not broken down completely may cause allergic reactions. Also, when you think of proteins, think nitrogen.

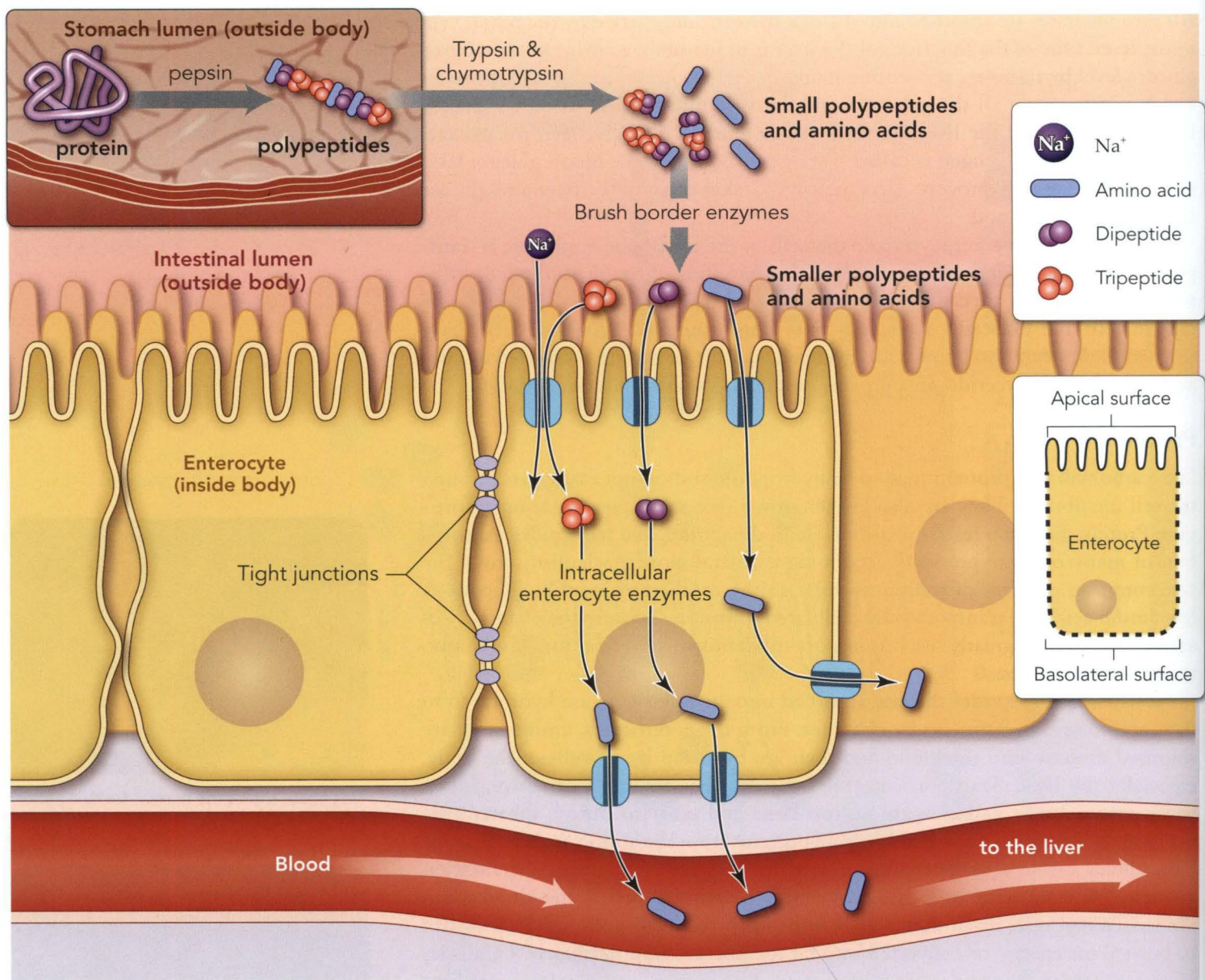


This photo shows the normal surface pattern of the jejunal mucosa.



This photo shows the jejunal mucosa of a person with celiac disease. Celiac disease is an uncommon condition caused by hypersensitivity to a component of gluten, a protein in wheat flour.

FIGURE 5.9 Protein Digestion and Absorption

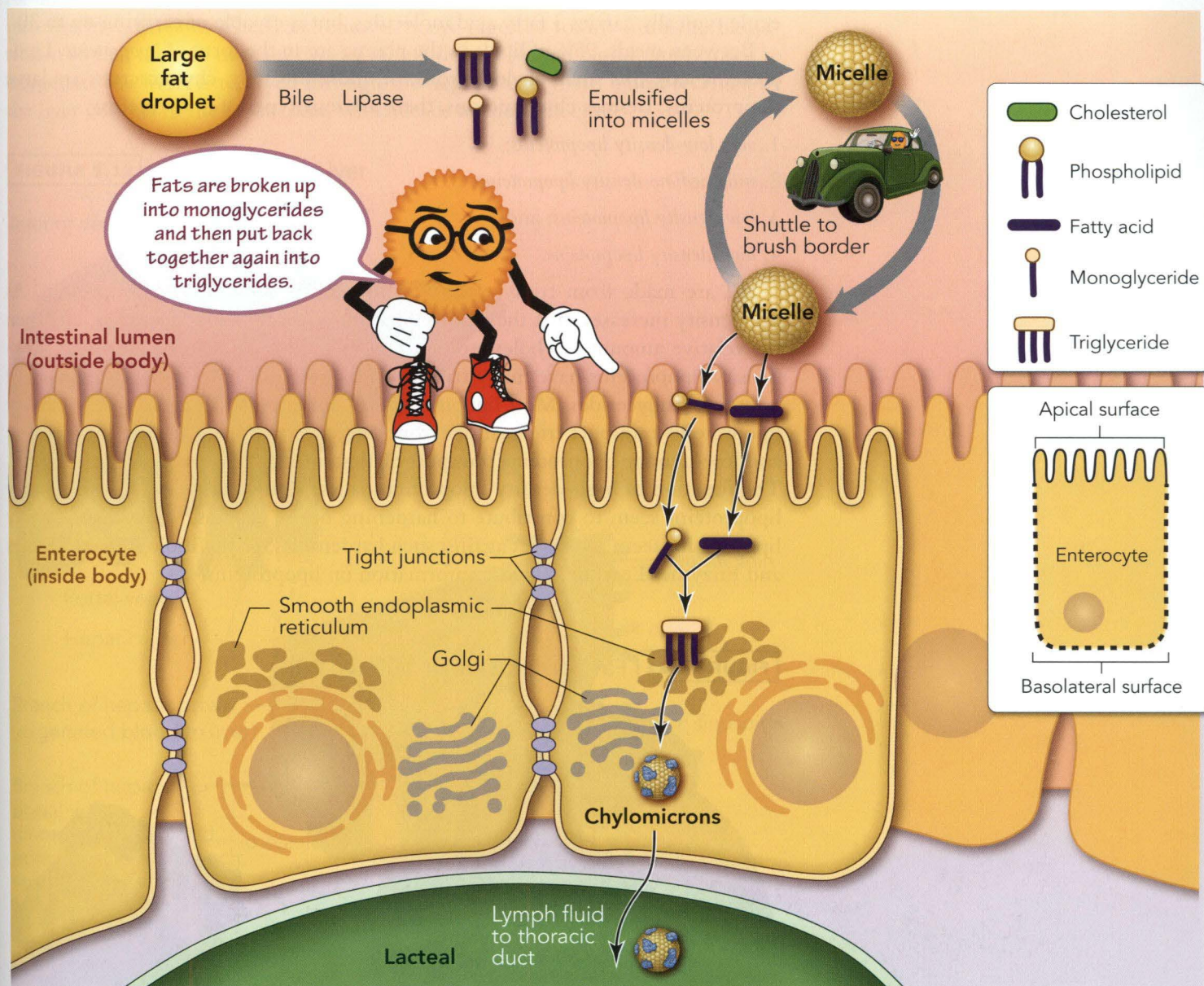


Fats

Because they are hydrophobic molecules, the absorption of fats encounters many challenges that are opposite to those of proteins and carbohydrates. Fats are not easily transported in the aqueous environments of the digestive lumen and the intracellular space, but they easily pass through hydrophobic cell membranes. Most dietary fat consists of triglycerides, which are broken down to monoglycerides and fatty acids in the digestive process. These components are then shuttled to the brush border by bile micelles. At the brush border, fats easily diffuse through the enterocyte membrane (Figure 5.10). After delivering their fats, the micelles return to the chyme to pick up more fat digestates. Micelles also carry small amounts of hydrolyzed phospholipids and cholesterol, which, like monoglycerides and fatty acids, diffuse through the enterocyte membrane.

Once inside the enterocytes, fats must be altered such that they can travel through the aqueous environment of the cell. Monoglycerides and fatty acids are converted back into triglycerides at the smooth endoplasmic reticulum. The newly synthesized triglycerides aggregate within the smooth endoplasmic reticular lumen along with some cholesterol and phospholipids. These amphipathic molecules orient themselves with their charged ends pointing outward toward

FIGURE 5.10 Fat Digestion and Absorption



the aqueous solution of the lumen. Apoproteins attach to the outside of these globules. (See the Biological Molecules and Enzymes Lecture in *Biology 1: Molecules* for more on apoproteins.) The globules move to the Golgi apparatus and are released from the cell via exocytosis. Most of these globules, now called *chylomicrons*, move into the lacteals of the lymph system. Note the distinguishing feature of fat metabolism: while carbohydrates and proteins move from the enterocyte into the bloodstream, fats are absorbed into the lymph system. Most ingested fat that is absorbed by this process moves through the lymph system and enters the large veins of the neck at the *thoracic duct*. Small amounts of more water soluble short chain fatty acids are absorbed directly into the blood of the villi.

The concentration of chylomicrons in the blood peaks about 1-2 hours after a meal, but falls rapidly as the fat digestates are absorbed into the cells of the body. The most significant absorption of fat occurs in the liver and adipose tissue. Chylomicrons stick to the side of capillary walls, where *lipoprotein lipase* hydrolyzes the triglycerides. The products immediately diffuse into fat and liver cells, where the triglycerides are reconstituted at the smooth endoplasmic reticulum. Thus, the first stop for most of the digested fat is the liver.

Keep in mind that fat is insoluble in water, so it typically requires a carrier (i.e. a lipoprotein or albumin). For the MCAT®, associate fat with efficient long-term energy storage: lots of calories (energy) per mass.

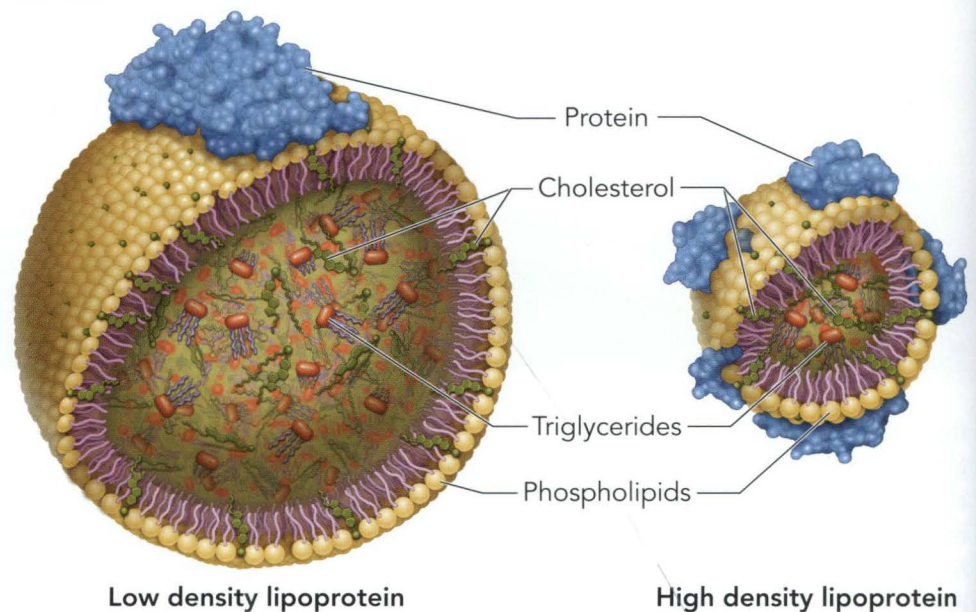
From adipose tissue, most fatty acids are transported in the form of *free fatty acid*, which combines with the protein **albumin** in the blood. A single albumin molecule typically carries 3 fatty acid molecules, but is capable of carrying up to 30.

Between meals, 95% of lipids in the plasma are in the form of *lipoproteins*. Lipoproteins look like small chylomicrons, or, more precisely, chylomicrons are large lipoproteins. Besides chylomicrons, there are four types of lipoproteins:

1. *very low-density lipoproteins*;
2. *intermediate-density lipoproteins*;
3. *low-density lipoproteins*; and
4. *high-density lipoproteins*.

All are made from triglycerides, cholesterol, phospholipids, and protein. As the density increases, first the relative amount of triglycerides decreases, and then the relative amount of cholesterol and phospholipids decreases. Thus, very low-density lipoproteins have many triglycerides, and high-density lipoproteins have very few triglycerides. Most lipoproteins are made in the liver. Very-low density lipoproteins transport triglycerides from the liver to adipose tissue. Intermediate and low-density lipoproteins transport cholesterol and phospholipids to the cells. The function of high-density lipoproteins is less well understood. Lower density lipoproteins seem to contribute to hardening of the arteries, while high-density lipoproteins seem to protect against such hardening. See the Biological Molecules and Enzymes Lecture for more information on lipoproteins.

FIGURE 5.11 Fat Transport Within LDL and HDL



The liver serves a wide variety of functions in the body. Think of the liver as a large warehouse where substances can be recycled into new products, stored for later use, or processed for distribution.

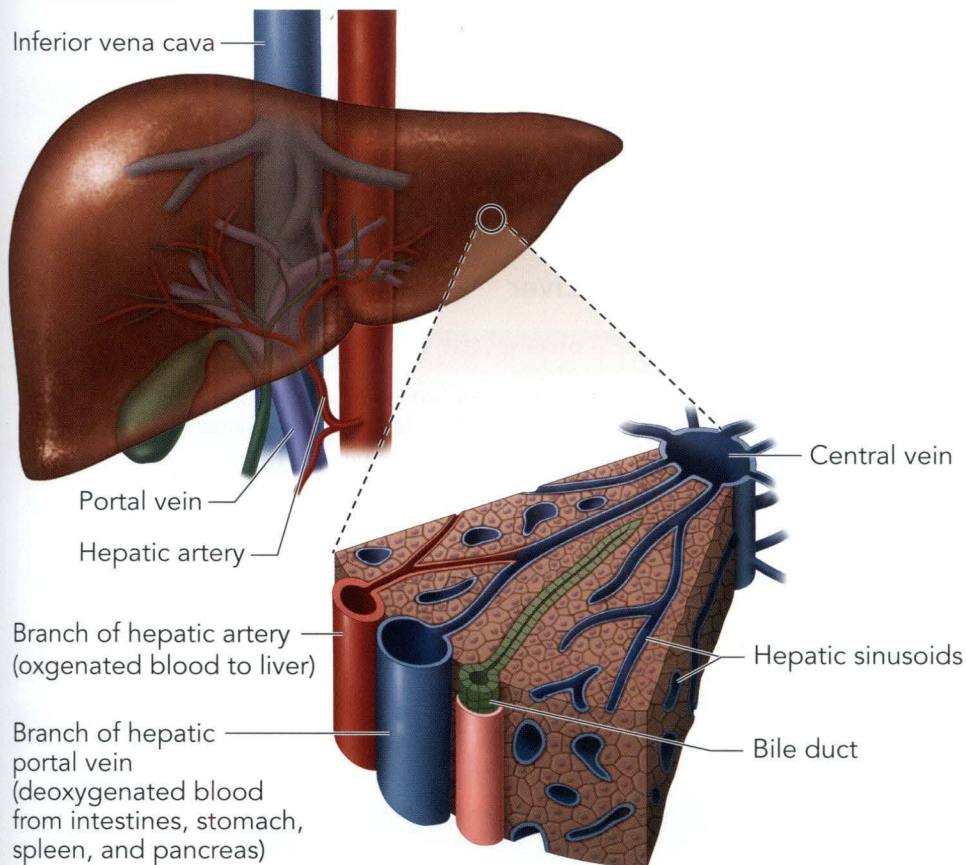
5.5

The Liver: Storage, Distribution, and Detox

The **liver** is located primarily in the upper right-hand quadrant of the abdomen adjacent to the organs of the digestive tract. Blood from the capillary beds of the intestines, stomach, spleen, and pancreas feeds into the large *hepatic portal vein*. The hepatic portal vein carries all of the blood from the digestive system to the liver so that the liver can process the blood before it is re-circulated throughout the rest of

the body. By processing the blood, the liver functions as a screening mechanism for all of the nutrients, toxins, or other molecules that are absorbed from the gut into the bloodstream. The liver removes many ingested toxins from the bloodstream so that they do not enter wider circulation. A second blood supply, used to oxygenate the liver, is received through the hepatic artery. All blood received by the liver collects in the *hepatic vein*, which leads to the vena cava.

FIGURE 5.12 Anatomy of the Liver



The liver has a wide variety of purposes that can be categorized as metabolic, storage, or immune functions.

Metabolic Functions of the Liver

1. **Carbohydrate metabolism:** The liver maintains normal blood glucose levels through **gluconeogenesis** (the production of glycogen and glucose from non-carbohydrate precursors), glycogenesis, and release of glucose stores according to the needs of the body.
2. **Fat metabolism:** The liver synthesizes bile from cholesterol and converts carbohydrates and proteins into fat. It oxidizes fatty acids for energy, and forms most lipoproteins. When the liver mobilizes fat for energy, it produces acids called *ketone bodies*. This often results in a condition called *ketosis* or *acidosis*. For the MCAT®, know that when the liver mobilizes fats or proteins for energy, the acidity of the blood increases.

Prothrombin and fibrinogen are important clotting factors. Albumin is the major osmoregulatory protein in the blood. Globulins are a group of proteins that include antibodies. However, antibodies are not produced in the liver. They are made by plasma cells.

3. **Protein metabolism:** The liver deaminates amino acids, forms urea from ammonia in the blood, synthesizes plasma proteins such as fibrinogen, prothrombin, albumin, and most globulins, and synthesizes nonessential amino acids.
4. **Detoxification:** Detoxified chemicals are secreted by the liver as part of bile or modified so that they can be excreted by the kidney.

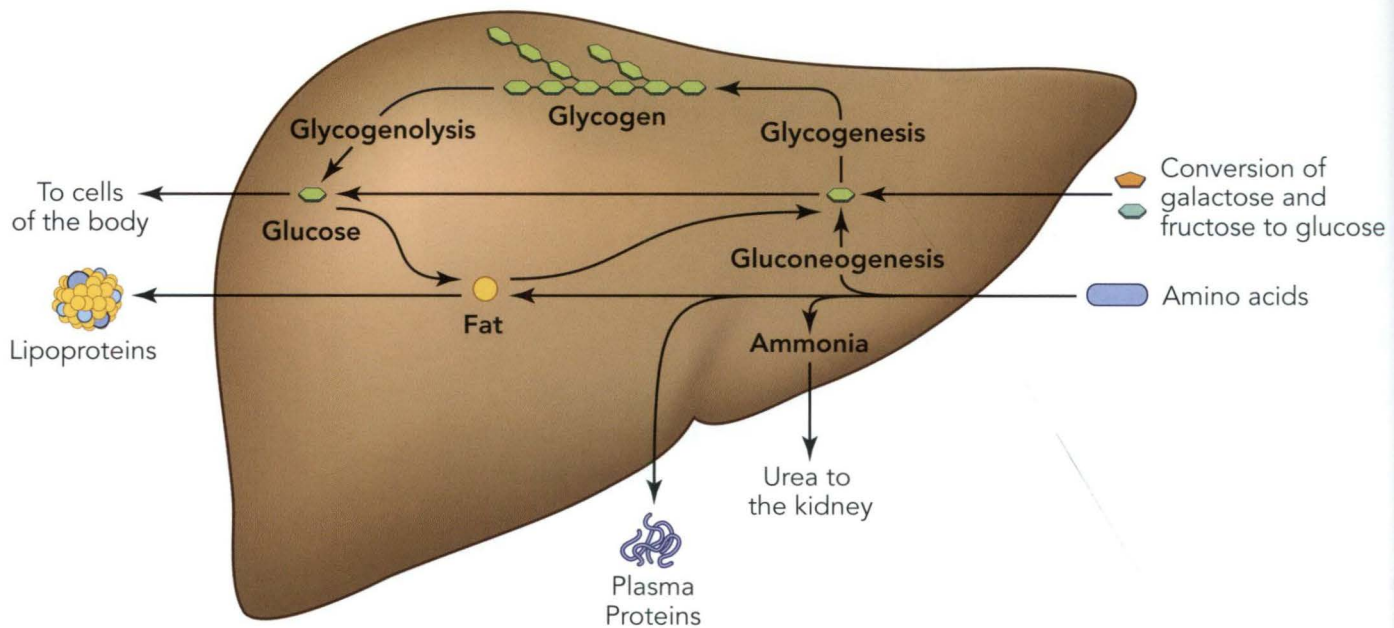
Storage Functions of the Liver

1. **Blood storage:** The liver can expand to act as a blood reservoir for the body.
2. **Glycogen storage:** The liver stores large amounts of glycogen as an energy reserve that can be used to regulate blood glucose levels.
3. **Vitamin storage:** The liver stores vitamins such as vitamins A, D, and B12. The liver also stores iron.

Immune Functions of the Liver

1. **Blood filtration:** *Kupffer cells* phagocytize bacteria picked up from the intestines.
2. **Erythrocyte destruction:** *Kupffer cells* also destroy irregular erythrocytes, although most irregular erythrocytes are destroyed by the spleen.

FIGURE 5.13 Functions of the Liver



These questions are NOT related to a passage.

Item 105

A stomach ulcer may increase the acidity of the stomach. The stomach cells most affected by a stomach ulcer are:

- ☐ A) goblet cells.
- ☐ B) parietal cells.
- ☐ C) chief cells.
- ☐ D) G cells.

Item 106

Which of the following occurs mainly in the liver?

- ☐ A) Fat storage
- ☐ B) Protein degradation
- ☐ C) Glycolysis
- ☐ D) Gluconeogenesis

Item 107

Dietary fat consists mostly of neutral fats called triglycerides. Most digestive products of fat:

- ☐ A) enter intestinal epithelial cells as chylomicrons.
- ☐ B) are absorbed directly into the capillaries of the intestines.
- ☐ C) are degraded to fatty acids by the smooth endoplasmic reticulum of enterocytes.
- ☐ D) enter the lymph system before entering the bloodstream.

Item 108

Which of the following is NOT true concerning the digestive products of dietary protein?

- ☐ A) They are used to synthesize essential amino acids in the liver.
- ☐ B) Some of the products are absorbed into the intestines by facilitated diffusion.
- ☐ C) Energy is required for the intestinal absorption of at least some of these products.
- ☐ D) Deamination of these products in the liver leads to urea in the blood.

Item 109

Cholera is an intestinal infection that can lead to severe diarrhea causing profuse secretion of water and electrolytes. A glucose-electrolyte solution may be administered orally to patients suffering from cholera. What is the most likely reason for mixing glucose with the electrolyte solution?

- ☐ A) When digested, glucose increases the strength of the patient.
- ☐ B) The absorption of glucose increases the uptake of electrolytes.
- ☐ C) Glucose is an electrolyte.
- ☐ D) Glucose stimulates secretion of the pancreatic enzyme, amylase.

Item 110

Most of the glycogen in the human body is stored in the liver and the skeletal muscles. Which of the following hormones inhibits glycogenolysis?

- ☐ A) Cortisol
- ☐ B) Insulin
- ☐ C) Glucagon
- ☐ D) Aldosterone

Item 111

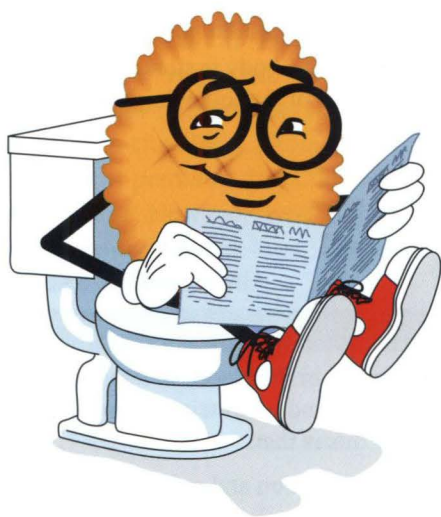
Free fatty acids do not dissolve in the blood, so they must be transported within the body bound to protein carriers. The most likely explanation for this is that:

- ☐ A) blood is an aqueous solution and only hydrophobic compounds are easily dissolved.
- ☐ B) blood is an aqueous solution and only hydrophilic compounds are easily dissolved.
- ☐ C) blood serum contains chylomicrons which do not bind to fatty acids.
- ☐ D) blood serum is lipid based and the polar region of a fatty acid will not be dissolved.

Item 112

Essential amino acids must be ingested because they cannot be synthesized by the body. In what form are these amino acids likely to enter the bloodstream?

- ☐ A) Single amino acids
- ☐ B) Dipeptides
- ☐ C) Polypeptides
- ☐ D) Proteins



I always keep track of where water and solutes are going by remembering that they will go back into my body or into the toilet. When water or a solute moves into the filtrate, it will eventually leave the body as urine going into the toilet. When water or a solute moves out of the filtrate into the medulla, the vasa recta, or the glomerulus, it's going back into my body. Waste products go into the toilet; things I want to keep stay in my body.

The kidney is all about blood composition, blood pressure, and excretion.

5.6

The Kidney: Excretion, Blood Pressure & Composition

The major functions of the **kidney** are:

1. maintaining homeostasis of body fluid volume and thus regulating blood pressure;
2. maintaining homeostasis of plasma solute composition and helping control plasma pH; and
3. excreting waste products, such as urea, uric acid, ammonia, and phosphate.

This section will examine the structure of the kidney and the rest of the urinary system in detail, including the role of each part of the nephron and the function of the juxtaglomerular apparatus. The section also examines the mechanisms that set up and maintain a concentration gradient in the medulla, allowing the kidney to make concentrated urine. The kidney participates in the control of blood pressure in the circulatory system. It is also linked to the metabolic and detoxification functions of the liver through excretion of specific drugs and toxins as well as the products of the urea cycle.

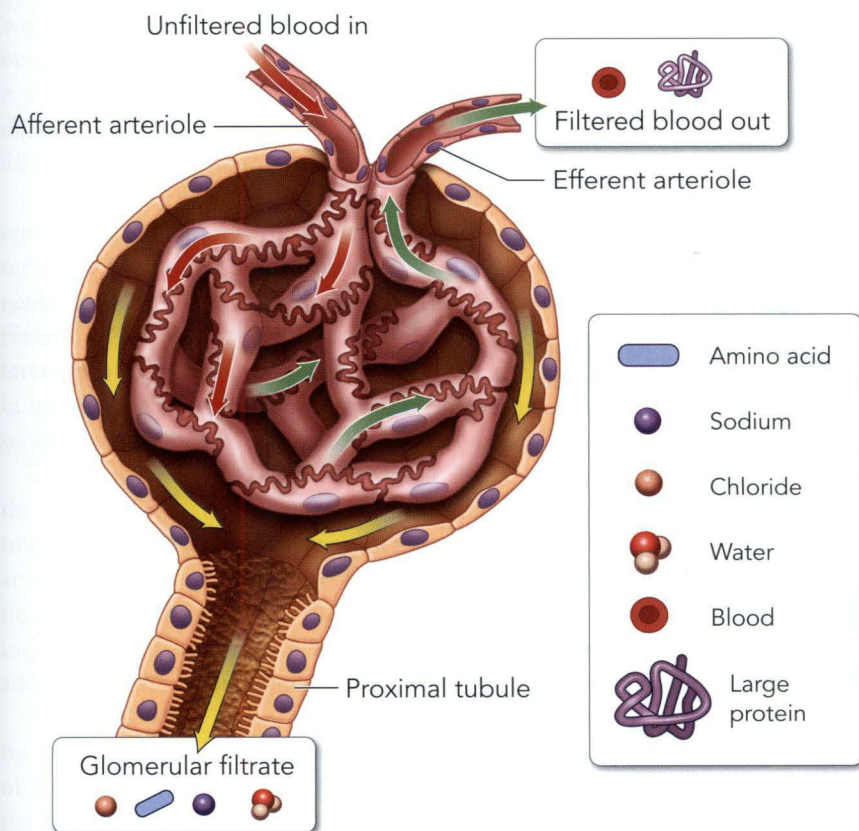
Each one of the two kidneys is a fist-sized organ made up of an outer **cortex** and an inner **medulla**. Urine is created by the kidney and emptied into the **renal pelvis**. The renal pelvis is emptied by the **ureter**, which carries urine to the **bladder**. The bladder is drained to the external environment by the **urethra**. The bladder keeps the **urethra** closed through the action of the urinary sphincter muscles to avoid leaking urine. During urination, the urinary sphincter muscle relaxes and a muscle in the bladder contracts to allow the release of urine.

The functional unit of the kidney is the **nephron**. Each human kidney contains approximately one million nephrons. Blood entering a nephron first flows into a capillary bed called the **glomerulus** (Figure 5.14). Together, **Bowman's capsule** and the glomerulus make up the **renal corpuscle**. **Hydrostatic pressure** forces some plasma through **fenestrations** of the glomerular endothelium and into Bowman's capsule. The fenestrations screen out blood cells and large proteins, preventing them from entering Bowman's capsule. The fluid that enters Bowman's capsule is called **filtrate** or **primary urine**. The retained blood cells and proteins circulate through the peritubular capillary beds.

Filtrate moves from Bowman's capsule to the **proximal tubule**. The proximal tubule is where **secretion** and most **reabsorption** takes place. Drugs, toxins, uric acid, bile pigments, and other solutes are secreted into the filtrate by cells of the proximal tubule and will eventually leave the body as part of the urine. Hydrogen ions are secreted by the proximal tubule through an **antiport** system driven by the sodium concentration gradient. By contrast to the transport system of glucose with sodium discussed earlier in this lecture, in this antiport system the proton crosses the membrane in the opposite direction to sodium.

Reabsorption in the proximal tubule allows the kidney to retain valuable nutrients that were inadvertently filtered out and to return these substances to the rest of the body through the capillary circulation. Reabsorption can occur via passive or active transport. Secondary active transport proteins in the apical membranes of proximal tubule cells carry out the reabsorption of nearly all glucose, most proteins, and other solutes. These transport proteins can become saturated. Once a solute has reached its transport maximum, any more solute is washed into the urine. The concentration of a solute that saturates its transport proteins is called the **transport maximum**. Some solutes that are not actively reabsorbed are reabsorbed

FIGURE 5.14 Glomerulus



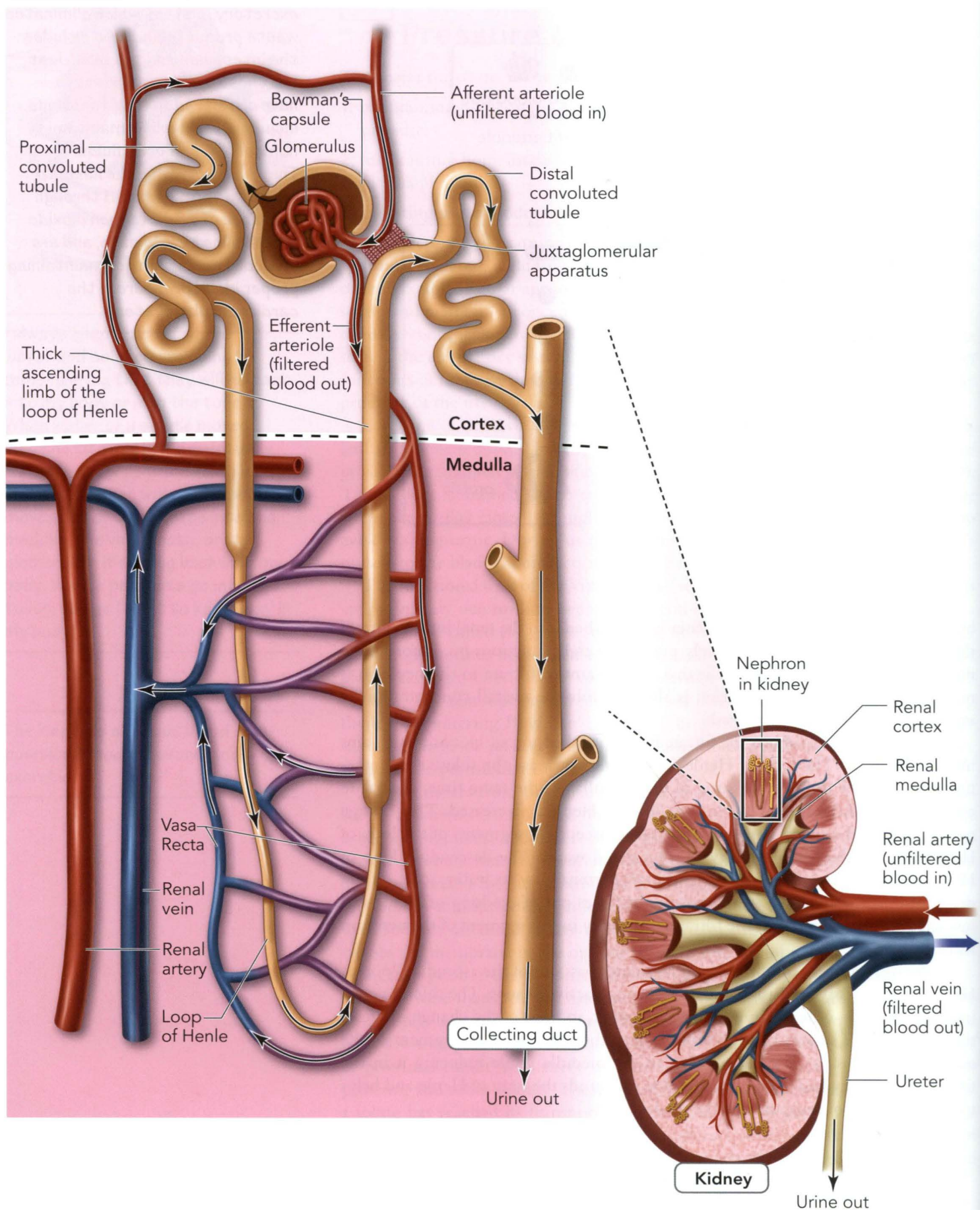
The kidneys are part of the excretory system, which eliminates waste products and also includes the intestines and the skin. Just like those organs, the kidneys have critical additional functions, including their role in maintaining homeostasis of body fluids. They also work with the lungs to maintain the plasma pH through a balance of acidic carbon dioxide and alkaline bicarbonate, and are critically important for maintaining proper blood pressure in the cardiovascular system.

by passive or facilitated diffusion. Water is reabsorbed into the renal interstitium of the proximal tubules across relatively permeable tight junctions by osmosis. The net result of the proximal tubule is that the amount of filtrate in the nephron is reduced and the solute composition is altered while the overall concentration of solutes in the filtrate is unchanged.

From the proximal tubule, the filtrate flows into the **loop of Henle**, which dips into the medulla. The loop of Henle functions to increase the solute concentration, and thus the osmotic pressure, of the medulla. At the same time, the solute concentration of the filtrate leaving the loop of Henle is decreased. This change occurs because the initial descending and final ascending segments of the loop of Henle differ in their permeability to solutes and water. The descending loop of Henle has low permeability to salt and high permeability to water, so as filtrate descends into the medulla, water passively diffuses out of the loop of Henle and into the medulla. As a result, the filtrate osmolarity in this segment of the nephron increases.

As the filtrate rises out of the medulla, solutes pass out of the ascending loop of Henle, first by passive diffusion and then through active pumps. The thick ascending loop of Henle is nearly impermeable to water, so most of the change is due to the movement of solutes from the filtrate into the medulla. This segment of the nephron increases solute concentration in the medulla while reducing it in the filtrate. A capillary bed called the *vasa recta* surrounds the loop of Henle and helps to maintain the concentration of the medulla.

FIGURE 5.15 The Nephron and Vasa Recta



Concentration of Urine: The Osmolarity Gradient

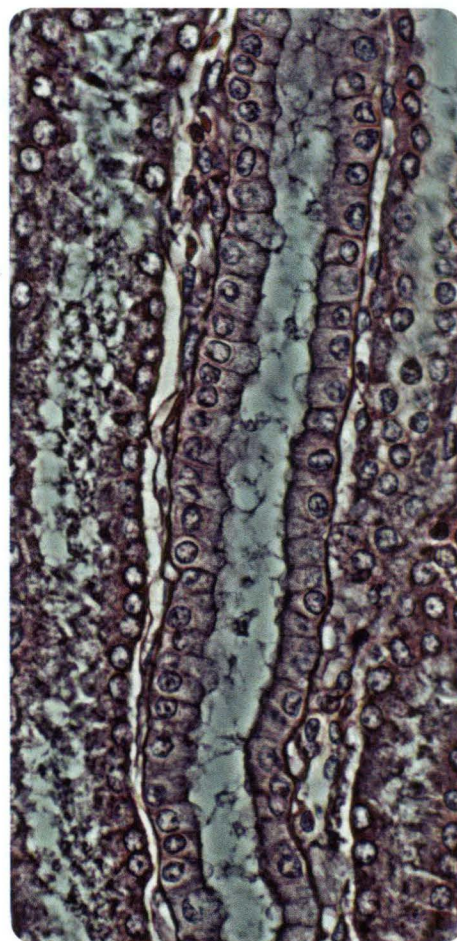
If the kidneys were not able to make concentrated urine, simply staying hydrated would require drinking gallons of water each day. This process is only possible because of the highly concentrated medulla that draws water out of the filtrate as it passes through the collecting duct. It is not necessary to understand all of the details presented here, but a general understanding of this process will be helpful for answering questions about the kidney on the MCAT®.

Processes known as the single effect, countercurrent multiplier, and countercurrent exchanger all work together to create an osmolarity gradient in the medulla. To understand how the gradient is established, it helps to imagine the nephron before it has set up the steady-state gradient within the medulla and the filtrate, as in the fetal kidneys. While reviewing this section, pay attention to differences in solute concentration in the various fluid compartments and differences in membrane permeability to water and solutes. Think about which way water or solutes would move if they were able to diffuse freely.

The loop of Henle has *countercurrent flow*, meaning that as filtrate moves through the descending and ascending loops it flows in opposite directions in parallel tubules that are very close together and separated only by a small amount of tissue and fluid. The vasa recta also has counter-current flow, but in the opposite direction of the loop of Henle; the blood in the vasa recta descends next to the ascending portion of the loop of Henle and ascends next to the descending portion. In addition to the main loop, the vasa recta has connecting horizontal capillaries.

The *single effect* is the process by which active transport of solute by pumps in the wall of the thick ascending loop creates a concentration gradient. The result of the single effect is that solute is more highly concentrated outside the tubule (in the medulla) than inside the tubule (in the filtrate). Water cannot diffuse across the thick wall of this segment of the ascending loop, so the gradient depends entirely on active pumping of solutes. The single effect creates a moderate osmotic gradient between the filtrate and interstitial fluid, up to a 200 mOsm concentration difference. (Recall that an osmole measures solute concentration in terms of solute particles per kilogram. Fluid with an osmolality of 1 Osm contains 1 mole of particles per kilogram, and a mOsm is 1/1000th of this concentration.) Water always tries to equalize concentrations of solutions and will diffuse down from an area with more water (less concentrated solutes) to an area with less water (more concentrated solutes). Though water cannot cross the wall of the ascending limb, it can diffuse freely through the wall of the descending loop of Henle. Since the medulla and the medullary interstitium (the fluid in the space between the cells of the medulla) have become more concentrated through the action of the pumps in the ascending limb, and since the descending limb is permeable to water, water moves out of the descending loop and into the medulla until these two areas have equal concentrations. The net result of the single effect is to dilute filtrate in the ascending limb while concentrating the medulla, and to concentrate filtrate in the descending limb of the loop of Henle.

The **counter-current multiplier mechanism** applies the single effect, which creates a static gradient, to a dynamic system where fluid is continually moving through the loop of Henle. In the body, the whole process is happening at once and is generally in homeostasis. However, to initially understand the counter-current multiplier mechanism, it is useful to imagine it as a series of discrete steps and then envision all of them happening at the same time, over and over again. These steps are: 1. pump salt from the filtrate to the medulla; 2. equilibrate water throughout the system; and 3. shift the filtrate along the tube.



Micrograph of the kidney's tubules, which work to move water and solutes into and out of the filtrate, depending on the body's needs.

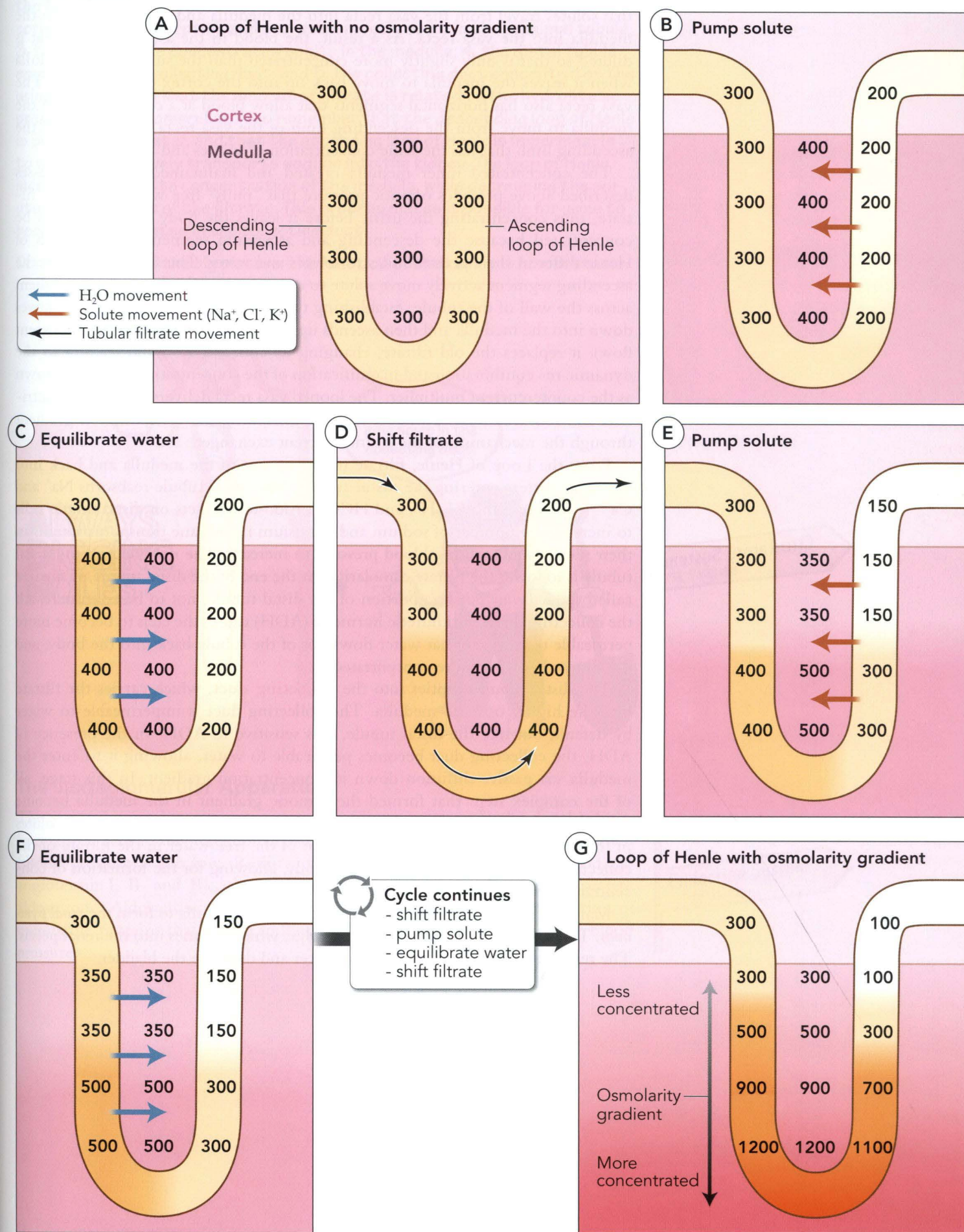
Time out! Don't try to memorize these numbers! They are provided as an illustration. The important thing to understand about the concentration gradient in the medulla is the self-perpetuating counter-current multiplier mechanism that sets it up. Remember the purpose of the medulla's concentration gradient: facilitating reabsorption of water into the body and, correspondingly, concentrating the urine.

In Figure 5.16 A, all of the filtrate in the loop and the entire medulla starts out at the same concentration of around 300 mOsm. In Figure 5.16 B, all of the active pumps in the ascending limb have pumped once to move solute out of the filtrate into the medullary interstitium and have set up their maximum gradient of a 200 mOsm difference across the wall (the single effect). In that instant, the concentration of filtrate in the entire ascending limb is 200 mOsm and the concentration of the entire length of the medulla is 400 mOsm. This change in concentration of the medulla affects the concentration of the filtrate in the descending limb through diffusion and equilibration, as described above. Water leaves the filtrate in the descending limb through diffusion and moves into the medulla to equilibrate the concentrations so that the concentrations of descending loop filtrate and the medulla are both 400 mOsm (Figure 5.16 C). But glomerular filtration continues to push the fluid along through the loop, so the concentrations quickly change. As shown in Figure 5.16 D, the concentrated filtrate in the descending limb gets pushed down and around (i.e., is shifted), bringing concentrated filtrate to the hairpin turn and to the bottom segment of the ascending limb. Meanwhile, the more dilute filtrate that was in the ascending limb gets pushed up, and some of it moves out of the loop.

At this point, the cycle repeats: pump salt, equilibrate water, shift filtrate. When the pumps in the ascending limb act again (Figure 5.16 E), they are still only able to set up a maximum concentration difference of 200 mOsm across the wall. In the more dilute upper segment where the filtrate concentration was at 200 mOsm, the action of the pumps creates a filtrate concentration of 150 mOsm and a medulla concentration of 350 mOsm. Unlike in the first cycle, the concentration is not the same through the whole ascending limb. In the more concentrated lower segment, where 400 mOsm filtrate that had been in the descending limb has shifted down and been pushed up into the lower part of the ascending loop, the pumps will create the same maximum gradient of a 200 mOsm difference across the wall. In the deeper section that starts out at a higher concentration, the action of the pumps establishes a new filtrate concentration of 300 mOsm and a medulla concentration of 500 mOsm. As in the first cycle, water diffuses through the permeable walls of the descending limb, allowing the filtrate to equilibrate with the medullary interstitium (Figure 5.16 F). Filtrate in the lower segment that has already been concentrated to 400 mOsm will become further concentrated to 500 mOsm, but the newer filtrate that entered the upper segment of the descending loop will only equilibrate to 350 mOsm. This process continues, repeating the steps of pump fluid, equilibrate water, and shift filtrate. As a result, an osmolarity gradient is established. The medulla is least concentrated in the upper region near the cortex and becomes progressively more concentrated in the deeper region (Figure 5.16 G).

Like all other body tissues, the medulla requires a steady supply of oxygen and nutrients as well as removal of waste products via capillary blood flow. A process called the countercurrent exchanger, involving the vasa recta, allows the needs of the medulla to be met while avoiding disruption of the balance of solutes described above. Recall that blood entering the kidneys (via either the vasa recta or the glomerulus) has an osmolarity of approximately 300 mOsm, and that capillaries throughout the body are permeable to both solutes and water. If capillaries were randomly organized throughout the concentrated medullary interstitium, solutes would diffuse into the capillaries and be transported away from the kidney, destroying the essential concentration gradient established by the loop of Henle and the countercurrent multiplier. The hairpin loop structure of the vasa recta, combined with particularly slow blood flow through these vessels, allows blood circulation to occur without major disruption of the medulla's concentration gradient. As blood descends through the vasa recta, it moves into increasingly concentrated areas of the medulla. In these areas, water diffuses out of the vasa recta and solutes are absorbed back in so that the blood at the bottom of the vasa recta loop is as concentrated as the most concentrated area of the medulla. As this more

FIGURE 5.16 Counter Current Multiplier Effect



concentrated blood ascends back up through the vasa recta, it passes through less concentrated areas of the medulla, where the free flow of water and solutes means that solutes travel from the vasa recta into the medulla and water flows from the medulla into the vasa recta. As a result, the blood in the ascending segment is diluted so that it is only slightly more concentrated than the surrounding medulla when it leaves the medulla to move back up into the cortex of the kidney. The vasa recta also has horizontal segments that allow blood at a certain depth of the medulla to move from the descending limb of the vasa recta to a section of the ascending limb that has the same concentration of solutes and water.

The concentrated inner medulla created and maintained by the processes described above provides osmotic pressure that “pulls” free water out of the filtrate, thus concentrating the urine before it leaves the body. The urine can be concentrated because the descending and ascending segments of the Loop of Henle differ in their permeabilities to solutes and water. The solute pumps in the ascending segment actively move solute to create an initial concentration gradient across the wall of the tubule, establishing the single effect. As new filtrate moves down into the medulla and then ascends up in the parallel tubule (countercurrent flow), it replaces the old filtrate, changing its concentration and leading to the dynamic re-equilibration and magnification of the concentration gradient known as the countercurrent multiplier. The looped vasa recta delivers oxygen and nutrients and removes waste products without disturbing the concentration gradient through the mechanism of the countercurrent exchanger.

From the Loop of Henle, filtrate moves up out of the medulla and back into the renal cortex, entering the **distal tubule**. The distal tubule reabsorbs Na^+ and Ca^{2+} while secreting K^+ , H^+ , and HCO_3^- . Aldosterone acts on distal tubule cells to increase the number of sodium and potassium membrane transport proteins in their membranes, causing blood pressure to increase. The net effect of the distal tubule is to lower the filtrate osmolarity. At the end of the distal tubule, in an area called the *collecting tubule* (a portion of the distal tubule, not to be confused with the collecting duct), antidiuretic hormone (ADH) causes the cells to become more permeable to water so that water flows out of the tubule back into the body, and the filtrate becomes more concentrated.

The distal tubule empties into the **collecting duct**, which carries the filtrate into the highly osmotic medulla. The collecting duct is impermeable to water by default, but like the distal tubule, it is sensitive to ADH. In the presence of ADH, the collecting duct becomes permeable to water, allowing it to enter the medulla via passive diffusion down its concentration gradient. In this stage, all of the complex steps that formed the osmotic gradient in the medulla become critically important. The osmotic pressure created by densely concentrated solutes in the medulla causes a substantial portion of the free water in the filtrate of the collecting duct to diffuse back into the body, allowing for the formation of concentrated urine.

Many collecting ducts line up side by side in the medulla to form the *renal pyramids*. The collecting ducts lead to a *renal calyx*, which empties into the renal pelvis. The renal pelvis drains urine into the ureter and down to the bladder.



Many details about the kidney are important for the MCAT®. Remember the function of each section of the nephron: 1. filtration occurs in the renal corpuscle; 2. reabsorption and secretion mostly occur in the proximal tubule; 3. the loop of Henle concentrates solute in the medulla; 4. the distal tubule empties into the collecting duct; and 5. the collecting duct concentrates the urine. Understand that the amount of filtrate is related to the hydrostatic pressure of the glomerulus. Also remember that the descending loop of Henle is permeable to water, and that the ascending loop of Henle is impermeable to water and actively transports sodium into the kidney. The loop of Henle increases the solute concentration of the medulla, while decreasing the solute concentration of the filtrate. This process makes it possible for urine to become concentrated in the collecting duct.

Don't lose sight of the big picture: the function of the kidney is homeostasis.



The Juxtaglomerular Apparatus

The **juxtaglomerular apparatus** monitors filtrate pressure in the distal tubule. Specialized cells in the juxtaglomerular apparatus secrete the enzyme renin when filtrate pressure is too low. Renin initiates a regulatory cascade that produces angiotensin I, II, and III, ultimately stimulating the adrenal cortex to secrete aldosterone. Aldosterone acts on the distal tubule, stimulating the formation of membrane proteins that absorb sodium and secrete potassium to increase blood pressure.

Endocrine System
BIOLOGY 2

These questions are NOT related to a passage.

Item 113

Bowman's capsule assists in clearing urea from the blood by:

- ☐ A) actively transporting urea into the filtrate using ATP-driven pumps.
- ☐ B) exchanging urea for glucose in an antiport mechanism.
- ☐ C) allowing urea to diffuse into the filtrate under filtration pressure.
- ☐ D) converting urea to amino acids.

Item 114

Tests reveal the presence of glucose in a patient's urine. This is an indication that:

- ☐ A) glucose transporters in the loop of Henle are not functioning properly.
- ☐ B) the patient is healthy, as glucose normally appears in the urine.
- ☐ C) the proximal tubule is over-secreting glucose.
- ☐ D) glucose influx into the filtrate is occurring faster than it can be reabsorbed.

Item 115

The epithelial cells of the proximal convoluted tubule contain a brush border similar to the brush border of the small intestine. The most likely function of the brush border in the proximal convoluted tubule is to:

- ☐ A) increase the amount of filtrate that reaches the loop of Henle.
- ☐ B) increase the surface area available for the absorption.
- ☐ C) slow the rate of at which the filtrate moves through the nephron.
- ☐ D) move the filtrate through the nephron with cilia-like action.

Item 116

If a patient were administered a drug that selectively bound and inactivated renin, which of the following would most likely result?

- ☐ A) The patient's blood pressure would increase.
- ☐ B) Platelets would be found in the urine.
- ☐ C) The amount of filtrate entering Bowman's capsule would increase.
- ☐ D) Sodium reabsorption by the distal tubule would decrease.

Item 117

Which of the following correctly orders the structures through which urine flows as it leaves the body?

- ☐ A) Urethra, urinary bladder, ureter, collecting duct
- ☐ B) Collecting duct, urinary bladder, urethra, ureter
- ☐ C) Collecting duct, ureter, urinary bladder, urethra
- ☐ D) Ureter, collecting duct, urethra, urinary bladder

Item 118

How are the blood levels of vasopressin and aldosterone in a dehydrated individual likely to compare with those of a healthy individual?

- ☐ A) Vasopressin and aldosterone levels are likely to be lower in a dehydrated individual.
- ☐ B) Vasopressin and aldosterone levels are likely to be higher in a dehydrated individual.
- ☐ C) Vasopressin levels are likely to be higher in a dehydrated individual, while aldosterone levels are likely to be lower.
- ☐ D) Vasopressin levels are likely to be lower in a dehydrated individual, while aldosterone levels are likely to be higher.

Item 119

An afferent arteriole in a glomerular tuft contains microscopic fenestrations which increase fluid flow. In a hypertensive patient (a patient with high blood pressure):

- ☐ A) these fenestrations would constrict, resulting in decreased urinary output.
- ☐ B) filtrate volume would be expected to be larger due to increased fluid pressure.
- ☐ C) filtrate volume would be expected to be smaller due to increased fluid pressure.
- ☐ D) urinary output would most likely be diminished due to increased solute concentration.

Item 120

For an individual with highly concentrated urine, filtrate entering the loop of Henle is likely to be:

- ☐ A) more concentrated than filtrate exiting the loop of Henle.
- ☐ B) less concentrated than filtrate exiting the loop of Henle.
- ☐ C) more voluminous than filtrate exiting the loop of Henle.
- ☐ D) less voluminous than filtrate exiting the loop of Henle.

TERMS YOU NEED TO KNOW

α -amylase	Fat metabolism	Microvilli
Albumin	Feces	Mouth
Antiport	Fenestrations	Mucous cells
Anus	Fundus	Nephron
Ascending colon	Gall bladder	Pancreas
Bacterial flora	Gastric juice	Pancreatic amylase
Bicarbonate ion	Gastrin	Parietal cells (oxyntic cells)
Bile	G cells	Pepsin
Blood filtration	Glomerulus	Pepsinogen
Blood storage	Gluconeogenesis	Peristalsis
Body	Glycogenesis	Protein metabolism
Bowman's capsule	Glycogenolysis	Proximal tubule
Brush border	Glycogen storage	Pylorus
Carbohydrate metabolism	Goblet cells	Reabsorption
Chief cells (peptic cells)	Hormones	Rectum
Chymotrypsin	Hydrochloric acid (HCl)	Secretion
Collecting duct	Hydrostatic pressure	Sigmoid colon
Cortex	Ileum	Small intestine
Detoxification	Ingestion	Sphincter
Descending colon	Jejunum	Stomach
Distal tubule	Juxtaglomerular apparatus	Transverse colon
Duodenum	Kidney	Triglycerides
Electrolyte absorption	Lacteal	Trypsin
Endocrine	Large intestine	Urea
Enteric nervous system	Lipase	Villi
Erythrocyte destruction	Liver	Vitamin storage
Esophagus	Loop of Henle	Water absorption
Excretory system	Lubrication	
Exocrine glands	Medulla	



DON'T FORGET YOUR KEYS

1. The three processes of the digestive system are digestion, absorption, and excretion. Surface area and length promote absorption.
2. From the kidney, substances travel in one of only two directions: "into the toilet" (filtration, secretion) and "back to the body" (reabsorption).
3. The nephron works by diffusion across membranes and active pumps in the ascending loop of Henle.

Muscle, Bone and Skin

6.1 Introduction

The musculoskeletal system and the integumentary system, which includes skin and hair, consist of organs that carry out a variety of functions including protection, movement, and regulation. This lecture will present the information about muscle, bone, and skin that is required for the MCAT®. It will start by covering the three main types of muscle in the body, including how the structure of each type relates to its specific function and how different types of muscle are controlled by separate portions of the nervous system. Next the lecture will discuss the functions of bone, such as the regulation of calcium levels that makes muscle contraction possible, and the process through which new bone is made to replace old bone. The lecture will then cover the basic structure and multiple purposes of human skin. Although each performs a variety of tasks, muscle, skin, and bone are united by their roles of protecting and regulating the internal environment of the body.



- 6.1 Introduction
- 6.2 Muscle
- 6.3 Skeletal Muscle: Physiology and Structure
- 6.4 Features of Cardiac Muscle
- 6.5 Smooth Muscle
- 6.6 Bone: Mineral Homeostasis and Structure
- 6.7 Cartilage and Joints
- 6.8 Skin

THE 3 KEYS

1. Somatic NS innervates voluntary muscles; autonomic NS innervates involuntary muscle.
2. See Ca^{2+} , think neuromuscular function and storage in bone.
3. The energy of an ATP molecule prepares the myosin head so that the muscle is ready and contraction is downhill in energy.

6.2 Muscle

There are three types of muscle tissue:

1. skeletal muscle;
2. cardiac muscle; and
3. smooth muscle.

The types of muscle each differ in structure, function, and nervous system innervation, but all have some properties in common. A muscle generates force by contracting its cells. The mechanisms by which muscle cells contract differ between the three types of tissue, as described later in this lecture. The major **functions of muscle** are:

1. body movement;
2. stabilization of body position;
3. movement of substances through the body; and
4. generating heat to maintain body temperature.

Know the three types of muscle and their four possible functions.

6.3 Skeletal Muscle: Physiology and Structure

Skeletal muscle (a type of **striated muscle**) is the tissue that is commonly called “muscle” in everyday language. Skeletal muscle is **voluntary muscle**, meaning that it can be consciously controlled to produce specific desired movements. It is innervated by the somatic nervous system. Skeletal muscle moves the body and allows activities like running or lifting weights. It is also involved in thermoregulation and the movement of fluids in the cardiovascular and lymphatic systems. This section will describe the functions of skeletal muscle, as well as the mechanism used by skeletal muscle to create movement.

Skeletal muscle connects one bone to another. Rather than attaching directly to the bone, the muscle is attached by a **tendon**. Note that connective tissue connecting muscle to bone is called a tendon; connective tissue connecting bone to bone is called a **ligament**. A muscle stretches across a joint in order to create movement at that joint when the muscle contracts. The *origin* of the muscle is usually its attachment on the larger bone closer to the midpoint of the body, which remains relatively stationary. The attachment at the other end of the muscle, known as its *insertion*, is on the smaller bone farther from the midpoint, which moves relative to the larger bone as the muscle contracts.

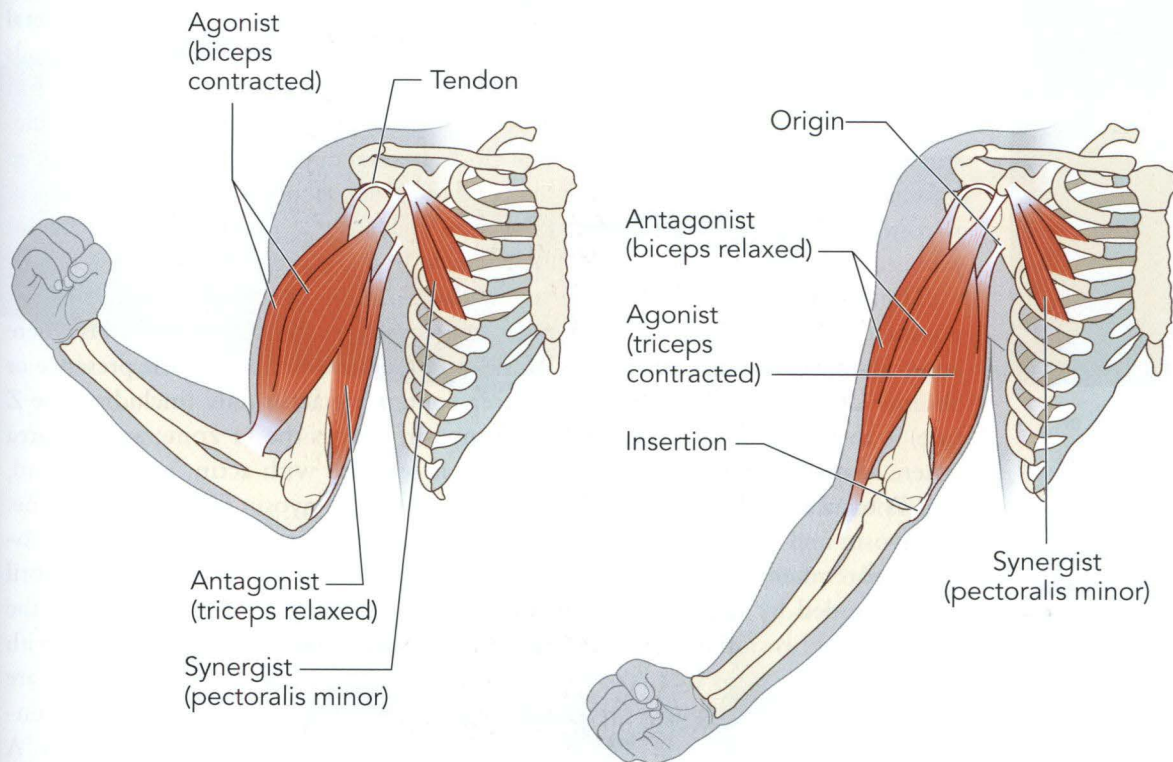
Muscles work in groups to perform movements efficiently. For each movement, the muscle whose contraction is primarily responsible for the movement is called the *agonist*. A second muscle, the *antagonist*, stretches in response to the agonist's contraction and opposes the movement so that the motion is smooth and controlled. The major upper arm muscles, the biceps and the triceps, provide an example of two groups of muscles that function antagonistically to each other. In addition to antagonistic muscles, movements usually involve *synergistic* muscles. A synergistic muscle assists the agonist by stabilizing the origin bone or by positioning the insertion bone during the movement. By acting together, agonistic, antagonistic, and synergistic muscles contribute to two major functions of skeletal muscle: movement and maintenance of posture.

Another function of skeletal muscle is that it provides **peripheral circulatory assistance**. Contraction of skeletal muscles helps squeeze blood and lymph through their respective vessels, aiding circulation.

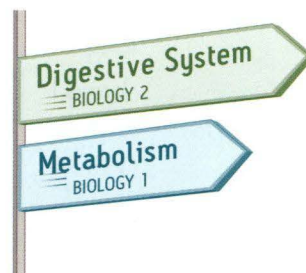
Nervous System
BIOLOGY 2

Circulatory System
BIOLOGY 2

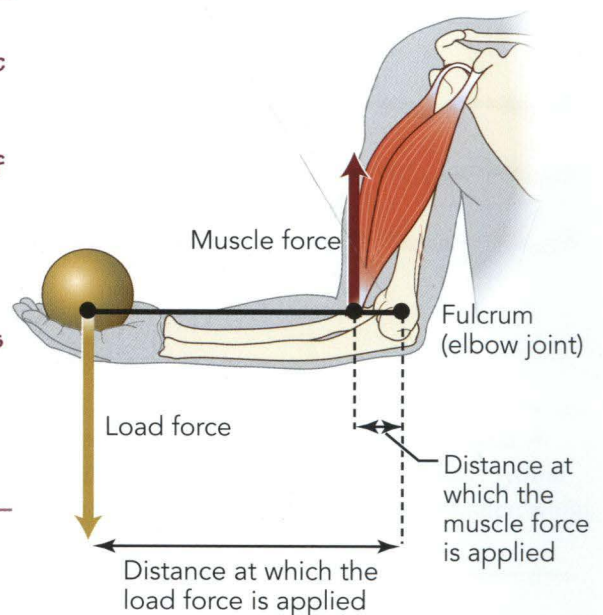
FIGURE 6.1 Agonist, Antagonist, and Synergist Muscles

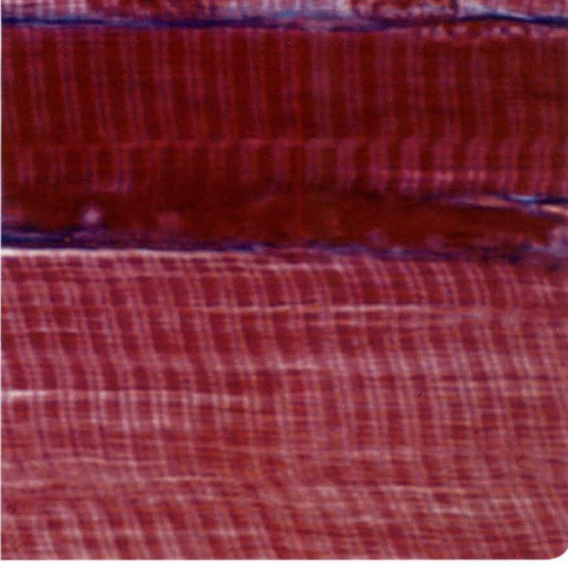


Skeletal muscle also participates in **thermoregulation**, meaning regulation of body temperature. Contraction of skeletal muscle produces large amounts of heat. The **shivering reflex** is the rapid contraction, or shaking, of skeletal muscle to warm the body. It is controlled by the hypothalamus upon stimulation by receptors in the skin and spinal cord. As described in the Digestive and Excretory Systems Lecture, skeletal muscle stores large amounts of glycogen. When necessary, the energy stored as glycogen can be metabolized and used to power muscle contractions that provide heat to the body.



A muscle uses leverage by applying a force to a bone at its insertion point and rotating the bone about the joint. This is a likely MCAT® topic because it applies the physics concept of levers and work to a biological system. Most (but not all) muscles act as class three lever systems in the body, meaning that the force applied by the contraction of the muscle (via the muscle attachment) is between the fulcrum (joint) and the load (the part of the body that moves). Class three levers, such as some muscles, use more force to perform a given amount of work than would be used if there were no lever at all. In other words, a greater force than mg is required to lift a mass m . This arrangement is advantageous because the shorter lever arm reduces the bulk of the body and increases the range and control of movement. You could see an MCAT® question or passage about the physics of levers in muscle movement.





The striated (striped) banding pattern of skeletal muscle fibers can be seen in this photo. The cross striations are the arrangements of proteins (actin and myosin) that cause the fibers to contract. Multiple nuclei (fuzzy pink) can be seen along the junction of the fibers (blue). Each cylindrical fiber is a single muscle cell.

Physiology of Skeletal Muscle Contraction

Skeletal muscle cells have unique physical features that facilitate their function in contraction. The smallest functional unit of the **contractile apparatus** in skeletal muscle is the **sarcomere** (Figure 6.2). A sarcomere is composed of many strands of two kinds of protein filaments: **thick filaments** made of **myosin** and **thin filaments** made of the globular protein **actin**. Several long myosin molecules wrap around each other to form one thick filament. Globular heads, known as *myosin heads*, protrude along both ends of the thick filament. The thin filament is composed mainly of a polymer of actin. Attached to the actin are the proteins **tropoin** and **tropomyosin**, which participate in the mechanism of contraction.

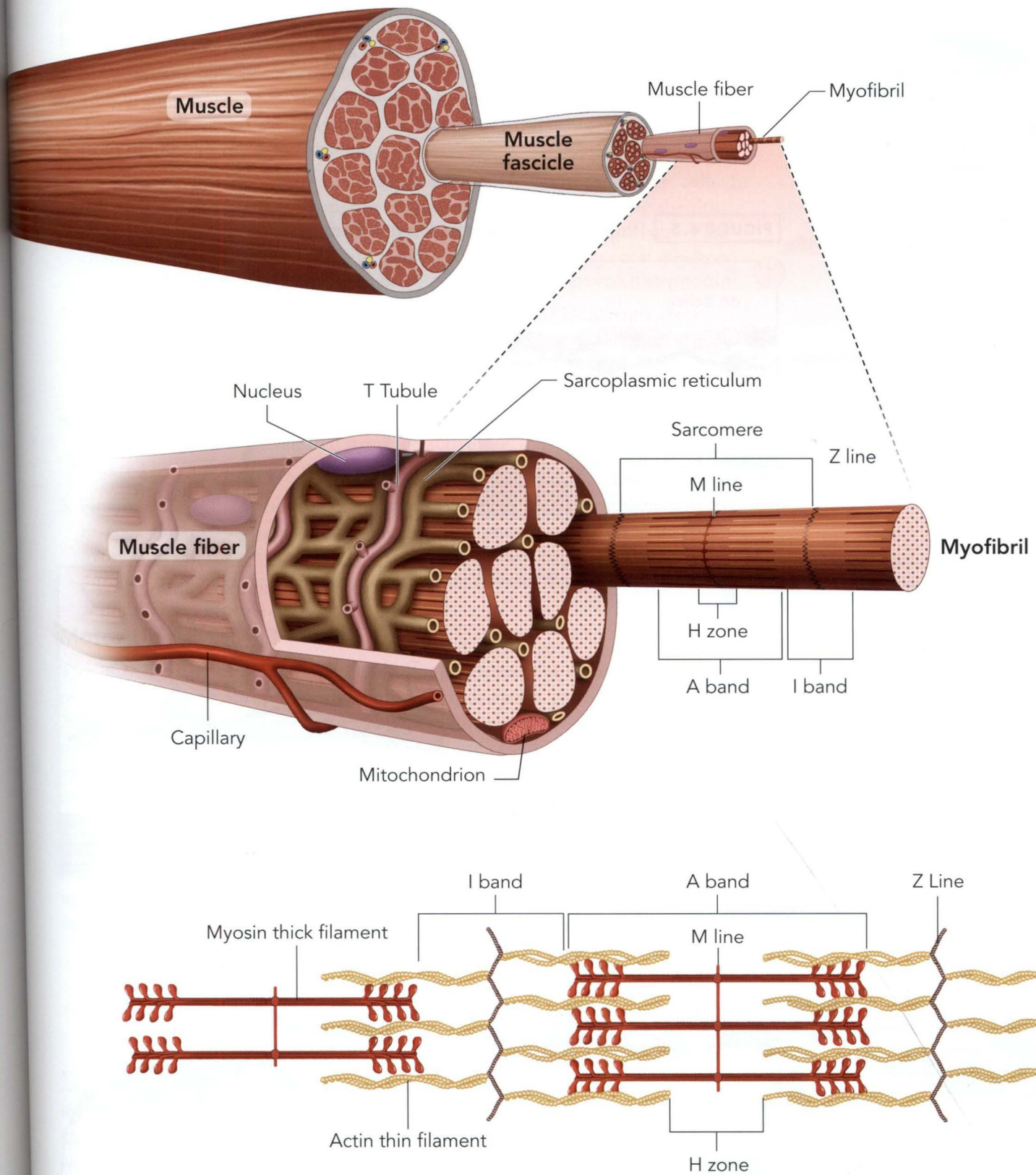
The myosin and actin filaments overlap and slide past each other when muscles contract and relax. The **Z line** separates one sarcomere from the next and is where actin filaments attach. Other areas of the sarcomere are defined by the presence or absence of actin and/or myosin. The area containing actin only (including the Z line) is the **I band**; the area containing myosin only is the **H zone**; and the area where myosin is present, including where it overlaps with actin, is the **A band**. The A band includes the H zone. The midline of the myosin fibers is the **M line**.

Myosin and actin filaments are laid side by side to form the cylindrical sarcomere. Sarcomeres are positioned end to end to form a *myofibril*. Each myofibril is surrounded by the specialized endoplasmic reticulum of the muscle cell, the **sarcoplasmic reticulum**. The lumen of the sarcoplasmic reticulum is filled with Ca^{2+} ions for reasons that will become clear. Lodged between the myofibrils are many mitochondria, which create the supplies of ATP required for muscular contraction. Each muscle cell contains many nuclei and is said to be *multinucleate*. A modified cellular plasma membrane called the *sarcolemma* wraps several myofibrils together to form a muscle cell (also called a myocyte or muscle fiber). Many muscle fibers are further bound into a *fasciculus*, and many fasciculae make up a single muscle.

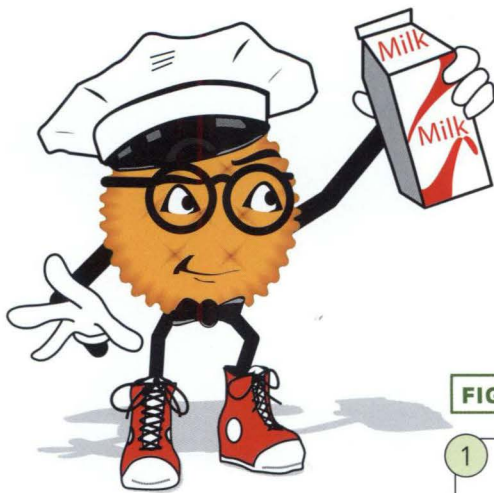
The contraction of skeletal muscle is controlled by the somatic nervous system. A **motor neuron** attaches to a muscle cell at a **motor end plate**, forming a **neuromuscular junction**. The action potential of the neuron releases **acetylcholine** into the synaptic cleft. The acetylcholine activates ion channels in the sarcolemma of the muscle cell, creating an action potential that propagates along the sarcolemma. The action potential moves deep into the muscle cell via small infoldings of the sarcolemma called **T-tubules**. T-tubules facilitate the uniform contraction of the muscle by allowing the action potential to spread through the muscle cell more rapidly. The action potential is transferred to the sarcoplasmic reticulum, causing voltage gated channels on the sarcoplasmic reticulum to open. As a result, the sarcoplasmic reticulum becomes more permeable to Ca^{2+} , which it releases around the sarcomere. The presence of Ca^{2+} allows the myosin and actin fibers of the sarcomere to slide across each other, causing the shortening (contraction) of the muscle fiber.

Nervous System
BIOLOGY 2

FIGURE 6.2 Structure of Skeletal Muscle

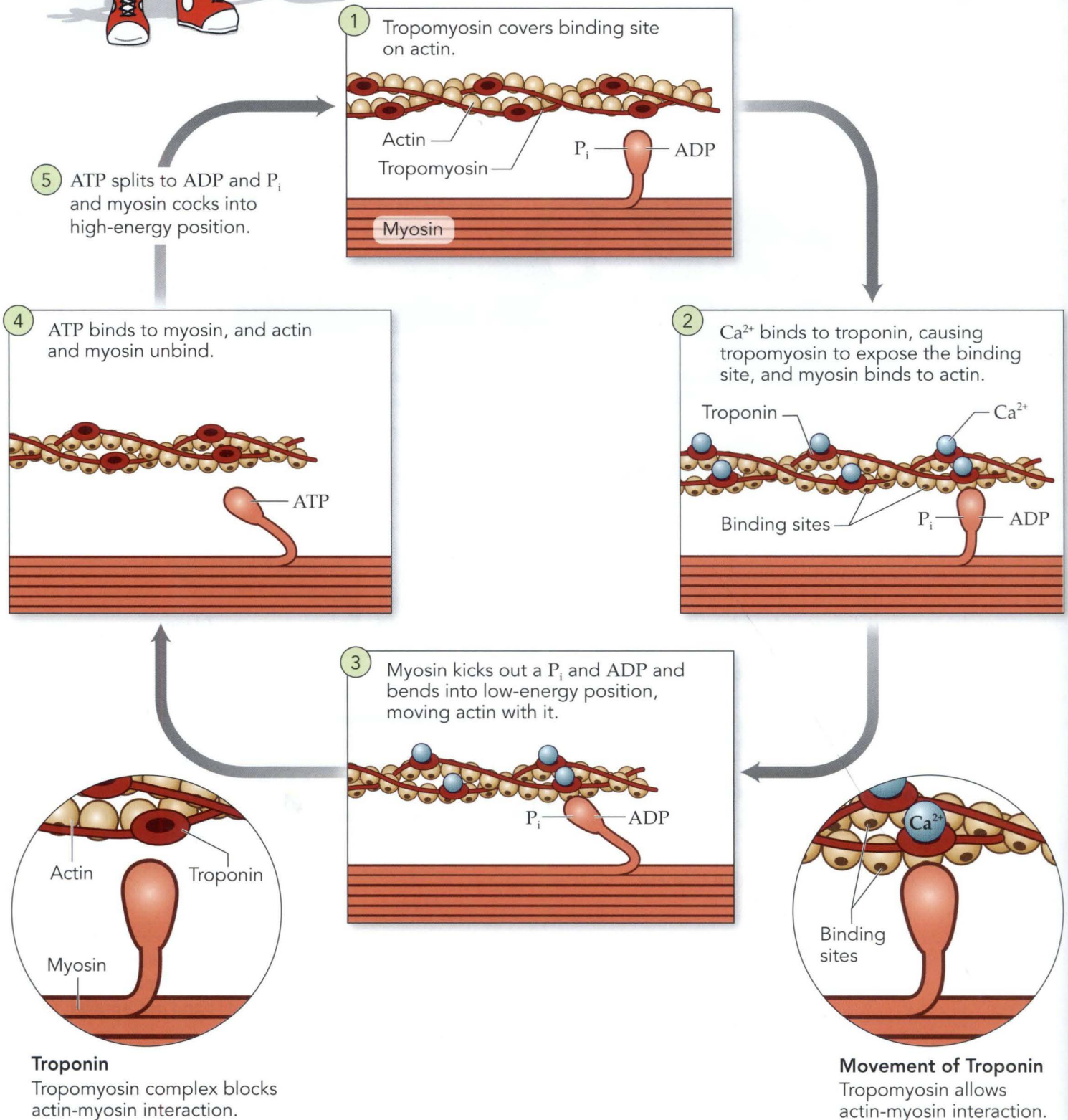


Take a minute to think about the labeled parts of the sarcomere: I band, A band, H zone, Z line, and M line. The diagram indicates that when the myosin and actin fibers slide past each other, the H zone and I band get smaller, while the A band does not change size.



Recognize the importance of calcium in muscle contraction, and make sure you're familiar with the functions of the sarcoplasmic reticulum and the T-tubules.

FIGURE 6.3 Physiology of Skeletal Muscle Contraction



According to the **sliding filament model**, myosin and actin work together by sliding alongside each other to create the contractile force of skeletal muscle. The process of contraction requires the expenditure of energy in the form of ATP. Each myosin head crawls along the actin in a 5 stage cycle (Figure 6.3).

1. In the resting state of muscle, the myosin heads of the thick filaments are in a high-energy “cocked” position with a phosphate and ADP group attached. Tropomyosin covers the active sites on the actin, preventing myosin heads from binding to the actin filament.
2. Somatic nervous input increases cytoplasmic Ca^{2+} levels in the muscle cells. In the presence of Ca^{2+} ions, troponin changes its configuration along the thin filament by pulling the tropomyosin back and exposing the active site. This change allows the myosin heads to bind to the actin, forming **cross-bridges** between the thick and thin filaments.
3. Next, the myosin head expels its phosphate and ADP and bends into a low energy position, dragging the actin along with it. This step is called the power stroke because it causes the shortening of the sarcomere and thus starts the muscle contraction.
4. In the fourth stage, a new ATP molecule attaches to the myosin head, causing the myosin head to be released from the active site. The active site is then covered by tropomyosin.
5. Finally, ATP splits into inorganic phosphate and ADP. The energy is used to re-cock the myosin head into the high-energy position. This cycle is repeated many times to form a contraction. At the end of each cycle, Ca^{2+} is actively pumped back into the sarcoplasmic reticulum to reset the gradient.

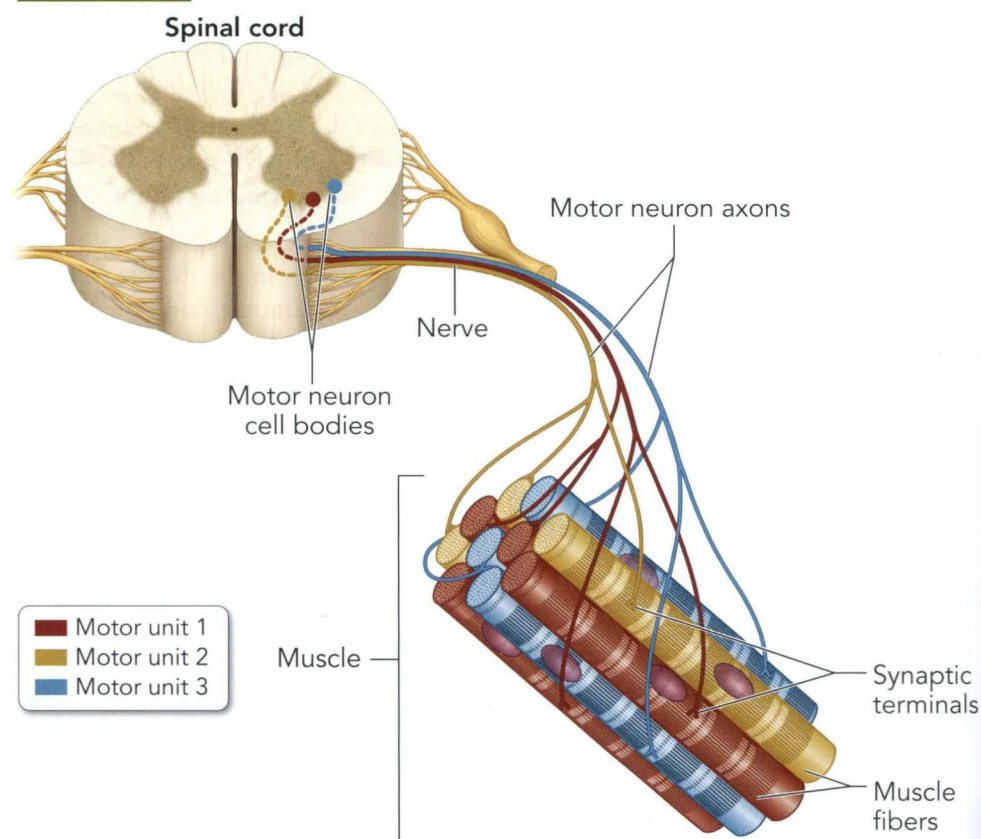
Motor Units

The muscle fibers of a single muscle do not all contract at once. If they did, the result would be an abrupt, poorly controlled movement. Instead, between 2 and 2000 fibers spread throughout the muscle are innervated by a single neuron. The neuron and the muscle fibers that it innervates are called a *motor unit*. Motor units are independent of each other. The force of a contracting muscle depends upon the number and size of active motor units, as well as the frequency of action potentials in each neuron of the motor unit. Smaller motor units are activated first, and larger motor units are recruited as needed. The result is a smooth increase in the force generated by the muscle. Muscles requiring intricate movements, like those in the finger, have small motor units. Muscles requiring greater force and less finesse, like those in the back, have larger motor units.

If I recruited my large motor units first, I would pick this mug up with so much force that all my root beer would wind up on the wall behind me. That's why I start with the small motor units and recruit larger ones as needed until I have just enough force to lift the mug to my mouth without spilling a drop.



FIGURE 6.4 Motor Unit



A motor unit consists of a nerve and all the muscle fibers with which it synapses.

Limitations of Skeletal Muscle and Skeletal Muscle Types

As any marathon runner or body builder knows, there are limits to how many times muscle can contract before it becomes fatigued. Fatigued muscles can no longer generate the same force of contraction. Since both nervous system input and energy from ATP are required for muscular contraction, **muscle fatigue** can result from nervous or metabolic causes. After sustained use of the same motor unit, the nerve supplying the unit can become temporarily unable to supply the signals necessary to continue frequent, high intensity contraction of the muscle. Metabolic fatigue can result from depletion of energy stores within the muscle or decreased sensitivity to the effects of calcium in the contracting muscle due to the buildup of waste products from metabolism.

Metabolism BIOLOGY 1

Metabolic processes are constantly occurring in muscle cells to produce the ATP that is used to fuel movement. Oxygen is the final acceptor of electrons in the electron transport chain, and thus plays an important role in metabolism. During moderate exercise, there is enough oxygen in the body to meet the increased metabolic demands through continuing aerobic respiration. During strenuous exercise, however, the oxygen demands of metabolism exceed the body's supply of oxygen. Under these conditions, muscle cells can switch from the citric acid cycle and oxidative phosphorylation to anaerobic glycolysis to produce the necessary ATP. The result is an excess of lactic acid, which must later be metabolized by the body when sufficient oxygen is again available. The need for increased oxygen after exercise in order to metabolize the excess lactic acid produced is known as **oxygen debt**.

The body contains types of skeletal muscle fibers that are specialized for specific purposes and respond differently to exercise and fatigue. The two main fiber types are **type I**, which are known as **slow twitch** (or *slow oxidative*) fibers, and **type II**, which are known as **fast twitch** fibers. Fast twitch fibers are further subdivided into two categories: *fast oxidative (type II A) fibers* and *fast glycolytic (type II B) fibers*.

Type I muscle fibers appear red because they contain large amounts of myoglobin, an oxygen storing protein similar to hemoglobin. Type I fibers also have large numbers of mitochondria, so they can efficiently use oxygen to generate ATP through aerobic metabolism. The fiber types differ in their **contractile velocity** (speed of contraction), maximum force production, and resistance to fatigue. Type I fibers have a relatively slow contractile velocity and produce a low amount of force. However, type I fibers have the advantage that they are slow to fatigue and thus can be employed for long periods of time. The large number of mitochondria and high myoglobin content of slow twitch fibers provide them with the ATP and oxygen necessary to operate for long periods without fatigue.

Myoglobin stores oxygen inside muscle cells. A molecule of myoglobin looks like one subunit of hemoglobin. It can store only one molecule of oxygen.

Type II A fibers are also red, but they have a fast contractile velocity. They are resistant to fatigue, but not as resistant as type I fibers. Type II B fibers have a low myoglobin content and thus appear white. They contract rapidly and are capable of generating great force, but they fatigue quickly. Type II B fibers contain large amounts of glycogen.

Most muscles in the body have a mixture of fiber types. The ratio of the mixture depends on the contraction requirements of the muscle and the genetics of the individual. The relative amounts of fiber types may influence a person's natural aptitude for athletic activities. Someone with a greater proportion of fast twitch fibers is likely to be naturally better at sprinting than someone with more slow twitch fibers, who would be better at running marathons. Large amounts of type I fibers are found in the postural muscles. There are large amounts of type II A fibers in the upper legs, while a greater proportion of type II B fibers is found in the upper arms.

Skeletal muscle cells are highly specialized and differentiated. Adult human skeletal muscle does not usually undergo mitosis to create new muscle cells. Instead, a number of changes occur over time to meet the need for increased strength when the muscles are exposed to forceful, repetitive contractions. These changes include increased diameter of the muscle fibers, increased numbers of sarcomeres and mitochondria, and lengthened sarcomeres. This increase in muscle cell diameter and change in muscle conformation is called *hypertrophy*.



If you're having trouble remembering the difference between type I and type II fibers, think of a rotisserie chicken. White meat (fast-twitch, type II fibers), such as the breasts, are used for short, intense bursts of activity like flapping the wings. The dark meat of the legs and thighs (slow-twitch, type I fibers) is used for sustained, low-intensity activities like wandering around the chicken coop.

Human muscle cells are so specialized that they have lost the ability to undergo mitosis. Only in rare cases does one muscle cell divide to form two cells.

TABLE 6.1 > Skeletal Muscle Fiber Types

	Contraction Time	Force Production	Resistance to Fatigue	Activity
Type I Slow (oxidative) twitch	Slow	Low	High	Aerobic
Type II A Fast (oxidative) twitch	Fast	High	Intermediate	Long-term anaerobic
Type II B Fast (glycolytic) twitch	Very fast	Very high	Low	Short-term anaerobic

These questions are NOT related to a passage.

Item 121

During a muscular contraction:

- ☐ A) both the thin and thick filaments contract.
- ☐ B) the thin filament contracts, but the thick filament does not.
- ☐ C) the thick filament contracts, but the thin filament does not.
- ☐ D) neither the thin nor the thick filament contract.

Item 122

Irreversible sequestering of calcium in the sarcoplasmic reticulum would most likely:

- ☐ A) result in permanent contraction of the muscle fibers, similar to what is seen in rigor mortis.
- ☐ B) create a sharp increase in bone density as calcium is resorbed from bones to replace the sequestered calcium.
- ☐ C) prevent myosin from binding to actin.
- ☐ D) depolymerize actin filaments in the sarcomere.

Item 123

Shivering increases body temperature by:

- ☐ A) serving as a warning that body temperature is too low, prompting the person to seek warmer locations.
- ☐ B) causing bones to rub together, creating heat through friction.
- ☐ C) increasing the activity of muscles.
- ☐ D) convincing the hypothalamus that body temperature is higher than it actually is.

Item 124

Muscles cause movement at joints by:

- ☐ A) inciting neurons to initiate an electrical "twitch" in tendons.
- ☐ B) increasing in length, thereby pushing the muscle's origin and insertion farther apart.
- ☐ C) filling with blood, thereby expanding and increasing the distance between the ends of a muscle.
- ☐ D) decreasing in length, thereby bringing the muscle's origin and insertion closer together.

Item 125

When one of a pair of antagonistic muscles contracts, what usually happens to the other muscle to produce movement?

- ☐ A) It acts synergistically by contracting to stabilize the moving bone.
- ☐ B) It relaxes to allow movement.
- ☐ C) It contracts in an isometric action.
- ☐ D) Its insertion slides down the bone to allow a larger range of movement.

Item 126

When undergoing physical exercise, healthy adult skeletal muscle is likely to respond with an increase in all of the following except:

- ☐ A) glycolysis.
- ☐ B) the citric acid cycle.
- ☐ C) mitosis.
- ☐ D) protein production.

Item 127

Which of the following statements regarding muscles that act as third class levers in the body is NOT true?

- ☐ A) They require more force to perform the allotted work than if no lever were present.
- ☐ B) The force of the muscle contraction is applied between the fulcrum and the load force.
- ☐ C) This arrangement increases the bulk of the body.
- ☐ D) This arrangement increases the precision of movement.

Item 128

Skeletal muscle contraction may assist in all of the following EXCEPT:

- ☐ A) movement of fluid through the body.
- ☐ B) body temperature regulation.
- ☐ C) posture.
- ☐ D) peristalsis.

6.4 Features of Cardiac Muscle

The human heart is composed mainly of **cardiac muscle** (Figure 6.5). Cardiac muscle is a specialized, electrically-excitabile tissue, which permits the propagation of the electrical signals that cause the heart to beat normally. Like skeletal muscle, cardiac muscle is striated, which means that it is composed of sarcomeres. However, each cardiac muscle cell contains only one nucleus. Cardiac muscle cells are separated from each other by *intercalated discs*. The intercalated discs contain gap junctions that allow an action potential to spread from one cardiac cell to the next via electrical synapses, synchronizing the contraction of groups of cardiac muscle cells. The coordination of contraction in cardiac muscle controls the efficient pumping of blood through the chambers of the heart. Because the heart must beat continuously for the entire length of a human life, the mitochondria of cardiac muscle are large and numerous to provide a constant supply of ATP. By contrast to skeletal muscle, which connects bone to bone via tendons, cardiac muscle is not connected to bone. Instead, cardiac muscle forms a net that contracts in upon itself like a squeezing fist.

Muscle is said to be involuntary when nervous control over its contractions does not reach the level of consciousness in the brain. In other words, your heart beats whether you think about it or not. For the MCAT®, it is important to know that skeletal muscle is voluntary while cardiac and smooth muscle are not.

Cardiac muscle is **involuntary muscle**. Unlike voluntary skeletal muscle, which is controlled by the somatic nervous system, involuntary muscle such as cardiac muscle receives nervous input from the autonomic nervous system. Although cardiac muscle is self-excitatory to some extent and modulates its own rhythm through the SA and AV nodes, input from the autonomic nervous system can affect contraction frequency and thus heart rate. For cardiac muscle, **sympathetic innervation** increases heart rate, while **parasympathetic innervation** via the *vagus nerve* decreases heart rate. Like skeletal muscle, cardiac muscle can grow by hypertrophy when it must work particularly hard.

The action potential of cardiac muscle exhibits a plateau after depolarization. The plateau is created by slow voltage-gated calcium channels, which allow calcium to enter and maintain the inside of the membrane at a positive potential difference. As a result, repolarization of cardiac muscle is slower and more frequent than that of skeletal muscle. The plateau lengthens the time of contraction, preventing a new action potential from starting in the middle of the previous contraction.

Remember the importance of calcium in the cardiac action potential. Without it, the heart would beat far too quickly to serve as a functional pump, and death would result.

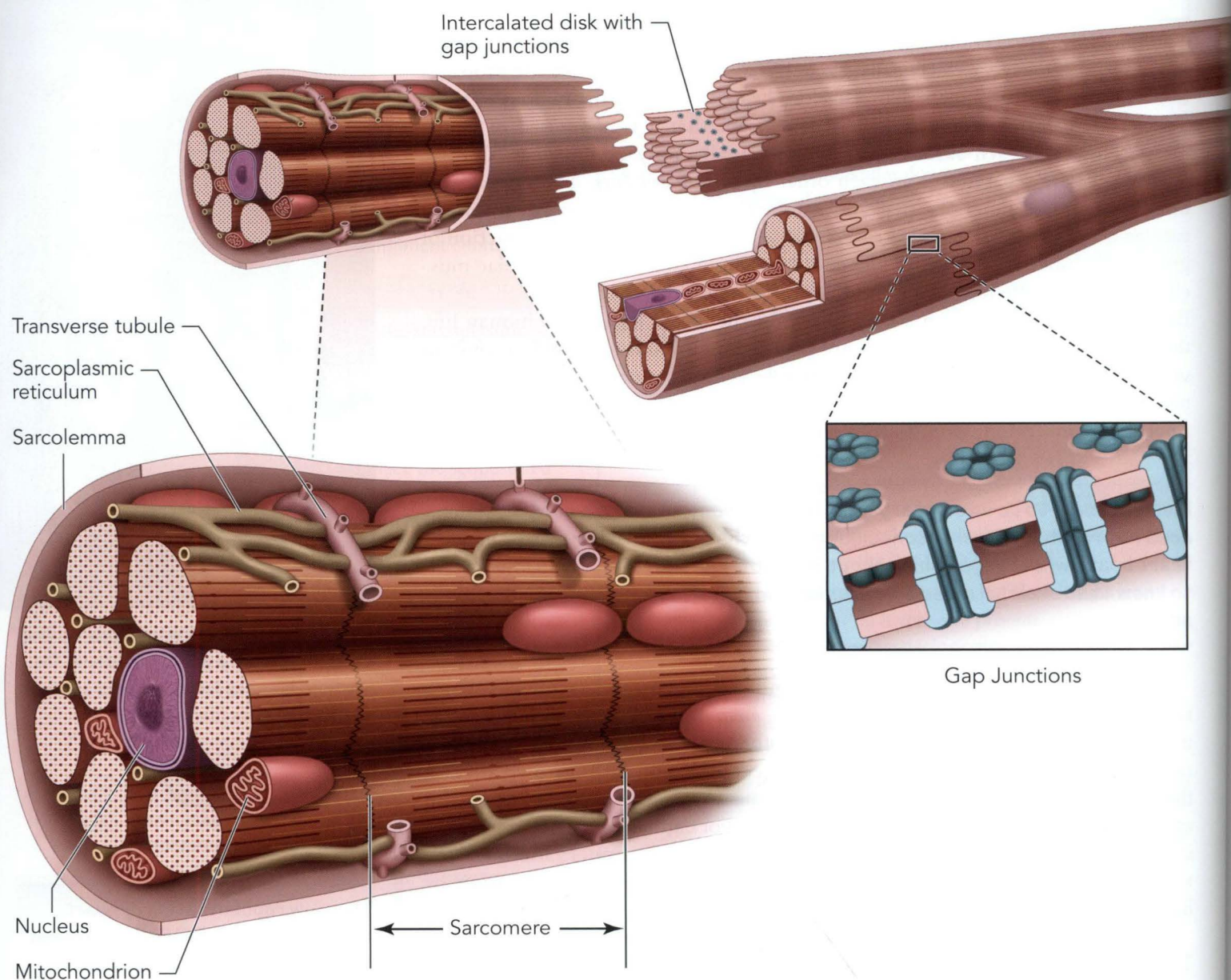


As seen through a light microscope, cardiac muscle cells form a net-like structure. The junctions between individual cells are the intercalated discs (dark lines).

Circulatory System BIOLOGY 2

The slow repolarization of heart muscle gives the heart enough time to refill with blood and prevents tetanus, the sustained contraction that can occur in skeletal muscle and could be deadly if it occurred in the heart.

FIGURE 6.5 Cardiac Muscle



One example of the purpose of smooth muscle is its role in digestion. Smooth muscle in the digestive organs helps push food along the digestive tract. Sympathetic innervation pauses digestion so that energy can be expended on other tasks, while parasympathetic innervation increases the rate of digestion.

6.5 Smooth Muscle

Smooth muscle composes the muscular layer of internal organs and blood vessels. Like cardiac muscle, smooth muscle cells contain only one nucleus and are also involuntary, so they are also innervated by the autonomic nervous system (Figure 6.6). Smooth muscles contain thick and thin filaments, but they are not organized into sarcomeres. In addition, smooth muscle cells contain **intermediate filaments**, which are attached to *dense bodies* spread throughout the cell. The thick and thin filaments are attached to the intermediate filaments, and, when they contract, they cause the intermediate filaments to pull the dense bodies together. Upon contraction, the smooth muscle cell shrinks length-wise.

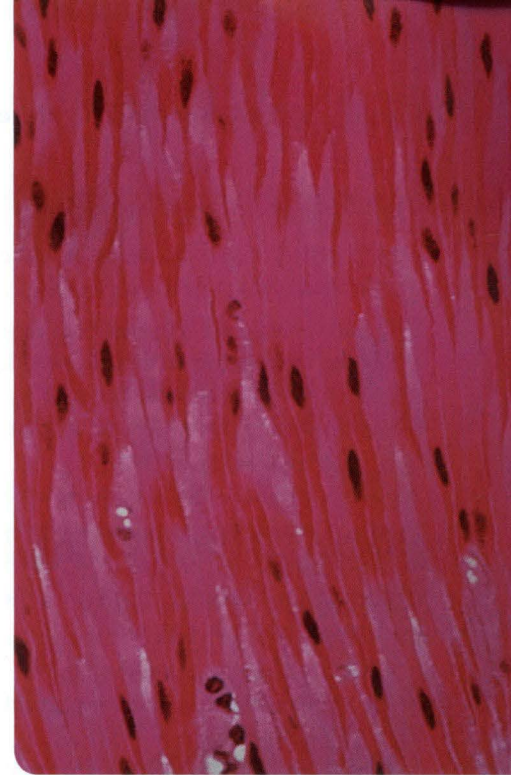
There are two types of smooth muscle: 1. *single-unit* and 2. *multi-unit*. Single-unit smooth muscle, also called *visceral smooth muscle*, is the most common. Single-unit smooth muscle cells are connected by gap junctions that spread the action potential from a single neuron through a large group of cells, allowing the cells to contract as a single unit. Electrical synapses via gap junctions in visceral muscle allow for faster signal transmission than would be possible with chemical synapses. The speed of transmission permits simultaneous contraction of the muscle cells in

a coordinated fashion. Single-unit smooth muscle is found in small arteries and veins, the stomach, intestines, uterus, and urinary bladder.

In multi-unit smooth muscle, each fiber is attached directly to a neuron. A group of multi-unit smooth muscle fibers can contract independently of other muscle fibers in the same location. Multi-unit smooth muscle is found in the large arteries, bronchioles, pili muscles attached to hair follicles, and the iris.

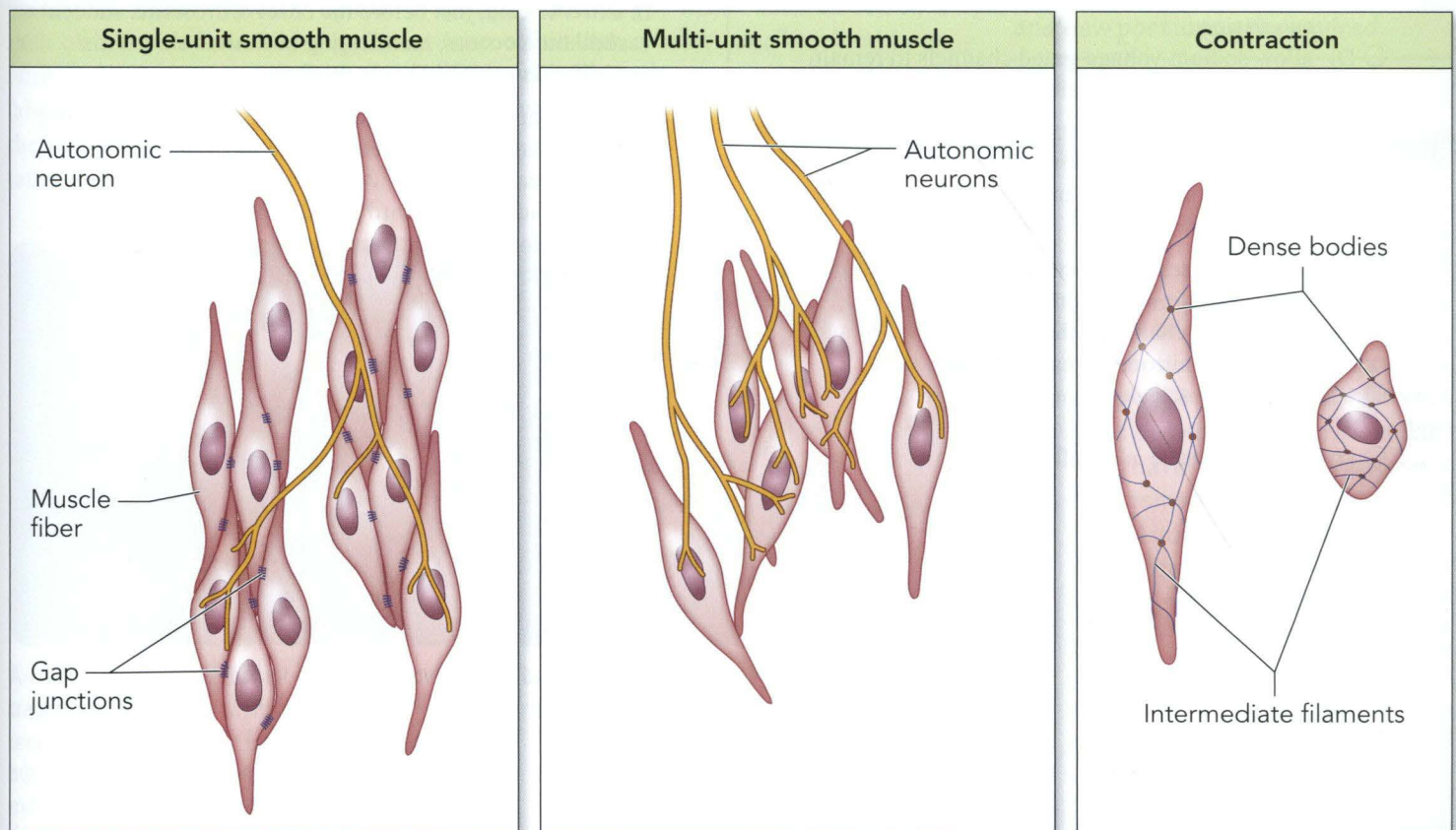
In addition to responding to neural signals, smooth muscle contracts or relaxes in the presence of hormones, or in response to changes in pH, O_2 and CO_2 levels, temperature, and ion concentrations.

If you see smooth muscle on the MCAT®, remember that it is primarily found in the walls of blood vessels and internal organs, especially the digestive tract and reproductive tract. In organ walls, it functions to cause contraction of the organ such as peristalsis in the digestive tract. In blood vessels, contraction of smooth muscle can constrict the vessel radius, helping to regulate blood flow. Smooth muscle is also present in certain other locations such as the iris of the eye and the arrector pili muscles of the skin, but if you see these examples on the MCAT®, they will likely be explained in a passage.



Smooth muscle is composed of spindle-shaped cells grouped in irregular bundles. Each cell contains one nucleus, seen here as a dark stained spot.

FIGURE 6.6 Smooth Muscle



These questions are NOT related to a passage.

Item 129

The function of gap junctions in the intercalated discs of cardiac muscle is to:

- ☐ A) anchor the muscle fibers together.
- ☐ B) ensure that an action potential is spread to all fibers in the muscle network.
- ☐ C) control blood flow by selectively opening and closing capillaries.
- ☐ D) release calcium into the sarcoplasmic reticulum.

Item 130

Which of the following muscular actions is controlled by the autonomic nervous system?

- ☐ A) The knee-jerk reflex
- ☐ B) Conduction of cardiac muscle action potential from cell to cell
- ☐ C) Peristalsis of the gastrointestinal tract
- ☐ D) Contraction of the diaphragm

Item 131

During an action potential, a cardiac muscle cell remains depolarized much longer than a neuron. This characteristic of the cardiac muscle cell most likely functions to:

- ☐ A) prevent the initiation of another action potential during contraction of the heart.
- ☐ B) ensure that adjacent cardiac muscle cells will contract at different times.
- ☐ C) keep the neuron from firing twice in rapid succession.
- ☐ D) allow sodium voltage-gated channels to remain open long enough for all sodium to exit the cell.

Item 132

All of the following statements are true concerning smooth muscle EXCEPT:

- ☐ A) Smooth muscle contractions are longer and slower than skeletal muscle contractions.
- ☐ B) A chemical change in the environment around smooth muscle may create a contraction.
- ☐ C) Smooth muscle does not require calcium to contract.
- ☐ D) Smooth muscle is usually involuntary.

Item 133

Which of the following muscles is under voluntary control?

- ☐ A) The diaphragm
- ☐ B) The heart
- ☐ C) The smooth muscle of the large intestines
- ☐ D) The iris

Item 134

Cardiac muscle is excited by:

- ☐ A) parasympathetic nervous excitation.
- ☐ B) constriction of T-tubules.
- ☐ C) increased cytosolic sodium concentration .
- ☐ D) increased cytosolic calcium concentration.

Item 135

When left alone, certain specialized cardiac muscle cells have the capacity for self-excitation. The SA node is a collection of such cells. The SA node is innervated by the vagus nerve. The frequency of self-excitation of the cardiac cells of the SA node is likely to be:

- ☐ A) slower than a normal heartbeat, because excitation by the vagus nerve decreases the heart rate.
- ☐ B) slower than a normal heartbeat, because excitation by the vagus nerve increases the heart rate.
- ☐ C) faster than a normal heartbeat, because excitation by the vagus nerve decreases the heart rate.
- ☐ D) faster than a normal heartbeat, because excitation by the vagus nerve increases the heart rate.

Item 136

In extreme cold, just before the onset of frostbite, sudden vasodilation occurs, manifesting in flushed skin. This vasodilation most likely results from:

- ☐ A) paralysis of smooth muscle in the vascular walls.
- ☐ B) paralysis of skeletal muscle surrounding the vascular walls.
- ☐ C) sudden tachycardia with a resultant increase in blood pressure.
- ☐ D) blood shunting due to smooth muscle sphincters.

Bone: Mineral Homeostasis and Structure

Bone is living tissue and is one of the major types of connective tissue in the body. The **functions of bone** are support of soft tissue, protection of internal organs, assistance in body movement, mineral (calcium) storage, blood cell production, and energy storage in the form of adipose cells in bone marrow. This section will cover the major cell types within bone, the process by which new bone is made, and the structure and classification of bones in the human body.

Bone tissue contains four types of cells surrounded by an extensive **calcium/protein matrix** composed of inorganic minerals (notably, calcium) and proteins.

1. **Osteoprogenitor** (or *osteogenic*) cells differentiate into osteoblasts.
2. **Osteoblasts** secrete collagen and organic compounds upon which bone is formed. They are incapable of mitosis. As osteoblasts release matrix materials around themselves, they become enveloped by the matrix and differentiate into osteocytes.
3. **Osteocytes** are also incapable of mitosis. They exchange nutrients and waste materials with the blood.
4. **Osteoclasts** resorb bone matrix, releasing minerals back into the blood. They are thought to develop from the white blood cells called monocytes.

Although bones vary in size, shape and composition, some general structural features are shared by most bones. A typical long bone (Figure 6.7) has a long shaft, called the *diaphysis*, and two ends, each composed of a *metaphysis* and *epiphysis*. A sheet of cartilage between the epiphysis and the metaphysis, called the *epiphyseal plate*, is where long bones grow in length when stimulated by growth hormone (GH) during childhood and adolescence.

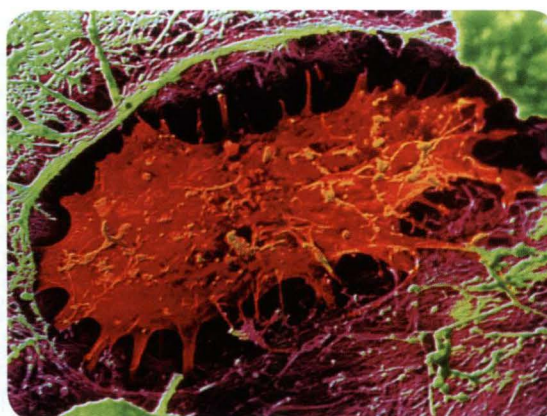
Each bone contains two main types of bone structure: spongy bone and compact bone. Bones typically consist of spongy bone on the inside surrounded by a shell of compact bone. **Spongy bone** (also called *trabecular* or *cancellous bone*) contains **red bone marrow**, the site of red blood cell development. **Compact bone** (also called **cortical bone**) surrounds a hollow area inside the diaphysis known as the *medullary cavity*, which holds yellow bone marrow. Yellow bone marrow contains adipose cells for fat storage.

Some organisms, such as lobsters, gain structural support and protection from having their skeleton on the outside in a shell-like exoskeleton. Humans and all other vertebrates have a skeleton on the inside, called an endoskeleton. Exo- and endoskeletons serve many of the same purposes, including structural support and protection, but it is crucial to know the difference between them.

Bone serves a wide variety of purposes in the human body. Like most other living tissue, bone must constantly replace itself. The main cell types in bone are used to break down and rebuild the structure of bone as older portions are worn out and new portions are required.



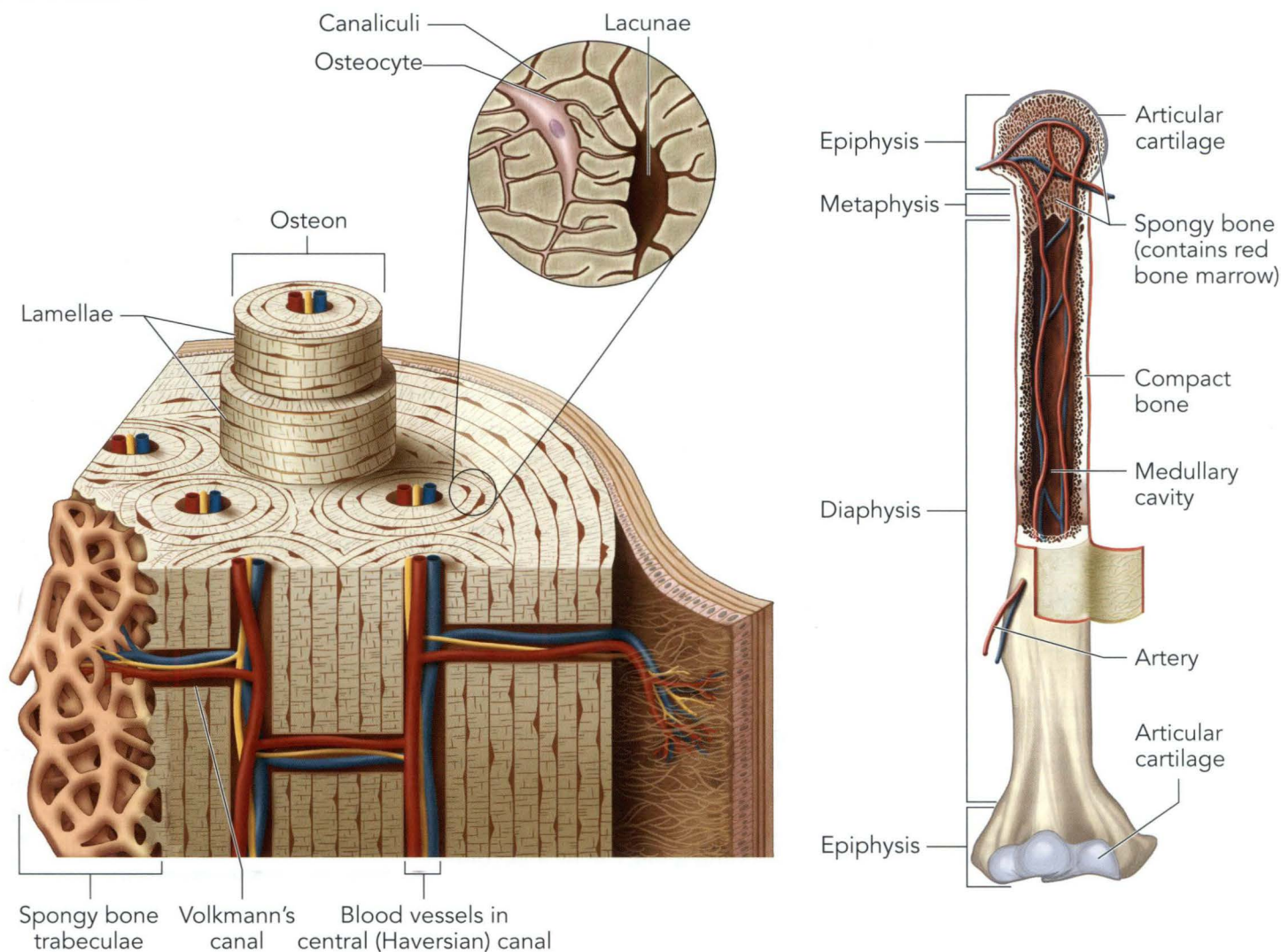
An osteocyte is an osteoblast that has become trapped within a bone cavity (lacuna). Osteocytes are responsible for bone formation, but eventually become embedded in the bone matrix and are only able to communicate with each other and the rest of the body through a system of canals and canaliculi.



A bone-making osteoblast cell is shown here surrounded by a dense network of collagen fibers.

Know the functions of osteoblasts, osteocytes, and osteoclasts. Osteoblast and osteoclast sound similar but have opposite functions. Remember: **osteoblasts Build bone, osteoclasts Consume it.**

FIGURE 6.7 Typical Long Bone Structure



Compact bone has a highly organized microstructure. Old parcels of bone are continuously replaced with new bone through the process of *remodeling*. In remodeling, osteoclasts burrow tunnels through compact bone. The osteoclasts are followed by osteoblasts, which lay down a new bone matrix onto the tunnel walls, forming concentric rings called *lamellae*. Osteoblasts leave open spaces in the center of the lamellae known as *Haversian canals*. The entire system of lamellae and a Haversian canal is called an *osteon* or *Haversian system*. The series of spaces within bone tissue allows for communication and nutrient exchange. Osteocytes are living cells that, once they have surrounded themselves with bone matrix, are isolated from other cells. Haversian canals contain blood and lymph vessels, and are connected by crossing canals called *Volkman's canals*. Osteocytes trapped between the lamellae exchange nutrients via spaces called *canaliculi*.

The remodeling of bone is subject to **endocrine control**. Parathyroid hormone helps regulate Ca^{2+} levels in the bloodstream by influencing bone. High levels of parathyroid hormone signal the osteoclasts to begin breaking down bone so that calcium stored as part of the bone matrix can be released into the blood. Other hormones, such as vitamin D, help restore calcium stores in the bone by promoting calcium absorption through the digestive system.

Endocrine System
BIOLOGY 2

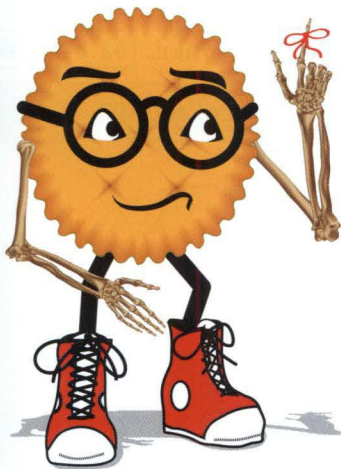
Bone's Function in Mineral Homeostasis

Osteoblasts use calcium from the blood to form new osteons. Conversely, when osteoclasts break down bone, they release that calcium into the bloodstream. Therefore, one of the important functions of bone is to help regulate the mineral content of the blood, particularly calcium levels. Calcium salts are only slightly soluble, so most calcium in the blood is not in the form of free calcium ions. Instead it is bound mainly by proteins and, to a much lesser extent, by phosphates (HPO_4^{2-}) and other anions. It is the concentration of free calcium ions (Ca^{2+}) in the blood that is important physiologically. Too much Ca^{2+} causes membranes to become hypo-excitability, leading to fatigue and memory loss; too little results in cramps and convulsions.

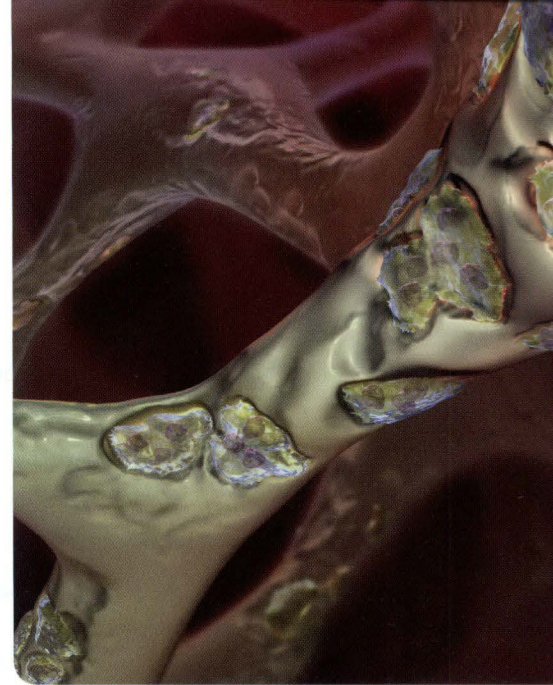
Most of the body's Ca^{2+} is stored in the bone matrix as the mineral *hydroxyapatite* [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$], which contributes to the strength of bones. Collagen fibers give bone great tensile strength (the ability to stretch without breaking). Hydroxyapatite crystals lie alongside collagen fibers, giving bone great compressive strength (the ability to compress under the weight of a load without breaking). Some Ca^{2+} is stored in bone in the form of slightly soluble calcium salts such as CaHPO_4 . These salts buffer plasma Ca^{2+} levels. Thus bone acts as a reservoir that can store minerals when excess Ca^{2+} and HPO_4^{2-} are present and release these minerals into the bloodstream as needed.

Bone Types and Structures

Bones can be categorized by shape. Most bones fall into one of four **specialized bone types**: 1. long; 2. short; 3. flat; or 4. irregular. **Long bones** have a shaft that is curved for strength. They are composed of compact and spongy bone. Leg, arm, finger, and toe bones are examples of long bones. **Short bones** are often roughly cuboidal in shape. Examples include the ankle and wrist bones. **Flat bones**, such as the skull, sternum, ribs, and shoulder blades, provide organ protection and large areas for muscle attachment. **Irregular bone** has an irregular shape and variable amounts of compact and spongy bone. The ossicles of the ear are irregular bones.



Remember that bone is not just for support, protection, and movement. Bone also stores calcium and phosphate, helping to maintain homeostasis in the concentration of these ions in the blood. Bone stores energy in the form of fat and is also the site of blood cell formation.



This computer-generated image shows multi-nucleated osteoclasts etching away trabecular bone in a process called bone resorption.

FIGURE 6.8 Bone Types

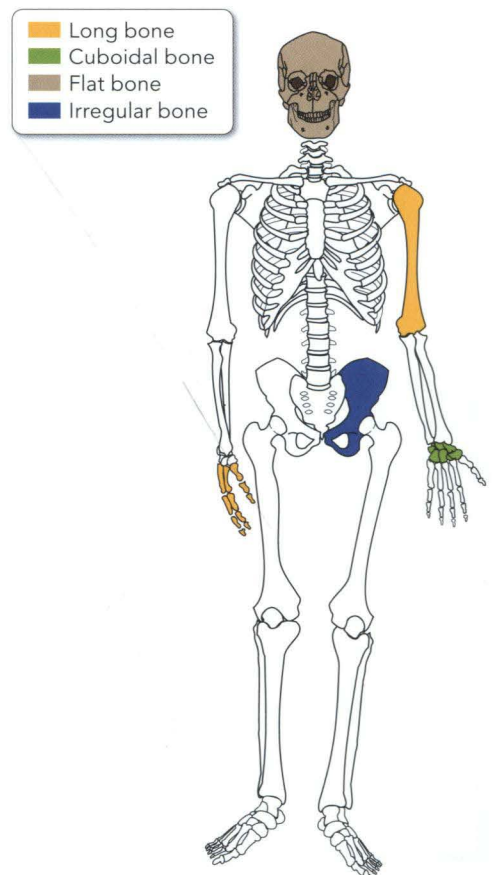
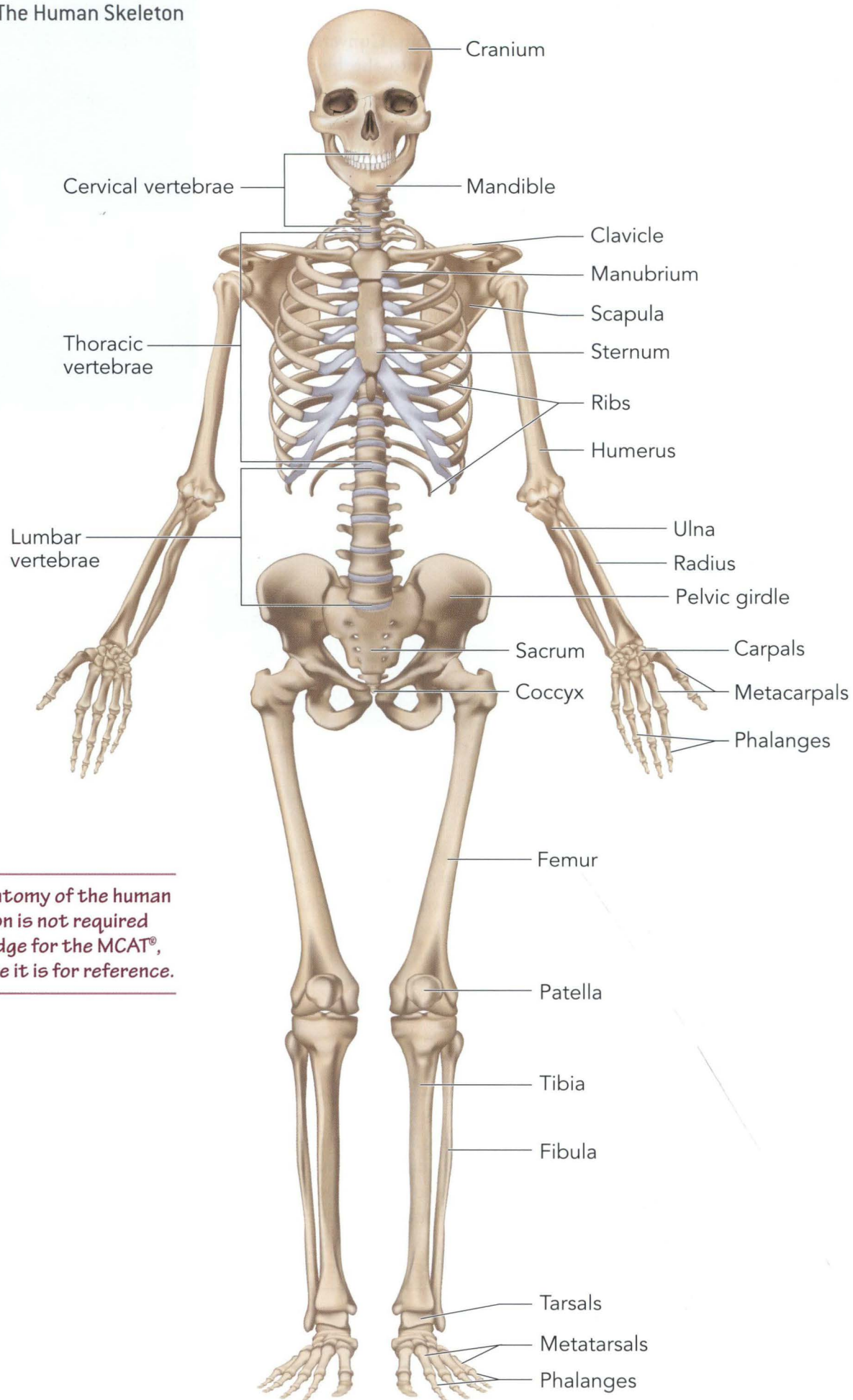


FIGURE 6.9 The Human Skeleton



The anatomy of the human skeleton is not required knowledge for the MCAT®, but here it is for reference.

Cartilage

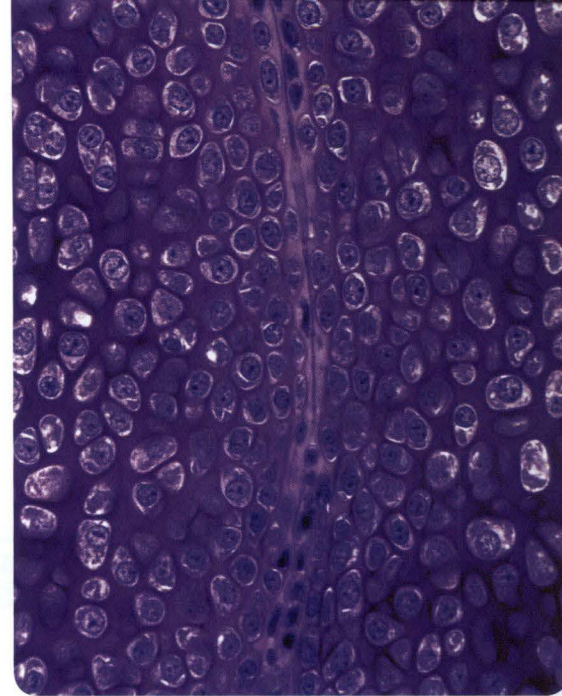
Cartilage is flexible, resilient connective tissue. It is composed primarily of collagen and has great tensile strength. Cartilage gives shape and structure to various body parts (such as the ears) and also serves the important function of providing cushion, connection, and elasticity to the joints of the body. Cartilage has no blood vessels or nerves except in its outside membrane. There are three types of cartilage: 1. *hyaline*; 2. *fibrocartilage*; and 3. *elastic*. Hyaline cartilage, which reduces friction and absorbs shock in joints, is the most common.

Cartilage serves the important function of cushioning and reducing friction at the joints. When cartilage wears away through damage or over-use, one bone will grind against the other, causing the painful condition of osteoarthritis.

Joints

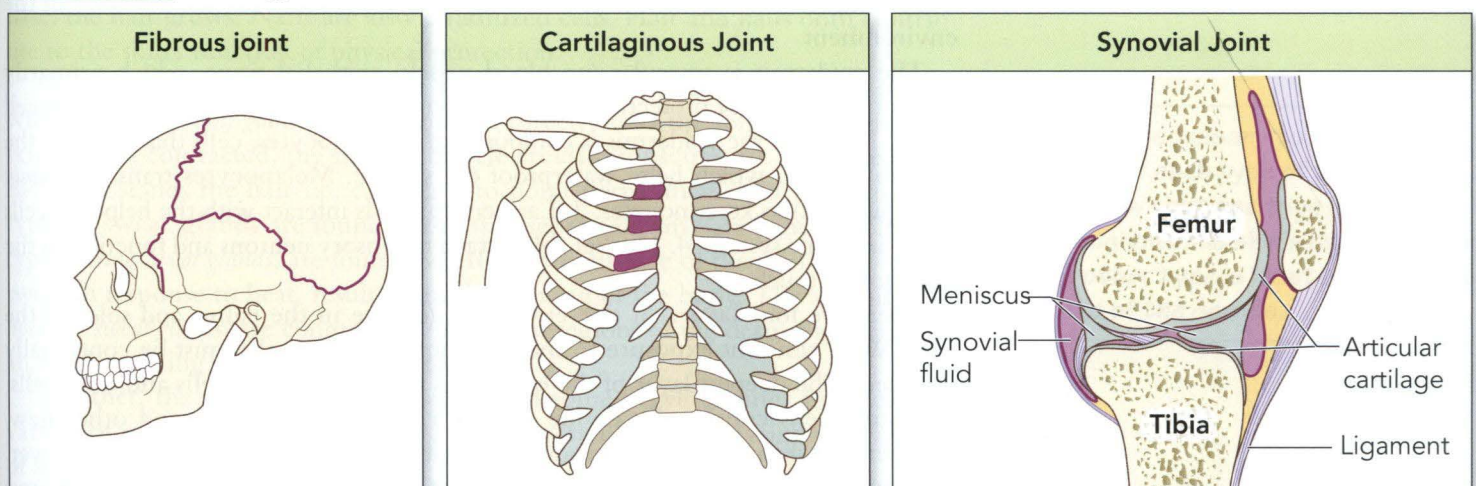
Joints are locations where bones connect in ways that allow for varying amounts of movement, depending on type. Joints are classified into three types according to their structures:

1. **Fibrous joints** occur between two bones held closely and tightly together by fibrous connective tissue, permitting extremely minimal movement. Teeth form fibrous joints with the mandible. After early childhood, skull bones form fibrous joints with each other, strengthening and hardening the skull.
2. **Cartilaginous joints** also allow little movement. They occur between two bones tightly connected by cartilage, such as the ribs and the sternum, or the pubic symphysis in the pelvis.
3. **Synovial joints** are the type of joint that are most familiar as “joints.” Bones joined by synovial joints are not bound directly by the intervening cartilage, so a wide range of movement is possible. Instead, they are separated by a capsule filled with *synovial fluid*. Synovial fluid provides lubrication and nourishment to the cartilage. In addition, the synovial fluid contains phagocytotic cells that remove microbes and particles. The shoulder and knee are two of the many examples of synovial joints in the body.



Hyaline cartilage is semi-rigid connective tissue composed of many chondrocytes (cartilage cells, pale purple). These cells synthesize an extracellular matrix (dark purple) of proteoglycans, collagen, and water that keeps them apart from each other in spaces known as lacunae. Hyaline cartilage is strong but compressible due to its high water content. It reduces friction between the bones in the knee joint as they move against each other.

FIGURE 6.10 Joint Types





This is a sample of skin from the back of a human hand.

Circulatory System
BIOLOGY 2

Nervous System
BIOLOGY 2

6.8 Skin

Skin may seem different from other organs, but like any other organ, it is a group of tissues working together to perform a specific function. Skin is the largest organ in the body and has a wide variety of functions, many of which contribute to homeostasis. Some important **functions of the skin** are:

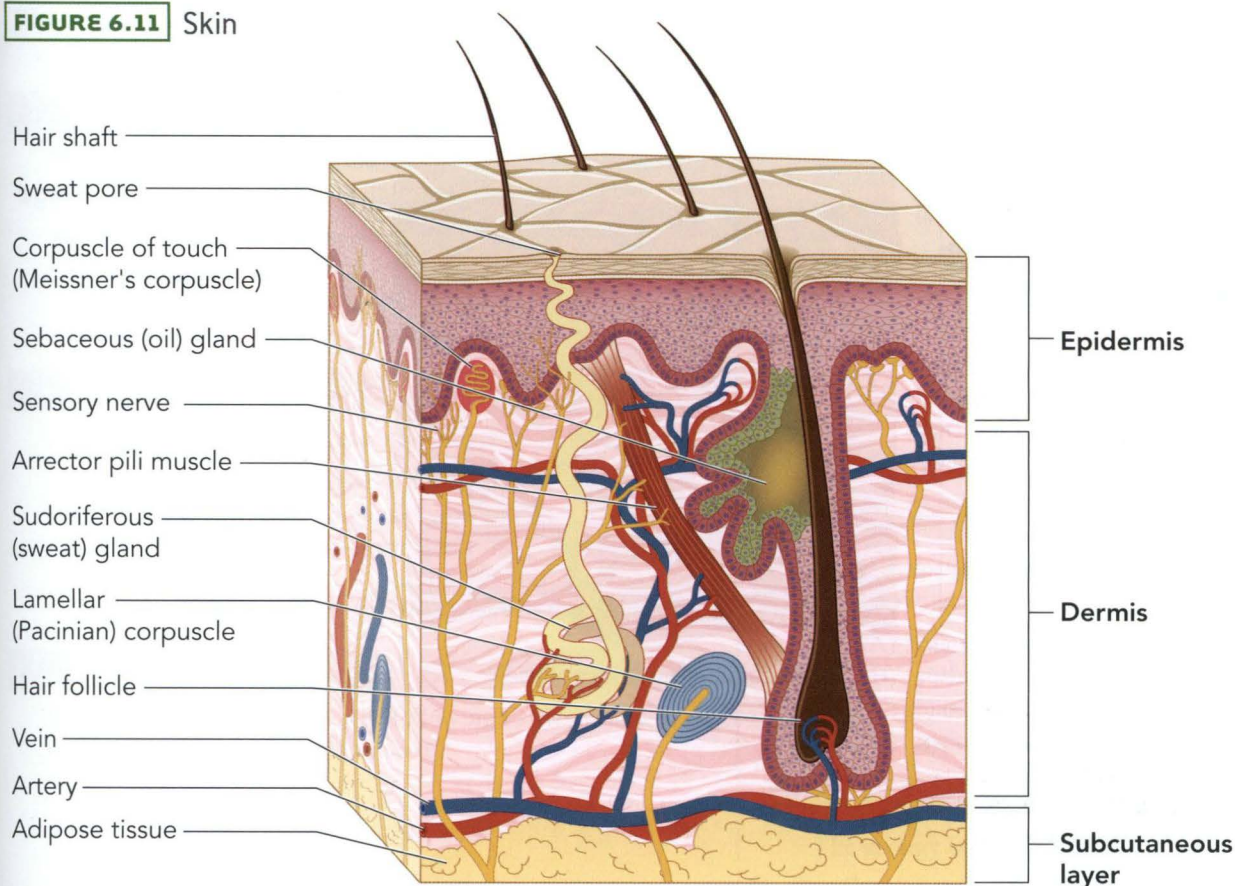
1. **Thermoregulation:** The skin helps to regulate body temperature. Blood conducts heat from the core of the body to skin. Some of this heat can be dissipated by the endothermic evaporation of sweat, but most is dissipated by radiation. Radiation is only effective if the body temperature is higher than room temperature. More blood can be directed to **surface capillaries** through **vasodilation** to allow for greater heat loss, or blood can be shunted away from the capillaries of the skin through the process of **vasoconstriction** to reduce heat loss. Thermoregulation of the body through **sweating**, vasoconstriction, and vasodilation is under the influence of hormonal control. Additionally, hairs can be erected via sympathetic stimulation of associated muscles, insulating warm air next to the skin. Skin has both warmth and cold receptors.
2. **Protection:** The skin is a physical barrier to **abrasion**, **disease organisms**, many chemicals, and ultraviolet radiation.
3. **Environmental sensory input:** The skin gathers information from the environment by sensing temperature, pressure, pain, and touch.
4. **Osmoregulation:** Skin is **relatively impermeable to water**, protecting against dehydration. However, some water and salts are excreted through the skin via diffusion. Both excretion and sweating are ways that skin contributes to osmoregulation, keeping the concentration of solutes in body fluids at the appropriate level.
5. **Immunity:** Besides being a physical barrier to bacteria, specialized cells of the epidermis are components of the immune system.
6. **Blood reservoir:** Vessels in the dermis hold up to 10% of the blood of a resting adult.
7. **Vitamin D synthesis:** Ultraviolet radiation activates a molecule in the skin that is a precursor to vitamin D. The activated molecule is modified by enzymes in the liver and kidneys to produce vitamin D.

The skin has two principal parts: 1. the superficial **epidermis**; and 2. the deeper **dermis**. Beneath both of these layers is a subcutaneous tissue called the *superficial fascia* or *hypodermis*. This subcutaneous **fat layer** is an important heat insulator for the body. It contributes to thermoregulation by helping to maintain normal core body temperatures on cold days when the skin approaches the temperature of the environment.

The epidermis is avascular (no blood vessels) epithelial tissue, which primarily serves the purpose of protection from the environment. It consists of four major cell types. 1. 90% of the epidermis is composed of **keratinocytes**, cells that produce the protein keratin, which helps waterproof the skin. 2. **Melanocytes** transfer *melanin* (skin pigment) to keratinocytes. 3. **Langerhans cells** interact with the helper T-cells of the immune system. 4. **Merkel cells** attach to sensory neurons and function in the sensation of touch.

There are four **layers of the epidermis** (or five in the palms and soles of the feet). With constant exposure to the environment, skin cells must be continually replaced. The deepest layer of the epidermis contains Merkel cells and stem cells. The stem cells continually divide to give rise to keratinocytes and other new, replacement skin cells. Once produced, keratinocytes are pushed to the top layer. As they rise, they accumulate keratin and die, losing their cytoplasm, nucleus, and

FIGURE 6.11 Skin



other organelles. When the cells reach the outermost layer of skin, they slough off the body. The process of keratinization, from birth of a cell to sloughing off, takes two to four weeks. The outermost layer of epidermis consists of 25 to 30 layers of flat, dead cells. Exposure to friction or pressure stimulates the epidermis to thicken, forming a protective **callus**.

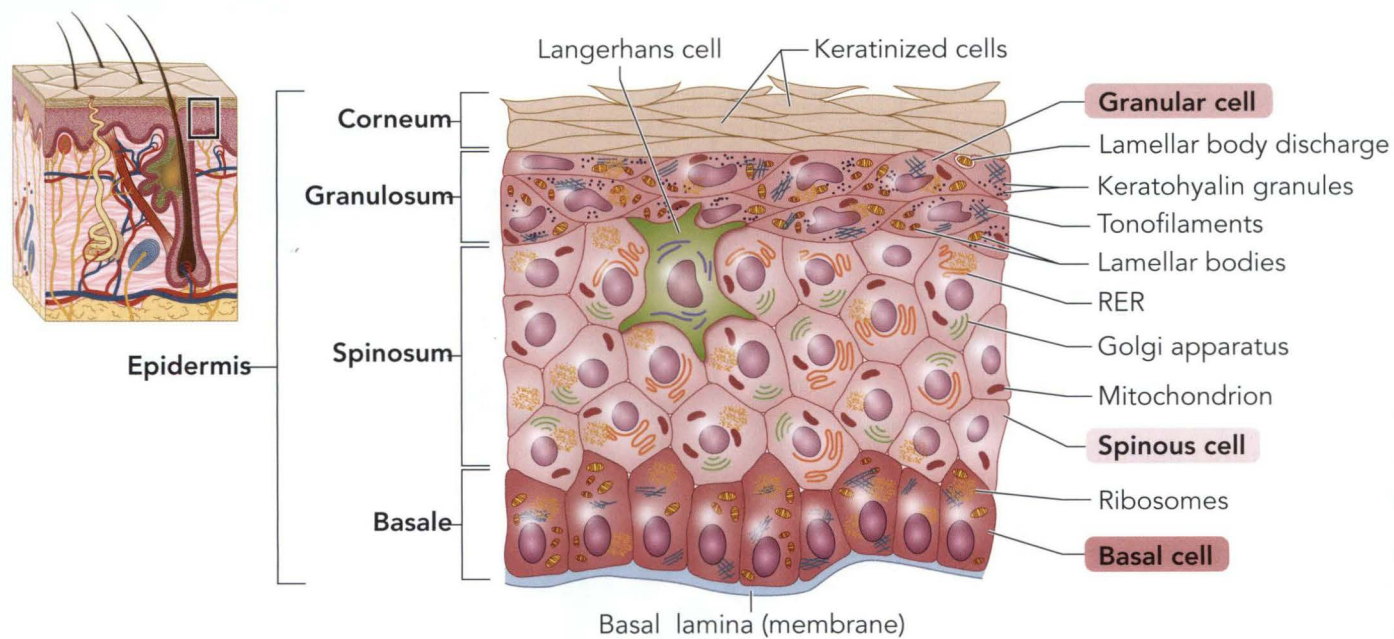
The dermis is connective tissue derived from mesodermal cells. This layer serves a variety of functions and is embedded with blood vessels, nerves, glands, and hair follicles. Collagen and elastic fibers in the dermis provide skin with strength, extensibility, and elasticity. The receptors that transmit the sensation of touch, including separate receptors for the sensations of pressure, pain, and temperature, are located in the dermis. *Hair follicles* are embedded in the dermis. **Hair** is a column of keratinized cells held tightly together. As new cells are added to its base, the hair grows. **Nails** are also keratinized cells. Hair and nails both contribute to the skin's function of physical protection.

The dermis also contains a wide variety of glands. Most hairs are associated with a *sebaceous (oil) gland* that empties oil directly into the follicle and onto the skin. When contracted, the smooth muscle **erectile musculature** associated with each hair stands the hair up, causing it to point perpendicular to the skin. Two types of **sweat glands** are found in the skin separate from hair follicles. The first type, *eccrine sweat glands*, are found over the entire surface of the skin and produce sweat in response to heat, resulting in the cooling of the body. The second type, *apocrine sweat glands*, are congregated in certain regions of the dermis and produce an acrid-smelling sweat in response to stress.

Together, the skin, hair, nails, glands, and some nerve endings function in a variety of roles, primarily concerning the protection of the body and preservation of homeostasis within an organism.

It is not necessary to know the names of each type of sweat gland, but know that one type is located throughout the skin's surface while the other type is located in certain areas of the dermis.

FIGURE 6.12 The Epidermis



These questions are NOT related to a passage.

Item 137

The production of which of the following cell types would most likely be increased by parathyroid hormone?

- ☐ A) Osteoprogenitors
- ☐ B) Osteocytes
- ☐ C) Osteoclasts
- ☐ D) Osteoblasts

Item 138

In a synovial joint, the purpose of synovial fluid is to:

- ☐ A) reduce friction between bone ends.
- ☐ B) keep bone cells adequately hydrated.
- ☐ C) occupy space until the bones of the joint complete their growth.
- ☐ D) maintain a rigid connection between two flat bones.

Item 139

Surgical cutting of which of the following tissues would result in the LEAST amount of pain?

- ☐ A) Muscle
- ☐ B) Bone
- ☐ C) Cartilage
- ☐ D) Skin

Item 140

In a synovial joint, the connective tissues holding the bones together are called:

- ☐ A) ligaments.
- ☐ B) tendons.
- ☐ C) muscles.
- ☐ D) osseous tissues.

Item 141

All of the following are functions of bone EXCEPT:

- ☐ A) mineral storage.
- ☐ B) structural support.
- ☐ C) blood temperature regulation.
- ☐ D) fat storage.

Item 142

All of the following are found in compact bone EXCEPT:

- ☐ A) yellow marrow.
- ☐ B) Haversian canals.
- ☐ C) canaliculi.
- ☐ D) Volkmann's canals.

Item 143

Hydroxyapatite, the mineral portion of bone, contains all of the following elements except:

- ☐ A) calcium.
- ☐ B) sulfur.
- ☐ C) phosphate.
- ☐ D) hydrogen.

Item 144

The spongy bone of the hips is most important for:

- ☐ A) red blood storage.
- ☐ B) red blood cell synthesis.
- ☐ C) fat storage.
- ☐ D) lymph fluid production.

TERMS YOU NEED TO KNOW

A band	H zone	Relatively impermeable to water
Abrasion	Hair	Sarcomere
Acetylcholine	I band	Sarcoplasmic reticulum
Actin	Immunity	Skeletal muscle
Blood reservoir	Intermediate filaments	Skin
Bone	Involuntary muscle	Shivering reflex
Calcium/protein matrix	Irregular bone	Short bones
Callus	Keratinocytes	Sliding filament model
Cardiac muscle	Langerhans cells	Slow twitch fibers (type I)
Cartilage	Layers of the epidermis	Smooth muscle
Cartilaginous joints	Ligament	Specialized bone types
Compact bone (cortical bone)	Long bones	Spongy bone
Contractile apparatus	M line	Striated muscle
Contractile velocity	Melanocytes	Surface capillaries
Cross-bridges	Merkel cells	Sweat glands
Dermis	Motor end plate	Sweating
Disease organisms	Motor neuron	Sympathetic innervation
Endocrine control	Muscle fatigue	Synovial joints
Endoskeleton	Myoglobin	Tendon
Environmental sensory input	Myosin	Thermoregulation
Epidermis	Nails	Thick filaments
Erectile musculature	Neuromuscular junction	Thin filaments
Excretion	Osmoregulation	Tropomyosin
Exoskeleton	Osteoblasts	Troponin
Fast twitch fibers (type II)	Osteoclasts	T-tubules
Fat layer	Osteocytes	Vasoconstriction
Fibrous joints	Oxygen debt	Vasodilation
Flat bones	Parasympathetic innervation	Vitamin D synthesis
Functions of bone	Peripheral circulatory assistance	Voluntary muscle
Functions of muscle	Protection	Z line
Functions of skin vitamin D synthesis	Red bone marrow	



DON'T FORGET YOUR KEYS

1. Somatic NS innervates voluntary muscles; autonomic NS innervates involuntary muscle.
2. See Ca^{2+} , think neuromuscular function and storage in bone.
3. The energy of an ATP molecule prepares the myosin head so that the muscle is ready and contraction is downhill in energy.

STOP!

DO NOT LOOK AT THESE EXAMS UNTIL CLASS.

**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 1**

Passage I (Questions 1-8)

Viruses possess two methods of reproduction, the lysogenic and the lytic cycles. Prophage viruses can be induced to become virulent in response to environmental conditions. One such condition is biofilm formation. Biofilms are composed of bacterial cells embedded in a self-generated polymer matrix. Lysogenic bacteria are theorized to play a role in biofilm formation by being induced into virulence when bacterial autolysin, a hydrolytic enzyme which cleaves cell walls, is produced. Researchers tested the hypothesis that the presence of prophage during conditions favoring biofilm formation in the gram-positive bacteria *Streptococcus pneumoniae* would cause increased biofilm formation.

Experiment 1

Researchers observed biofilm growth of two strains of *S. pneumoniae*, R36A and R36AP. The difference between these two strains was the presence of prophage in R36AP. Wild type strains were observed, along with strains which had genes for the bacterial autolysin *LytA* and the phage lysin *Svl* knocked out (Figure 1).

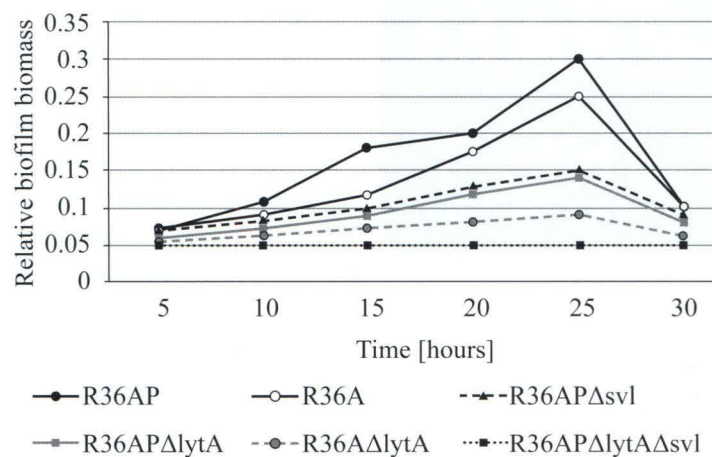


Figure 1. Effect of lysogeny and phage induction in *Streptococcus pneumoniae* biofilm development

Experiment 2

Extracellular DNA is a key component of the biofilm matrix. Varying amounts of DNase I were incubated with R36A and R36AP. The relationship between concentration of DNase I and biofilm growth was observed for R36A and R36AP (Figure 2).

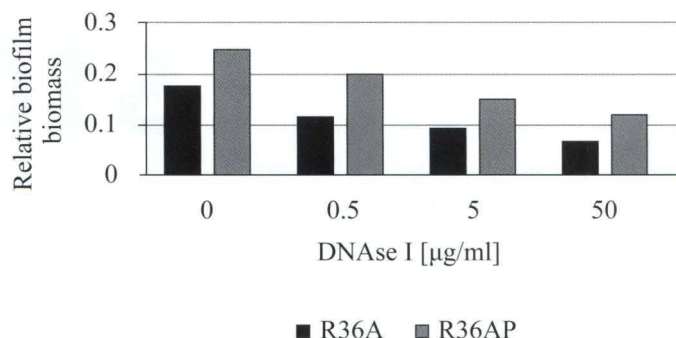


Figure 2 Effect of adding DNase I on *Streptococcus pneumoniae* biofilm mass

Experiment 3

To further test the role of extracellular DNA on biofilm growth, DNA was taken from R36A and salmon sperm and incubated with both strains. Growth was observed (Figure 3).

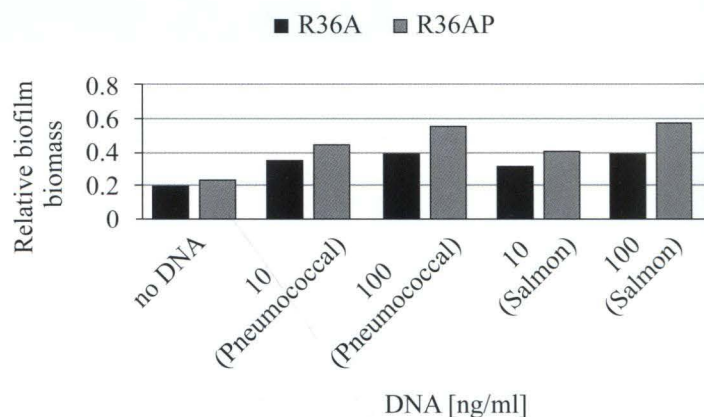


Figure 3 Effect of adding external DNA on *Streptococcus pneumoniae* biofilm mass

This passage was adapted from "Prophage Spontaneous Activation Promotes DNA Release Enhancing Biofilm Formation in *Streptococcus pneumoniae*." Carrolo M, Frias MJ, Pinto FR, Melo-Cristino J, Ramirez M. *PLoS ONE*. 2010. 5(12) doi: 10.1371/journal.pone.0015678 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

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1. During the lytic cycle, which component of the host *S. pneumoniae* is most likely to be under phage control?
 - A. Nucleus
 - B. Ribosomes
 - C. Mitochondria
 - D. Endoplasmic Reticulum
 2. Which of the following cell wall components does phage lysin most likely disrupt?
 - A. Peptidoglycan
 - B. Phospholipids
 - C. Lipopolysaccharides
 - D. Lipid A
 3. According to Figure 1, what effect does phage lysin have on biofilm growth?
 - A. Consistently higher growth rates
 - B. Higher growth rates, but only in the presence of autolysin
 - C. Variable effects depending upon the amount of time that has passed
 - D. No clear answer can be derived from this data
 4. What is the most likely reason for the loss of biofilm mass between 25 and 30 hours in figure 1?
 - A. Nutrient degradation and/or depletion from biofilm overgrowth leads to population decrease.
 - B. The released lysin will begin to break down some of the extracellular matrix components.
 - C. The virulent bacteriophage can now spread, infecting and killing host cells which compose the biofilm.
 - D. After population hits a critical size, the number of cells begins to increase but the size of the slime matrix begins to decrease.
 5. How does DNase affect biofilm mass?
 - A. It increases mass by cross-linking matrix DNA.
 - B. It decreases mass by degrading intracellular DNA. This in turn causes some of the bacteria to lose their autolysin gene and prevents them from rupturing to contribute to biofilm.
 - C. It decreases mass by reacting with extracellular DNA and producing a product which cannot cross-link into the extracellular matrix.
 - D. It decreases mass by degrading extracellular DNA.
 6. Why did the researchers choose to incorporate salmon DNA in experiment 3?
 - A. Salmon have genes encoding for proteins that can increase the rate of biofilm formation
 - B. To serve as a control and ensure that the *S. pneumoniae* DNA is uniquely contributing to the biofilm growth
 - C. To serve as a control and ensure that the *S. pneumoniae* DNA is not uniquely contributing to the biofilm growth
 - D. To compare the effects of bacterial and animal DNA on biofilm growth
 7. What would happen if both DNase and extracellular DNA were incubated with an *S. pneumoniae* strain which was forming a biofilm?
 - A. There would be net growth of biofilm mass compared to the strain alone.
 - B. There would be net loss of biofilm mass compared to the strain alone.
 - C. There would be no net effect on biofilm growth.
 - D. This question can't be answered with the information provided.
 8. What shape is *S. pneumoniae*?
 - A. Rod shaped
 - B. Round
 - C. Helical
 - D. Cuboidal
-

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Passage II (Questions 9-15)

In a healthy cell, smooth endoplasmic reticulum (ER) performs several functions including carbohydrate metabolism, lipid synthesis, and oxidation of foreign substances such as drugs, pesticides, toxins and pollutants.

The smooth ER synthesizes several classes of lipids, including triacylglycerols which are stored in the ER lumen, cholesterol and its steroid hormone derivatives, and phospholipids for incorporation into the various membranous cell structures. Phospholipids are synthesized only along the cytosol side of the ER membrane. They are then selectively flipped to the other side of the cell membrane by phospholipid translocators.

Most detoxification reactions in the smooth ER involve oxidation. Such reactions usually involve the conversion of hydrophobic compounds into hydrophilic compounds, and are governed by a system of enzymes called mixed-function oxidases. Cytochrome P-450, a group of iron-containing integral membrane proteins, is a central component of one mixed-function oxidase system. Mixed function oxidases also govern the oxidation of nonpolar endogenous compounds, such as steroids and fatty acids. Ingestion of the depressant phenobarbital triggers an increase in smooth ER and mixed-function oxidases but not in other ER enzymes.

Previous work has shown that cytochrome P450 activity is enhanced in phospholipid rich environments. This provides a possible mechanism for increasing cytochrome P450 activity in response to toxic foreign substances. Researchers sought to determine what effect a highly toxic substance would have on phospholipid levels by studying the effects of Carbofuran, an organic compound which is used as a pesticide.

Experiment 1

Carbofuran was injected into the abdominal cavity of live catfish. After two days, the catfish were sacrificed. Liver membrane fractions were isolated, and lipid and phospholipid levels were measured. (Figure 1).

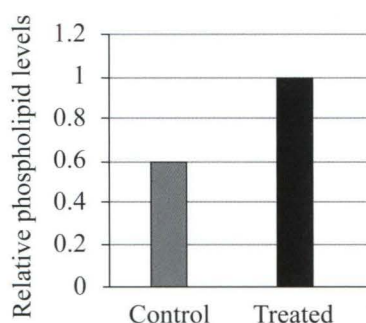


Figure 1 Carbofuran treated fish liver cells

This passage was adapted from "Membrane Phospholipid Augments Cytochrome P4501A Enzymatic Activity by Modulating Structural Conformation during Detoxification of Xenobiotics". Ghosh MC and Ray AK. *PLoS ONE*. 2013. 8(2) doi: 10.1371/journal.pone.0057919 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

9. Which of the following tissues would be expected to have especially well developed smooth ER?
 - A. Skeletal muscle
 - B. Adrenal cortex
 - C. Intestinal epithelium
 - D. Cardiac muscle
10. Where are many of the enzymes necessary for phospholipid synthesis likely to be located?
 - A. ER lumen
 - B. Cytosol
 - C. Lysosome
 - D. Golgi complex
11. How do phospholipids most likely affect Cytochrome P450 activity?
 - A. By upregulating P450 production
 - B. By downregulating P450 degradation
 - C. By modulating structural conformation of P450
 - D. By providing a pathway for exocytosis
12. The primary structure of mixed function oxidases is most likely synthesized at the:
 - A. smooth ER.
 - B. rough ER.
 - C. Golgi apparatus.
 - D. cellular membrane.
13. Which of the following endogenous compounds would a mixed-function oxidase most likely detoxify?
 - A. Estradiol
 - B. Lysine
 - C. Carbofuran
 - D. Ethanol
14. Some cells, called adipocytes, specialize in the storage of triacylglycerols synthesized by the smooth ER. The primary function of adipocytes is to:
 - A. maintain chemical homeostasis of the body.
 - B. filter and remove toxins.
 - C. provide for cholesterol synthesis.
 - D. serve as a reservoir of stored energy.
15. If a third group of fish was treated with both phenobarbital and Carbofuran, their phospholipid levels would be expected to be:
 - A. higher than both the control and experimental group.
 - B. higher than the control but lower than the experimental group.
 - C. lower than both the control and experimental group.
 - D. higher than the experimental but lower than the control group.

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Passage III (Questions 16-20)

The cell membrane is generally impermeable to most of the ions necessary for the normal functions of the cell. However, ion channels are embedded into the cell membrane to allow regulated entry and exit of ions. Without these, necessary functions such as metabolism and cell signaling would not be possible.

The selectivity of K^+ channels in cellular membranes allows the passage of K^+ ions while restricting passage of the chemically similar Na^+ ions. This differential permeability maintains the electrical potential across cellular membranes. Using isothermal titration calorimetry (ITC), researchers studied how K^+ channels discriminate between potassium and sodium ions by measuring ion binding to the *Streptomyces lividans* K^+ channel (KcsA) under equilibrium conditions. Two solutions containing equal amounts of KcsA were created. A solution of KCl was titrated into one of the solutions, and a solution of NaCl was titrated into the other. The heat exchange created during the titrations is shown in Figure 1.

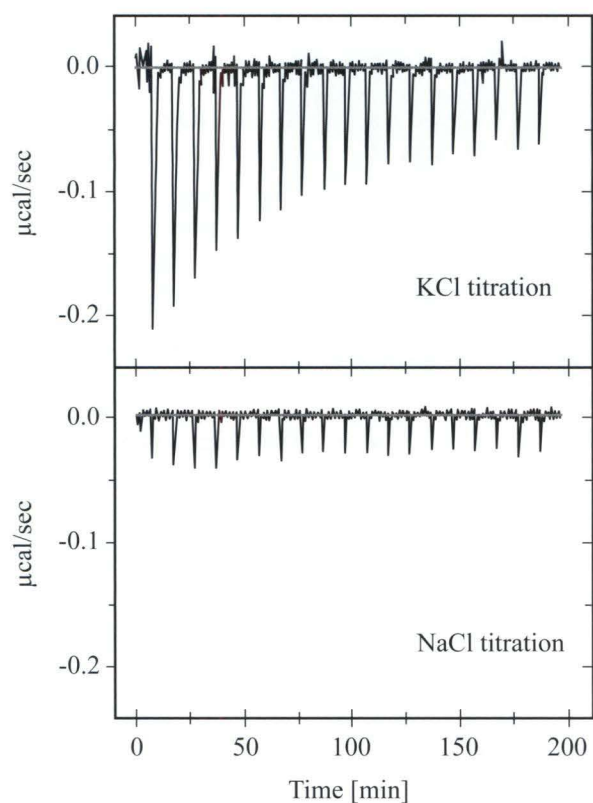


Figure 1 ITC titration of alkali metal cations binding to KcsA

Each downward deflection in the graph represents the heat exchange brought about by an injection of KCl or NaCl. Heat exchange can occur from the heat of diluting the titrant or from the net heat of transfer of ions from solution to the channel, both exothermic processes.

The same procedure was also carried out with other ions. For the ions that exhibited binding to KcsA, the values of ΔG for their reactions with the channel were obtained. The results are shown in Table 1.

Ion	Radius	ΔG° (kcal M^{-1})
Na^+	0.95 Å	
K^+	1.33 Å	-4.54 ± 0.06
Rb^+	1.48 Å	-5.29 ± 0.29
Cs^+	1.69 Å	-4.53 ± 0.17
Mg^{2+}	0.65 Å	
Ca^{2+}	0.99 Å	
Ba^{2+}	1.35 Å	-5.03 ± 0.15

Table 1 ΔG obtained for ion binding with KcsA

This passage was adapted from "Structural and Thermodynamic Properties of Selective Ion Binding in a K^+ Channel." Lockless SW, Zhou M, MacKinnon R. *PLoS Biology*. 2007. 5(5) doi: 10.1371/journal.pbio.0050121 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

16. According to the data shown in Table 1, which factor was found to be a significant determinant of ion channel permeability?
 - A. The charge of the ion
 - B. The size of the ion
 - C. The concentration of ions in solution
 - D. The number of ion channels in solution
17. Ion channels are necessary for ion transport across a cell membrane because:
 - A. hydrophobic ions cannot pass through the hydrophilic center of the cellular membrane.
 - B. ions are generally too large to pass through the tight connections between cell surface lipids.
 - C. the lipid bilayer creates a doubly impenetrable barrier.
 - D. the polar ions cannot pass through the non-polar lipid bilayer.
18. KcsA transports K^+ ions from the intracellular space to the extracellular space, down an electrochemical gradient created by an Na^+/K^+ ATPase pump. This is an example of which type of transport?
 - A. Primary active transport
 - B. Secondary active transport
 - C. Facilitated diffusion
 - D. Osmosis

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19. Which conclusion is supported by the results shown in Figure 1?

- A. Larger ions pass through ion channels more easily than smaller ions.
- B. The cellular membrane contains surface proteins that allow passage of ions into the cell.
- C. Na^+ ions do not bind to KcsA.
- D. K^+ is an exothermic ion.

20. According to the fluid mosaic model, K^+ channels:

- A. are transported from the nucleus to the outer membrane.
 - B. create the electrochemical gradient necessary for cellular functions.
 - C. contain a hydrophobic portion that allows them to insert into the membrane.
 - D. create energy for the cell.
-

Questions 21 through 23 are **NOT** based on a descriptive passage.

21. Which of the following **LEAST** describes the process of evolution?

- A. A heritable change in genes
- B. A change in the total frequency of alleles in a population
- C. A phenotypic shift based on inbreeding
- D. Two different species developing from a common ancestor

22. Which of the following must be present for a population to be considered in Hardy-Weinberg equilibrium?

- A. Natural selection
- B. Large population size
- C. Non-random mating
- D. Emigration

23. Which of the following does **NOT** correctly describe a characteristic that is true of eukaryotic cells but not prokaryotic cells?

- A. Eukaryotic cells have a membrane-bound nucleus.
- B. Eukaryotic DNA is coiled with histone proteins.
- C. Eukaryotic cells contain ribosomes.
- D. Eukaryotic flagella are composed of microtubules.

STOP. IF YOU FINISH BEFORE TIME IS CALLED, CHECK YOUR WORK. YOU MAY GO BACK TO ANY QUESTION IN THIS TEST BOOKLET.

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DO NOT LOOK AT THESE EXAMS UNTIL CLASS.

**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 2**

Passage I (Questions 24-30)

Circadian rhythms, regular cycles of physiological activity throughout the day, are generated by a central clock located in the hypothalamic suprachiasmatic nucleus (SCN) and subordinate clocks in peripheral tissues. The SCN clock responds to external cues, such as light, and drives peripheral clocks via circadian output pathways. Both the central and peripheral clocks are operated by feedback loops of circadian genes, including *Period1* and 2. It has been proposed that cell proliferation *in vivo* is paced by both central and peripheral clocks. Disruption of circadian rhythm, which has been linked with increased cancer risk, would then promote tumor development due to loss of the homeostasis of cell cycle control.

The central clock generates a robust circadian rhythm in sympathetic nervous system (SNS) signaling via direct and indirect targeting of neurons located in the hypothalamic autonomic paraventricular nucleus. *In vivo*, the SNS controls peripheral tissues by releasing the hormones epinephrine and norepinephrine that target adrenergic receptors (ADRs) on the cell membrane. Norepinephrine is directly released from postganglionic sympathetic neurons, whereas epinephrine is released from chromaffin cells located in the adrenal medulla. Chromaffin cells are controlled by preganglionic sympathetic neurons and are themselves modified sympathetic postganglionic neurons.

Scientists proposed that jet-lag disrupts the homeostasis of multiple circadian output pathways including the SNS. To test this hypothesis, they studied urine epinephrine levels in mice with mutations of the circadian genes *Period1* and 2 (*Per1^{-/-};Per2^{m/m}*) and weight-matched controls (*Wt*).

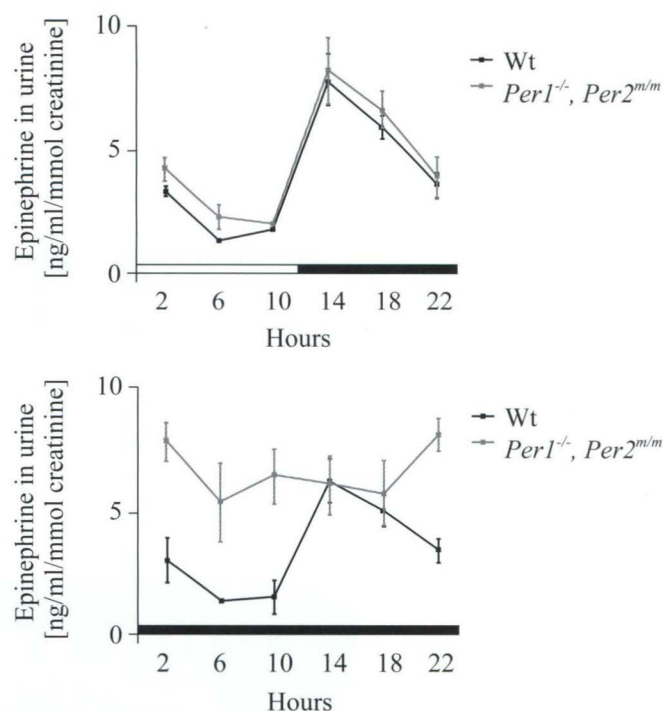


Figure 1 Urine epinephrine levels in *Per*-mutant mice and weight-matched controls during 24 hr light/dark and dark/dark cycles

This passage was adapted from "Disrupting Circadian Homeostasis of Sympathetic Signaling Promotes Tumor Development in Mice." Lee S, Donehower LA, Herron AJ, Moore DD, Fu L. *PLoS ONE*. 2010. 5(6) doi:10.1371/journal.pone.0010995 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

24. Which of the following cell types most likely contain adrenergic receptors?
 - A. Chromaffin cells
 - B. Sympathetic postganglionic neurons
 - C. Parasympathetic postganglionic neurons
 - D. Cardiac muscle cells
25. Suppose that the researchers wanted to determine whether there were significant differences between the *Per* mutant mice and weight-matched controls in urine epinephrine levels at each time measured. Which of the following tests would they most likely use?
 - A. ANOVA
 - B. T-test
 - C. Correlation
 - D. Chi-square
26. Which is **LEAST** likely to be affected by the circadian rhythm of SNS signaling?
 - A. The arteries of the heart
 - B. The iris musculature of the eye
 - C. The diaphragm
 - D. Sweat glands

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27. When combined with the data shown in Figure 1, which finding would provide greatest support to the hypothesis that jet lag contributes to tumor formation in *Per* mutant mice?
- The circadian rhythm of SNS signaling encourages activation of the *Myc* oncogene.
 - In humans, deregulation of the *Per* gene is associated with increased risk for a variety of cancers.
 - Rhythmic SNS signaling plays a role in regulation of cell proliferation.
 - Previous studies have shown that *Per1^{-/-};Per2^{m/m}* mice are deficient in cell cycle regulation and cancer-prone.
28. Which of the following is most likely **NOT** associated with activation of chromaffin cells?
- Increased heart rate
 - Elevated blood glucose levels
 - Increased basal metabolism
 - Constricted pupils
29. Suppose that the researchers chose to follow groups of human subjects with differing degrees of jet lag over time and record their urine levels of epinephrine. The ability to conclude causality for any observed effect would be limited because:
- the subjects would not all be *Per* mutant.
 - in an observational study design, urine levels of epinephrine cannot be obtained.
 - the requirement of temporality would not be met.
 - the subjects would not be randomly assigned into groups.
30. Which of the following would increase the amount of norepinephrine in the synapse between postganglionic neurons and their effectors?
- Inhibition of the enzyme that catalyzes norepinephrine breakdown
 - Increased reabsorption by the postganglionic neuron
 - Inhibition of norepinephrine reuptake
- I only
 - I and III only
 - II and III only
 - I, II and III

Passage II (Questions 31-37)

Photoreceptors, the sensory receptor cells of the visual system, are a specialized class of neurons found in the retina. Unlike most neurons, photoreceptors are depolarized and release neurotransmitters in their baseline state. When the photoreceptor pigment rhodopsin absorbs a photon, the cell becomes impermeable to cations and hyperpolarizes. This effect is largely due to hydrolysis of the second messenger cyclic GMP (cGMP) and the subsequent closure of cGMP-sensitive cation channels.

To return to a depolarized state after light stimulation, photoreceptors must undergo the process known as recovery, which is largely dependent on the synthesis of new cGMP by retinal membrane guanylyl cyclase (RetGC). RetGCs are activated by guanylyl cyclase activating proteins (GCAPs), whose activity is dependent on free Ca^{2+} concentrations within the cell. In the dark, intracellular Ca^{2+} levels are high, and GCAPs are inhibited. Under illumination, however, Ca^{2+} levels fall, and GCAPs can more easily stimulate RetGCs to produce cGMP.

There are two main GCAPs in mammals, with differing intrinsic sensitivities to Ca^{2+} : GCAP1 and GCAP2. Experimenters explored the differences between the two by generating mutant mice lacking functional GCAP1 (*GCAP1^{-/-}*).

Experiment 1

Retinas from wild type (WT) and *GCAP1^{-/-}* mice were exposed to buffers containing varying Ca^{2+} concentrations, and cGMP levels were measured. (Figure 1)

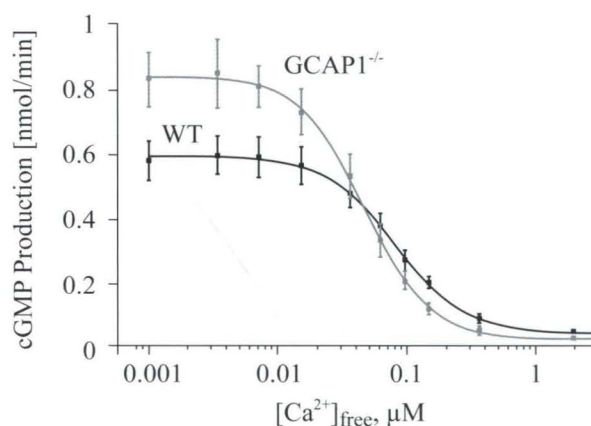


Figure 1. Effects of $[\text{Ca}^{2+}]$ on cGMP production in WT and *GCAP1^{-/-}* retinas.

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Experiment 2

Experimenters calculated ratios of RetGC activity to baseline (activity in the absence of Ca^{2+}) as Ca^{2+} levels were increased. (Figure 2)

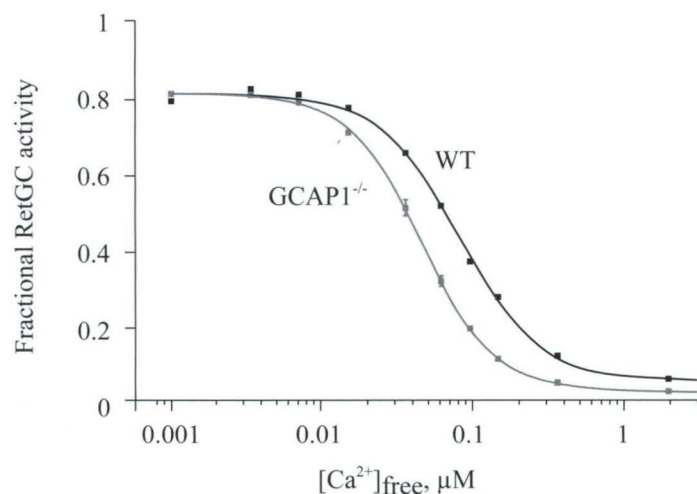


Figure 2 RetGC activity as a fraction of baseline as $[\text{Ca}^{2+}]$ increases in WT and GCAP1^{-/-} retinas.

This passage is adapted from "Enzymatic Relay Mechanism Stimulates Cyclic GMP Synthesis in Rod Photoresponse: Biochemical and Physiological Study in Guanylyl Cyclase Activating Protein 1 Knockout Mice." Makino CL, Wen XH, Olshevskaya EV, Peshenko IV, Savchenko AB, Dizhoor AM. *PLoS ONE*. 2012. 7(10) doi:10.1371/journal.pone.0047637 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

31. Electrophysiological recordings allow researchers to monitor the electrical activity of single neurons or entire nerves in real time. Field electrodes can detect general stimulation for an entire brain region, while techniques such as patch recording measure areas as small as a single subcellular compartment. Suppose the researchers wanted to measure the circuit effects of GCAP1 deletion on an animal's ability to recognize familiar objects in the photoreceptor field. What region of the visual pathway should they record from?
 - A. Horizontal cells of the retina
 - B. Central inferotemporal area of the temporal lobe
 - C. Optic chiasm
 - D. Magnocellular layers of the lateral geniculate nucleus
32. Which of the following best explains the results shown in Figure 2?
 - A. Knocking out GCAP1 had no effect on activating proteins.
 - B. Knocking out GCAP1 reduced the number of activating proteins by 50%.
 - C. GCAP1 is more sensitive to calcium than GCAP2.
 - D. GCAP2 is more sensitive to calcium than GCAP1.
33. The experimenters also studied photoreceptor recovery *in vivo* by generating mutant mice that produce fluorescently tagged cGMP and imaging the retina at specific time points after bleaching the photoreceptors with pulses of visible light. This experiment focused only on rod photoreceptors. What adjustments might the researchers make to repeat this study in specific cone cell types?
 - A. Use pulses of the entire visible spectrum.
 - B. Use pulses of light with wavelengths below 300 nm.
 - C. Use pulses of light of only one wavelength.
 - D. Use fluorescently tagged cAMP.
34. Given the passage information, which of the following must be FALSE?
 - I. GCAP1 is necessary for generating new photoreceptor action potentials.
 - II. GCAP1 is necessary for normal photoreceptor recovery.
 - III. GCAP2 is necessary for normal photoreceptor recovery.
 - A. I only
 - B. II only
 - C. I and II only
 - D. II and III only
35. Which of the following is **NOT** needed by photoreceptors for normal functioning?
 - A. GCAP1
 - B. Insulin
 - C. cGMP
 - D. Vitamin A
36. The amount of light reaching the retina is controlled by the radial and circular muscles of the iris. Would adrenergic signaling onto these muscles be expected to increase or decrease photoreceptor recovery?
 - A. Increase due to pupil dilation
 - B. Increase due to pupil constriction
 - C. Decrease due to pupil dilation
 - D. Decrease due to pupil constriction
37. Based on the information in Figure 2, which of the following best explains why cGMP production increased at low Ca^{2+} levels in GCAP1^{-/-} mice in Figure 1?
 - A. Compensatory increase in GCAP2
 - B. Decreased Ca^{2+} sensitivity of GCAP2
 - C. Decreased RetGC activity
 - D. Increased photobleaching due to active rhodopsin

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Passage III (Questions 38-43)

Cholinergic receptors are subdivided into two broad classifications: nicotinic and muscarinic. The nicotinic acetylcholine receptor (nAChR) is a ligand-gated sodium channel that regulates Na,K-ATPase and is stimulated by nicotine. The nAChR specifically co-immunoprecipitates with both α_1 and α_2 isoforms of the Na,K-ATPase α -subunit and phospholemman (PLM), a muscle-specific auxiliary subunit of Na,K-ATPase which modulates sodium pump activity. Na,K-ATPase is the only known receptor for the poison ouabain.

Active transport by Na,K-ATPase generates a negative membrane potential, V_{pump} , due to the net outward transfer of one positive charge per transport cycle (3 Na^+ out per 2 K^+ in). V_{pump} adds directly to the Nernst potential arising from the ion concentration differences, resulting in the following equation for resting membrane potential (RMP): $\text{RMP} = E_{\text{Nernst}} + V_{\text{pump}}$.

Stimulation of Na,K-ATPase activity by acetylcholine (ACh) produces membrane hyperpolarization by shifting Na^+ channels from the inactive to available conformation. While nanomolar concentrations of nicotine have been shown to stimulate the Na,K-ATPase α_2 isoform by this mechanism, *in vivo* effects of cigarette smoking on the activity of these nAChRs remains largely uncharacterized.

Nicotine was administered orally to rats for 21-31 days at a dosage shown to produce a plasma nicotine pattern similar to that seen in smokers. The effect on diaphragm muscle removed from euthanized rats is shown in Figure 1.

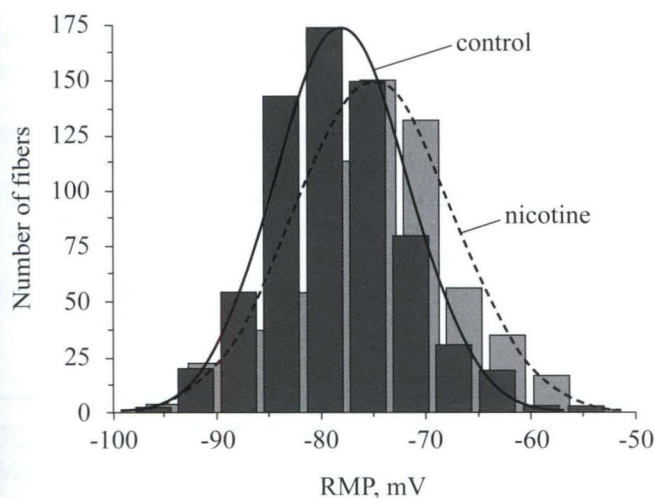


Figure 1 Distribution histogram of resting membrane potentials in the diaphragm of control (black bars) and nicotine-treated rats (light gray bars)

This passage was adapted from "Chronic Nicotine Modifies Skeletal Muscle Na,K-ATPase Activity through Its Interaction with the Nicotinic Acetylcholine Receptor and Phospholemman." Chibalin AV, Heiny JA, Benziane B, Prokofiev AV, Vasiliev AV, Kravtsova VV, Krivov II. *PLoS ONE*. 2012. 7(3) doi:10.1371/journal.pone.0033719 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

38. Based on the passage information, where is phospholemman most likely to be found?
 - A. The dendrites
 - B. The soma
 - C. The presynaptic membrane
 - D. The postsynaptic membrane
39. According to Figure 1, what was the primary result of nicotine exposure in rats?
 - A. Increased muscular excitability
 - B. Decreased muscular excitability
 - C. Increased neuronal excitability
 - D. Decreased neuronal excitability
40. Suppose that repeating the experiment described in the passage with administration of ouabain resulted in equivalent RMPs among both the experimental and control group. What would this suggest about the findings from Experiment 1?
 - A. The change in RMP resulted from a change in V_{pump} .
 - B. The change in RMP resulted from a change in E_{Nernst} .
 - C. The change in RMP was unrelated to changes to E_{Nernst} or V_{pump} .
 - D. The change in RMP was due to experimental error.
41. Which conclusions are compatible with the results shown in Figure 1?
 - I. Nicotine exposure results in overexpression of Na,K-ATPase α_2 isoform.
 - II. Nicotine exposure results in underexpression of Na,K-ATPase α_2 isoform.
 - III. Nicotine exposure results in desensitization of the nAChR.
 - A. I only
 - B. I and III only
 - C. II and III only
 - D. I, II, and III
42. The Nernst potential measures the equilibrium potential across a neuronal membrane. All of the following help to establish the resting potential of a neuronal membrane EXCEPT:
 - A. selective permeability of the cell membrane.
 - B. the Na^+/K^+ pump.
 - C. the Na^+ voltage gated channels.
 - D. the electrochemical gradient of multiple ions.

43. Myasthenia gravis is an autoimmune neuromuscular condition that results in production of antibodies that block acetylcholine receptors at the postsynaptic muscular junction. Symptoms include muscle fatigue. Based on the passage, how might cigarette smoking affect sufferers of myasthenia gravis?

- A. Symptoms would improve because the resting membrane potential would increase.
 - B. Symptoms would worsen because the resting membrane potential would increase.
 - C. Symptoms would improve because the resting membrane potential would decrease.
 - D. Symptoms would worsen because the resting membrane potential would decrease.
-

Questions 44 through 46 are **NOT** based on a descriptive passage.

44. In saltatory conduction:

- A. an action potential jumps along a myelinated axon from one node of Ranvier to the next.
- B. an action potential moves rapidly along the membrane of a Schwann cell, which is wrapped tightly around an axon.
- C. an action potential jumps from the axon of one neuron to the dendrites of the next.
- D. ions jump from one node of Ranvier to the next along an unmyelinated axon.

45. All of the following are true concerning a typical motor neuron **EXCEPT**:

- A. the K^+ concentration is greater inside the cell than outside the cell.
- B. K^+ voltage-gated channels are more sensitive than Na^+ voltage-gated channels to a change in membrane potential.
- C. Cl^- concentrations contribute to the membrane resting potential.
- D. the action potential begins at the axon hillock.

46. Which of the following statements regarding the thalamus is true?

- A. The thalamus maintains homeostasis in many physiological activities by coordinating between nervous and endocrine signaling.
- B. The major neural pathways for both visual and auditory information pass through the thalamus.
- C. Higher-level processing of the complex features of multiple types of sensory information take place in the thalamus.
- D. The thalamus is a critical site of processing for olfactory information.

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**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 3**

Passage I (Questions 47-53)

Peptide hormones and catecholamines, a class of tyrosine derivatives, bind to membrane-bound receptors on their effector cells and act via second messenger systems.

One common second messenger system works as follows: the bound hormone receptor activates a protein inside the cell, called a G-protein. Once activated, the G-protein exchanges GDP for GTP, causing a portion of the G-protein to dissociate. The dissociated portion may stimulate or inhibit *adenylyl cyclase*, another membrane bound protein. Inhibitory G-proteins are called G_i -proteins; stimulating G-proteins are called G_s -proteins. After acting on adenylyl cyclase, the dissociated portion of the G-protein hydrolyzes GTP to GDP in order to become inactive and recombine with its other portion. Adenylyl cyclase converts ATP to cyclic AMP (cAMP). cAMP activates *protein kinase A*, which causes changes in protein phosphorylation throughout the cell.

Dopamine (DA) is a catecholamine that can act as a hormone. Depending on the type of receptor that it binds to, hormonal dopamine can have either a stimulatory or inhibitory effect on adenylyl cyclase. *Dopamine receptor D1* (D1R) and *D2* (D2R), for example, act antagonistically to one another.

DA signaling can affect the release of the hormone prolactin (PRL) and the cytokine leptin. Since both of these molecules are secreted by human adipose tissue, researchers investigated the effects of DA on two adipocyte cell lines, SW872 and LS14. Preliminary results indicated that each cell line primarily expressed just one receptor type but that other receptor types might be expressed in limited quantity.

Experiment 1

SW872 cells were treated with either DA, raclopride (RAC), an antagonist of D2R, or both. PRL release and cAMP levels were monitored. (Figure 1)

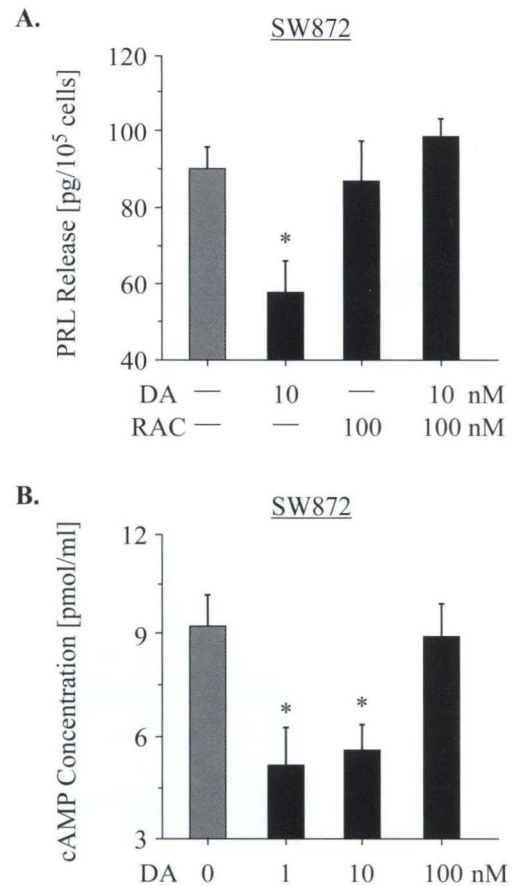


Figure 1 A. Prolactin release from SW872 cells treated with DA and D2R antagonist RAC. **B.** cAMP concentration in SW872 cells treated with various concentrations of DA.

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Experiment 2

Leptin release was monitored in LS14 cells after treatment with DA or SKF38393 (SKF), a D1R agonist; see Figure 2.

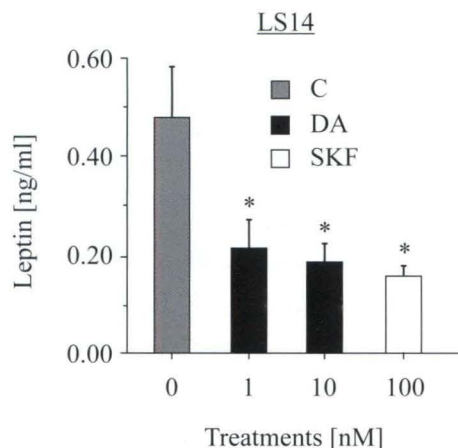


Figure 2 Leptin secretion from LS14 cells after treatment with DA or D1R agonist SKF

This passage was adapted from "Dopamine Receptors in Human Adipocytes: Expression and Functions." Borchardin DC, Hugo ER, Idelman G, De Silva A, Richtand NW, Loftus J, Ben-Jonathan N. *PLoS ONE*. 2011. 6(9) doi:10.1371/journal.pone.0025537 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

47. Cortisol is similar to dopamine in that the changes it causes can vary widely among different types of effector cells. Cortisol most likely binds to a receptor protein:
 - A. on the cell membrane.
 - B. in the cytosol.
 - C. on the nuclear membrane.
 - D. just outside the cell.
48. Excess DA is usually converted to the catecholamines epinephrine and norepinephrine. Based on passage information, which of the following would you expect to find in a recently pregnant mother with high prolactin levels?
 - A. Low blood DA levels
 - B. Increased heart rate
 - C. Decreased heart rate
 - D. High blood leptin levels
49. What is the most likely explanation for the results shown in Figure 1?
 - A. DA binds mainly to D1R and activates G_s -proteins.
 - B. DA binds mainly to D2R and activates G_s -proteins.
 - C. DA binds mainly to D1R and activates G_i -proteins.
 - D. DA binds mainly to D2R and activates G_i -proteins.

50. The catecholamine epinephrine binds to several types of receptors called adrenergic receptors. Heart muscle cells contain β_1 -adrenergic receptors, whereas the smooth muscle cells of the gut contain many α_2 -adrenergic receptors. Which of the following is most likely true concerning these two types of receptors?
 - A. β_1 -adrenergic receptors activate G_s -proteins, whereas α_2 -adrenergic receptors activate G_i -proteins.
 - B. β_1 -adrenergic receptors activate G_i -proteins, whereas α_2 -adrenergic receptors activate G_s -proteins.
 - C. Both β_1 -adrenergic receptors and α_2 -adrenergic receptors activate G_i -proteins.
 - D. Both β_1 -adrenergic receptors and α_2 -adrenergic receptors activate G_s -proteins.
51. *Vibrio cholerae*, the bacterium responsible for cholera, releases an enterotoxin which acts on G_s -proteins of the intestinal mucosa inhibiting their GTPase activity. Which of the following is most likely to occur inside an intestinal mucosal cell of an individual infected with cholera?
 - A. Decreased activation of protein kinase A
 - B. Increased electrolyte concentration
 - C. Decreased rate of hormones binding to membrane bound receptors
 - D. Increased concentration of cAMP
52. Which of the following best explains why 100nM DA had no significant effect on cAMP levels in SW872 cells? (Figure 1B)
 - A. High DA levels activate a minority of G_s -activating D1Rs.
 - B. High DA levels activate a minority of G_i -activating D1Rs.
 - C. High DA levels cause an increase in cyclic AMP transcription.
 - D. cAMP is not dependent on DA signaling.
53. Glucagon works via a G-protein system. Which of the following best explains why glucagon stimulates glycogen breakdown in liver cells, but stimulates lipid breakdown in fat cells? Glucagon is broken down by a cAMP- dependent phosphorylase.
 - A. Fat cells contain a G_s -protein while liver cells contain a G_i -protein.
 - B. Liver cells don't contain *adenylyl cyclase*.
 - C. The two cell types contain a different set of proteins phosphorylated by protein kinase A.
 - D. Glycogen and lipid breakdown are not governed by cAMP levels.

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Passage II (Questions 54-59)

Leptin is a small, non-glycosylated peptide known to modulate satiety and energy homeostasis. However, leptin has also been implicated in the regulation of embryo implantation and the maintenance of pregnancy. Leptin is synthesized in the placenta, and pregnancy leads to elevated leptin levels. Scientists hypothesize that leptin expression in the placenta is regulated by the peptide hormone human chorionic gonadotropin (hCG).

hCG has many important functions during the course of pregnancy, including stimulation of progesterone production. Progesterone is secreted for the duration of gestation, initially by the corpus luteum, and later by the placenta. hCG is already expressed in eight-cell embryos and is secreted in high local concentrations by the blastula entering the uterine cavity. It can be detected in maternal plasma or urine shortly after trophoblast cells, which form the outermost layer of the blastula, implant in the uterine endometrium.

Binding of hCG to its receptor generates signal transduction through activation of associated G-proteins, causing an increase in cyclic adenosine monophosphate (cAMP) and a consequent activation of protein kinase A (PKA).

In a series of experiments on trophoblast-derived BeWo tumor cells, scientists investigated the regulation of leptin expression in trophoblast cells.

Experiment 1

To measure the effect of hCG on leptin mRNA expression and intracellular cAMP concentration, BeWo cells were treated with hCG. Leptin mRNA expression and intracellular cAMP concentration were measured. The results are shown in Figures 1 and 2.

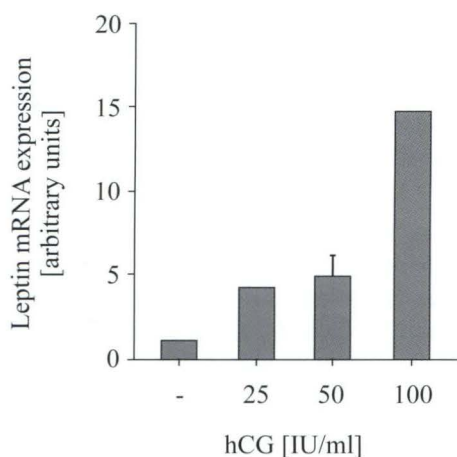


Figure 1. Leptin mRNA expression in BeWo cells treated with hCG

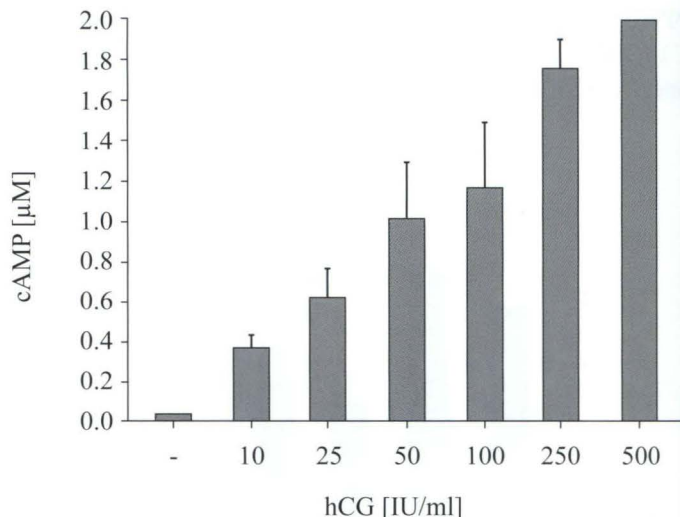


Figure 2. cAMP expression in BeWo cells treated with hCG

Experiment 2

To measure the effect of cAMP on leptin mRNA expression in the presence of high concentrations of hCG, BeWo cells were treated with cAMP and/or high concentrations of hCG. Results are shown in Figure 3.

HCG 100 IU/ml	-	+	-	+
cAMP 100 mM	-	-	+	+

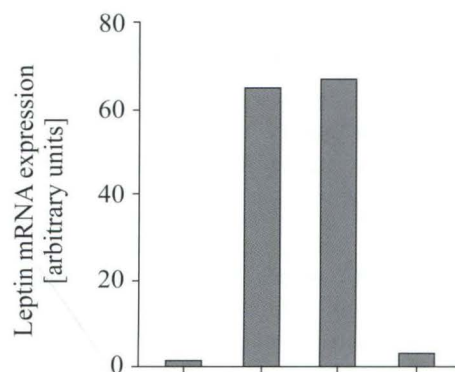


Figure 3 Impact of cAMP on BeWo cell leptin expression under the influence of high concentrations of hCG.

This passage was adapted from "The Alternative Epac/cAMP Pathway and the MAPK Pathway Mediate hCG Induction of Leptin in Placental Cells." Maymó JL, Pérez Pérez A, Maskin B, Dueñas JL, Calvo JC, Margalet VS. *PLoS ONE*. 2012. 7(10) doi:10.1371/journal.pone.0046216. For use under the terms of the Creative Commons CCBY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

54. The data obtained from experiments 1 and 2 best support which of the following conclusions?
- At high levels, cAMP interferes with hCG stimulation of leptin expression.
 - The hCG stimulatory effect on leptin expression is blocked by PKA activation.
 - cAMP induces leptin stimulation by hCG at high hormone concentrations.
 - hCG inhibits leptin mRNA expression and suppresses cAMP levels.

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55. During pregnancy, which of the following hormones promotes maintenance of the uterine endometrium?
- FSH
 - hCG
 - Oxytocin
 - Progesterone
56. Syncytiotrophoblast cells in the placenta manufacture and release hCG. Which of the following statements most accurately describes the release and transport of hCG?
- hCG is released by exocytosis and dissolves in the blood.
 - hCG is released by simple diffusion and dissolves in the blood.
 - hCG is released by exocytosis and binds to carrier proteins.
 - hCG is released by simple diffusion and binds to carrier proteins.
57. The corpus luteum is:
- a permanent ovarian structure that functions as an endocrine tissue.
 - a temporary ovarian structure derived from a ruptured follicle.
 - an endocrine tissue present in an implanted embryo.
 - the remnants of a disintegrated corpus albicans.
58. Which of the following is the most likely reason why BeWo tumor cells were used to investigate the regulation of leptin expression in trophoblast cells?
- hCG inhibits leptin expression in both trophoblast and BeWo cells.
 - Leptin deficiency promotes BeWo cell growth.
 - BeWo cells maintain many characteristics of trophoblast cells.
 - hCG activates cAMP expression in both trophoblast and BeWo cells.
59. Which of the following hormones is most likely to have an effect similar to that depicted in Figure 2?
- Progesterone
 - LH
 - Estrogen
 - Cortisol

Passage III (Questions 60-67)

Gametogenesis is regulated through positive and negative feedback loops that act at the level of the hypothalamus, pituitary, and gonad. Gonadotropin-releasing hormone (GnRH), which is released from the hypothalamus, acts on the anterior pituitary to cause release of the glycoproteins luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

In females, oogenesis occurs in the ovaries. The oocyte, together with surrounding theca and granulosa cells, compose a follicle. LH and FSH act on theca and granulosa cells, respectively, to stimulate steroid production and follicle maturation. When stimulated by LH, theca cells supply androgens to granulosa cells, which convert them to estrogens that exert negative feedback on GnRH, LH, and FSH production.

In males, spermatogenesis occurs in the seminiferous tubules of the testes. LH and FSH act on the Leydig and Sertoli cells of the testis, respectively, to stimulate steroidogenesis and spermatogenesis. Inhibins produced by Sertoli cells and androgens produced by Leydig cells, including testosterone, feedback negatively to reduce GnRH, LH, and FSH levels.

Scientists interested in the effects of gonadotropins and testosterone on mRNA transcript production in Leydig and Sertoli cells performed the following experiment. Mice received an injection of the GnRH antagonist acyline (ACY) every 24 hours for 4 days, followed by a single injection of LH 2 hours after the last ACY injection. Measurements were taken before as well as 1 and 4 hours after LH administration.

Blood levels of LH, FSH, and testosterone are shown in Figure 1.

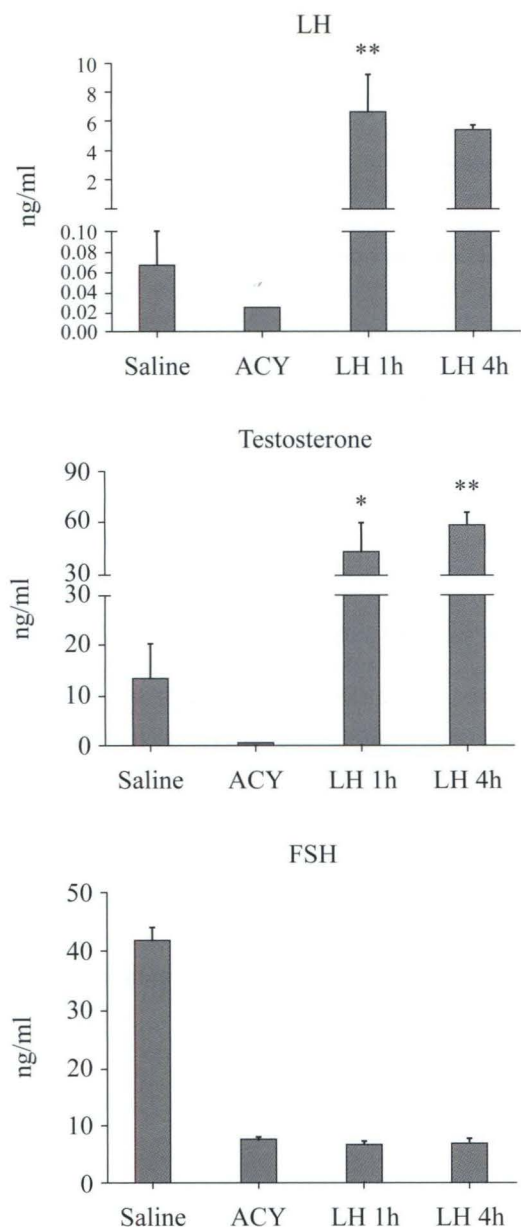


Figure 1. Effect of gonadotropin deprivation and LH restoration on blood levels of LH, FSH, and testosterone

Leydig cells were found to respond robustly to both gonadotropin deprivation and LH restoration with acute changes in mRNA transcript production.

In a second experiment, Sertoli cells were found to respond minimally to either gonadotropin deprivation or FSH and testosterone restoration with minor changes in mRNA transcripts production.

This passage was adapted from "RiboTag Analysis of Actively Translated mRNAs in Sertoli and Leydig Cells In Vivo." Sanz E, Evanoff R, Quintana A, Evans E, Miller JA, Ko C, Amieux PS, Griswold MD, McKnight GS. *PLoS ONE*. 2013. 8(6) doi:10.1371/journal.pone.0066179 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

60. The follicle in its earliest stages is called a primordial follicle. The primordial follicle most likely contains a:
 - A. haploid, primary oocyte.
 - B. diploid, primary oocyte.
 - C. haploid, secondary oocyte.
 - D. diploid, secondary oocyte.
61. Based on the information presented in the passage, which of the following pairs of cell types possesses the most similar developmental history?
 - A. Theca cells and Sertoli cells
 - B. Leydig cells and granulosa cells
 - C. Leydig cells and theca cells
 - D. Granulosa cells and oocytes
62. Androgens are sometimes taken by athletes to improve performance. Which of the following may be a side effect of taking large quantities of androgens?
 - A. Infertility due to decreased endogenous testosterone production
 - B. Infertility due to decreased secretion of GnRH
 - C. Increased fertility due to decreased endogenous testosterone production
 - D. Increased fertility due to increased Sertoli cell activity
63. Are the results shown in Figure 1 to be expected given the control pathways described in the passage?
 - A. No, because LH stimulates FSH production.
 - B. No, because LH inhibits androgen production.
 - C. Yes, because LH inhibits FSH production.
 - D. Yes, because LH stimulates androgen production.
64. The gonadotropins LH and FSH most likely alter mRNA production by:
 - A. acting as a transcription factor.
 - B. activating a second messenger system.
 - C. binding to a receptor in the cytoplasm.
 - D. binding to a receptor in the nucleus.
65. Which of the following are released into the fallopian tube during ovulation?
 - I. The follicle
 - II. The secondary oocyte
 - III. Granulosa cells
 - A. I only
 - B. II only
 - C. II and III only
 - D. I, II, and III

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66. What is the most likely reason that acyline was used in experiments on the effects of gonadotropins and testosterone on mRNA transcript production in Leydig and Sertoli cells?
- A. Acyline is expressed in Leydig and Sertoli cells.
 - B. Acyline induces expression of gonadotropins and testosterone.
 - C. Acyline inhibits the activity of GnRH.
 - D. Acyline is a product of spermatogenesis.
67. A vaccine that stimulates the body to produce antibodies against a hormone has been suggested as a long term male contraceptive. In order to insure that the vaccine has no adverse effects on androgen production, which hormone should be targeted?
- A. FSH
 - B. LH
 - C. GnRH
 - D. Testosterone
-

Questions 68 through 69 are **NOT** based on a descriptive passage.

68. A competitive inhibitor of TSH binding to TSH receptors on the thyroid would lead to a rise in the blood levels of which of the following?
- A. TSH
 - B. Thyroxine
 - C. PTH
 - D. Epinephrine
69. Which of the following hormones most likely acts as the substrate molecule for synthesis of cortisol and aldosterone in the fetal adrenal gland?
- A. HCG
 - B. Estrogen
 - C. LH
 - D. FSH
-

STOP. IF YOU FINISH BEFORE TIME IS CALLED, CHECK YOUR WORK. YOU MAY GO BACK TO ANY QUESTION IN THIS TEST BOOKLET.

STOP!

DO NOT LOOK AT THESE EXAMS UNTIL CLASS.

**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 4**

Passage I (Questions 70-76)

In the 1930s a line of “nude” mice was derived; these mice develop normal numbers of B cells, but lack a thymus and are impaired in producing antibodies. Early models of humanized mice used for human immune system reconstitution were generated in the late 1980s by infusion of human peripheral blood mononuclear cells into a line derived from nude mice. However, the level of reconstitution in such mice was very low and consisted mainly of human T cells. Impairment of human T and B cell function in these humanized mice has been attributed to the lack of expression of Human Leukocyte Antigens (HLA), since HLA molecules are required for development of human T cells that, in turn, are essential for stimulation of B cells. HLA molecules are the human-specific form of major histocompatibility complex (MHC) molecules, which are involved in both the process of clonal selection that selects immature T cells for maturation and the display of foreign particles in the immune system response.

Experiment 1

To test the hypothesis that expression of HLA class II molecules in humanized mice allows development of functioning human CD4 T cells, scientists generated mice expressing HLA-DR4 molecules (DRAG mice). Adult DRAG mice were infused with human hematopoietic stem cells (HSC). Littermates lacking expression of HLA-DR4 molecules were used as controls. The results are shown in Figure 1.

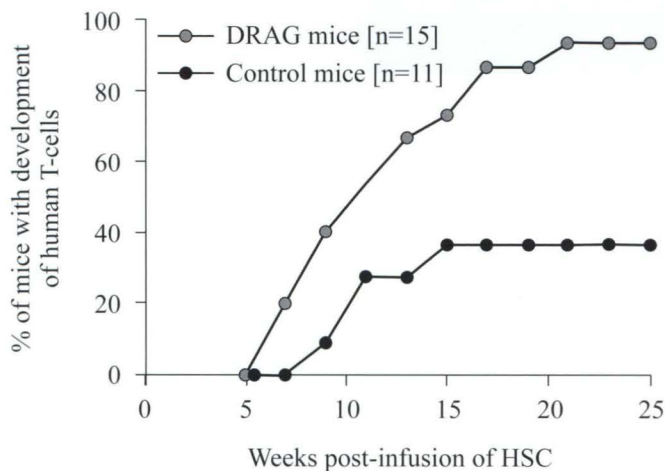


Figure 1 Percent of DRAG and control mice that showed development of human T cells following infusion with human hematopoietic stem cells

Experiment 2

Directly following Experiment 1, the researchers removed human T cells that had developed in the DRAG and control subjects. They then stimulated the T cells with PMA/ionomycin, which leads to the production of cytokines such as interleukins (IL) in functioning T cells. (Interleukins are peptide hormones that stimulate the proliferation of other T cells.) The results are shown in Figure 2.

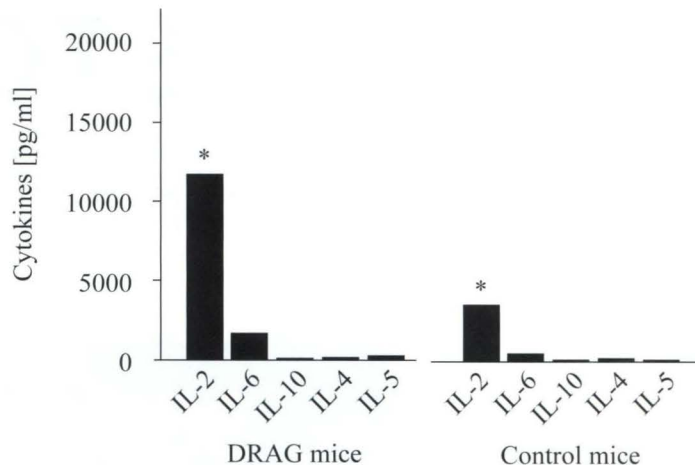


Figure 2 Levels of different types of interleukins secreted by human T cells from DRAG and control mice following stimulation with PMA/ionomycin

This passage was adapted from “Expression of HLA Class II Molecules in Humanized NOD. Rag1KO.IL2R γ KO Mice Is Critical for Development and Function of Human T and B Cells.” Danner R, Chaudhari SN, Rosenberger J, Surls J, Richie TL, Brumeau TD, Casares S. *PLoS ONE*. 2011. 6(5) doi:10.1371/journal.pone.0019826 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

70. Which of the following best describes the conclusions that can be drawn from the data?
- Compared to control mice, a greater percentage of DRAG mice showed reconstitution of T cells at every time point after infusion with HSC.
 - Compared to control mice, a greater percentage of DRAG mice showed reconstitution of T cells starting 15 weeks after infusion with HSC.
 - Compared to control mice, a greater percentage of DRAG mice showed reconstitution of T cells starting 5 weeks after infusion with HSC, and these T cells secreted higher levels of interleukins.
 - Compared to DRAG mice, a greater percentage of control mice showed reconstitution of T cells starting 5 weeks after infusion with HSC, and these T cells secreted higher levels of interleukins.
71. Which of the following is a cell that nude mice would be unable to produce?
- An antibody
 - A T cell
 - A B cell
 - A macrophage

GO ON TO THE NEXT PAGE.

72. In an early experiment with a humanized mouse model, researchers injected nude mice (hosts) with lymphocytes from the thymus of a human donor and then with an antigen. After antibodies were produced, lymphocyte samples were removed from the spleens of the nude mice, and the cells originating from the host or donor were selectively destroyed from separate samples, leaving a sample of only host cells and a sample of only donor cells. The host cells were still able to produce antibodies against the antigen, but the donor cells could not. This finding indicates that:

A. antibodies are produced by T cells.
 B. antibodies are produced by B cells only after exposure to T cells.
 C. nude mice are unable to produce antibodies.
 D. nude mice are unable to produce T cells.

73. According to the information given in the passage, interleukins most likely act:

A. via a second messenger by binding to a membrane bound protein receptor.
 B. by diffusing through the membrane of the helper T cell and binding to a receptor in the cytosol.
 C. at the transcriptional level by binding directly to nuclear DNA.
 D. via the nervous system.

74. All of the following arise from hematopoietic stem cells in bone marrow EXCEPT:

A. helper T cells.
 B. B lymphocytes.
 C. erythrocytes.
 D. osteoblasts.

75. Which of the following is most likely to create the humoral immune system response mediated by MHC class II molecules?

A. A bacterial infection
 B. A cell infected by a virus
 C. A tumor
 D. A foreign tissue graft

76. Which of the following is a feature of the study described that may limit the researchers' ability to draw conclusions about the hypothesis of interest?

A. B cell reconstitution in DRAG mice was not measured.
 B. The researchers did not test the functioning of reconstituted human T cells in DRAG mice.
 C. No wild-type mice were used as controls.
 D. Only control mice that showed reconstitution of human T cells in could be used as controls in the second part of the experiment.

Passage II (Questions 77-83)

The function of plasma cells in the immune system is to secrete specific proteins called antibodies, also called immunoglobulins, which bind to antigens and mark them for destruction. One plasma cell can only make antibodies that are specific for a single antigenic determinant of a single antigen. The general structure of an antibody is shown in Figure 1.

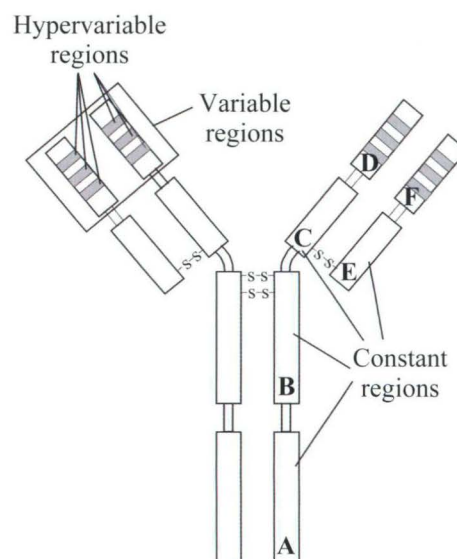


Figure 1 The basic monomeric structure of an antibody

Treatment of antibodies with the protease papain yields three fragments: two identical Fab fragments and one Fc fragment. The Fc fragment is nearly identical in all antibodies. Treatment of antibodies with mercaptoethanol, which cleaves disulfide bonds, results in two light chain polypeptides and two heavy chain polypeptides. Both the light and heavy chains possess constant, variable, and hypervariable regions in their amino acid structures. The light chain contains no part of the Fc region.

Selected peptides encompassing sequences of the Fc (Fc-peptides) from the major classes of Igs (IgG, IgM, IgA), were synthesized in order to evaluate their antifungal activity. Fc-peptides with fungicidal activity that might be released in vivo by proteolysis of Igs may represent a link between adaptive and innate immunity. Such peptides, moreover, could constitute novel lead molecules for devising new antifungal agents.

Selected Fc-peptides were preliminarily tested at the concentration of 100 $\mu\text{g/ml}$ of various fungal strains. Peptides exhibiting fungicidal activity at this concentration were further tested at scalar dilutions to determine the half maximal effective concentration (EC_{50}) values. The results for the Fc-peptides N10K and H4L are shown in Table 1.

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Fungicidal activity				
N10K		H4L		
Fungal Strain	%*	EC ₅₀ ** (95% confidence intervals) [mol/liter] × 10 ⁻⁶	%	EC ₅₀
<i>C. albicans</i> SC5314	100	1.004 (0.947-1.065)	84.34	n.d
<i>C. albicans</i> CA-6	100	2.939 (2.578-3.351)	57.04	n.d
<i>C. albicans</i> SA40	100	1.763 (1.670-1.861)	55.99	n.d
<i>C. albicans</i> AID568	100	1.745 (1.396-2.180)	59.82	n.d
<i>C. albicans</i> UM4	100	2.784 (2.622-2.956)	64.63	n.d
<i>C. glabrata</i> OMNI32	100	3.584 (3.390-3.788)	80.49	n.d
<i>C. neoformans</i> 6995	100	2.948 (2.645-3.288)	85.08	n.d
<i>M. furfur</i> 101	100	2.833 (1.900-4.226)	92.04	n.d

Table 1 *In vitro* fungicidal activity of Fc-peptides against fungal strains.

This passage was adapted from "Peptides of the Constant Region of Antibodies Display Fungicidal Activity." Polonelli L, Ciociola T, Magliani W, Zanello PP, D'Adda T, Galati S, De Bernardis F, Arancia S, Gabrielli E, Pericolini E, Vecchiarelli A, Arruda DC, Pinto MR, Travassos LR, Pertinhez TA, Spisni A, Conti S. *PLoS ONE*. 2012. 7(3) doi:10.1371/journal.pone.0034105 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

77. What level of protein structure is disrupted by mercaptoethanol?
- Primary
 - Secondary
 - Tertiary only
 - Tertiary and quaternary
78. Which of the following can be concluded based on the data shown in Table 1?
- N10K is more effective as a fungicidal agent against *M. furfur* 101 than *C. glabrata* OMNI32.
 - N10K is more effective as a fungicidal agent against *C. glabrata* OMNI32 than *M. furfur* 101.
 - It cannot be determined whether N10K is more effective as a fungicidal agent against either fungal strain.
 - N10K is not effective as a fungicidal agent against either fungal strain.
79. Which of the following labeled segment(s) from the antibody in Figure 1 most likely attaches to an antigen?
- A
 - D and F
 - D but not F
 - C and D

80. Which of the following structures in the plasma cell most likely produces IgG, IgM, and IgA antibodies?
- Ribosomes in the cytosol
 - Rough endoplasmic reticulum
 - Smooth endoplasmic reticulum
 - Cellular membrane
81. Which of the following statements concerning the immune system is **NOT** true?
- Plasma cells which provide immunity against one disease may also provide immunity against a closely related disease.
 - Two antibodies from the same plasma cell must bind to the same antigen type.
 - Plasma cells arise from T lymphocytes.
 - Memory B cells help the immune system to respond to the same antigen more quickly during a secondary immune response.
82. Which of the following labeled segments shown in Figure 1 could contain N10K?
- A or B
 - A, B, C, or D
 - A, B, C, or E
 - C, D, E, or F
83. Why does fungicidal activity of Fc peptides represent a possible link between innate and adaptive immunity?
- Fungicidal activity of a region that varies between antibodies indicates a way that antibodies could play a role in adaptive immunity.
 - Fungicidal activity of a region that varies between antibodies indicates a way that antibodies could play a role in innate immunity.
 - Fungicidal activity of a region that is constant across all antibodies indicates a way that antibodies could play a role in adaptive immunity.
 - Fungicidal activity of a region that is constant across all antibodies indicates a way that antibodies could play a role in innate immunity.

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Passage III (Questions 84-89)

Oxygen in erythrocytes is stored by hemoglobin, which consists of four polypeptide chains, each containing a heme group with a single oxygen binding site. The organic portion of the heme binds the iron atom at its center with four nitrogen atoms, leaving it with a +2 oxidation state. Carbon monoxide (CO) is a byproduct of the breakdown of the heme group, catalyzed by heme oxygenase (HO). An isolated heme group binds CO 25,000 times as strongly as it binds to O_2 . However, the binding affinity of hemoglobin and myoglobin for CO is only about 200 times as great as for O_2 .

The oxygen carrier in skeletal muscle tissue is myoglobin, which is very similar to hemoglobin but has only one polypeptide chain. Myoglobin does not show a decreased affinity for O_2 over a broad range of pH or in the presence of CO_2 . Hemoglobin has a lower affinity for oxygen than does myoglobin, partially due to 2,3-diphosphoglycerate (2,3-DPG), a chemical in erythrocytes that affects the characteristic sigmoidal oxygen dissociation curve of hemoglobin.

Under a variety of pathological conditions, hemoglobin and myoglobin—collectively known as respiratory hemoproteins (RH)—can leak into blood plasma and undergo auto-oxidation via electron transfer from the heme iron to oxygen. Oxidized RH (metRH) can damage the vascular system, particularly in association with peroxides (H_2O_2). Recent studies have indicated that both metRH and peroxides induce HO activity; it has been proposed that CO might turn on the reducing potential of peroxides and thus facilitate the formation of redox-inactive carboxyRH. Researchers tested this hypothesis by allowing metHb and H_2O_2 to interact in the presence of CO in vitro. The results are shown in Figure 1.

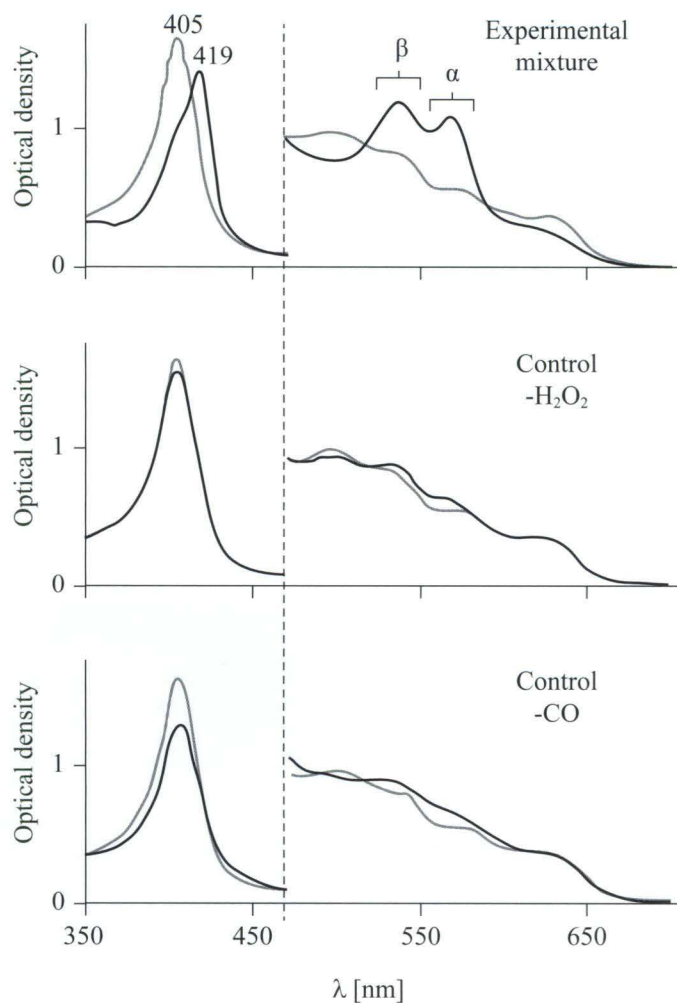


Figure 1 Light absorption spectra of reaction mixtures before (light line) and after (heavy line) incubation with a CO atmosphere

This passage was adapted from "Carbon Monoxide Promotes Respiratory Hemoproteins Iron Reduction Using Peroxides as Electron Donors." Sher EA, Shakhai M, Shakhai N. *PLoS ONE*. 2012. 7(3) doi:10.1371/journal.pone.0033039 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

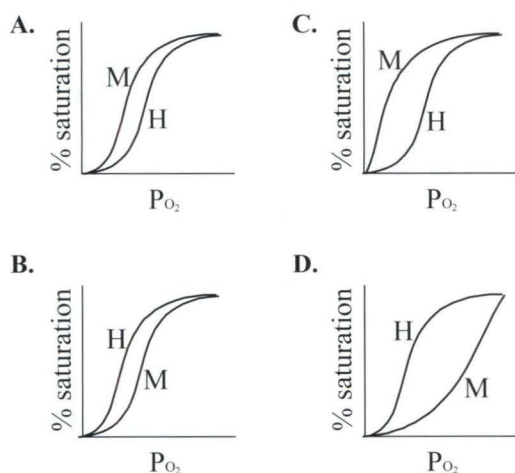
84. Which of the following most likely acted as the evolutionary selective pressure which led to the decreased affinity of hemoglobin and myoglobin for CO as compared to the isolated heme group?
- The emergence of industrial societies, which significantly increased the level of environmental CO
 - The products of aerobic respiration
 - The endogenous production of CO due to the breakdown of heme
 - Carbonic acid in the blood

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85. Which of the following pieces of information, if true, would provide the greatest support to the hypothesis of the experiment described in the passage when combined with the results shown in Figure 1?

- A. The CO concentrations used in the experiment were similar to those found *in vitro* in the absence of any pathological condition
- B. The light absorption spectrum of carboxy hemoglobin is characterized by peaks at around 419 nm, 540 nm, and 569 nm
- C. Free hemoglobin can in some cases protect against peroxide-induced oxidative damage
- D. Among plants, peroxides commonly function as reducing agents

86. Which of the following gives the oxygen dissociation curves for hemoglobin (H) and myoglobin (M)?



87. Increased concentration of lactic acid due to active skeletal muscle most likely results in which of the following?

- A. Increased off-loading of O_2 by both hemoglobin and myoglobin
- B. Increased off-loading of O_2 by hemoglobin but not myoglobin
- C. Decreased off-loading of O_2 by both hemoglobin and myoglobin
- D. Decreased off-loading of O_2 by hemoglobin but not myoglobin

88. In a healthy human body, where is 2,3-DPG likely to have its greatest effect?

- A. In the alveoli
- B. In the capillaries of the lungs
- C. In the muscle cells of the heart
- D. In the capillaries of skeletal muscle

89. Which of the following is LEAST likely to increase the breathing rate of an individual?

- A. Increased pH in the blood
- B. Low oxygen levels in the blood
- C. Increased muscle activity
- D. Increased CO_2 levels in the blood

Questions 90 through 92 are **NOT** based on a descriptive passage.

90. Which of the following is **NOT** true concerning the lymphatic system?

- A. The lymphatic system removes large particles and excess fluid from the interstitial spaces.
- B. The lymphatic system is a closed circulatory system.
- C. The lymphatic system contains lymphocytes that function in the body's immune system.
- D. Most fatty acids in the diet are absorbed by the lymphatic system before entering the bloodstream.

91. Which of the following is a cell that does **NOT** contain a nucleus?

- A. Erythrocyte
- B. Platelet
- C. Macrophage
- D. B lymphocyte

92. Clonal selection is:

- A. the first stage of the innate immune response.
- B. phagocytic destruction of antigens.
- C. the binding to an antigen by an antibody.
- D. the process by which certain immature lymphocytes are selected for maturation.

STOP. IF YOU FINISH BEFORE TIME IS CALLED, CHECK YOUR WORK. YOU MAY GO BACK TO ANY QUESTION IN THIS TEST BOOKLET.

STOP.

STOP!

DO NOT LOOK AT THESE EXAMS UNTIL CLASS.

**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 5**

Passage I (Questions 93-99)

Since fats are not soluble in the aqueous solution in the small intestine, fat digestion would be very inefficient were it not for bile salts and lecithin, which increase the surface area upon which lipase can act. In addition, bile forms micelles that travel to the brush border of the intestine, where they are absorbed by enterocytes.

Once inside the enterocyte, fatty acids are taken up by the smooth endoplasmic reticulum and new triglycerides are formed. These triglycerides combine with cholesterol and phospholipids to form triglyceride-rich lipoproteins (TRL) called chylomicrons that are secreted through exocytosis to the basolateral side of the enterocyte. From there, the chylomicrons move to the lacteal in the intestinal villus.

Chylomicrons are just one member of the lipoprotein families which transport lipids through the blood. The other members are very low density lipoproteins (VLDL), low density lipoproteins (LDL), and high density lipoproteins (HDL). Lipolysis of chylomicrons by lipoprotein lipase (LPL) results in the formation of smaller remnants that are depleted of triglycerides and enriched in cholesteryl esters. Elevated non-fasting triglyceride (TG) levels and elevated levels of remnants may lead to accelerated atherosclerosis and cardiovascular disease.

The mechanism that leads to high non-fasting TG levels involves decreased hepatic clearance of TRL remnants, which is mediated by syndecan-1 heparan sulfate proteoglycan (HSPG). Dysfunction of syndecan-1 HSPG has been shown to disrupt defective hepatic remnant clearance. One gene responsible for HSPG assembly and disassembly is *SULF2*.

Experiment 1

Scientists tested whether the presence of the G allele in the *SULF2* gene contributes to difficulty in lipid clearance in humans by monitoring blood lipid levels (mmol/L) after standardized consumption of dietary fats. Participants were classified according to genotype (AA, AG, or GG) and blood lipid levels were recorded prior to the administration of the meal and at 3, 4, 6, and 8 hours after eating. Results are shown in Figure 1.

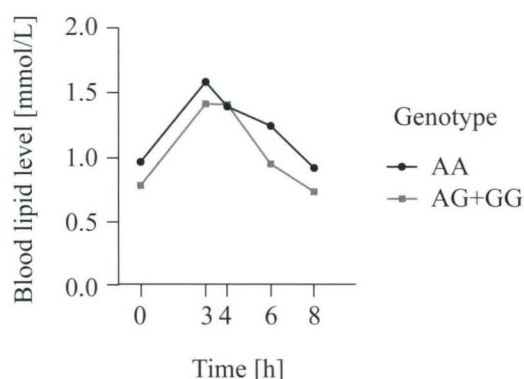


Figure 1 Blood lipid levels 0, 3, 4, 6, and 8 hours after eating

This passage was adapted from "Genetic Variation in *SULF2* Is Associated with Postprandial Clearance of Triglyceride-Rich Remnant Particles and Triglyceride Levels in Healthy Subjects." Matikainen N, Burza MA, Romeo S, Hakkarainen A, Adiels M, Folkersen L, Eriksson P, Lundbom N, Ehrenborg E, Orho-Melander M, Taskinen MR, Borén J. *PLoS ONE*. 2013. 8(11) doi:10.1371/journal.pone.0079473 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

93. The process by which bile increases the surface area of dietary fat is called:

- A. lipolysis.
- B. adipolysis.
- C. malabsorption.
- D. emulsification.

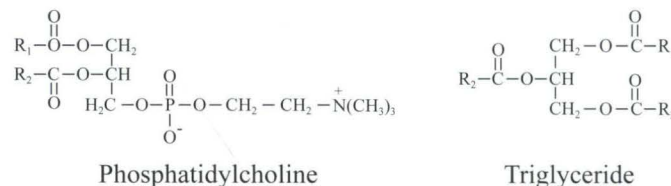
94. Most dietary fat first enters the bloodstream:

- A. from the right lymphatic duct into arterial circulation.
- B. from the thoracic duct into venous circulation.
- C. from the small intestine into capillary circulation.
- D. from the intestinal enterocyte into the lacteal.

95. Most tests for serum cholesterol levels do not distinguish between HDLs and LDLs. Life insurance rates generally increase with increasing serum cholesterol levels. Which of the following supports the claim that it is important to determine whether HDLs or LDLs are responsible for high serum cholesterol when evaluating a patient's risk for coronary heart disease?

- A. The risk from coronary heart disease doubles from an HDL level of 60mg/100ml to 30mg/100ml.
- B. The incidence of coronary heart disease rises in linear fashion with the level of serum cholesterol.
- C. The optimal serum cholesterol for a middle aged man is probably 200mg/100ml or less.
- D. VLDL is the main source of plasma LDL.

96. Considering the chemical structures of the fats below, which lipid may form part of the surface of a lipoprotein and which will be located in the interior of the lipoprotein?



- A. Triglyceride on the surface; phosphatidylcholine in the interior
- B. Both on the surface
- C. Phosphatidylcholine on the surface; triglyceride in the interior
- D. Both in the interior

97. Results from Experiment 1 suggest that:

- A. polymorphisms in genes responsible for HSPG assembly or disassembly associate with blood lipid clearance ability.
- B. the A allele affects blood lipid clearance, while the G allele has no effect.
- C. blood lipid clearance ability in heterozygotes is intermediate between that of individuals homozygous for AA and those homozygous for GG.
- D. individuals carrying the G allele clear lipids more slowly.

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98. Why might the remnant particles from lipolysis of chylomicrons contribute to cardiovascular disease even more than low-density lipoproteins?
- Remnant particles are larger than LDLs and cannot cross the endothelium as efficiently.
 - Remnants contain more triglycerides than LDLs
 - Remnants contain more cholesteryl esters than LDLs
- II only
 - I and II only
 - I and III only
 - I, II, and III
99. A patient that has had his pancreas surgically removed would most likely need to supplement his diet with the following enzymes EXCEPT:
- lactase.
 - lipase.
 - amylase.
 - proteases.

Passage II (Questions 100-107)

The *renal clearance* (C) of a solute is a measure of the rate at which it is cleared from blood plasma by excretion. C is expressed as volume of plasma cleared per unit time, and assumes that 100% of the solute is filtered from the blood into the lumen of the nephron.

$$C = \frac{U \times V}{P}$$

where U is the urine concentration of the solute, V is the urine flow rate, and P is the plasma concentration of the solute. The clearance rate of any substance that is freely filtered and is not reabsorbed or secreted is equal to the glomerular filtration rate (GFR). Normal GFR is approximately 125 mL/min.

Renal hyperfiltration, defined as $GFR \geq 135$ mL/min, has been associated with the progression of kidney disease, including diabetic nephropathy. Since renal hyperfiltration represents a state of intrarenal *renin-angiotensin-aldosterone system* (RAAS) activation, researchers hypothesized that hyperfiltration in patients with type I diabetes mellitus (DM) would be associated with higher BP and elevated levels of circulating RAAS mediators.

To test this hypothesis, a cohort of patients with type I DM and hyperfiltration (DM-H) was compared to patients with type I DM and normofiltration (DM-N) and healthy control (HC) patients. Researchers determined GFR by measuring the concentration of *inulin*—a nonmetabolizable polysaccharide that is freely filtered and neither reabsorbed nor secreted—in the blood and urine. GFR was found to be higher for DM-H patients than for either DM-N or HC patients. The data are shown by cohort in Table 1.

	HC	DM-N	DM-H
Concentration in plasma (mg/mL)	9.50×10^{-5}	1.05×10^{-4}	1.00×10^{-4}
Urine flow rate (mL/min)	0.75	0.80	1.00
Concentration in urine (mg/mL)	1.45×10^{-2}	1.50×10^{-2}	1.50×10^{-2}

Table 1 Concentrations of inulin (mg/mL) in blood plasma and urine

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Researchers then measured systemic blood pressure, renal blood flow, and concentrations of circulating RAAS mediators. The results are shown in Table 2.

	HC	DM-N	DM-H
Systolic BP (mmHg)	109	111	117
Diastolic BP (mmHg)	63	64	67
Effective RBF (mL/minute/1.73m ²)	629	662	891
Renin (pg/mL)	20.0	5.7	5.3
Angiotensin II (pg/mL)	12.5	3.2	3.5
Aldosterone (ng/dL)	276.1	85.9	41.8

Table 2 Blood pressure, effective renal blood flow, and concentrations of circulating RAAS mediators under conditions of normal blood glucose concentration

This passage was adapted from "Renal Hyperfiltration and Systemic Blood Pressure in Patients with Uncomplicated Type I Diabetes Mellitus." Yang GK, Maahs DM, Perkins BA, Cherney DZL. *PLoS ONE*. 2013. 8(7) doi:10.1371/journal.pone.0068908 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

100. Which of the following must be true of a solute that has a *renal clearance* greater than the GFR?
 - A. The solute is being reabsorbed by the nephron.
 - B. The solute is being secreted by the nephron.
 - C. The plasma concentration of the solute must be greater than the plasma concentration of inulin.
 - D. The solute has exceeded its transport maximum.
101. According to the data in Table 1, average GFR in patients with type I diabetes mellitus and hyperfiltration is approximately:
 - A. 130 mL/min.
 - B. 135 mL/min.
 - C. 145 mL/min.
 - D. 150 mL/min.
102. Inulin is neither secreted nor reabsorbed by the kidney. Which of the following must also be true for the clearance of inulin to accurately represent the GFR?
 - A. The filtration rate of inulin is less than its excretion rate.
 - B. The filtration rate of inulin is greater than its excretion rate.
 - C. The concentration of inulin in the filtrate is equal to its concentration in the plasma.
 - D. Inulin is completely filtered from the plasma in a single pass through the kidney.
103. *Inulin* is most likely:
 - A. smaller than an amino acid.
 - B. the same size as albumin.
 - C. the same size as a red blood cell.
 - D. larger than glucose.

104. The blood concentration of creatinine, a naturally occurring metabolite of skeletal muscle, tends to remain constant. Creatinine flows freely into Bowman's capsule, and only negligible amounts of creatinine are secreted or absorbed. A patient with a normal GFR has a urine output of 1 mL/min with a creatinine concentration of 2.5 mg/mL. What is the patient's plasma concentration of creatinine?
 - A. 2 mg/100 mL
 - B. 5 mg/100 mL
 - C. 2 mg/mL
 - D. 5 mg/mL
105. Which of the following would LEAST affect the *renal clearance* of a solute?
 - A. Solute size and charge
 - B. Solute plasma concentration
 - C. Glomerular hydrostatic pressure
 - D. Inulin plasma concentration
106. The data in Table 2 support the conclusion that hyperfiltration in patients with type I diabetes mellitus is associated with:
 - A. higher blood pressure and elevated levels of circulating RAAS mediators.
 - B. lower blood pressure and elevated levels of circulating RAAS mediators.
 - C. higher blood pressure and suppressed levels of circulating RAAS mediators.
 - D. lower blood pressure and suppressed levels of circulating RAAS mediators.
107. The organic dye *p*-aminohippuric acid (PAH) is not only filtered from the plasma in the glomerulus but also secreted into the filtrate by the renal tubules. As a result, 90% of the PAH in the blood enters the filtrate. If an individual has a hematocrit of 50%, and a PAH clearance of 650 mL/min, what is his approximate *renal blood flow* (RBF)?
 - A. 325 mL/min
 - B. 650 mL/min
 - C. 1300 mL/min
 - D. 2600 mL/min

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Passage III (Questions 108-113)

The *renin-angiotensin-aldosterone system* (RAAS) regulates renal blood flow (RBF), glomerular filtration rate (GFR), and systemic blood pressure (BP).

Renin, a proteolytic enzyme, is synthesized and stored in the juxtaglomerular granular cells of the afferent arterioles. Each of the stimuli that initiates renin release—including sympathetic stimulation of β -adrenergic receptors on the juxtaglomerular cells, low blood pressure in the renal arterioles, and low rate of NaCl transport across the macula densa of the distal tubule—is either a direct or indirect consequence of low systemic blood pressure.

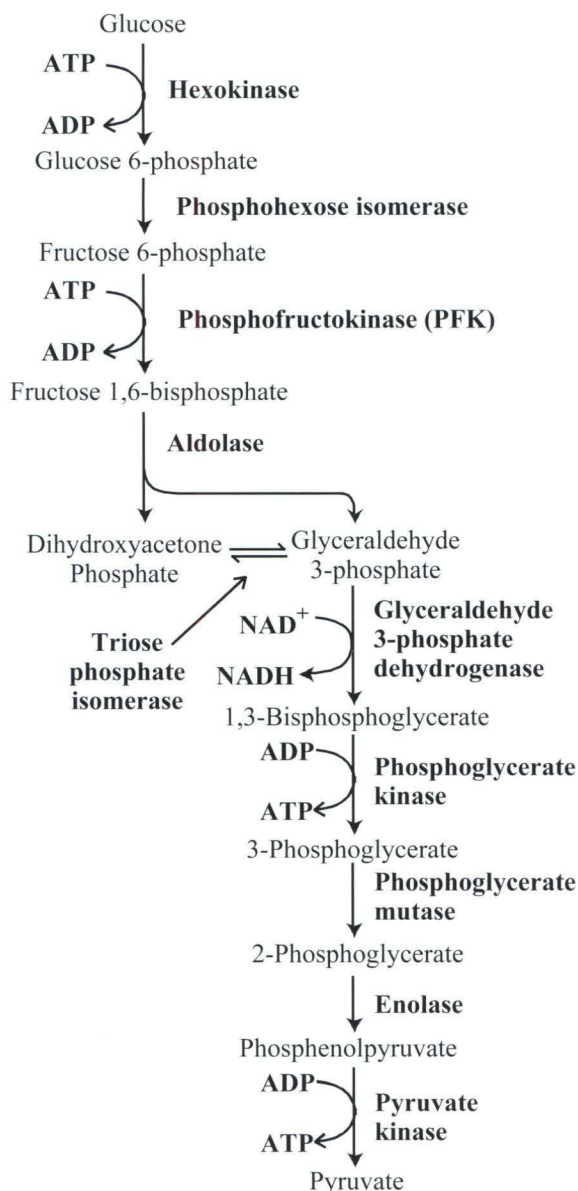


Figure 1. Initiation of renin release involves both the macula densa and juxtaglomerular cells of the nephron

Once in the blood, renin decreases the resistance of the afferent arterioles and converts *angiotensinogen*, an inactive plasma protein, into *angiotensin I*. When angiotensin I (Ang I) encounters *angiotensin converting enzyme* (ACE), it is converted to *angiotensin II* (Ang II). Ang II, a potent vasoconstrictor, increases the resistance of the efferent arterioles and promotes synthesis

and release of *aldosterone*, a steroid hormone that increases Na^+ reabsorption in the distal tubule and collecting ducts.

Dysfunction of brain *renin-angiotensin system* (RAS) components is implicated in the development of hypertension. Studies have suggested that Ang II-induced hypertension may be mediated by increased production of proinflammatory cytokines (PIC), including tumor necrosis factor (TNF).

Researchers experimentally investigated the effects of TNF inhibition on Ang II-induced hypertension. Rats were subjected to intracerebroventricular infusion of entanercept, a TNF inhibitor, with and without concurrent subcutaneous infusion of Ang II. Mean arterial pressure (MAP) and ratio of heart weight to body weight (HW/BW) were measured.

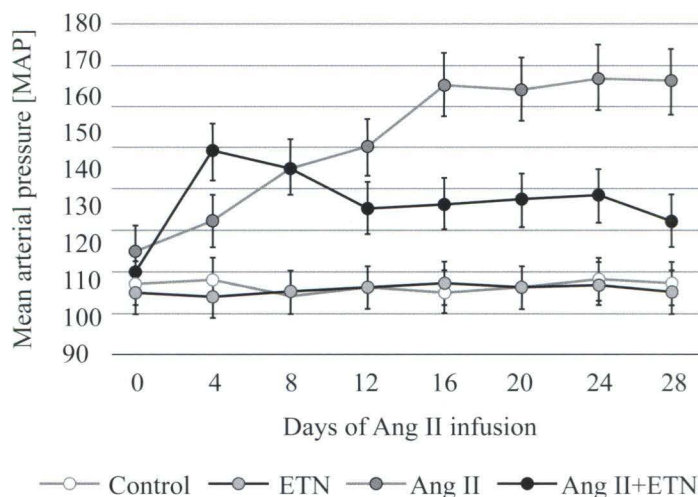


Figure 2 Effects of angiotensin II and central TNF blockade on mean arterial pressure

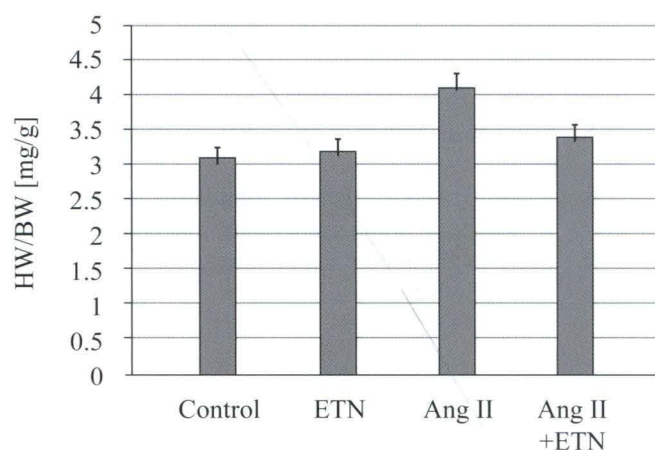


Figure 3 Effects of angiotensin II and central TNF blockade on cardiac hypertrophy

This passage was adapted from "Inhibition of TNF in the Brain Reverses Alterations in RAS Components and Attenuates Angiotensin II-Induced Hypertension." Sriramula S, Cardinale JP, and Francis J. *PLoS ONE*. 2013. 8(5) doi:10.1371/journal.pone.0063847. For use under the terms of the Creative Commons CCBY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

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108. The most likely cellular mechanism of action of aldosterone is:
- A. modification of existing cellular proteins.
 - B. initiation of a cAMP second messenger system.
 - C. diffusion into the nucleus followed by activation or repression of one or more genes.
 - D. initiation of a signal transduction system.
109. Based on passage information, renin most likely promotes conversion of angiotensinogen to angiotensin I by:
- A. acting as a cofactor.
 - B. acting as a covalent modulator.
 - C. lowering the energy of activation.
 - D. increasing the probability of protein-ligand binding.
110. According to Figures 2 and 3, for those rats subjected to Ang II infusion, central TNF blockade tended to:
- A. increase mean arterial pressure and increase heart weight to body weight ratio.
 - B. increase mean arterial pressure and decrease heart weight to body weight ratio.
 - C. decrease mean arterial pressure and increase heart weight to body weight ratio.
 - D. decrease mean arterial pressure and decrease heart weight to body weight ratio.
111. The renin-angiotensin-aldosterone system increases all of the following EXCEPT:
- A. urine volume.
 - B. blood pressure.
 - C. Na^+ reabsorption.
 - D. K^+ excretion.
112. Increased Na^+ reabsorption resulting from increased concentration of aldosterone most likely raises systemic blood pressure by increasing:
- A. water reabsorption in the distal tubule and collecting duct.
 - B. blood osmolarity, thereby stimulating thirst.
 - C. K^+ excretion in the distal tubule and collection duct.
 - D. hypothalamic secretion of vasopressin.
113. Amino acids are reabsorbed in the proximal tubule by a secondary active transport system that uses energy stored in the concentration gradient of Na^+ . Apical symport proteins move both Na^+ and amino acids from the tubule lumen into the proximal tubule cells. Because increased reabsorption of Na^+ in the proximal tubule leads to decreased delivery of Na^+ past the macula densa, a high protein diet would most likely lead to which of the following:
- I. decreased resistance of the afferent arterioles.
 - II. decreased resistance of the efferent arteriole.
 - III. increased glomerular filtration rate.
- A. I and II only.
 - B. I and III only.
 - C. III only.
 - D. I, II, and III.
-

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Questions 114 through 115 are **NOT** based on a descriptive passage.

114. The ability to produce a concentrated urine is primarily based on the presence of functional kidney nephrons. The most important structure involved in concentrating urine within the nephron is the:
- A. glomerulus.
 - B. proximal convoluted tubule.
 - C. loop of Henle.
 - D. Bowman's capsule.

115. Which of the following statements about digestion is **NOT** true?

- A. Carbohydrate metabolism begins in the mouth.
- B. Most dietary protein is absorbed into the body in the stomach.
- C. The large intestine is a major source of water reabsorption.
- D. The liver produces bile for storage in the gallbladder.

STOP. IF YOU FINISH BEFORE TIME IS CALLED, CHECK YOUR WORK. YOU MAY GO BACK TO ANY QUESTION IN THIS TEST BOOKLET.

STOP!

DO NOT LOOK AT THESE EXAMS UNTIL CLASS.

**30-MINUTE
IN-CLASS EXAM
FOR LECTURE 6**

Passage I (Questions 116-123)

The functional unit of a skeletal muscle cell is the sarcomere. The protein polymers actin and myosin lie lengthwise along a sarcomere creating the various regions shown in Figure 1.

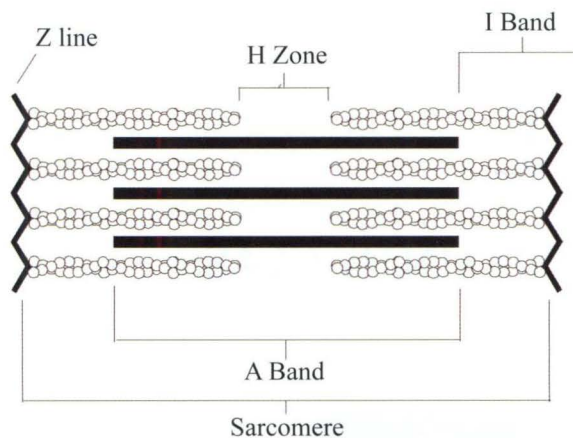


Figure 1 Schematic representation of a sarcomere

In skeletal muscle, the release of calcium by sarcoplasmic reticulum (SR) Ca^{2+} release channels (RyR1s) is the primary determinant of contractile filament activation. The action potential that initiates muscle contraction is delivered deep into each muscle cell via tubular invaginations in the sarcolemma or cell membrane called T-tubules. The change in membrane potential is transferred to the sarcoplasmic reticulum, which causes it to become permeable to Ca^{2+} ions and to release its large stores of calcium into the cytosol, setting off a chain reaction that causes conformational changes in troponin and tropomyosin that allow for the creation of a muscular contraction. The Ca^{2+} ions are removed from the cytosol by extremely efficient calcium pumps via active transport. Once the Ca^{2+} has been sequestered back into the lumen of the sarcoplasmic reticulum, the Ca^{2+} ions are bound by calsequestrin (CASQ1). Much research has been focused on CASQ1 and its role in SR Ca^{2+} buffering as well as its potential for modulating RyR1. Scientists explored the role of CASQ1 by examining muscle contraction in mice with genetic ablation of CASQ1 expression.

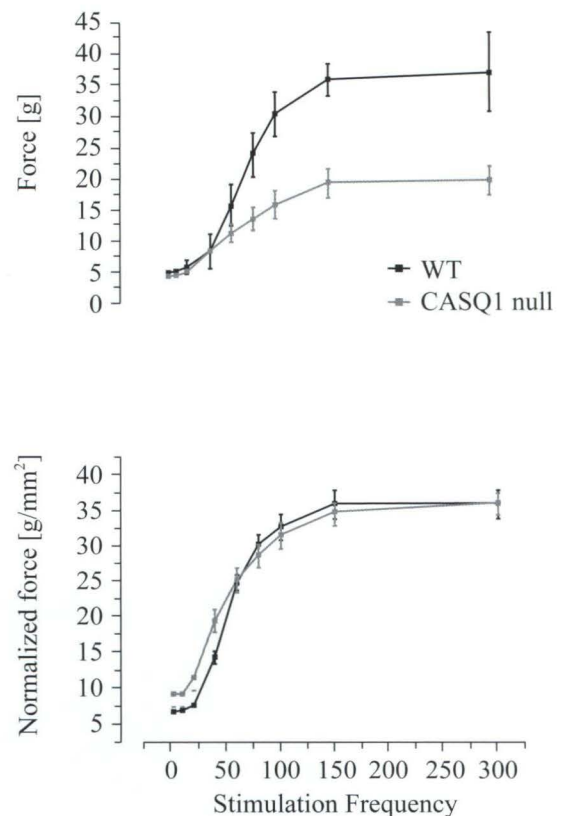


Figure 2 Relationships between force and stimulation frequency in wild-type ($n=8$) and CASQ1 ablated (CASQ1 null) mice ($n=8$). **A.** Absolute values of isometric force vs. stimulation frequencies. **B.** Force values normalized by cross-sectional area (CSA) of muscle vs. stimulation frequency.

Although the direct source of energy for muscle contraction comes from ATP, the ATP concentration in actively contracting muscle remains virtually constant. In addition, it has been shown that inhibitors of glycolysis and cellular respiration have no effect on ATP levels in actively contracting muscle over the short term. Instead, phosphocreatine donates its phosphate group to ADP in a reaction catalyzed by creatine kinase. Phosphocreatine levels are replenished via ATP from glycolysis and cellular respiration.

This passage was adapted from "Mice Null for Calsequestrin 1 Exhibit Deficits in Functional Performance and Sarcoplasmic Reticulum Calcium Handling." Olojo RO, Ziman AP, Hernández-Ochoa EO, Allen PD, Schneider MF, Ward CW. *PLoS ONE*. 2011. 6(12) doi:10.1371/journal.pone.0027036 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

116. Muscle cell T-tubules function to:

- A.** create an action potential within a muscle cell.
- B.** receive the action potential from the presynaptic neuron.
- C.** deliver the action potential directly to the sarcomere.
- D.** supply Ca^{2+} to the cytosol during an action potential.

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117. According to the passage, calsequestrin:
- A. lowers the free Ca^{2+} ion concentration inside the lumen of the sarcoplasmic reticulum
 - B. raises the free Ca^{2+} ion concentration inside the lumen of the sarcoplasmic reticulum
 - C. gathers Ca^{2+} for release into the cytosol
 - D. pumps Ca^{2+} into the sarcoplasmic reticulum
118. Which of the following is/are true based on the results of Figure 2?
- I. At high stimulation frequencies, absolute force is greater in wild-type mice than CASQ1 null mice.
 - II. At low stimulation frequencies, normalized force is slightly greater in CASQ1 null mice than wild-type mice.
 - III. Normalized force is more similar between CASQ1 null and wild-type mice than absolute force.
- A. I only
 - B. III only
 - C. I and III only
 - D. I, II, and III
119. Which of the following additions to the study involving CASQ1 ablation and force production would likely be **LEAST** helpful in increasing the validity of the findings?
- A. Age-matching CASQ1 and wild-type mice
 - B. Including experimental data on higher stimulation frequencies
 - C. Increasing the sample size of mice
 - D. Including force data normalized to muscle volume
120. If a creatine kinase inhibitor were administered to an active muscle cell, which of the following would most likely occur?
- A. ATP concentrations would diminish while muscle contractions continued.
 - B. Phosphocreatine concentrations would diminish while muscle contractions continued.
 - C. ATP concentrations would remain constant while the percent saturation of myoglobin with oxygen would diminish.
 - D. Cellular respiration and glycolysis would increase to maintain a constant ATP concentration.
121. All of the following are true concerning skeletal muscle cells EXCEPT:
- A. skeletal muscle cells contain more than one nucleus.
 - B. human skeletal muscle cells continue normal cell division via mitosis throughout adult life.
 - C. skeletal muscle cells contain more than one sarcomere.
 - D. during muscle contraction, only the H band and the I band change length.
122. Which of the following is most likely NOT true concerning the uptake of Ca^{2+} ions from the cytosol during muscle contraction?
- A. It requires ATP.
 - B. The mechanism involves an integral protein of the sarcolemma.
 - C. It occurs against the concentration gradient of Ca^{2+} .
 - D. It is rapid and efficient.
123. Which of the following best accounts for the differences between absolute and CSA-normalized force in wild-type and CASQ1 null mice?
- A. Wild-type mice are larger than CASQ1 null mice.
 - B. CASQ1 null mice are smaller than wild-type mice.
 - C. Wild-type mice are able to achieve greater contractile frequency than CASQ1 null mice.
 - D. CASQ1 null mice are able to achieve greater contractile frequency than wild-type mice.

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Passage II (Questions 124-129)

The human fetus has a cartilaginous endoskeleton which is gradually replaced with bone before and after birth until adulthood. Bone forms within and around the periphery of small cartilaginous replicas of adult bones. After it is formed, adult bone is continuously remodeled through the activity of osteoblasts and osteoclasts. *Osteoblasts* differentiate from *fibroblasts* of the perichondrium. *Osteoclasts* differentiate from certain phagocytotic blood cells.

Although studies indicate that both nutrition and amount of load-bearing exercise affect bone density and volume in humans, the full process by which osteoblast and osteoclast activity is regulated in the body is not fully understood. Gastrointestinal peptides are increasingly being linked to processes controlling the regulation of bone mass, particularly under conditions of altered energy balance. Peptide YY (PYY) is a gut-derived peptide of the neuropeptide Y family that is released post-prandially into the bloodstream in proportion to calorie intake. PYY acts to inhibit food intake and increase satiety. It has been shown to be upregulated under some conditions that are also associated with low bone mass. Anorexic conditions and bariatric surgery for obesity both influence circulating levels of PYY and have a negative impact on bone mass.

Experiment 1

To determine the effect of PYY expression on bone mass, scientists compared bone mineral density (BMD) and bone mineral content (BMC) in control and germline PYY knockout (PYY^{-/-}) mice. The results for female mice are shown in Figure 1.

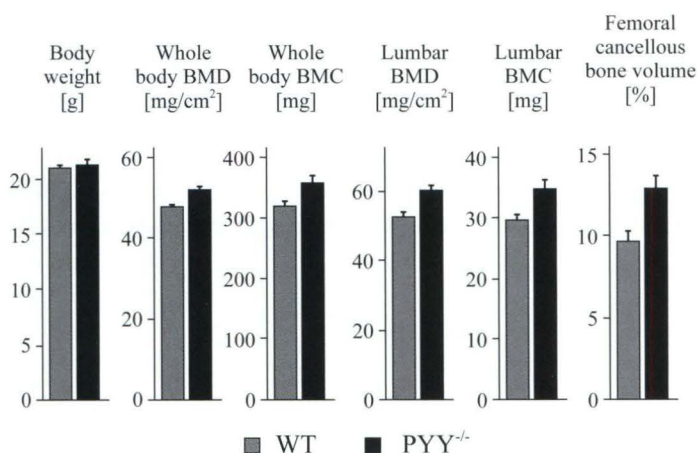


Figure 1 Bone mineral density and bone mineral content in wild-type and PYY knockout mice

Experiment 2

To further evaluate the effects of PYY expression on the regulation of bone mass, scientists examined femoral bone structure in control and conditional adult-onset PYY over-expressing mice (PYYtg). Results for female mice are shown in Figure 2.

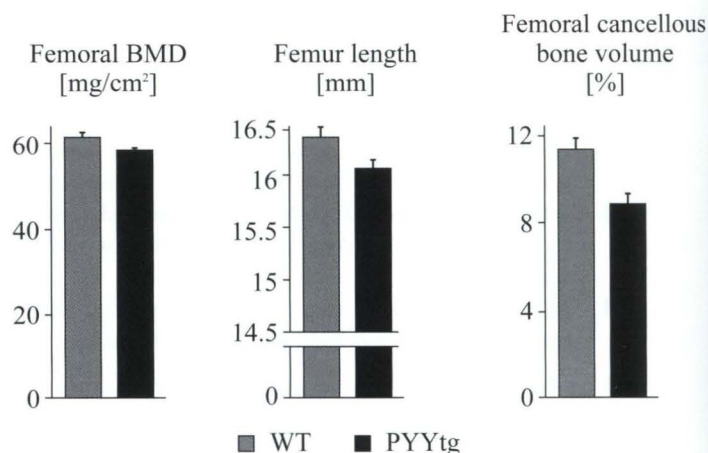


Figure 2 Attributes of femoral bone morphology for wild-type and conditional adult-onset PYY over-expressing mice

This passage was adapted from "Peptide YY Regulates Bone Remodeling in Mice: A Link between Gut and Skeletal Biology." Wong IPL, Driessler F, Khor EC, Shi Y-C, Hörner B, Nguyen AD, Enriquez RF, Eisman JA, Sainsbury A, Herzog H, Baldock PA. *PLoS ONE*. 2012. 7(7) doi:10.1371/journal.pone.0040038 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

124. Based on the results in Figure 1, which of the following **CANNOT** be true regarding PYY^{-/-} mice in comparison with wild-type mice?
 - A. They have increased osteoclast activity and increased osteoblast activity.
 - B. They have increased osteoclast activity and decreased osteoblast activity.
 - C. They have decreased osteoclast activity and increased osteoblast activity.
 - D. They have decreased osteoclast activity and decreased osteoblast activity.
125. Which of the following changes to the study methodology would make the results of Experiment 1 more reliable?
 - A. Standardizing for mouse body mass between study groups
 - B. Examining male and female mice separately
 - C. Standardizing for amount of exercise between study groups
 - D. Sampling bone from a greater number of locations within the body

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126. Suppose researchers studied bone mass in a mouse genotype they created to be a hybrid of $PYY^{-/-}$ and PYY^{tg} . Which of the following would be true regarding the $PYY^{-/-}$ - PYY^{tg} hybrid?
- Femoral bone would likely decrease, but lumbar bone would likely increase.
 - Deviation from wild-type bone phenotype would likely be age-dependent.
 - It is not possible to predict the net effect on whole body bone phenotype based on the information given.
- II only
 - III only
 - I and II only
 - II and III only
127. Which of the following hormones most likely stimulates osteoclasts?
- Parathyroid hormone
 - Calcitonin
 - Epinephrine
 - Prostaglandin
128. All of the following statements are true concerning bone EXCEPT:
- bone is connective tissue.
 - bone is innervated and has a blood supply.
 - yellow bone marrow stores triglycerides as a source of energy for the body.
 - bone is the only nonliving tissue in the body.
129. Which of the following cells most likely arises from the same stem cell in the bone marrow as an erythrocyte?
- Osteoblast
 - Fibroblast
 - Osteoclast
 - Chondrocyte

Passage III (Questions 130-136)

The rate at which a muscle can perform work, or the muscle power, varies over time and is given in Table 1.

Time	Power (kg m/min)
First 10 seconds	7000
Next 1.5 minutes	4000
Next 30 minutes	1700

Table 1 Muscle power variance over time

Energy for muscle contraction is derived directly from ATP. However, a muscle cell's original store of ATP is used up in less than 4 seconds by maximum muscle activity. Three systems work to maintain a nearly constant level of ATP in a muscle cell during muscle activity: the phosphagen system; the glycogen-lactic acid system; and the aerobic system. The phosphagen system makes use of phosphocreatine, which contains a high energy phosphate bond that is used to replenish ATP stores from ADP and AMP. This system can sustain peak muscular activity for about 10 seconds. The glycogen-lactic acid system is relied upon for muscular activity lasting beyond 10 seconds but not more than 1.6 minutes. This system produces ATP from glycolysis. Aerobic metabolism of glucose, fatty acids and amino acids can sustain muscular activity for as long as the supply of nutrients lasts.

The recovery of muscle after exercise involves replacement of oxygen. Before exercise, the body contains approximately 2.5 liters of oxygen, but this oxygen store is used up in approximately 1 minute of heavy exercise. After heavy exercise, oxygen uptake increases dramatically at first and then levels back down to normal over a 1 hour period. The extra oxygen taken in is called the oxygen debt, and is about 11.5 liters.

Although the above is true for muscle in general, muscle fiber types vary in endurance, force production, and contractile and metabolic properties. Some of these differences are represented in Table 2.

	Slow Twitch Oxidative (Type I)	Fast Twitch Oxidative (Type IIA)	Fast Twitch Glycolytic (Type IIB)
Time to peak tension	1.0	0.4	0.4
Oxidative potential	1.0	0.7	0.2
Glycolytic potential	1.0	1.5	2.0
[Phosphocreatine]	1.0	1.2	1.2
[Glycogen]	1.0	1.3	1.5
[Triacylglycerol]	1.0	0.4	0.2

Table 2 Contractile and metabolic properties of human skeletal muscle fiber types. All values are expressed as a fold-change relative to slow-twitch oxidative fibers

GO ON TO THE NEXT PAGE.

Proportion of muscle fiber types can influence susceptibility to metabolic diseases such as diabetes. Insulin sensitivity correlates with the proportion of ST oxidative fibers. Specifically, insulin-stimulated glucose transport is greater in skeletal muscle enriched with ST muscle fibers, thus priming ST muscles for accelerated glucose uptake and metabolism.

This passage was adapted from "Skeletal Muscle Fiber Type: Influence on Contractile and Metabolic Properties." Zierath JR and Hawley JA. *PLoS Biology*. 2004. 2(10) doi:10.1371/journal.pbio.0020348 for use under the terms of the Creative Commons CC BY 3.0 license (<http://creativecommons.org/licenses/by/3.0/legalcode>).

130. Based upon the information in Table 1, which of the following are the most likely rates of molar production of ATP for the phosphagen system, the glycogen-lactic acid system, and the aerobic system respectively?
- A. 1.7 M/min, 4 M/min, 7 M/min
 - B. 2 M/min, 2 M/min, 2 M/min
 - C. 4 M/min, 3 M/min, 2.5 M/min
 - D. 4 M/min, 2.5 M/min, 1 M/min
131. Why is the oxygen debt greater than the amount of oxygen stored in the body?
- A. Exercise increases the hemoglobin content of the blood so that it can store more oxygen.
 - B. Heavy breathing after exercise takes in more oxygen.
 - C. In addition to replenishing the stored oxygen, oxygen is used to reconstitute the phosphagen and lactic acid systems.
 - D. In addition to replenishing the stored oxygen, oxygen is used to reconstitute the phosphagen, lactic acid, and aerobic systems.
132. During the aging process, the ratio of fast twitch to slow twitch fibers increases. All of the following might be expected to accompany that transition EXCEPT:
- A. decreased concentration of phosphocreatine.
 - B. diminished insulin sensitivity.
 - C. decreased oxidative capacity.
 - D. increased concentration of glycogen.

133. According to the passage, muscle fiber types differ in all of the following characteristics EXCEPT:
- A. contractile velocity.
 - B. maximum force production.
 - C. resistance to fatigue.
 - D. amount of oxygen debt.
134. As shown in Table 2, type I fibers have a greater density of mitochondria than type II fibers. Which of the following helps explain this discrepancy?
- I. Type II fibers contract with more force than type I fibers.
 - II. Type I fibers have greater endurance than type II fibers.
 - III. Type I fibers make greater use of the aerobic system than type II fibers.
- A. II only
 - B. III only
 - C. II and III only
 - D. I, II and III
135. In which of the following sports do athletes most likely rely primarily upon the phosphagen system for muscle contraction?
- A. Tennis
 - B. Boxing
 - C. Diving
 - D. Cross-country skiing
136. Which of the following is depleted first in the body of an athlete exercising at maximal capacity?
- A. Phosphocreatine
 - B. ATP
 - C. Glycogen
 - D. Glucose

GO ON TO THE NEXT PAGE.

Questions 137 through 138 are **NOT** based on a descriptive passage.

137 All of the following are true concerning the musculoskeletal system **EXCEPT**:

- A. Skeletal muscles function by pulling one bone toward another.
- B. tendons connect muscle to muscle.
- C. ligaments connect bone to bone.
- D. the biceps works antagonistically to the triceps.

138. Which of the following statements concerning bone is **FALSE**?

- A. Bone functions as a mineral reservoir for calcium and phosphorous.
- B. Bone contains cells that differentiate into red and white blood cells.
- C. Bone acts as a thermostat for temperature control of the body.
- D. Bone provides a framework by which muscles can move the body.

STOP. IF YOU FINISH BEFORE TIME IS CALLED, CHECK YOUR WORK. YOU MAY GO BACK TO ANY QUESTION IN THIS TEST BOOKLET.

ANSWERS & EXPLANATIONS

FOR
30-MINUTE IN-CLASS EXAMINATIONS

ANSWERS TO THE 30-MINUTE IN-CLASS EXAMS

Lecture 1	Lecture 2	Lecture 3	Lecture 4	Lecture 5	Lecture 6
1. B	24. D	47. B	70. C	93. D	116. C
2. A	25. B	48. B	71. B	94. B	117. A
3. A	26. C	49. D	72. B	95. A	118. D
4. A	27. C	50. A	73. A	96. C	119. B
5. D	28. D	51. D	74. D	97. A	120. A
6. C	29. D	52. A	75. A	98. C	121. B
7. D	30. B	53. C	76. D	99. A	122. B
8. B	31. B	54. A	77. D	100. B	123. A
9. B	32. D	55. D	78. C	101. D	124. B
10. B	33. C	56. A	79. B	102. C	125. C
11. C	34. A	57. B	80. B	103. D	126. D
12. B	35. B	58. C	81. C	104. A	127. A
13. A	36. A	59. B	82. A	105. D	128. D
14. D	37. A	60. B	83. D	106. C	129. C
15. A	38. D	61. C	84. C	107. C	130. D
16. B	39. A	62. B	85. B	108. C	131. C
17. D	40. A	63. D	86. C	109. C	132. A
18. B	41. C	64. B	87. B	110. D	133. D
19. C	42. C	65. C	88. D	111. A	134. C
20. C	43. B	66. C	89. A	112. B	135. C
21. C	44. A	67. A	90. B	113. B	136. A
22. B	45. B	68. A	91. A	114. C	137. B
23. C	46. B	69. B	92. D	115. B	138. C

MCAT® BIOLOGICAL SCIENCES

Raw Score	Estimated Scaled Score
22-23	132
20-21	131
19	130
18	129
17	128
15-16	127
14	126
12-13	125

MCAT® BIOLOGICAL SCIENCES

Raw Score	Estimated Scaled Score
11	124
9-10	123
8	122
6-7	121
5	120
3-4	119
1-2	118

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 1

Passage I

1. **B is correct.** There were two ways to approach this problem. It could have been noted that viruses hijack ribosomes during the lytic cycle to produce new virions. Alternatively, the fact that prokaryotes lack membrane-bound organelles could have been used to eliminate answer choices A, C, and D because none of these structures are present in a prokaryotic cell.
2. **A is correct.** The bacteria is gram-positive, meaning that its cell wall is composed of primarily peptidoglycan. It would make sense to attack the primary component of the cell wall when attempting to break the structure up. The other choices are all components in gram-negative cell walls. If phage lysin worked by breaking any of these structural components up, it would probably not be very effective at lysing the gram-positive bacteria *S. pneumoniae*.
3. **A is correct.** Losing the phage lysin always results in a lower growth rate when compared to the bacteria that normally possessed it. To see this, compare any two of the strain variants which differ only in the presence or absence of the phage lysin gene, Svl. R36AP has a higher growth rate than R36APΔSvl. R36APΔLytA has a higher growth rate than R36APΔLytAΔSvl (Note that the Δ sign is being used to indicate that the gene has been knocked out). This answer would also be the most reasonable guess if you had trouble reading the graph but understood the process that was being described. If the phage lysin plays a role in breaking the cell wall apart, and this is a critical step in the formation of biofilm, it stands to reason that the phage lysin should always increase the rate of biofilm formation. However, note that questions such as this do not always have intuitive answers and are ultimately about interpretation of graphical data. If the data had somehow shown lysin decreasing the growth rate, you would have to choose that answer even though it didn't make intuitive sense.
4. **A is correct.** This is the most reasonable explanation for loss of biofilm. The presence of lysin degrading the matrix would cause it to consistently slow the biofilm growth rate down as more and more of it was released rather than causing a sharp drop at the end. When the virulent bacteriophage spreads and causes other bacterial cells to lyse it is contributing to the biofilm, not degrading it. Answer D doesn't make sense, biofilms are composed of lysed cells and a polymer made up of, among other things, extracellular DNA. As the cells are lysing they should probably be contributing to the matrix, not using it up.
5. **D is correct.** Figure 2 shows that DNase decreases growth rate, so answer choice A is out. The experiment is looking at the effects of DNase on extracellular DNA, so choice B is out. DNase's name indicates that it is an enzymes. Enzymes don't react with their substrate, they facilitate its reaction with other substrates, so choice C is out.
6. **C is correct.** The researchers wanted to make sure that any extracellular DNA would contribute to the biofilm's growth, so they used a second type of DNA in addition to the *S. pneumoniae* DNA. If they had not used the salmon DNA, there would be suspicion that there was something about *S. pneumoniae*'s DNA in particular that was increasing growth. There were two ways to approach this. The first would be to note that the experiment stated that it was testing the effects of extracellular DNA in general with no mention of the source of DNA. The other way to approach this question would be in reverse. Does the *S. pneumoniae* DNA appear to affect growth more than salmon, or vice-versa? In fact, both of these DNA sources seem to have similar effects for any given dose. The implication is there is not something special about either *S. pneumoniae* DNA or salmon DNA, knocking out both answer choice A and answer choice B. Answer choice D is fairly specific, and there is nothing in the passage that indicates that researchers were interested in comparing bacterial and animal DNA in particular. Note that choice C also fits in with experiment 2, which looked at how growth rate was affected by general extracellular DNA degradation.
7. **D is correct.** DNase degrades extracellular DNA and decreases its amount while adding in extracellular DNA would increase the amount of DNA. Choice C would only be accurate in the unique case where the amounts of DNase and extracellular DNA cancelled each other out. In any other case, there would some net effect depending upon which of the factors was contributing more.
8. **B is correct.** Streptococcus. Coccus implies that the shape of the bacteria is round.

Passage II

9. **B is correct.** The smooth ER plays a role in both steroid hormone synthesis and metabolism. The adrenal cortex produces mineral corticoids and glucocorticoids, all of which are steroid hormones. The smooth ER is primarily concerned with the synthesis and breakdown of compounds. Muscle cells are primarily concerned with ion transport in order to facilitate muscle contractions – the analogous structure they contain is the sarcoplasmic reticulum, which is smooth ER that has different proteins to handle ion flow. Intestinal epithelial cells are responsible for nutrient uptake from the digestive tract and into the intestinal lumen– we would expect them to have large amounts of organelles involved in transport, such as the Golgi apparatus and secretory vesicles.
10. **B is correct.** The passage directly states that phospholipids are produced on the cytosol side of the ER membrane. The lumen is on the opposite side of the ER membrane.
11. **C is correct.** Phospholipids are stated to be incorporated into membranous cell structures. Cytochrome P450 is said to be composed of integral proteins, meaning it is in the cell membrane. Since Cytochrome P450 is an integral protein, it is likely produced in the rough ER (remember that secretory AND integral proteins are produced in the rough ER). This means that its upregulation and downregulation would probably occur at the level of gene expression or by posttranslational modification, neither of which newly produced phospholipids should affect. Cytochrome P450 is an integral protein, meaning it is not going to be exocytosed.
12. **B is correct.** Mixed function oxidases are proteins, meaning they are synthesized in either the rough ER or on free floating ribosomes in the cytosol. Since cytosol isn't a choice here, rough ER is picked by default. Note that even if cytosol were present, you could make an educated guess that rough ER was the right answer by having noticed that the only specific protein listed as being a major part of a mixed-function oxidase is cytochrome P450, which is an integral protein.
13. **A is correct.** Mixed function oxidases are said to oxidize steroids – estradiol is a steroid hormone. Note that the question asks for an endogenous substance, which means that the answer choice has to be something produced by the body. This means that neither ethanol nor Carbofuran can be the correct answer choice. Lysine is an amino acid which holds a positive charge. If you knew this but did not know what estradiol was, you could have guessed at the answer by having noted that mixed function oxidases convert hydrophobic compounds into hydrophilic ones.
14. **D is correct.** This is what adipocytes are by definition – adipose tissue, or body fat, is stored energy. The question implies that adipocytes are serving as a reservoir for triacylglycerols, which hints at the correct answer. B and C are both stated functions of the smooth ER, not of the adipocytes.
15. **A is correct.** Phenobarbital has been stated to increase smooth ER levels and mixed-function oxidase levels. This effect would be compounded when Carbofuran was added, leading to higher levels of phospholipids than either the group which only had Carbofuran added or the control group which had no foreign substances added.

Passage III

16. **B is correct.** First of all, Table 1 does not give data regarding concentration of number of ions in solution, so C can be eliminated. D can be eliminated because the passage states that the concentration of the ion channel was the same in each solution. Now you only have to choose between A and B. The passage states that ΔG was only obtained for those ions that exhibited binding with the K^+ channel. Only ions that bind to the channel will be able to pass through it, so identifying the characteristic that determines permeability is as simple as comparing the ions that do and do not have a recorded value of ΔG . According to Table 1, ΔG was obtained for some of the 1^+ cations and some of the 2^+ cations, so there is no reliable trend for charge. A can be eliminated. Table 1 also shows that only K^+ and ions with larger atomic radii than K^+ have ΔG values recorded. This demonstrates that the ion channel is specifically reacting with ions based on their size, making B the correct answer. While the charge of an ion can affect ion channel permeability, this experiment demonstrated that the size of the ion was the important factor in this instance.

17. **D is correct.** A can be eliminated because ions are hydrophilic (polar), not hydrophobic (nonpolar), and the center of the lipid bilayer is hydrophobic, not hydrophilic. B is incorrect because if ions were nonpolar, they would be able to pass through the membrane just as small nonpolar molecules can. Although choice C describes the structure of the cellular membrane accurately, this has nothing to do with the inability of ions to pass through. D is correct because it accurately describes the characteristics of the ions and cellular membrane that prevent free passage of ions through the membrane.
18. **B is correct.** The reference to an ATPase indicates that energy input from ATP is used in the mechanism described, which means that the type of transport involved is "active." This means that A or B must be the answer. Primary active transport moves ions against their concentration gradient, so A is incorrect. Secondary active transport allows ions to diffuse down an electrochemical gradient that is created by another cellular mechanism (usually primary active transport). In the example given in the passage and question stem, the Na^+/K^+ ATPase is creating a cell-made gradient, which the K^+ ions then travel down using the K^+ channel.
19. **C is correct.** Figure 1 does not provide any evidence for or against the statements made in A and B, so these answer choices can be eliminated. According to the passage, the downward deflections in Figure 1 represent heat exchange caused by dilution of the titrant or binding of ions to KcsA. The heat exchange associated with dilution of the titrant should be the same for both KCl and NaCl, so any difference between the graphs must reflect a difference in binding of ions to the channel. Therefore, the fact that the deflections in the graph for the KCl titration are greater than those in the NaCl titration must indicate that K^+ binds to the channel while Na^+ does not. This makes C the correct answer. D is incorrect because an ion cannot be intrinsically exothermic or endothermic.
20. **C is correct.** As described by the fluid mosaic model, proteins inserted into the membrane must have a hydrophobic portion that can interact with the hydrophobic lipids that make up the cell membrane. A is incorrect because K^+ channels are not synthesized in the nucleus. Just like any other protein, they are made at the rough endoplasmic reticulum. C is incorrect because the K^+ channels themselves do not "create" the gradient, although they participate in its creation. Also, the fluid mosaic model does not address the electrochemical gradient referred to in choice C. D is not a true statement; the K^+ channels do not create energy for the cell.

Stand-alones

21. **C is correct.** Evolution has to do with genetic change. It can be defined either at an individual level when a change occurs in genes that can be passed down to subsequent generations (choice A) or at the level of the population where a change in the total gene pool (allelic frequencies) constitutes evolution (choice B). During speciation, new species evolve from older species, which illustrates the process of evolution on a macro-scale (choice D). The only answer choice that doesn't necessarily involve evolution is choice C. Inbreeding, which increases the number of homozygous individuals in a population, can create a phenotypic shift, or change in the frequencies of phenotypes, without changing the overall allelic frequencies of that population.
22. **B is correct.** Recall that Hardy-Weinberg equilibrium describes a population in which no evolution is occurring. Natural selection and non-random mating contribute to evolution by the selection and propagation of certain genes at greater frequencies than others. Emigration contributes to evolution by the introduction of new genetic information into a population. Choice B is correct because a large population size is necessary to protect the population from evolution caused by genetic drift.
23. **C is correct.** Eukaryotic cells have a membrane-bound nucleus and membrane-bound organelles, while prokaryotic cells do not. Eukaryotic DNA is coiled around histone proteins; prokaryotic DNA is "naked" and lacks histone proteins. Eukaryotic flagella are composed of microtubules while those of prokaryotic cells are made of flagellin. Choice C is correct because both eukaryotic and prokaryotic cells contain ribosomes (although prokaryotic ribosomes are smaller).

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 2

Passage I

24. **D is correct.** The passage states that chromaffin cells are modified sympathetic postganglionic neurons, so A and B will have similar receptors; this similarity alone is enough to eliminate both answer choices. Also note that postganglionic neurons usually respond to acetylcholine from preganglionic neurons, not epinephrine. Parasympathetic postganglionic neurons will also respond to acetylcholine rather than epinephrine. Process of elimination leaves D as the best answer. You could also pick D by remembering that cardiac cells are innervated by both branches of the autonomic nervous system, so they must have both cholinergic and adrenergic receptors.
25. **B is correct.** Familiarize yourself with the differences between commonly-used statistical tests. One important distinction is between those used with categorical and continuous dependent variables. This experimental setup involves a categorical independent variable (weight-matched control versus *Per* mutant) and a continuous dependent variable (urine epinephrine levels). Chi-square analysis is used for categorical dependent variables, so D can be eliminated. The other three choices are appropriate for continuous dependent variables, but C can be eliminated because correlation describes a relationship between two variables rather than establishing significant differences between groups. Of the answer choices that are left, either could technically be used, but the question asks which is most *likely*. An ANOVA can be used to compare two groups, but it is usually used when there are three or more groups. In this case there are only two groups, so a t-test is more likely than an ANOVA.
26. **C is correct.** This question seems as though it requires detailed knowledge about circadian rhythms, but you only need to know which answer choices are innervated by the sympathetic nervous system. An organ that does not receive signals from the SNS can't be affected by a circadian rhythm of SNS signaling. Know that the diaphragm is skeletal muscle and is not innervated by the autonomic nervous system. The answer can also be found by process of elimination. Recall that the SNS signals the iris to constrict in dark environments in order to dilate the pupil (allowing you to hunt in the dark); B can be eliminated. Sweat glands and the arteries of the heart also respond to SNS signaling as part of the fight-or-flight response, so A and D are also incorrect.
27. **C is correct.** The data in Figure 1 indicate that jet lag disrupts the circadian rhythm of SNS signaling, since epinephrine urine levels in *Per* mutant mice experiencing jet lag (the dark/dark cycle) do not follow the regular peak seen in these mice during a normal light/dark cycle. What is needed to support the hypothesis suggested in the question stem is a link between this disruption of the SNS circadian rhythm and tumor growth; the correct answer will provide this link. Choice A undermines the hypothesis rather than supporting it. An oncogene promotes tumor formation, so if the normal SNS circadian rhythm activates the *Myc* oncogene, the disruption associated with jet lag would prevent tumor formation. B might seem tempting, but it does not provide direct evidence of a link between the SNS circadian rhythm and tumor formation (and it also refers to humans rather than the *Per* mutant mice featured in the experiment and question stem). C is a better answer, since it implies that a disruption of the circadian rhythm of SNS signaling would lead to dysregulated cell proliferation, which is associated with tumor formation. D is not as good an answer: the effects of jet lag found in this experiment could explain the finding described in choice D, but the evidence is less direct than that provided by choice C.
- As this example shows, starting with a loose prediction of what the correct answer will look like can be helpful in finding the best answer choice when there are a number of choices that seem like plausible answers.
28. **D is correct.** As stated in the passage, chromaffin cells release epinephrine, an SNS neurotransmitter. A, B, and C all describe processes that are associated with the "flight-or-flight" response triggered by SNS activation. Constricted pupils would be associated with PNS activation rather than SNS activation (and thus would occur in response to acetylcholine, rather than epinephrine). Even if you didn't remember that pupil constriction occurs in response to acetylcholine rather than epinephrine, the question can be answered by process of elimination. You should associate increased heart rate, elevated blood glucose, and increased basal metabolism with epinephrine and SNS activation.

29. **D is correct.** Although A is presumably a true statement, it does not limit the ability to draw conclusions of causality about the effect of jet lag on urine epinephrine levels. You might be tempted to pick B, which correctly points out that the study design is observational; know that it is often difficult to draw conclusions of causality in an observational study. However, it is not true that urine epinephrine levels cannot be obtained in this study design, so B is wrong. D is the better answer choice because it correctly describes a specific reason that the observational study described here limits conclusions of causality. The subjects cannot be assigned randomly into groups that experience different degrees of jet lag. C is incorrect because the subjects are followed over time, so the researchers would be able to determine whether jet lag preceded changes in urine epinephrine levels. If jet lag and urine epinephrine were assessed at only one point in time, the requirement of temporality would not be met.
30. **B is correct.** This question requires reasoning about the processes that regulate the amount of neurotransmitter in synapses. It also indicates how important it is to take the time to read the question stem closely: a rushed test-taker might read “decrease” rather than “increase,” and you can bet that an answer choice will be included that is opposite to the correct one. Choice I is correct; notice that the enzyme is associated with norepinephrine breakdown, so inhibition of this enzyme would increase the amount of neurotransmitter available. C does not contain choice I and can be eliminated. Choice II is not correct; reabsorption decreases the amount of neurotransmitter in the synapse. D contains choice II, so it can be eliminated. Choice III is correct; reuptake is the process of clearing the neurotransmitter from the synapse, so the inhibition of reuptake allows more neurotransmitter to remain in the synapse. A can be eliminated because it does not include choice III. This leaves B, the correct answer.

Passage II

31. **B is correct.** The information in the question about electrophysiology is extraneous. The question is really asking: which region of the visual pathway is most associated with object recognition? This question is testing your knowledge of the ventral (“what”) pathway and the dorsal (“where”) pathway. Recall that the “what” pathway is largely responsible for object recognition, and involves the temporal lobe. The retina, optic chiasm, and LGN (answers A, C, and D) are important earlier in visual processing, and will contain both “what” and “where” information. You probably did not recognize terms like central inferotemporal area and magnocellular layer in answer choices B and D, but the fact that they are part of the temporal lobe and LGN is enough to answer the question. Note that even if you didn’t remember that the temporal lobe is the endpoint of the “what” pathway, you could answer this question simply with the knowledge that higher-level visual processing like object recognition takes place in the cerebral cortex. B is the only answer choice that references a lobe of the cerebral cortex rather than an earlier part of the visual pathway.
32. **D is correct.** This question requires you to understand that the wild type and mutant mice both have GCAP2, while only the WT mice have GCAP1. You also must realize that lower fractions in Figure 2 reflect a greater change from baseline and thus a greater sensitivity to calcium. Figure 2 shows that when GCAP1 is knocked out, RetGC activity is unaffected at low calcium levels but lower than wild type at higher calcium levels. The difference between the GCAP1^{-/-} and wild type mice at higher concentrations must be due to the activity of GCAP1 in the WT mice, indicating that GCAP1 is LESS sensitive to calcium than GCAP2. This means that Answer C is incorrect and D is correct. Answer B could be a true statement, but is not shown by Figure 2 and would not explain why the deficit in RetGC activity is not seen at low calcium levels. Answer A does not make sense – knocking out an activating protein by definition has an effect on activating proteins – and is not supported by the data.
33. **C is correct.** This question is asking you to think about the difference between rods and cones. Know that rods, which are incapable of detecting color, respond to all wavelengths of light in the visible spectrum. Cones, on the other hand, are more finely tuned to smaller wavelength ranges. To properly perform this experiment in a subset of cone cells, you would need to use light with wavelengths corresponding to the range for that particular cell type. None of the answer choices state this exactly, so we need to find the one that is most correct. Answer A would be correct for rods rather than cones, so it can be eliminated. Answer B would have the researchers using a wavelength outside of the visible spectrum. Neither rods nor cones would respond to these wavelengths, so B can also be eliminated. Nothing in the passage or lecture indicates that cones use cAMP for recovery – answer D is also incorrect. This leaves only C. Using light of only one wavelength would make the experiment specific to a specific subset of cones, as long as the cones respond to that wavelength. Although C doesn’t give you all the detail you might have expected from the correct answer, it is more correct than any of the other choices.

34. **A is correct.** Choice I must be incorrect: It is important to know that photoreceptors do not send action potentials and instead hyperpolarize when stimulated, and this process was referenced at the beginning of the passage. Answer choices B and D can be eliminated because they do not contain I. To choose between A and C, you have to determine whether II must be false. Based on the deficits in cGMP production seen in the passage when GCAP1 is knocked out, there is no reason to believe it is not necessary for normal recovery. The key word here is normal; i.e., in the wild type phenotype. Thus choice II is false, and the answer is A. Always use this process of elimination when presented with questions in this format, but to double check yourself, quickly look at choice III as well. The passage gives no indication that GCAP2 is not also necessary. It is *possible* that GCAP2 is totally redundant and unnecessary, but remember that the question is asking you for an answer that *must* be false.
35. **B is correct.** The passage information tells you that cGMP is necessary for normal photoreceptor recovery, and the experiments show that GCAP1 is also needed. Answer choices A and C can be eliminated. Recall that vitamin A is a precursor for the pigment rhodopsin, another crucial molecule in the functioning of photoreceptors. D can also be eliminated. One way that neurons (including photoreceptors) are unique from other cells in the body is that they do not depend on insulin for glucose uptake. This makes answer B correct. This question is on the edge of requiring more detail than you would need for the MCAT®, but you can at least eliminate A and C based on the passage, and it's a good idea to know that neurons are not dependent on insulin.
36. **A is correct.** First you need to think about adrenergic signaling onto the iris. What is adrenergic signaling (a.k.a. epinephrine/norepinephrine signaling) associated with? The sympathetic nervous system. Recall that sympathetic activation leads to the "fight or flight" response, which includes pupil dilation. This narrows the potential correct answers down to A and C. The next step is to think about what happens to the retina as the pupil dilates. More light should enter the eye, leading to more hyperpolarization of photoreceptors. This should in turn lead to more photoreceptor recovery. The passage also tells us that Ca^{2+} levels decrease under greater illumination, which should lead to more activation of RetGC and increased recovery.
37. **A is correct.** This is a particularly difficult question. Start by eliminating answers that must be incorrect. Answer C tells you that the effect is due to decreased RetGC activity, but this would lead to a *decrease* in cGMP production, not an increase. C can be eliminated. Answer D is a distractor answer choice that is not relevant, as the experiment in question does not involve light or rhodopsin, and can also be eliminated. This leaves only A and B. Note that the passage told us that GCAP1 and 2 have different *intrinsic* sensitivities to calcium. In other words, the sensitivity of GCAP2 does not depend on the presence or absence of GCAP1, and should not have changed in this experiment. For this reason, B is also incorrect. This leaves choice A. An increase in production of GCAP2 to replace the missing GCAP1 would explain an increase in cGMP production at low calcium levels. At higher concentrations of calcium the increase should be negated, since experiment 2 shows that GCAP2 is inhibited at lower calcium levels than GCAP1.

Passage III

38. **D is correct.** As the nAChR immunoprecipitates with phospholemman, we can assume that they are structurally connected. Therefore, we can conclude that phospholemman is present wherever nicotinic acetylcholine receptors are. We know that acetylcholine is a neurotransmitter and neurotransmitters are released across the synapse, from the presynaptic neuron to the postsynaptic membrane.
39. **A is correct.** First, you can immediately eliminate C and D because Figure 1 represents the effect of nicotine exposure on muscle fibers, not neurons. Then examine Figure 1 to determine whether muscular excitability increased or decreased. The figure shows that the experimental condition (exposure to nicotine) causes the distribution to shift to the right, while the shape of the distribution remains the same. This indicates that there is a mean increase in the resting membrane potential among the experimental group. Thus, exposure to nicotine results in a net membrane depolarization. Associate depolarization with increased excitability and hyperpolarization with decreased excitability, since depolarization brings a membrane closer to the threshold potential that would trigger an action potential. B can be eliminated, leaving A as the correct answer.

40. **A is correct.** The passage states that the sodium-potassium pump is the only known receptor for ouabain, that Na,K-ATPase generates V_{pump} , and that the RMP is the sum of E_{Nernst} and V_{pump} . C can immediately be eliminated: by definition, the change in RMP must be due to a change in E_{Nernst} and/or V_{pump} . If administration of ouabain eliminates any difference in RMP, the difference between the experimental and control groups in RMP seen in Experiment 1 cannot be due to a difference in the Nernst potential, which is unaffected by ouabain. B can be eliminated. The differences in RMP between the experimental and control group must result from differences in Na,K-ATPase activity, making A the correct answer. You might be tempted by D, but there is no information given to indicate that experimental error is involved.
41. **C is correct.** Notice to start that I and II are opposite from each other, so both cannot be included in the correct answer. Even if you did not understand the question, you could eliminate D.
- The experimental findings are an increased RMP in skeletal muscle among nicotine-exposed rats, so the conclusions must be compatible with this result. The passage states that nicotine exposure results in stimulation of the α_2 isoform of Na,K-ATPase and also states that stimulation of the sodium-potassium pump results in hyperpolarization. Since the results indicate depolarization, stimulation by nicotine must cause the isoform to be underexpressed rather than overexpressed; II is correct, and I is incorrect. Since answer choice C is the only one that does not contain choice I, it must be the correct answer. However, as usual, it is best to check yourself by quickly considering all of the choices. Considering III, the sodium-potassium pump could have simply become desensitized to the stimulus due to constant stimulation. As a result, a given amount of nicotine would produce less stimulation of the enzyme and less hyperpolarization would occur, resulting in a lower potential. This too fits with the experimental findings.
42. **C is correct.** The resting membrane potential, as quantified by the Nernst potential, is a voltage (and thus a potential) that results from the imbalance of charges across a membrane. If the membrane were not selectively permeable to ions, all ions would be able to cross the membrane and reach equilibrium, preventing the formation of a potential. A can be eliminated. Multiple ions contribute to the overall charges on either side of the membrane, so D can be eliminated. (Know that the resting potential is primarily determined by the electrochemical gradients of K^+ and Na^+ .) Finally, the sodium-potassium pump also contributes to the uneven distribution of ions across the membrane, as it pumps potassium ions in and sodium ions out of the cell. This means B can be eliminated. The voltage gated sodium channels modulate the balance of ions during an action potential but play no role in maintaining the resting state of the neuron. Recall that the rapid depolarization achieved during an action potential is achieved by the sudden rush of Na^+ ions into the cell after the opening of voltage gated sodium channels, which are closed in the neuron at rest.
43. **B is correct.** Blocking acetylcholine receptors would result in inhibited stimulation of nAChRs. As stated in the text, stimulation of nAChRs results in hyperpolarization, so the inhibition seen in myasthenia gravis (MG) sufferers would instead lead to depolarization at the neuromuscular synapse. Depolarization is an increase in resting membrane potential, so C and D can be eliminated. Since exposure to nicotine results in an increased RMP and myasthenia gravis also results in an increased RMP, smoking would exacerbate the symptoms of myasthenia gravis rather than alleviating them. A can be eliminated.

Stand-alones

44. **A is correct.** Choice A describes saltatory conduction accurately. If you didn't remember the exact mechanism of saltatory conduction, at least know that it allows faster movement of an action potential down the axon of a single neuron. C can be eliminated, since it refers to movement from one neuron to another. You should also remember that saltatory conduction has to do with a "jump," making A or D the most likely answer. Furthermore, saltatory conduction occurs only in myelinated axons. D can be eliminated, and A is correct.
45. **B is correct.** You should know that Na^+ channels are more sensitive than K^+ channels. That's why they open first after the threshold potential is reached, causing the influx of Na^+ ions that depolarizes the neuronal membrane. A is a true statement. Recall that when voltage-gated K^+ channels open, K^+ diffuses *out* of the cell, moving it back towards resting potential; this would not occur if K^+ concentration were not greater inside than outside the cell. C is also true. Although K^+ and Na^+ are by far the major determinants of the resting membrane potential, Cl^- has a small contribution. Finally, D is correct. You should know that the action potential starts at the junction between the soma and axon, which is called the axon hillock.

46. **B is correct.** You should think of the thalamus as a “way station” for most types of sensory information, with the notable exception of the olfactory system. D can be eliminated. The thalamus does not carry out the higher-level processing described in choice C. Instead, the thalamus preserves and communicates sensory information to the cerebral cortex, which is where this type of processing does take place. C can be eliminated. Choice A applies to the *hypothalamus*, not the thalamus. For the MCAT®, you must be aware of the major functions of both the thalamus and hypothalamus.

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 3

Passage I

47. **B is correct.** You should recognize cortisol as a steroid hormone. Remember that steroid hormones act by diffusing through the effector cell membrane and binding with a receptor in the cytosol. No hormones bind with receptors attached to the nuclear membrane or unattached outside of the cell, so C and D are incorrect. A is true for peptide and catecholamine hormones, and is also incorrect.
48. **B is correct.** This is a feedback loop question – a common MCAT® question type for the endocrine system. Remember that the test usually gives you some condition (in this case, high prolactin levels) and expects you to understand how it will affect the feedback loop, not the other way around. Since the passage indicates that dopamine inhibits the release of prolactin, high prolactin levels will lead to high dopamine levels; A is incorrect. The question stem explains that excess dopamine is converted into epinephrine and norepinephrine, so high dopamine levels will yield high levels of those hormones. Remember that epinephrine and norepinephrine have similar effects to the sympathetic nervous system as hormones, including raising heart rate. Answer B is correct, and C is incorrect. According to the passage, another consequence of high dopamine levels should be decreased secretion of leptin, so D is incorrect.
49. **D is correct.** Figure 1B indicates that dopamine, except in high concentration, inhibits production of cAMP. Thus it is reasonable to conclude that, in SW872 cells, dopamine activates G_i-proteins. A and B, therefore, should be eliminated. Figure 1A indicates that dopamine inhibits prolactin release, except in the presence of a D2R antagonist. Recall that an antagonist is a substance that opposes the action of another. This suggests that dopamine typically inhibits prolactin release by binding to D2R. C, therefore, should be eliminated. Together, Figures 1A and 1B indicate that DA binds to D2R and activates G_i-proteins, making D the best answer choice.
50. **A is correct.** When you see epinephrine, heart, and gut, you should immediately think of the sympathetic nervous system. Remember that epinephrine has similar effects as a hormone. Sympathetic signaling stimulates heart muscle cells and inhibits the smooth muscle cells of the gut. Since all of the answer choices involve differences in G_s- and G_i-protein expression, the most correct answer is the one that has epinephrine stimulating heart cells through G_s-proteins and inhibiting gut cells through G_i-proteins. This is answer A. Answer B is incorrect because it describes the opposite scenario. Neither C nor D makes a distinction between the two cell types in terms of G-protein expression, making them incorrect. It is possible that B, C, or D could be proven correct with more information about downstream signaling molecules, but they are not the best answers given the available information. This is a common occurrence on the MCAT®.
51. **D is correct.** Removing the GTPase activity of a G_s-protein means it cannot hydrolyze GTP and stop activating adenylyl cyclase. The passage indicates that this should lead to a buildup of cAMP. D is correct. Higher levels of cAMP would lead to *more* protein kinase A activation, not less, so A is incorrect. B is a distractor – nothing in the passages mentions electrolyte levels – and can be discarded. The passage makes no mention of hormone-receptor binding being dependent on G-protein activity, so C is also incorrect.
52. **A is correct.** The passages state that D2R and D1R act antagonistically to each other, meaning one activates G_s-proteins and the other works through G_i-proteins. Since experiment 1 showed that binding to D2R activates G_i-proteins, it is reasonable to conclude that D1R acts on G_s-proteins; B can be eliminated. Answer C seems tempting, but remember that cAMP is a free nucleotide, not a protein, and thus is not transcribed. D is directly contradicted by Figure 1B, and must be false. This leaves A. To understand why A is correct, think about probabilities – passage information indicates SW872 cells predominately express D2R, meaning that a DA molecule has a higher probability of binding to a D2R than a D1R, and is thus more likely to activate G_i-proteins. At a certain DA concentration, however, all DA receptors will be saturated, including some D1Rs. This should lead to activation of G_s-proteins, potentially offsetting the inhibitory D2R signaling.

53. **C is correct.** Remember that different effector cells respond differently to the same hormone because of variability in receptors and other molecules further down signaling cascades. The two answer choices closest to this definition are A and C. The question stem states that both liver phosphorylases are stimulated by cAMP, indicating the G_s -proteins are necessary. A, which says liver cells express G_i -proteins, must be incorrect, and C is correct. B is incorrect because the question tells us that glucagon works on liver cells through a cAMP-dependent mechanism, which requires adenylyl cyclase. D directly contradicts information in the question stem, and must be incorrect.

Passage II

54. **A is correct.** Experiment 1 simply demonstrates that increased hCG is associated with increased expression of both leptin and cAMP in BeWo cells. D contradicts this finding and thus can be eliminated. The results of Experiment 1 suggest that hCG acts through a cAMP second messenger system to increase leptin expression. Experiment 2 complicates things by suggesting that at high levels, cAMP interferes with hCG stimulation of leptin expression in BeWo cells. A fits both of these findings. B can be eliminated because neither experiment 1 nor experiment 2 examines the effect of PKA activation on leptin expression. C can be eliminated because it contradicts the results of experiment 2.
55. **D is correct.** You must know the basic function(s) of each of the hormones introduced in this lecture. One of the functions of progesterone is maintenance of the uterine endometrium.
56. **A is correct.** Use your knowledge of hormone polarity to answer this question. The passage introduces hCG as a peptide hormone. Peptide hormones are polar and, therefore, are unlikely to diffuse through the non-polar interior of the cellular membrane. B and D can be eliminated. Because peptide hormones are polar, they can dissolve in the polar blood and do not require protein carriers. Therefore, C can be eliminated. The best choice is A.
Even if you did not notice that hCG was referred to as a peptide hormone or did not remember that peptides are polar, you could at least eliminate B. A substance that is able to diffuse through the cellular membrane must be nonpolar and thus would not be able to dissolve in the blood.
57. **B is correct.** The ruptured follicle develops into the corpus luteum, which later disintegrates. A can be eliminated because the corpus luteum is a temporary ovarian structure. C can be eliminated because the corpus luteum develops following ovulation; an implanted embryo does not ovulate. D can be eliminated because it is the corpus albicans that is the remnants of a disintegrated corpus luteum, not the other way around.
58. **C is correct.** Trophoblast-derived BeWo tumor cells were most likely used because they were similar to trophoblast cells but easier to obtain and culture. A can be eliminated because hCG promotes rather than inhibits leptin expression in trophoblast and BeWo cells. B can be eliminated because the passage gives no indication that leptin deficiency promotes BeWo cell growth. D, while true, is not the best answer. D simply states that hCG activates the cAMP second messenger system in trophoblast and BeWo cells. This is the effect that hCG has on every cell to which it binds. C is a better answer because it explains why BeWo cells could be used in place of trophoblast cells.
59. **B is correct.** To answer this question, first refer back to Figure 2 and note that it depicts cAMP expression as a function of increasing hormone concentration. Recall that cAMP is a second messenger system commonly activated by the binding of a peptide hormone to its receptor. The correct answer will be a peptide hormone. Progesterone, estrogen and cortisol are all steroid hormones. Only LH is a peptide hormone.

Passage III

60. **B is correct.** At birth, the female ovary contains primary oocytes enclosed in primary follicles and arrested in prophase I of meiosis. Prior to the completion of meiosis I, oocytes are diploid. Therefore, B is the best answer choice.
61. **C is correct.** According to the passage, LH stimulates both theca cells and Leydig cells to produce androgens. Because theca cells perform the same function under the influence of the same hormone, it seems likely that they share a similar development history. For this reason, C is the best answer choice.

62. **B is correct.** Androgens are male hormones like testosterone. As the passage states, testosterone inhibits GnRH. GnRH stimulates FSH and LH which are required for gamete production. Choice A is wrong because, although there would be a decrease in testosterone production, the intake of exogenous androgens more than makes up for this decrease. Otherwise, there would be no point in taking androgens. C and D are wrong for the reasons that B is correct.
63. **D is correct.** The results presented in Figure 1 are to be expected given the control pathways presented in the passage. According to the passage, GnRH stimulates release of both LH and FSH. Therefore, A, which states that LH stimulates FSH production can be eliminated. LH, the passage explains, stimulates the Leydig cells to produce androgens, including testosterone, which exert negative feedback on gonadotropin release. Therefore, B, which states that LH inhibits androgen and C, which states that LH—rather than testosterone—inhibits FSH production can be eliminated. D, which states that LH stimulates androgen production, is the best choice.
64. **B is correct.** The passage states that LH and FSH are glycoproteins. In general, polar peptide hormones cannot pass through the non-polar interiors of cellular and nuclear membranes and, instead, bind to receptors on the cell membrane. For this reason, A, C, and D, all of which suggest that LH and FSH can pass through cellular and/or nuclear membranes, can be eliminated. By binding to a cell membrane receptor, peptide hormones can activate second messengers that translate hormone signals into intracellular activity. Therefore, B, which states that LH and FSH activate second messenger systems, is the best response.
65. **C is correct.** The follicle bursts on ovulation and remains behind as the corpus luteum. The secondary oocyte and corona radiata are released into the body cavity and swept into the fallopian tubes by fimbriae. The corona radiata consists of the zona pellucida and some granulosa cells.
66. **C is correct.** The passage states that acyline is a GnRH antagonist. An antagonist is a substance that opposes the action of another. Therefore, C, which states that acyline inhibits the activity of GnRH is the best choice. A, B, and D are false statements, and can, therefore, be eliminated.
67. **A is correct.** FSH blockage would prevent spermatogenesis by interfering with Sertoli cells and would not interfere with Leydig cells, which produce androgens. The others would affect testosterone production.

Stand-alones

68. **A is correct.** TSH acts on the thyroid to promote synthesis of T_3 and T_4 , also known as thyroxine. T_3 and thyroxine, in turn, inhibit release of TSH from the anterior pituitary. If a competitive inhibitor were to bind to TSH receptors on the thyroid, it would prevent TSH from promoting synthesis of T_3 and thyroxine. In the absence of negative feedback from T_3 and thyroxine, the anterior pituitary would continue to produce TSH, causing a rise in TSH blood levels.
69. **B is correct.** To answer this question correctly, you must recognize that cortisol and aldosterone are both steroid hormones. Most likely, another steroid hormone will act as a substrate molecule for their synthesis. Estrogen is the only steroid hormone listed; hCG, LH, and FSH are all peptide hormones. Therefore, A, C, and D can be eliminated. B is the best answer.

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 4

Passage I

70. **C is correct.** This question tests graphical interpretation and also shows the importance of reading every answer choice. A is true, but is not the best answer because it is not as complete as choice C, which describes the findings of both parts of the experiment. B is wrong because Figure 1 shows that DRAG mice had higher percentage reconstitution from the time that measurements started at 5 weeks after infusion, although 15 weeks is the point at which the percentage of control mice leveled off while the percentage of DRAG mice continued to increase. D flips the findings for DRAG and control mice.

71. **B is correct.** As stated in the passage, nude mice do not have a thymus. T cells require a thymus for maturation, so nude mice would not be able to produce T cells. You might be tempted to pick A because the passage states that nude mice are impaired in antibody production, but an antibody is not a cell. The MCAT® may be misleading in this fashion, so read the question closely. The passage says that nude mice are able to produce B cells, so C is incorrect. D is wrong because there is no passage information to imply that nude mice would not be able to produce macrophages.
72. **B is correct.** The passage states that nude mice do not produce antibodies but do produce B cells. Since nude mice have no thymus, they cannot produce T cells. As stated in the question stem, the nude mice are able to produce antibodies after injection of T cells, so C can be eliminated. Since antibodies are produced in the nude mice only after exposure to the donor T cells, either the donor T cells or the host B cells are producing antibodies. Since the B cells continue to produce antibodies after the T cells are removed, B cells produce antibodies only after exposure to helper T cells. This makes B correct. The findings indicate that T cells do not produce antibodies (consistent with your prior knowledge), so A is wrong. Notice that D is a true statement, but is not indicated by the findings of the experiment described and thus does not answer the question.
73. **A is correct.** To answer this question, you must recognize that it is testing your knowledge of how different types of hormones exert their effects, rather than requiring specific knowledge about interleukins. The passage stated that interleukins are peptide hormones, so this question is really asking: "How do peptide hormones act on their effectors?" A correctly describes the mechanism used by peptide hormones, which cannot diffuse through the membrane because they are large and polar. B describes the actions of steroid hormones. C is not correct for any type of hormone; steroid hormones can affect DNA at the transcriptional level but must first bind to a receptor in the cytosol. D is incorrect, as hormones are part of the endocrine system, not the nervous system.
74. **D is correct.** You should know that all blood cells arise from the same stem cells in the bone marrow. The thymus is required for maturation of T cells, but is not where they are originally produced. D is the only answer choice that is not a type of blood cell.
75. **A is correct.** Humoral immunity is directed against an exogenous antigen (one found outside the cell) such as fungi, bacteria, viruses, protozoans, and toxins. Cell mediated immunity (T cells) works against infected cells, cancerous cells, skin grafts, and tissue transplants.
76. **D is correct.** The correct answer must 1) be a feature of the study, 2) potentially limit the ability to draw conclusions, and 3) relate to the hypothesis of interest. Any answer choice that does not meet these three requirements can be eliminated. The hypothesis, as stated in the passage, is that expression of HLA in humanized mice will allow these mice to develop functioning T cells. A can be eliminated because it does not relate to this hypothesis. B is wrong because it is not a feature of the study described: the researchers did test the functioning of T cells in DRAG mice in the second part of the experiment. C is a feature of the experimental design, but the littermates of the DRAG mice that failed to express HLA-DR4 are more similar to the DRAG mice and thus are better suited for the control group than wild-type mice. D describes a feature of the study design: to compare the functioning of reconstituted T cells between DRAG mice and control mice, only the 40% of control mice that actually produced T cells could be used. The sample sizes were already fairly small, so decreasing the number of subjects even further limits the ability to draw conclusions by statistical analysis.

Passage II

77. **D is correct.** Quaternary structure consists of the joining of separate polypeptide chains. Since the passage says that multiple polypeptide chains remain after the treatment of an antibody with mercaptoethanol, it must be quaternary structure that was disrupted. D is the only answer choice that references quaternary structure, so it must be correct. However, you should also know that disulfide bonds are involved in tertiary structure, so mercaptoethanol also disrupts tertiary structure.

78. **C is correct.** First, D can be eliminated because the passage states that EC_{50} values were only determined for peptides demonstrating fungicidal activity. You should next consider choice C. If it is impossible to differentiate between the effectiveness of N10K for the different strands, you shouldn't waste time trying! Looking at Table 1, notice that confidence intervals are provided. Recall that the confidence interval indicates a range within which there is a 95% certainty of finding the actual value. Comparing the confidence intervals for the two fungal strains should show whether there is a difference in effectiveness. The confidence interval for the EC_{50} associated with *M. furfur* 101 is quite large and overlaps considerably with that associated with *C. glabrata* OMNI32. As a result, you cannot conclude whether there is a significant difference, making C the correct answer.

But what if the confidence intervals did not overlap, and you did have to determine which strain N10K was more effective against? The answer would be the one associated with the LOWEST EC_{50} . If a lower concentration is needed to achieve half the maximal response, the peptide is more effective (analogous to the association between a lower K_m and greater enzyme-substrate affinity). No prior knowledge of EC_{50} is required, but the MCAT® could ask you to make this kind of inference.

79. **B is correct.** This question requires reasoning about antigen-antibody recognition and the general features of antibodies. Recall that each type of antibody is highly specific to a certain antigen. Presumably the constant regions would not be able to contribute to this antigen-antibody specificity, so the part of the antibody that attaches to the antigen is more likely to include the variable and hypervariable regions. The figure shows that segments A and C are both constant regions, so answer choices A and D can be eliminated. D and F both contain variable and hypervariable regions, and there is no information in the passage or figure to indicate that these segments differ in structure or function, so answer choice C can be eliminated and choice B is the best answer.
80. **B is correct.** Although this question refers to the specific classes of antibodies involved in the experiment described in the passage, only your background knowledge of protein production is needed to find the answer. You should know that proteins for secretion are produced at the rough endoplasmic reticulum, rather than on free ribosomes; A can be eliminated and B is correct. But if you didn't remember the distinction between protein production at ribosomes in the cytosol versus in the rough ER, you could at least eliminate C and D, since the smooth ER and cellular membrane are not involved in protein synthesis.
81. **C is correct.** You should know that plasma cells arise from B cells, not T cells, making C the correct answer. You could also arrive at the answer by eliminating the other answer choices. A is a true statement. The pathogens or disease carriers may be different but carry similar antigens. This may seem contradictory to antigen-antibody specificity, but notice that the answer choice says that the plasma cells "may" provide immunity and that the disease must be "closely related." B is a true statement; the passage states that a single antibody secretes antibodies that are all specific to the same antigen. D correctly describes the function of memory B cells.
82. **A is correct.** You know that the peptides featured in the passage experiment, including N10K, are all from the Fc region of the antibody. This question is really just asking you to identify which segments are in the Fc region. Recall that the Fc fragment is constant among almost all antibodies. The Fc fragment must not contain any variable or hypervariable regions, and thus does not include segments D or F. Answer choices B and D can be eliminated. A hasty test-taker might conclude that all of the constant regions are part of the Fc fragment and choose C. However, remember that the Fc region and two identical Fab regions are released when the antibody is treated with papain. Examining Figure 1 shows that there is no way that a fragment made up of segments A, B, C, and E could be accompanied by two other fragments that are identical to each other. It must be the case that only segments A and B are part of the Fc region. C can be eliminated, and A is correct.

The line of reasoning described here is fairly complex and probably time-consuming. On the real MCAT®, you might want to answer the question intuitively and mark it for review if you have time. Simply looking at the figure and remembering that D and F cannot be part of the Fc fragment, it makes sense to think that the region containing AB is the one Fc fragment and that the remaining regions, which contain D and F, are the two identical Fab fragments.

83. **D is correct.** You can immediately eliminate A and B, since the Fc region does NOT vary between different antibodies. Choosing between C and D requires an understanding of the essential difference between innate and adaptive immunity: innate immunity is the initial, non-specific line of defense, while adaptive immunity provides is specific to the given antigen. A region that is constant across all antibodies is non-specific and thus could play a role in innate immunity; this makes D the correct answer. You can also decide between C and D simply by realizing that antibodies are usually considered to be part of adaptive immunity. The statement given in C thus gives no new information linking adaptive and innate immunity.

Passage III

84. **C is correct.** We want to know why hemoglobin evolved to have less affinity for CO than the heme group has for CO (as explained in the passage). This would only happen if there was some advantage to not binding with CO, and there would only be an advantage if CO were present. So what explains the presence of CO in the cell? Since the passage tells us that the breakdown of heme produces CO, this is a logical source. Thus the production of CO by the breakdown of heme favored the selection of a form of oxygen carrier that had less affinity for CO. This makes C the correct answer. Another way to answer the question is to eliminate the other choices. The emergence of industrial societies was far too recent to account for such a broad evolutionary change; A is wrong. You should know that the products of aerobic respiration are carbon dioxide and water; thus choice B has nothing to do with CO and can be eliminated. As for choice D, there is no simple mechanism that an MCAT® test-taker should know that would result in CO from carbonic acid in the blood.

85. **B is correct.** When evaluating the answer choices, keep in mind that the question asks for the evidence that provides GREATEST support. There may be multiple answers that provide some support, but one will be the best answer. The reference to Figure 1 in the question stem is a big hint that might cause you to evaluate B first. B provides additional information about the results and turns out to be the correct answer, since carboxy hemoglobin (one of the types of carboxyRH, along with carboxy myoglobin) is the product that the researchers hypothesized would result from the experimental reaction mixture. However, note that even without the information provided by choice B, you can tell from the figure that the light spectrum of the experimental reaction mixture differs from the control mixtures. You could intuit that this probably reflects the occurrence of the reaction hypothesized by the researchers. Thus, the results shown in the figure could still be considered in tandem with the other answer choices.

A describes an element of the experimental design; if it improved the study's validity, it would help support the hypothesis. At first glance, A may seem to be a good choice, but recall from the passage that *pathological* conditions involve leakage of RH into the plasma. Furthermore, the oxidation of free RH is associated with raised levels of CO via the activation of HO. CO concentrations in the plasma will thus be higher in the context of pathological conditions associated with metRH, and thus the concentrations used in the experiment should be similar to the concentrations found in pathological conditions. A can be eliminated. C and D do not directly relate to the experimental hypothesis and thus do not provide strong support for or against it; both can be eliminated.

86. **C is correct.** The passage states that M has a greater affinity for O₂ than does hemoglobin. Thus, at a given pressure the M saturation will always be higher. B and D can be eliminated. It also states that 2,3-DPG is found in red blood cells and affects the characteristic sigmoidal oxygen dissociation curve for hemoglobin. The M curve should not be sigmoidal because it is not exposed to 2,3-DPG. The M curve shown in A is sigmoidal, so A can be eliminated and C is correct.

In this case there was sufficient passage information to answer the question, but for the MCAT® it's a good idea to be familiar with the oxygen dissociation curves of hemoglobin and myoglobin.

87. **B is correct.** To answer this question, you must first realize that lactic acid lowers pH. According to the passage, the oxygen affinity of myoglobin is not affected by pH changes, so A and C can be eliminated. The passage did not discuss changes in hemoglobin's affinity for oxygen, but this is required knowledge for the MCAT®. Decreased pH (increased hydrogen ion concentration) causes a rightward/downward shift in the oxygen dissociation curve; in other words, hemoglobin's affinity for oxygen is reduced. D can be eliminated, and B is correct.

88. **D is correct.** The passage states that 2,3-DPG is found in red blood cells. The capillaries contain red blood cells, so A or C will be the best answer. As per the passage, 2,3-DPG lowers the oxygen affinity of hemoglobin and thus affects its characteristic sigmoidal oxygen dissociation curve. 2,3-DPG must have its greatest effect at a part of the curve where affinity is low—i.e., where oxygen saturation occurs at a slow rate, as reflected by a flat curve. Although the oxygen dissociation curve flattens at very high concentrations of O_2 , this is presumably due to saturation (i.e., close to 100% of the hemoglobin molecules already have bound oxygen) rather than resulting from the action of 2,3-DPG. The other flattened region of the curve is at low pressures of O_2 ; this must be where the 2,3-DPG has the greatest effect. Low levels of O_2 would be found in the capillaries of skeletal muscle rather than those of the lungs, so D is the correct answer.

89. **A is correct.** Raised pH means lowered H^+ concentration, which leads to slowed breathing to prevent excessive loss of CO_2 (recall that CO_2 is associated with lowered pH). Thus an increase in pH would lead to decreased breathing rate, making A the correct answer. B is incorrect because low blood oxygen levels is likely to lead to increased breathing rate. Similarly, C is incorrect because increased muscle activity leads to low blood oxygen levels and thus faster breathing. D is the opposite of A: increased CO_2 levels would lead to lowered pH and increased breathing rate.

Notice that B and C are very similar answer choices, while A and D are opposites. This means that you could eliminate both B and C right off the bat: they must both have the same effect, so neither can be the one that is different from all other answer choices. Since A and D are opposites, one of them has to be the correct answer.

Stand-alones

90. **B is correct.** The lymphatic system is an open system, meaning something goes in one end and out the other. In contrast, the blood flows in a closed system. A, B and D all correctly describe major functions of the lymphatic system.

91. **A is correct.** You should know that erythrocytes (red blood cells) do not contain nuclei. Think of them as essentially being bags of hemoglobin. Platelets also do not contain nuclei, but they are not cells, so B is wrong.

92. **D is correct.** Clonal selection allows only those lymphocytes that demonstrate the ability to recognize foreign antigens and avoid responding to self antigens to mature; those that violate either of these conditions are destroyed.

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 5

Passage I

93. **D is correct.** You should know the word emulsification.

94. **B is correct.** You should narrow this down to A or B from the passage. The thoracic duct delivers lymph to the venous circulation from the lower part of the body and the left arm. This question requires that you know either that the thoracic duct delivers the fat to the blood, or that the lymphatic ducts empty their contents into the veins, not the arteries. Even if you haven't memorized the fact that lymphatic ducts empty into the venous system, you can figure it out by remembering that the function of the lymph system is generally to clear things out from arterial circulation, so it would not make sense for the lymph system to dump directly back in to the arteries. This question is on the trivial side for an MCAT® question, but it is not impossible that they would ask it.

95. **A is correct.** Only A shows that serum cholesterol level alone might not indicate a health risk to the patient. The HDLs might cause a high serum cholesterol but indicate a healthy patient.

96. **C is correct.** Remember that the purpose of chylomicrons (and other lipoproteins) is to transport water-insoluble fats through the aqueous environment of the bloodstream. This means that chylomicrons must consist of polar fat molecules surrounded and protected by amphipathic molecules. Triglycerides are non-polar fats and are transported in the interior of the chylomicron. Phosphatidylcholine is amphipathic, so it can contribute to the surface of the chylomicron. Phosphatidylcholine's non-polar end faces the interior of the chylomicron while its polar end faces the aqueous environment of the bloodstream.
97. **A is correct.** The blood lipid levels differ between genotype categories at every time point. Answer B is incorrect because the experimental setup does not allow for the results to draw this conclusion. Drawing this conclusion would require a comparison of lipid levels with a control group who have neither the A nor the G allele. The present experimental setup can only answer the question of whether there is a difference between genotypes studied. For answer C, again the experimental setup does not allow this conclusion because heterozygotes are lumped in with the AG + GG group rather than being examined separately. The graph indicates that individuals carrying the G allele clear lipids more quickly, making answer choice D incorrect.
98. **C is correct.** For questions that use Roman numeral choices, you can use strategy to limit the time you spend. Notice Roman numeral II is included in all answer choices except choice C. Lipolysis increases the levels of triglycerides in the blood but remnants do not CONTAIN higher levels of triglycerides than LDLs. Therefore, II is incorrect and answer C must be the correct choice. To double check quickly review the other answer choices. Roman numeral I is true because of all the kinds of lipoproteins, chylomicrons have the lowest density (even lower than VLDL) because they carry the greatest ratio of fat to protein. From the amount of fats they carry, these structures are relatively large and have a more difficult time efficiently crossing the epithelium. The passage states that remnants are enriched in cholesteryl esters so III is also true making C the correct answer.
99. **A is correct.** You should know the major pancreatic enzymes: trypsin (works on proteins), chymotrypsin (works on proteins), lipase (works on lipids), and amylase (breaks starch into disaccharides). Disaccharides are broken down by intestinal enzymes. Lactase breaks down lactose, a disaccharide in milk.

Passage II

100. **B is correct.** The passage states that renal clearance is equal to GFR for a substance that is not reabsorbed or secreted. Since the question refers to a scenario in which GFR and renal clearance do not have the same value, either reabsorption or secretion must be occurring, making A or B the correct answer. If clearance is greater than filtration, then the urine must be receiving an additional supply of the substance from some other source; this is consistent with secretion. Reabsorption would instead cause clearance to be lower than filtration. A can be eliminated, and B is correct.
101. **D is correct.** You are not given enough information to calculate GFR directly, but the passage explains that the clearance rate of any substance that is freely filtered and does not undergo reabsorption or secretion is equal to GFR. Inulin, the solute involved in the experiment described in the passage, meets these conditions, so to answer the question you simply need to calculate clearance rate of inulin. You are told that clearance rate, C , is equal to $\frac{U \times V}{P}$. According to Table 1, $U = 1.50 \times 10^{-2}$ mg/mL, $V = 1.00$ mL/min, and $P = 1.00 \times 10^{-4}$ mg/mL. Therefore, C equals 1.5×10^2 mL/min, or 150 mL/min.

- 102. C is correct.** You know from the passage that clearance rate is equal to GFR only if there is no reabsorption or secretion, and the question stem reminds you that inulin does not undergo either of these processes. You can eliminate A, which suggests that inulin is secreted, and B, which suggests that inulin is reabsorbed. The glomerular filtration rate (GFR) is the volume of fluid that filters into Bowman's capsule per unit time. To select between C and D, you should look for a restatement of the other requirement described in the passage: that the substance be freely filtered. Freely filtered does not mean completely filtered; it just means that the kidney's filtration barriers do not select for or against the substrate, and thus its filtrate concentration equals its plasma concentration. Therefore, you should have eliminated D, which states that inulin must be completely filtered, and selected C, which states that inulin's filtrate concentration must equal its plasma concentration.
- 103. D is correct.** The passage states that inulin is a polysaccharide, so it must be larger than glucose. This alone is enough to choose D, but you should also know that a red blood cell is too large to be filtered, so inulin must be smaller. Albumin is just small enough to be filtered but its negative charge prevents filtration, but this knowledge concerning albumin is not required for the MCAT® or this question, since you know that D must be true of any polysaccharide.
- 104. A is correct.** Because creatine is freely filtered and neither secreted nor reabsorbed, its clearance rate is equal to the glomerular filtration rate.

$$GFR = C_{\text{creatinine}} = \frac{U \times V}{P}$$

The question asks for the plasma concentration, P , of creatine in an individual with normal GFR. The passage states that normal GFR is 125 mL/min. The urine concentration of creatine, U , and the urine flow rate, V , are given in the question stem. Therefore, you can solve for P .

$$P = \frac{U \times V}{GFR} = \frac{2.5 \frac{\text{mg}}{\text{mL}} \times 1 \frac{\text{mL}}{\text{min}}}{125 \frac{\text{mL}}{\text{min}}} = 0.02 \frac{\text{mg}}{\text{mL}} = \frac{2 \text{ mg}}{100 \text{ mL}}$$

Notice that even without doing calculations, you can narrow the choices down to A or B since you know that the numerator, 2.5, is being divided by a denominator, 125, that is 2 orders of magnitude larger. To then choose between A and B, you just need to divide 2.5 by 1.25.

- 105. D is correct.** Since the formula for clearance includes solute concentration in the urine, urine flow rate, and solute concentration in the plasma, you can eliminate any answer choices that involve these variables. Thus B can be eliminated. The rate at which a substance is cleared depends, in part, on the rate at which it flows out of the glomerulus and into Bowman's capsule. Since kidney filtration barriers select against substances of a certain size and charge, you can eliminate A. Because pressure differences drive fluid flow, C can be eliminated. D is the best answer choice; the plasma concentration of a substance that is neither secreted nor absorbed should not appreciably affect the clearance rate of another solute.
- 106. C is correct.** In Table 2, the column labeled DM-H presents the data for patients with type I diabetes mellitus and hyperfiltration. Average systolic and diastolic pressure is higher for DM-H patients than for either DM-N or HC patients, so B and D can be eliminated. By contrast, renin, ANG II, and ALD concentrations are lower for DM-H patients than for either DM-N or HC patients. In other words, levels of circulating RAAS mediators are suppressed. Therefore, A can be eliminated and C is the best answer choice.
- 107. C is correct.** Hematocrit is the percentage of red blood cells, by volume, in the blood. A hematocrit of 50% means that 50% of blood volume consists of red blood cells and 50% is plasma. The renal blood flow, then, is twice the renal plasma flow. Because the PAH clearance approximates the renal plasma flow, the renal blood flow is approximately twice the PAH clearance. $2(650 \text{ mL/min}) = 1300 \text{ mL/min}$.

Passage III

108. **C is correct.** Aldosterone is a steroid hormone. Steroid receptor-hormone complexes enter the nucleus and act as transcription factors that activate or repress one or more genes. In this way, steroid hormones induce new protein synthesis. Only peptide and amine hormones induce modification of existing proteins. While some steroid hormones do bind to membrane receptors that use second messenger systems, the use of signal transduction pathways, for example cAMP second messenger systems, is more commonly ascribed to peptide hormones. In general, steroid hormones are associated with slower genomic rather than rapid non-genomic responses.
109. **C is correct.** The passage states that renin is a proteolytic enzyme. An enzyme is a catalyst, and a catalyst lowers the energy of activation of a reaction.
110. **D is correct.** Intracerebroventricular infusion of entanercept, a TNF inhibitor, results in central TNF blockade. Figures 2 and 3 show that, compared to Ang II rats, Ang II + ENT rats tended to have decreased mean arterial pressure and decreased heart weight to body weight ratio.
111. **A is correct.** Ang II increases blood pressure by increasing vasopressin secretion, stimulating thirst, constricting blood vessels, and increasing sympathetic output to the heart and blood vessels. Because aldosterone increases the activity of the $\text{Na}^+\text{-K}^+\text{-ATPase}$ pump, it increases both Na^+ reabsorption and K^+ excretion, and, thereby, indirectly increases blood pressure. Neither renin nor angiotensin nor aldosterone increases urine volume.
112. **B is correct.** Again, aldosterone increases the activity of the $\text{Na}^+\text{-K}^+\text{-ATPase}$ pump, thereby increasing both Na^+ reabsorption and K^+ excretion in the distal tubule and collecting duct. Increased K^+ excretion, however, does not lead to increased blood pressure. Instead, increased Na^+ reabsorption increases blood osmolarity, leading to increased thirst and increased blood volume. In this way, aldosterone indirectly increases blood pressure. Na^+ and water reabsorption are separately regulated in the distal tubule and collecting duct. It is only in the proximal tubule that water reabsorption freely follows Na^+ reabsorption. Secretion of vasopressin, the hypothalamic hormone that regulates water reabsorption in the distal tubule and collecting duct is stimulated by Ang II, not aldosterone.
113. **B is correct.** Decreased delivery of sodium past the macula densa stimulates renin release by the juxtaglomerular granular cells. Renin decreases the resistance of the afferent arterioles and converts angiotensinogen to angiotensin II, which, in turn, *increases* the resistance of the efferent arterioles. Both decreasing the resistance of the afferent arterioles and increasing the resistance of the efferent arterioles increases the glomerular filtration rate. The former increases both renal blood flow and glomerular filtration rate, whereas the latter decreases renal blood flow but increases glomerular filtration rate.

Stand-alones

114. **C is correct.** Urine is concentrated in the collecting ducts, but the loop of Henle plays the major role in allowing this process to occur by establishing a concentration gradient between the collecting duct and the medulla.
115. **B is correct.** Carbohydrate metabolism begins in the mouth with the breakdown of sugars by the enzyme amylase. Water reabsorption is a major function of the large intestine. The gallbladder is a storage receptacle for the bile produced by the liver. B is the only false choice because, while protein DIGESTION begins in the stomach, the small intestine is the major site for ABSORPTION of nutrients.

EXPLANATIONS TO IN-CLASS EXAM FOR LECTURE 6

Passage I

116. **C is correct.** T-tubules are invaginations of the sarcolemma that deliver the action potential directly to the sarcoplasmic reticulum along the center of each sarcomere. The function of T-tubules is implied by the passage assertion that T-tubules allow action potentials to be “delivered deep into each muscle cell.”
117. **A is correct.** From the passage you know that Ca^{2+} is bound to calsequestrin in the sarcoplasmic reticular lumen. This lowers the concentration inside the lumen, which weakens the gradient that the calcium pumps must work against.
118. **D is correct.** This question is purely graphical interpretation. Graph 2A shows that wild-type (WT) mice dramatically exceed CASQ1 null mice at high stimulation frequencies. Graph 2B shows that, at low stimulation frequencies, CASQ1 null mice actually exceed WT mice in normalized force. A comparison of graphs 2A and 2B shows that the differences between CASQ1 and WT mice are, in general much smaller in normalized than absolute force.
119. **B is correct.** The patterns of force production as stimulation frequencies increase in graphs 2A and 2B are regular and non-erratic. While there is always a chance that the pattern could change if data from a larger range of frequencies were collected, extrapolating from the present data, there is no reason to believe that measurements at higher frequencies would be more informative; thus B is the best answer choice. Regarding answer choice A, it is reasonable to expect that young mice might be stronger than old mice. Hence, age-matching mice in different experimental groups would help prevent confounding factors (such as differential age-related strength or other age-related health problems) from influencing the outcomes of absolute force production. For choice C, both CASQ1 null and wild-type mice were studied with a small sample size ($n = 8$), so increasing sample size would help scientists know if their results were more generally applicable to a larger population of mice. Choice D would be helpful because the current normalization procedure (cross-sectional area normalized force) accounts for muscle thickness in force production but does not take into account muscle length, or total size.
120. **A is correct.** From the passage, the function of creatine kinase is to allow phosphocreatine to give or receive a phosphate group to or from ATP. This is what maintains ATP levels during muscle contraction. The passage states that cellular respiration is not fast enough to maintain ATP levels at a constant level (so D is wrong). However, muscular contractions would continue because there would still be a store of ATP available. B is wrong because the inhibition of the enzyme that breaks down phosphocreatine would cause a buildup of phosphocreatine rather than a decrease. The passage does not suggest any mechanism that would support answer choice C.
121. **B is correct.** This question is a little bit trivial for the MCAT®, but is still within the realm of possibility. You should be aware that some cell types in the human body, such as muscle cells and neurons, are so specialized that they have lost the ability to undergo mitosis.
122. **B is correct.** The mechanism involves an integral protein of the sarcoplasmic reticulum, not the sarcolemma. The passage says that uptake is active, so it requires ATP and can occur against the concentration gradient of Ca^{2+} , meaning that A and C are incorrect. Notice that since A and C must both be true if either is true, both could be eliminated even if you didn't remember that Ca^{2+} uptake is an active process.
123. **A is correct.** Graph 2A shows that wild-type mice, in general, produce greater amounts of force than CASQ1 mice, but in graph 2B when force is normalized by cross-sectional area of the muscle, those differences mostly disappear. This is due to the fact that wild-type mice have larger muscle mass which contributes to their greater force production. Choice A could help explain why wild-type mice would have larger muscle mass. If choice B were true, the opposite effect would occur (an exaggeration of differences in the graph of normalized force). Choices C and D do not address how normalization by cross-sectional area affects force.

Passage II

124. **B is correct.** The graphs in Figure 1 and the language of the passage indicate that, in comparison to wild-type mice, $PYY^{-/-}$ mice have increased bone mineral density and bone mineral content. You should know that osteoclasts resorb bone while osteoblasts build new bone. These two processes happen simultaneously. In order to have the possibility of net bone gain in comparison to wild-type mice, $PYY^{-/-}$ mice must have decreased osteoclast activity (less breakdown), increased osteoblast activity (more build-up) or both of these conditions. The only choice in which neither condition is met is choice B – a situation in which no net bone gain is possible.
125. **C is correct.** This question is about identifying possible confounding factors in the experiment. A seems like a good idea, but Figure 1 shows body mass to be virtually identical between the two study groups so standardizing by weight is not likely to make the results much more reliable. B is also a good idea, but since the data presented are for female mice only, we know the researchers have already done this and therefore it wouldn't be a change to the methodology. The study states explicitly that exercise can influence bone density and volume. Therefore it is possible that differing amounts of exercise between study groups could be a considerable confounding variable – making C the best answer. D could be helpful, but two kinds of whole body measurements are already displayed in Figure 1. In light of the choices, C is a better answer than D.
126. **D is correct.** Option I may be tempting because femoral bone mass decreases in PYY^{tg} mice while lumbar bone increases in $PYY^{-/-}$ mice. However, there is nothing to suggest that the effects of these genotypes are sampling site-specific. In fact, whole body measurements indicate that PYY expression has a whole body effect. Therefore option I can be discarded and answer choice C can be eliminated. Option II is likely true because the passage states that the PYY^{tg} genotype has a conditional, adult-onset phenotype while the knockout genotype presumably affects expression right away. The experiments show that, in general, $PYY^{-/-}$ mice have increased bone while PYY^{tg} mice have decreased bone. Presumably, each genotype might cancel out the effect of the other to some degree. However, it is not possible from the information given to know which effect might be stronger or whether there are unexpected phenotypic outcomes from the interaction of the two genotypes. Option III is also true, making D the best answer choice.
127. **A is correct.** There are two pieces of MCAT®-required knowledge that will help you answer this question: 1. Parathyroid hormone is released in order to increase blood calcium levels and 2. Bone tissue is the body's major repository for storing calcium and other minerals. When osteoclasts break down bone, the calcium that was contained in the bone becomes available to the circulatory system. Parathyroid hormone increases blood calcium by breaking down bone via stimulation of osteoclasts.
128. **D is correct.** There are several types of connective tissue in the body, of which bone and cartilage are two. Bone is living tissue containing blood and nerves. One of its main functions is the storage of yellow fat within the bone marrow. Even if you didn't have all of this background knowledge you should be able to narrow down the answer choices to B and D. If bone were a living tissue, why would it receive its own blood and nerve supply? Logic dictates that either B or D should be false.
129. **C is correct.** The passage states that osteoclasts are differentiated from phagocytotic blood cells. Erythrocytes are also a type of blood cell and all blood cells differentiate from the same precursor. The fact that osteoblasts and osteoclasts were the focus of the passage while the other two answer choices were not discussed should have made you give careful consideration to choices A and C. Be careful, though, the correct answer choice is not necessarily one that was discussed in the passage.

Passage III

130. **D is correct.** The phosphagen system, glycogen-lactic acid system, and aerobic system take place primarily in the first, second, and third time categories laid out in Table 1, so that each time category may be considered to represent a system. The values in answer choice D are in the same ratio as the values of power given in the table. Since ATP concentration remains relatively constant within the cell, it makes sense that ATP production rate would mirror muscle power for these systems.

131. **C is correct.** The body must reconstitute the phosphagen system, which requires ATP to make phosphocreatine. Oxygen is required to make ATP. The heavier than normal breathing that follows exercise for approximately 1 hour takes in oxygen to convert most of the lactic acid produced by the glycogen-lactic acid system back into glucose. (This is done principally in the liver.) Choice A is wrong because the time frame is too short to make new hemoglobin. B is a true statement, but does not answer the question. D is wrong because the passage states that aerobic metabolism can continue indefinitely or as long as nutrients last. Nutrients are not replenished with oxygen, but with food.
132. **A is correct.** The last paragraph of the passage states that slow twitch fibers are associated with increased insulin sensitivity, so the change to fast twitch fibers would decrease insulin sensitivity, eliminating answer choice B. Answering this question requires a correct interpretation of Table 2. Fast twitch fibers have INCREASED (not decreased) phosphocreatine concentration, decreased oxidative potential, and decreased glycogen concentration compared to slow twitch fibers. Therefore, as the ratio of fast twitch fibers increases, these traits would accompany that change.
133. **D is correct.** You should know from background knowledge that muscle fiber types differ in contractile velocity, force production, and endurance. However, this question can also be answered from a careful reading of the passage. The passage states that "muscle fiber types vary in endurance, force production, and contractile and metabolic properties" and Table 2 demonstrates that type II fibers have greater contractile velocity than type I fibers. Although oxygen debt is discussed, no differentiation of oxygen debt between fiber types is mentioned.
134. **C is correct.** All three statements are true. Fast twitch (type II) fibers do contract with more force than slow twitch (type I) fibers, while slow twitch fibers have greater endurance and therefore require the replacement of more ATP through aerobic respiration during sustained periods of contraction. However, option I does not help explain why type I fibers have a greater density of mitochondria, so C is the best answer. You should know that mitochondria are involved in energy production, and thus should recognize the validity of option III by making the connection between mitochondria and their role in energy production through aerobic respiration. Option II is also about type I fibers requiring more energy. However, option I is about type II fibers requiring more energy and, taken out of context, would actually suggest that type II fibers would have more mitochondria than type I fibers; therefore, II does not answer the question and is not included in the correct answer.
135. **C is correct.** The passage states that the phosphagen system can only sustain peak muscle activity for approximately 10 seconds. Only answer choice C is an event that lasts for a period of 10 seconds or less.
136. **A is correct.** The passage states that ATP levels remain nearly constant during muscle activity, so choice B can be eliminated. While glycogen can be converted to make more glucose, and glucose can be metabolized to make more ATP, the passage also states that phosphocreatine is the first substance used to maintain those stable ATP levels and is therefore the first to be depleted. Notice that you could eliminate C immediately even in the absence of other information, since glucose (choice D) would be depleted before glycogen, which is a storage molecule.

Stand-alones

137. **B is correct.** Tendons connect muscle to bone. Muscle pulls on bone, not on other muscles.
138. **C is correct.** Bone does not act as a thermostat for the body. Choices A, B, and D describe important functions of the skeletal system.

ANSWERS & EXPLANATIONS

FOR
QUESTIONS IN THE LECTURES

ANSWERS TO THE LECTURE QUESTIONS

Lecture 1	Lecture 2	Lecture 3	Lecture 4	Lecture 5	Lecture 6
1. A	25. B	49. D	73. B	97. C	121. D
2. C	26. D	50. C	74. C	98. D	122. C
3. A	27. A	51. B	75. A	99. D	123. C
4. D	28. C	52. C	76. B	100. A	124. D
5. D	29. A	53. D	77. C	101. A	125. B
6. C	30. D	54. B	78. B	102. D	126. C
7. C	31. A	55. B	79. A	103. A	127. C
8. B	32. B	56. B	80. D	104. C	128. D
9. D	33. D	57. C	81. D	105. B	129. B
10. B	34. A	58. C	82. C	106. D	130. C
11. A	35. B	59. D	83. A	107. D	131. A
12. A	36. B	60. A	84. A	108. A	132. C
13. D	37. A	61. D	85. D	109. B	133. A
14. A	38. A	62. A	86. A	110. B	134. D
15. A	39. D	63. C	87. A	111. B	135. C
16. A	40. A	64. D	88. D	112. A	136. A
17. C	41. C	65. C	89. B	113. C	137. C
18. B	42. A	66. A	90. D	114. D	138. A
19. D	43. B	67. A	91. D	115. B	139. C
20. A	44. B	68. C	92. D	116. D	140. A
21. B	45. D	69. D	93. D	117. C	141. C
22. C	46. B	70. C	94. C	118. B	142. A
23. A	47. C	71. C	95. A	119. B	143. B
24. B	48. C	72. D	96. D	120. A	144. B

EXPLANATIONS TO QUESTIONS IN LECTURE 1

1. **A is correct.** Retroviruses inject viral RNA into host cells. This RNA is then reverse transcribed into DNA. In DNA form, it can then be integrated into the host genome, and replicated along with host DNA, especially in the lysogenic life cycle. Once the virus is in the host, the reverse transcriptase gene is transcribed, and the enzyme can then convert viral RNA into DNA. The DNA can then be transcribed by the cell, and the resulting mRNA is translated by the host's ribosomes.
2. **C is correct.** Domains are far larger than orders, so if two species are in the same order, they must be in the same domain. A single class encompasses several orders; two different families can belong to the same order. A common mnemonic for taxonomic ranks is Kings Play Cards On Fridays Generally Speaking (Kingdom, Phylum, Class, Order, Family, Genus, Species), going from most encompassing to least. Two species in the same order could very well live in different habitats or biomes, as genetic relatedness does not restrict location.
3. **A is correct.** Most animal viruses enter host cells via receptor-mediated endocytosis. Thus, a receptor is required to recognize the specific appropriate host cell. Unlike bacteriophages, animal viruses do not leave capsids outside host cells. Finally, no virus can reproduce independently, as a defining characteristic of viruses is reproduction within a host cell.
4. **D is correct.** Eubacteria have cell walls containing peptidoglycan. Bacterial cell membranes do not contain cholesterol. Finally, ribosomes are present in all cells, eukaryotic or prokaryotic.
5. **D is correct.** Bacteriophages can only infect those bacteria who have the specific receptor that the virus can attach to and use to enter the cell body. Viruses do not reproduce until they enter a cell. Integration of the viral genome also does not occur until after infection. Finally, bacterial cell wall penetration is the first step of infection, right after attachment to the receptor. As the question asks what occurs before infection, it is presumably also asking for the step that occurs first, and that is receptor attachment.
6. **C is correct.** Transformation is the process of picking up stray DNA from the environment and incorporating it. As the DNA is already on the agar, the originally sensitive bacteria most likely underwent transformation and incorporated the resistance genes. Transduction is transfer of genes via a viral vector, and while that could potentially occur here, transformation would definitely have to occur first. Sexual reproduction and conjugation involve transfer and swapping of genes between multiple bacteria, and the resistance genes are on the extracted DNA in the environment, not a bacterium that could conjugate or do sexual reproduction.
7. **C is correct.** Catastrophic events will not cause significant genetic drift to a large, homogeneous (well-mixed) population. These kinds of events only significantly disrupt small and/or nonhomogeneous populations. Emigration, selection, and mutation all affect the HW equilibrium, regardless of population size.
8. **B is correct.** The bacterial cell wall would be most affected, as peptidoglycan is a key component of bacterial cell walls. It is not a significant part of any of the other structures listed.
9. **D is correct.** The flagella of bacteria are made from the protein flagellin. Microtubules are a main building block of the other three organelles.
10. **B is correct.** The nucleolus disappearing is one of the defining events of prophase. The nucleolus is the site of rRNA transcription, not translation. It is not membrane bound and is not to be confused with the nucleoid of prokaryotes.

11. **A is correct.** Anytime a compound moves against its electrochemical gradient across a membrane, it is active transport. The sodium electrochemical gradient was established by the expenditure of ATP, making this secondary active transport. Facilitated and passive transport both go down the concentration gradient. Osmosis does as well, and is restricted to water.
12. **A is correct.** The smooth ER plays a major role in detoxification, and the liver detoxifies the body, so it is most likely a liver cell. The other options do not have a significant role that would suggest more than normal smooth ER.
13. **D is correct.** Ribosomes are made of RNA and protein. They do not have a phospholipid bilayer.
14. **A is correct.** The smooth endoplasmic reticulum helps to detoxify alcohol in the liver. The nucleus runs the cell and makes nucleic acids; the Golgi body packages materials for transport. The rough endoplasmic reticulum makes proteins for use outside the cell.
15. **A is correct.** The hydrolytic enzymes of lysosomes are activated by a low pH achieved by pumping protons into the interior. Choices B and C can be ruled out immediately, as the pH change described is the opposite of what actually occurs based on the proton movement. Finally, the enzymes in lysosomes require a low pH to be active, so choice D is unlikely.
16. **A is correct.** Peptide hormones are synthesized in the rough ER. Insulin and glucagon are two major peptide hormones synthesized in the pancreas, so a pancreatic cell is most likely. The other cell types do not perform any major functions that would require more than normal amounts of rough ER.
17. **C is correct.** The sodium-potassium pump transports both ions against their concentration gradient. If they were moving along the gradient, a pump, and energy input, would not be necessary. The sodium-potassium pump is also a form of primary active transport. Energy is used to pump ions against their gradients.
18. **B is correct.** In secondary active transport, one molecule diffuses down its gradient, and this favorable change is paired with the unfavorable movement of another molecule against its gradient. This is happening here with sodium and glucose. Primary active transport uses energy, usually ATP, to pump something against its gradient. Passive and facilitated diffusion both involve molecules only going down their gradient.
19. **D is correct.** The main characteristics that need to be considered here are size and polarity. Carbon dioxide is a small molecule, and is nonpolar and hydrophobic. Thus, it can go straight through the hydrophobic cell membrane. All other molecules are polar, and larger, and would most likely require some sort of transporter to enter a cell.
20. **A is correct.** Protein hormones bind to structures on the plasma membrane, as proteins are often large and hydrophilic, so they cannot go through the membrane easily. The only option within the cell is binding to a nuclear receptor. Typically, only steroid hormones will bind to a nuclear receptor. All other options are located on the cell membrane, and protein hormones are likely to use them.
21. **B is correct.** I and II are true, but desmosomes are anchored to the cytoskeleton and are stronger than tight junctions.
22. **C is correct.** The red blood cells would burst. The osmolarity in the cells is much higher than the pure water, with no solutes. Thus, water would continuously flow into the cells until they burst. Cells stay the same size in an isotonic solution. They would expand in a slightly hypotonic solution, but not in a solution as hypotonic as pure water. Finally, shrinking occurs in a hypertonic solution, which is not the case for pure water.

23. **A is correct.** Adult neurons are not preparing for, or in the process of cell division. Cells in the G_0 phase cease to divide, describing these neurons perfectly. All other phases listed are preparing for cell division, producing DNA, organelles, and other components necessary for mitosis.
24. **B is correct.** Desmosomes are used purely for cell-to-cell adhesion, and not so much for communication. Gap junctions allow molecules and ions to flow freely between the two cells, and are used for communication. Membrane and nuclear receptors also bind signaling molecules in cell-to-cell communication.

EXPLANATIONS TO QUESTIONS IN LECTURE 2

25. **B is correct.** A signal which is being received from another neuron is typically transmitted to the dendrites of a postsynaptic neuron. It then travels to the cell body and finally down the axon; however, synapses are found all along the neuron and a signal may begin anywhere on the neuron. Although an action potential moves in all directions along an axon, the cell body and dendrites do not normally contain enough sodium channels to conduct the action potential for any length.
26. **D is correct.** This question is testing your knowledge of an action potential. The major ions involved in the action potential are sodium and potassium. An action potential is an all or nothing response which is determined by depolarization caused by the opening of sodium channels. Blocking sodium channels is the only way given that would block an action potential.
27. **A is correct.** The sodium/potassium pump moves potassium inside the membrane. Potassium is positively charged making the inside of the membrane more positive. The resting potential is measured with respect to the inside.
28. **C is correct.** A negative potential is created inside the cell so excess positive charge is pumped out of the cell. Since both sodium and potassium are positively charged, this is accomplished by pumping more positive charge out than is allowed in, hence the uneven number of ions in the pump. Inside the cell, potassium levels are high and sodium levels are low. Without this pump, sodium and potassium would eventually move down their concentration gradients and the negative resting potential would be lost.
29. **A is correct.** Although the nervous and endocrine systems are both involved in communication throughout the body, they differ in speed and specificity. The nervous system provides fast, specific signals. Since the endocrine system involves the release of hormones into the bloodstream, its effects are both slower to occur and more generalized than those of the nervous system, usually affecting a wider range of cells.
30. **D is correct.** Choice A must be wrong because the resting membrane potential of a neuron is primarily dependent on the electrochemical gradient of K^+ because the cell membrane is much more permeable to it than Na^+ . A change in the balance of intracellular and extracellular potassium ion concentrations must cause a change in the resting membrane potential. Choice B can be eliminated because the new resting membrane potential, and thus the change caused by a change in intracellular K^+ , can be predicted by using the Nernst equation, as mentioned in the question stem. The easiest way to choose between C and D is to recall that under normal conditions the intracellular K^+ concentration is greater than the extracellular concentration, causing a negative resting membrane potential. If the intracellular K^+ concentration increases, the resting membrane potential must become even more negative.

31. **A is correct.** The electrochemical gradient of K^+ is the most significant contributor to the resting membrane potential, so choices C and D can be eliminated. Note that if the membrane became impermeable to potassium, the electrochemical gradient of potassium would be disrupted; in other words, choice C would have to be correct if choice D is true, another reason to eliminate both answers. Leakage of Na^+ down its electrochemical gradient also contributes to the resting membrane potential, making it slightly less negative than the equilibrium potential of potassium, so choice B is incorrect. The electrochemical gradient of Cl^- makes only a minor contribution to the resting membrane potential compared to those of K^+ and Na^+ , so choice A is the correct answer.
32. **B is correct.** For the MCAT®, it is important to know the changes in the membrane potential that occur in different stages of the action potential. Depolarization of the membrane due to the flow of positive sodium ions into the cell is the first step of the action potential. Thus the correct answer must be either A or B. Hyperpolarization is the brief drop to an unusually low membrane potential at the end of the action potential, occurring after repolarization, the step that returns the membrane to a negative potential. Thus choice A can be eliminated and B is correct.
33. **D is correct.** Acetylcholinesterase is an enzyme that degrades acetylcholine. Remember that enzymes are often named by their substrate followed by the suffix 'ase'. Since acetylcholine is the substrate of this enzyme, not the product, Choice C is incorrect. Choice B is incorrect because acetylcholine, not the enzyme acetylcholinesterase, is what binds to the acetylcholine receptor. If this enzyme is inhibited, then acetylcholine will not be catabolized as quickly, and it will bind and release repeatedly with postsynaptic receptors.
34. **A is correct.** White matter is composed primarily of myelinated axons.
35. **B is correct.** Invertebrates do not have myelinated axons to accelerate nervous impulse transmission. Instead, they rely upon increased size. Vertebrata is a subphylum of Chordata which is characterized by a dorsal nerve chord at some point in their development.
36. **B is correct.** The cerebellum controls finely coordinated muscular movements, such as those that occur during a dance routine. Involuntary breathing movements are controlled by the medulla oblongata. The knee-jerk reflex is governed by the spinal cord.
37. **A is correct.** Every type of synapse in the peripheral nervous system uses acetylcholine as its neurotransmitter except the second (the neuroeffector) synapse in the sympathetic nervous system. As the "effector," it can be reasoned that this synapse is the end organ synapse. An effector is an organ or a muscle, something that responds to neural innervation by making something happen in the body.
38. **A is correct.** Parasympathetic stimulation results in "rest and digest" responses, or responses that are not involved in immediate survival or stress. Choice B is a sympathetic response, as is choice C. Choice D is mediated by skeletal muscles, which do not receive autonomic innervation.
39. **D is correct.** In order to prevent conflicting contractions by antagonistic muscle groups, reflexes will often cause one muscle group to contract while also sending an inhibitory signal to its antagonistic muscle group. Motor neurons exit ventrally from the spinal cord, not dorsally, so choice A is out. Reflex arcs (at least somatic ones) are usually confined to the spinal cord; they do not require fine control by the cerebral cortex. This eliminates choice B. Reflex arcs may be integrated by an interneuron in the spinal cord. Choice C is out as well.
40. **A is correct.** The central nervous system is comprised of the brain and spinal cord. An effector is organ or tissue affected by a nervous impulse.

41. **C is the right answer.** Pressure waves, or sound, are converted to neural signals by hair cells in the organ of Corti in the cochlea. The retina is related to the eye and vision, and is a distractor.
42. **A is correct.** All of the answer choices can be converted to electrical signals by the human body that can then be transmitted to the central nervous system, but choices B, C, and D are converted by chemoreceptors, while choice A, light, is converted by electromagnetic receptors.
43. **B is correct.** As light enters the eye, it first passes through the clear cornea and then passes through the aqueous humor that fills the anterior chamber of the eye. The lens divides the anterior chamber from the posterior chamber. After the light passes through the lens, it enters the posterior chamber, which is filled with vitreous fluid. After passing through the vitreous fluid, the light strikes the posterior wall of the eye, where the retina is located. The photoreceptors (rods and cones) of the retina work to convert the stimulus into an electrical signal to be sent to the CNS.
44. **B is correct.** One of the significant features of the olfactory system is that information about olfactory stimuli has a direct route to the amygdala and hippocampus, rather than first being processed in the cortex. Choice B is not a true statement and is the correct answer. The other answer choices accurately describe features of the olfactory system. Note that, as stated in choice D, olfactory sensory information bypasses the thalamus in its path to the cortex. This aspect of the olfactory system is unique among the sensory systems and must be known for the MCAT®.
45. **D is correct.** This question is a straightforward test of knowledge about the different types of sensory receptors. Nociceptors contribute to the sensation of pain, making choice D the correct answer. Chemoreceptors detect chemical stimuli, as in the olfactory and taste systems; mechanoreceptors detect touch and pressure; and photoreceptors respond to photons.
46. **B is correct.** The vestibular system contributes to the maintenance of balance, as described in choice B. Although the structures of the vestibular system are located in the inner ear, which contains structures involved in hearing, the vestibular and auditory systems have separate functions, and choice A is incorrect. Choice C describes the functions of the somatosensory system. The detection of pheromones occurs in the olfactory system.
47. **C is correct.** Choice A is incorrect because the optic nerve conveys visual information to the brain for advanced processing, rather than carrying out such processing itself. Processing of "what" and "where" information takes place in the temporal and parietal lobe, respectively. Choice B can be eliminated because the lateral geniculate nucleus is in the brain (in the thalamus) and thus cannot be said to convey information "to the brain," although it does send information to another part of the brain (the primary visual cortex in the occipital lobe). This statement describes the optic nerve, rather than the LGN. Choice C accurately describes the role that photoreceptors play in the visual system. Choice D is wrong because hair cells are part of the auditory system, not the visual system. The function that is incorrectly assigned to hair cells in choice D is actually carried out by cones in the retina.
48. **C is correct.** Sensory adaptation is the adaptive phenomenon where sensory receptors become less sensitive to a repeated stimulus, facilitating the ability to detect new stimuli. Choice C accurately describes sensory adaptation. Choice A is a distractor, intended to be appealing simply because it includes the word "adaptation." Similarly, choice D misuses the word; the phenomenon described in choice D is transduction, not adaptation. Choice B describes summation, a different feature of the nervous system.

EXPLANATIONS TO QUESTIONS IN LECTURE 3

49. **D is correct.** Aldosterone, as we can tell by its name, is a steroid (any hormone whose name ends in “sterone” or something similar is a steroid). This eliminates choice A, because steroid hormones do not need cell membrane receptors or second-messenger systems. They simply diffuse across the cell membrane. Choice B can be eliminated because the adrenal cortex is aldosterone’s source, not its target tissue. Answer choice C describes how neurotransmitters act at a synapse. For the most part, endocrine hormones act by being released into the blood stream and having effects at target tissues. Epinephrine, also produced in the adrenal gland, is the exception. It has roles as both a hormone and neurotransmitter. Aldosterone exerts its effect as is written in answer choice D, increasing the production of sodium-potassium pump proteins.
50. **C is correct.** This is a negative feedback question. If another source of aldosterone exists in the body besides the adrenal cortex, negative feedback (through the renin-angiotensin system and increased blood pressure) would suppress the level of aldosterone secreted by the adrenal cortex. Answer choice A is out because the levels of renin in the blood would decrease, not increase; aldosterone release would increase blood pressure, and renin is released in response to low blood pressure. Oxytocin plays no role in blood pressure (vasopressin does) and would not be affected by this tumor. Choices C and D are both possibilities, but the adrenal cortex would definitely respond to negative feedback, while the tumor is a wild card. At this point, choice C is the best answer. In fact, this is a good choice because normally, hormone-secreting tumors will not respond to negative feedback. Because the behavior of the tumor is unpredictable, choice D can be ruled out.
51. **B is correct.** All hormones bind to a protein receptor, whether at the cell membrane, in the cytoplasm, or in the nucleus of the cell. Steroids and thyroxine require a transport protein to dissolve in the aqueous solution of the blood. However, protein hormones do not. Steroids are derived from cholesterol, not protein precursors. Steroids, unlike protein hormones, do not act through a second messenger system.
52. **C is correct.** Acetylcholine acts through a second messenger system, and is not a second messenger itself. The other choices, cAMP, cGMP, and calmodulin are all examples of second messengers.
53. **D is correct.** Steroids are lipid soluble. Different steroids may have different target cells. For instance, estrogens are very selective while testosterone affects every, or nearly every, cell in the body. Steroids act at the transcription level in the nucleus, and are synthesized by the smooth endoplasmic reticulum.
54. **B is correct.** Exocrine function refers to enzyme delivery through a duct. Answer choices C and D refer to hormones, which are always part of the *endocrine* function of a gland, so they can be eliminated. Releasing digestive enzymes straight into the blood would be a very bad idea. The same enzymes that help digest food would have no problem digesting the cells of the body.
55. **B is correct.** Steroids act at the level of transcription by regulating the amount of mRNA transcribed. Because steroids diffuse into the cell and head for the nucleus, choice C can be eliminated – translation happens in the cytoplasm, not the nucleus. Although some steroid hormones have an effect on cellular growth, they don’t all control replication. In a cell, reactions are typically regulated by controlling relative concentrations of the enzyme and/or inhibitors (i.e. through regulation of transcription or translation).
56. **B is correct.** This is another negative feedback question. T3 and T4 (thyroxine) production is controlled by a negative feedback mechanism involving TSH (thyroid stimulating hormone) from the anterior pituitary. If there is an exogenous source of thyroxine the body will sense the higher level and react by decreasing levels of TSH. If there is enough thyroxine around the anterior pituitary doesn’t need to produce TSH to tell the thyroid to produce more thyroxine. Parathyroid hormone production is not affected by thyroxine levels.

57. **C is correct.** Epinephrine release leads to "fight or flight" responses, as does sympathetic stimulation. Choice A is out because insulin causes cells to take up glucose. In fact, in the "flight or fight" response, it is advantageous for blood glucose levels to be higher and insulin secretion is suppressed. Choice B is out because acetylcholine is a neurotransmitter; it has few, if any, known hormonal actions. Choice D is out because aldosterone is involved in sodium reabsorption by the kidney; it has no role in "fight or flight" responses.
58. **C is correct.** The nervous and endocrine systems are the two systems that respond to changes in the environment. In general, the endocrine system's responses are slower to occur but last longer. Think about the difference in your reaction when you stub your toe – a nervous system response- and when you get stressed – and endocrine response.
59. **D is correct.** The only important thing to recognize from the question is that high insulin levels exist. Then go to the basics; insulin decreases blood glucose. Telling the liver to make more glucose through gluconeogenesis will raise the blood glucose and is the job of glucagon. Although glucagon will definitely be released in response to the dangerously low blood glucose levels, it is not the direct result of high insulin.
60. **A is correct.** This is an important distinction to be made. The hormones of the posterior pituitary are synthesized in the bodies of neurons in the hypothalamus, and transported down the axons of these nerves to the posterior pituitary. Remember the hormones produced in the anterior pituitary are FLAT PG. The hormones produced in the hypothalamus are regulating hormones used to control the release of other hormones from the pituitary. The kidney is the target organ of vasopressin, not where it is produced.
61. **D is correct.** Calcitonin builds bone mass – it "tones the bone". If there were excess levels of calcitonin this would increase bone tissue mass. Parathyroid hormone increases blood calcium levels in part by breaking down bone. Being more sensitive to parathyroid hormone would certainly lead to a decrease in bone tissue mass. Defective intestinal calcium absorption would lead to low blood calcium levels and activation of parathyroid hormone in an attempt to restore blood calcium. Parathyroid hormone would break down bone to release the calcium into the blood. Menopause contributes to osteoporosis by reducing estrogen levels leading to diminished osteoblastic activity. Choice D has the opposite effect of any of the other choices, so it can also be picked in this way. The answer that is different from the rest will often be correct.
62. **A is correct.** Thyroxine (T_4) is produced by the thyroid gland. The anterior pituitary hormones are FLAT PG (FSH, LH, ACTH, TSH, Prolactin, GH). Choice A would result from mixing up thyroxine, T_4 , with thyroid stimulating hormone, or TSH.
63. **C is correct.** Glucagon increases blood sugar, a good thing while running a marathon. An increased heart rate would be expected in someone who had just run 25 miles. Blood flow to the small intestine would be rerouted to where it was needed – the heart, lungs, and leg muscles. Remember, rest and digest, the body doesn't want to waste blood flow for digestion while finishing the last mile of a marathon.
64. **D is correct.** Parathyroid hormone is all about raising blood calcium levels. It stimulates osteoclast (bone resorption) activity, decreasing bone density. It also works in the kidney to slow calcium lost in urine. It controls blood calcium levels via these two mechanisms. Because parathyroid hormone has to do with blood calcium levels choices A and B can be eliminated because they do not contain option III. Then, option I is in both remaining answers, so it does not need to be carefully considered. Afterwards, determine if parathyroid hormone impacts renal calcium reabsorption, which it does.

65. **C is correct.** Answer choice A looks good (testosterone does stimulate the testes to descend) until the question states that the person is a physically mature male. The testes normally descend during late fetal development. Choice B is out because increased testosterone would cause puberty to occur early, and would not change the timing of puberty if it's already happened (dealing with a physically mature male). Choice D is out because it is unknown whether any direct mechanism by which testosterone increases body temperature exists. More testosterone does enhance secondary sex characteristics even in a physically mature male. Think about athletes using steroids (often exogenous testosterone) to have bigger muscles.
66. **A is correct.** Increased secretion of estrogen sets off the luteal surge, which involves increased secretion of LH and leads to ovulation. Choice B is close, but estrogen stimulates a surge in LH, not FSH. Choice C describes what takes place when there are decreasing levels of estrogen. Progesterone is not secreted by the anterior pituitary: it is secreted by the placenta or the corpus luteum.
67. **A is correct.** The epididymis is where the sperm goes to mature and be stored until ejaculation. Leydig cells, next to the seminiferous tubules, secrete testosterone. Choice C is the job of the Fallopian tubes in a female. FSH and LH are secreted by the anterior pituitary.
68. **C is correct.** Decreased progesterone secretion results from the degeneration of the corpus luteum, which occurs because fertilization of the egg and implantation didn't happen. Choice A is out because thickening of the endometrial lining occurs while estrogen and progesterone levels are high, not while progesterone secretion is decreasing. Choice B can be eliminated because increased estrogen secretion causes the luteal surge, and because the luteal surge occurs earlier in the cycle. Choice D is out because while the flow phase does follow decreased progesterone secretion, it does not occur as a result of increased estrogen secretion.
69. **D is correct.** The layer of cilia along the inner lining of the Fallopian tubes serves to help the egg cell move towards the uterus, where it will implant if it has been fertilized. (Fertilization usually happens in the Fallopian tubes.) Choice A describes what the ciliary lining in the respiratory tract does. Choice B may sound good, but the Fallopian tubes are far enough away from the external environment that protection from its temperature fluctuations is not an issue. Choice C would seem to gum up the whole "continuation of the species" plan. The cilia would most likely try to improve the odds of fertilization rather than decrease it.
70. **C is correct.** The adrenal cortex makes many other steroid based hormones, as well as testosterone. Again, the anterior pituitary hormones are FLAT PG. LH does stimulate the production of testosterone, but testosterone is not produced in the anterior pituitary. The pancreas produces insulin and glucagon. The adrenal medulla produces epinephrine and norepinephrine.
71. **C is correct.** Mammalian eggs undergo holoblastic cleavage where division occurs throughout the whole egg. At a first glance, this question appears to ask for somewhat obscure knowledge about meroblastic cleavage. However, choices A, B, and D can be eliminated because they are part of human embryonic cleavage, so it is unnecessary to know meroblastic or holoblastic cleavage.
72. **D is correct.** Generally, the inner lining of the respiratory and digestive tracts, and associated organs, come from the endoderm. The skin, hair, nails, eyes and central nervous system come from ectoderm. Everything else comes from the mesoderm. The gastrula is not a germ layer.

EXPLANATIONS TO QUESTIONS IN LECTURE 4

73. **B is correct.** Hyperventilation results in loss of CO_2 , leading to lower concentrations of carbonic acid in the blood, and an increase in pH. Hypoventilation would result in the reverse. Breathing into a bag would increase the CO_2 content of the air and lead to acidosis. Excess aldosterone may lead to metabolic alkalosis due to hydrogen ion exchange in the kidney, so an insufficiency in aldosterone might lead to acidosis.
74. **C is correct.** The rate of gas exchange in the lungs would decrease, as carbonic anhydrase catalyzes the reaction involving carbonic acid and carbon dioxide. The carbon dioxide in the blood would not be expelled as quickly with lowered carbonic anhydrase activity. Catalysts increase the rate of a reaction. If the catalyst is inhibited, the rate decreases. Since the reaction moves in one direction in the lungs, and the opposite direction in the tissues, choice A is ambiguous. Unless one believes that a carbonic anhydrase inhibitor will affect transcription or degradation of hemoglobin, choices B and D are equivalent. If one were true, the other should also be true, so both can be ruled out.
75. **A is correct.** Cellular respiration produces carbon dioxide, which, in turn, lowers blood pH. Increased cardiac contractions and blood velocity would likely increase oxygen delivery to muscle tissue. During heavy exercise, capillaries dilate in order to deliver more oxygen to the active tissues. Nitrogen is irrelevant to respiration.
76. **B is correct.** The increased red blood cell count and hemoglobin concentration in the blood after reinjection increase the blood's ability to deliver oxygen to the tissues, often a limiting factor in endurance competitions. Choice A is wrong because, while this may happen, it is not the primary benefit of blood doping in the context of sports. Choice C is wrong because only blood cells are reinjected, so the body's hydration status is unaffected. Choice D is wrong because, while blood is less viscous with a lower concentration of red blood cells, the whole blood is being removed, not just red blood cells are being taken out. The blood viscosity does not change.
77. **C is correct.** Carbon dioxide is produced in the tissues. It is transported by the blood to the lungs, where it is expelled by diffusing into the alveoli. Since the concentration gradient carries CO_2 into the capillaries from the tissues and from the blood into the alveoli, it can be reasoned that there is a higher concentration of CO_2 in the tissues than in the alveoli. Choice A is wrong because blood CO_2 concentration will not change in the veins; it has nowhere to go. Choice B is wrong because CO_2 is expelled into the lungs at the pulmonary capillaries, so CO_2 that was present in the pulmonary arteries (before the capillaries) will largely be gone in the pulmonary veins (after the capillaries). Choice D describes the opposite of the concentration gradient that actually exists for CO_2 between the systemic tissues and the systemic capillaries.
78. **B is correct.** The person would need increased vascularity to deliver more blood to the tissues because the blood would carry less oxygen. Red blood cells carry oxygen, and an increase would be helpful in a low oxygen environment. Increased pulmonary ventilation would continuously introduce fresh oxygen into the alveoli and circulation. Finally, increased diffusing capacity increases the efficiency of gas exchange, helping to compensate for the lower oxygen content at high altitude.
79. **A is correct.** Constricted air passages is the key clue. The bronchioles are surrounded by smooth muscle and small enough to constrict. Cartilage does not constrict, while muscle does. The skeletal muscle in the thorax does not constrict the air passages. The alveoli are not part of the air passages.
80. **D is correct.** Heavy exercise manifests increased carbon dioxide production that leads to increased carboxyhemoglobin. Heavy exercise generates hydrogen ions in many ways, including by lactic acid fermentation and increased carbon dioxide in the blood. Increased metabolism contributes to increased temperature during exercise.

81. **D is correct.** The atrioventricular node, which sits at the junction between the atria and the ventricles, pauses for a fraction of a second before passing an impulse to the ventricles.
82. **C is correct.** Stroke volume must be the same for both ventricles. If it weren't, there would be a never-ending backlog of blood in one or the other circulations, ending with the faster circulation running dry. To keep the whole system running smoothly, both halves of the circulation must pump the same quantity of blood with each stroke.
83. **A is correct.** The cardiac action potential is spread from one cardiac muscle cell to the next via ion movement through gap junctions. Desmosomes are primarily for cell adhesion and are not as involved with signaling. Tight junctions do not allow the same movement of ions that gap junctions do. Acetylcholine is a signaling molecule, but it is not the one used to spread the cardiac action potential.
84. **A is correct.** Less oxygenated blood will reach the systemic system because some oxygenated blood will be shunted from the aorta to the lower pressure pulmonary arteries. The pulmonary circulation will carry blood that is more oxygenated than normal, since highly oxygenated blood from the aorta is mixing with deoxygenated blood on its way to the lungs. The entire heart will pump harder in order to compensate for less efficient oxygen.
85. **D is correct.** Oxygenated blood returning from the lungs feeds into the heart at the left atrium. From there, it flows into the left ventricle, which pumps it to the systemic circulation. The right atrium and the right ventricle pump deoxygenated blood to the lungs.
86. **A is correct.** Blood loss is likely to be more rapid during arterial bleeding due to the greater blood pressure in the arteries. Low oxygen intake would not affect blood volume. Lastly, excess sodium consumption would increase osmolarity of blood, increasing blood volume.
87. **A is correct.** The not-so-subtle physics reference is a trick. Bernoulli's equation, which would indicate a greater pressure at the greater cross-sectional area, doesn't work here. The blood pressure in a human is greatest in the aorta and drops until the blood gets back to the heart. The longer the blood has travelled since leaving the heart, the lower the pressure at that point.
88. **D is correct.** The capillaries are one cell thick and blood moves slowly in them to allow for efficient oxygen exchange. Gas exchange does not occur in the larger blood vessels.
89. **B is correct.** "Swollen glands" are actually swollen lymph nodes that are bulging with immune cells gearing up to fight the invasion. Choice A is not what is going on here. Choice C is out because an inflammatory response would draw fluid into the inflamed area, not drain it away. Choice D is also just a goofy answer.
90. **D is correct.** Immunoglobulins, or antibodies, are involved in the humoral immune system, or the B cell system. Choice A is out because cytotoxic T cells work in cell mediated immunity. Choice B is out because stomach acid plays a role in the nonspecific innate immunity; humoral immunity is specific and acquired. Choice C is unrelated.
91. **D is correct.** Antibodies bind to antigens through interactions between the antibody's variable region and the antigen. Antibodies do not phagocytize anything, so choice A is out. Antibodies are produced by plasma cells, they don't normally bind to them; choice B is out. Plasma cells are derived from stem cells in the bone marrow. Antibodies will not usually prevent their production. Choice C is out.
92. **D is correct.** Fluid that is picked up by the lymphatic tissues is returned to the circulation at the right and left lymphatic ducts, which feed into veins in the upper portion of the chest. The rest of the options are false.

93. **D is correct.** Old erythrocytes are destroyed in the spleen and the liver, not in lymph nodes. B-lymphocytes often reside in lymph nodes, while bacteria and proteins from the tissue can be brought to lymph nodes by immune cells.
94. **C is correct.** The innate immune response does not involve humoral immunity (B-cells) or cell mediated immunity (T-cells). The innate immune system responds to any and every foreign invader with the white blood cells called granulocytes as well as with inflammation and other actions.
95. **A is correct.** Intracellular proteins, including those that would be produced by a virus, are processed by the endogenous pathway and expressed on MHC I. Choice B and C have matched the wrong pathway and MHC type. Lastly, the exogenous pathway leads to presentation of extracellular antigens on MHC II.
96. **D is correct.** Positive and negative selection are the two ways that T-cells are selected. In positive selection, only T-cells that can successfully interact with MHCs survive. In negative selection, potentially auto-immune, self-reactive T-cells are selected against. Type I Diabetes results from self-reactive T-cells, so negative selection has failed. Choices A and B are unrelated to T-cell selection.

EXPLANATIONS TO QUESTIONS IN LECTURE 5

97. **C is correct.** Pepsin works primarily in the stomach, and has an optimum pH around 2.0. It denatures in the environment of the small intestine, where the pH is between 6 and 7. Choice A is wrong because pepsin isn't working at all in the small intestine; it won't be working synergistically with trypsin. Choice B is wrong because pepsinogen is activated in the stomach by low pH. Choice D is wrong because pepsin is a catalyst, which makes it a protein; amylase digests starch.
98. **D is correct.** The best answer is choice D because only choice D is both true and reveals a benefit for enzymes to be inactive while in the pancreas. Choice A may seem logical but would only apply to lipase. Choice B is false; zymogens are in inactivated precursor form. Choice C is true but is not an adequate explanation.
99. **D is correct.** The stomach doesn't digest carbohydrates, making D the least affected answer choice. If stomach acid secretion is obstructed then: A) fewer bacteria will be killed in the stomach; B) less pepsinogen will be activated; C) the pH will rise.
100. **A is correct.** All macronutrients are digested through hydrolysis, or the breaking of bonds by adding water. Reduction does not necessarily take place. Glycolysis and phosphorylation are generally processes relating to metabolic, not digestive, processes.
101. **A is correct.** The major function of the large intestine is to absorb water, making choice B wrong and choice A the correct answer. Choice C is incorrect because fat is digested primarily in the small intestine. Choice D is incorrect because urea is secreted by the kidney.
102. **D is correct.** Amylases digest sugars; nucleases digest nucleic acids into nucleotides; lipases digest fats; and proteases digest proteins.
103. **A is correct.** Pancreatic exocrine function includes enzymes such as chymotrypsin, pancreatic amylase, and lipase made in the pancreas and secreted through a duct. This eliminates choices B, C, and D. Bile is not an enzyme. It is made in the liver and stored in the gallbladder, which makes choice A the correct answer.

104. **C is correct.** Chemical digestion of carbohydrates begins in the mouth and chemical digestion of proteins begins in the stomach. Both the stomach and the mouth are also large contributors to physical breakdown of food. However, most chemical digestion occurs in the first part of the small intestine, the duodenum, making C the best answer. By the time food reaches the ileum, it is mostly digested. The primary function of the ileum is the absorption of nutrients from the broken-down food.
105. **B is correct.** The question stem gives the clue that the correct answer will have to do with the secretion of HCl. Parietal cells secrete HCl, making choice B the best answer. Goblet cells secrete mucus. Chief cells secrete pepsin. G cells secrete gastrin into the blood.
106. **D is correct.** Gluconeogenesis is the production of glycogen from non-carbohydrate precursors. This function is performed mainly in the liver. Glycolysis can be performed by any cell, eliminating choice C. Fat storage takes place in adipocytes which can be found throughout the body, making choice A an incorrect answer. Protein degradation occurs in all cells, which eliminates choice B.
107. **D is correct.** Choice A is incorrect because fat digestates are shuttled into intestinal epithelial cells by micelles, not chylomicrons (which primarily transport fats through the lymph and blood). Most fat digestates first enter the lymph as chylomicrons via lacteals, which eliminates choice B and makes choice D the best answer. In choice C, it is true that triglycerides are degraded into fatty acids during digestion, but the second part of the answer choice is not true; smooth endoplasmic reticulum synthesizes triglycerides.
108. **A is correct.** 'Essential' means that the body cannot synthesize them. Nonessential amino acids are synthesized by the liver. Choices B and C are true because amino acids are absorbed through both facilitated and active transport. Choice D is true; urea is the end product of amino acid deamination in the liver.
109. **B is correct.** Glucose is not an electrolyte (eliminating choice C), but sodium is an electrolyte and the absorption of glucose increases the absorption of sodium because glucose is absorbed in a symport mechanism with sodium; choice B is the best answer. The focus of the question is on reestablishing water and electrolyte balance. Choices A and D are irrelevant to this goal and can be eliminated.
110. **B is correct.** The primary function of aldosterone is in the regulation of salt, so choice D is less relevant and can be eliminated. Glycogenolysis converts stored glycogen into products ready for metabolism. Cortisol and glucagon are energy mobilizers and work to increase blood glucose levels. Insulin has the opposite effect and decreases blood sugar levels in several ways. One of the ways that it accomplishes this goal is by inhibiting glycogenolysis, making choice B the correct answer.
111. **B is correct.** This is a knowledge-based question. The knowledge that blood is an aqueous solution is required. This eliminates choice D and makes it apparent that either choice A or B must be the correct answer. Since hydrophilic compounds easily dissolve in aqueous solutions while hydrophobic ones do not, choice A is incorrect and choice B is the correct answer. As a double-check, choice C must be incorrect because chylomicrons are a combination of proteins and fats and, therefore, DO bind fatty acids.
112. **A is correct.** Single amino acids are the most basic building blocks, while dipeptides, polypeptides and proteins represent increasingly large and complex structures composed of amino acids. During digestion, macromolecules are broken down into their basic nutrients, making choice A the correct answer.
113. **C is correct.** The only process available for the removal of wastes by the Bowman's capsule is diffusion, aided by the hydrostatic pressure of the blood. The mechanisms mentioned in choices A, B, and D do not take place.

114. **D is correct.** Glucose is normally completely reabsorbed from the filtrate and thus does not appear in the urine, making choice B an incorrect answer. When glucose does appear in the urine, the glucose transporters in the PCT (not in the loop of Henle, as stated in choice A) are unable to reabsorb all of the glucose from the filtrate. Choice C is wrong because the proximal tubule does not secrete glucose.
115. **B is correct.** Choice A is incorrect because villi do not increase the volume of filtrate that reaches the loop of Henle. The purpose of the brush border is to increase the surface area available to reabsorb solutes from the filtrate. The brush border is made from villi, not cilia, and so has no effect on the direction or rate of fluid movement, making choice C and D irrelevant. The question suggests a similar function to the brush border in the small intestine, further confirming choice B.
116. **D is correct.** Renin secretion catalyzes the conversion of angiotensin I to angiotensin II, which increases the secretion of aldosterone. If renin is blocked, then aldosterone cannot cause increased synthesis of sodium absorbing proteins, and sodium absorption decreases, making D the correct answer. Under these circumstances, blood pressure would decrease, not increase; choice A can be eliminated. Platelets are irrelevant; choice B is incorrect. Choice C is incorrect because the effect of inactivating renin primarily impacts sodium reabsorption, not rate of flow through the nephron.
117. **C is correct.** This is the correct order of structures. A collecting duct receives the output from many nephrons. The contents of many collecting ducts empty into the ureter which carries its contents to the urinary bladder. Urine is then eliminated from the body through the urethra.
118. **B is correct.** Vasopressin is antidiuretic hormone, which will rise in response to dehydration increasing water retention. Aldosterone is a mineral corticoid released by the adrenal cortex in response to low blood pressure. In a severely dehydrated person, blood volume would be low, likely resulting in diminished blood pressure. Aldosterone levels would rise in response to low blood pressure.
119. **B is correct.** Under the circumstances described, high blood pressure would result in more fluid being forced into Bowman's capsule, making choice B the best answer. There is no reason to assume that the increased pressure would result in constriction of the fenestrations; choice A is not a strong answer. Filtrate volume could be expected to be larger (not smaller) due to increased fluid pressure, so choice C is false and can be eliminated. The question stem does not provide insight into the solute concentration of the person in question, so choice D cannot be correct.
120. **A is correct.** The main purpose of the loop of Henle is to concentrate the medulla via a net loss of solute from the loop to the medulla. As indicated in the lecture, the filtrate leaving the loop of Henle generally has a lower solute concentration than the filtrate which entered. The process of concentrating the medulla is critical to the function of other parts of the nephron; a medulla with a high concentration of solute allows for the passive absorption of water from the filtrate in other areas of the nephron.

EXPLANATIONS TO QUESTIONS IN LECTURE 6

121. **D is correct.** Neither actin (the thin filament) nor myosin (the thick filament) changes its length during a muscular contraction; instead, during contraction, the actin and myosin filaments interact to pull the actin filaments toward the center of the myosin filaments. As a result, the proportion of actin and myosin overlap increases and the sarcomere shortens.
122. **C is correct.** Permanent sequestering of calcium in the sarcoplasmic reticulum would prevent calcium from binding to troponin, which is what causes the conformational change that moves tropomyosin away from the myosin binding sites on actin. Choice A would occur if calcium were present and ATP were not. Loss of ATP would prevent the myosin from releasing from actin, resulting in rigor mortis-like conditions. Choice B is incorrect because resorption of calcium from bone would result in a decrease in bone density, not an increase. Choice D is incorrect because loss of calcium would not cause depolymerization of actin filaments. If this actually occurred, it would pose a serious problem every time calcium was re-sequestered into the SR after the completion of a contraction.
123. **C is correct.** Shivering results from the increase of muscle tone. When muscle tone increases beyond a certain critical point, it creates the familiar indiscriminate muscle activity typical of shivering. While shivering may serve as a warning, it does more than that, and that is not its primary purpose so choice A can be eliminated. Choice B is untrue; in fact, healthy joints contain elements such as cartilage and synovial fluid to help PREVENT bones from rubbing together, which can cause damage to the bones. Choice D is not a logical solution because convincing the hypothalamus that body temperature is higher than it is would not actually address the problem of low body temperature.
124. **D is correct.** Muscles cause movement by contracting, not lengthening, eliminating choices B and C. The contraction brings the origin and insertion closer together, usually by moving the insertion. Neurons cause contractions in muscles, not tendons, and the neural signals are not initiated by the muscle. This eliminates choice A.
125. **B is correct.** Resist the temptation to choose A, which refers to the action of synergist muscles. Choice B is correct because antagonistic muscles move bones in opposite directions relative to a joint. Therefore, in order to produce movement, one must relax while the other contracts. An isometric contraction by the antagonistic muscle would inhibit movement, eliminating choice C. The insertion of a muscle refers to its attachment site on a bone, which cannot slide or change locations, making D an incorrect choice.
126. **C is correct.** All muscles will need more energy, which can be obtained through the metabolic processes of glycolysis and the citric acid cycle, as well as increased protein if they are being used rigorously, making choices A, B, and D accurate. However, in humans, mature skeletal muscle cells usually do not divide, so no mitosis occurs.
127. **C is correct.** Choices A, B, and D are true: third class levers require more force to perform a certain amount of work than if no lever were present due to the fact that the force of the muscle acts between the fulcrum and the load force. The need for greater force to perform smaller movements increases the body's capacity for precision movement (as opposed to the opposite – small forces producing huge movements). The arrangement of muscles in order to act as third class levers actually reduces the bulk of the body making C false and the correct answer.
128. **D is correct.** Choices A, B, and C are all functions of skeletal muscle. Muscular contraction can assist in venous blood movement and lymph fluid movement. Shivering is an example of temperature regulation by skeletal muscle. Skeletal muscles help to hold the body erect and maintain posture. Peristalsis refers to the muscular contraction which pushes partially digested food through the digestive tract; it is accomplished through the action of smooth (not skeletal) muscle.
129. **B is correct.** Gap junctions provide direct contact between adjacent cardiac muscle cells and allow for the rapid spread of the action potential throughout the heart. The gap junctions do not anchor muscle fibers together (a task which is accomplished by other types of cardiac cell-cell junctions); nor do they control capillaries or the release of calcium.

130. **C is correct.** The key to correctly answering this question is the knowledge that skeletal muscle is innervated by the somatic nervous system while smooth muscle is innervated by the autonomic nervous system. The muscles of the leg for the knee-jerk reaction and the diaphragm are all skeletal muscles. Therefore, choices A and D can be eliminated outright. An action potential in cardiac muscle is conducted from cell to cell by gap junctions, making choice B an incorrect answer. Peristalsis is a smooth-muscle activity, and is, therefore, controlled by the autonomic nervous system making C the correct answer.
131. **A is correct.** The heart requires long, steady contractions in order to pump blood effectively, so the longer amount of time spent in a state of depolarization prevents the occurrence of contractions in quick succession. Adjacent cardiac cells must contract together to produce coordinated and effective pumping; choice B can be eliminated. Neurons are not the focus of the question, and the answer choice about neurons is not logical. Faster repolarization of the neuron would allow for more rapid firing so choice C is eliminated. Sodium flows into the cell, not out. Therefore, choice D is incorrect as well.
132. **C is correct.** Smooth muscle contains thick and thin filaments, so it requires calcium to contract, making choice C the correct answer. Choices A, B, and D are all true regarding smooth muscle, which tends to have slower, lengthier contractions. Smooth muscle is also under involuntary control through the autonomic nervous system. Under some conditions, changes in the chemical environment can result in contraction of smooth muscles cells.
133. **A is correct.** This question requires the knowledge that smooth muscle and cardiac muscle are involuntary, and then to recognize muscle types of the different structures. Skeletal muscle is under voluntary control. Of the muscles listed, only the diaphragm is skeletal muscle.
134. **D is correct.** Choice A is a tempting answer because cardiac muscle is under the control of the autonomic nervous system and parasympathetic innervation is part of the autonomic nervous system. However parasympathetic input does not excite the cardiac muscle, but rather represses heart rate. T-tubules are invaginations of the sarcolemma and their constriction does not result in cardiac muscle excitation. All muscles contract in response to increased cytosolic calcium concentration, which makes choice C incorrect and makes choice D the right answer.
135. **C is correct.** Choices A and D are not logical and can be eliminated. To decide between choices B and C, it is necessary to know that the vagus nerve is a parasympathetic nerve, which slows the heart rate from the pace naturally set by the SA node. Without inhibitory input from the vagus nerve, the heart would normally beat at 100 – 120 beats per minute.
136. **A is correct.** The word dilation here is the give-away. Smooth muscle in the walls of blood vessels must be relaxing in order to allow dilation. While some of the other answer choices could result in greater blood flow reaching the extremities, none of the other choices (paralysis of skeletal muscle, tachycardia, or blood shunting) necessarily result in vasodilation as indicated in the question stem.
137. **C is correct.** Parathyroid hormone is released when blood calcium levels are low and need to be increased. Choice C is correct because osteoclast activity breaks down bone tissue and releases the stored calcium back into the blood. Therefore, need for higher blood calcium levels increases osteoclast activity and osteoclast count. An increased number of osteoblast would have the opposite of the desired effect, making choice D incorrect. Increased osteocyte and osteoprogenitor numbers would have minimal effects on blood calcium concentrations, making C the best answer.
138. **A is correct.** Synovial fluid acts as a lubricant, decreasing friction between the ends of the bones as they move. Bone cells receive circulation to keep them adequately hydrated; they do not need synovial fluid for this purpose, eliminating choice B. Synovial fluid persists in adults, after bones have stopped growing, so choice C must be wrong. Synovial fluid is found in synovial joints, which allow movement. Its purpose is not to prevent movement. Choice D can be eliminated.

139. **C is correct.** Of the tissues listed, only cartilage does not contain nerves. Therefore, the cutting of cartilage would result in much less pain than cutting skin, muscle, or bone.
140. **A is correct.** Bands of connective tissue attaching bone to bone are called ligaments. Tendons attach bone to muscle, eliminated choice B. Choice C is incorrect because muscles are not a type of connective tissue. Choice D is incorrect because osseous tissues make up bone and would contribute to the formation of one continuous bone rather than the connection between two bones.
141. **C is correct.** Bone does not regulate body or blood temperature. It does store calcium and phosphate, support and protect the body, produce blood cells, and store fat.
142. **A is correct.** Haversian canals, canaliculi, and Volkmann's canals are some of the structural features that are found within compact bone on a microscopic level. Yellow bone marrow is usually found in the medullary cavity of long bones.
143. **B is correct.** Hydroxyapatite is made up of calcium and phosphate in a compound that includes hydroxyl groups as well. This question can be answer by process of elimination. The fact that bone acts as a storage place for phosphate and calcium is required knowledge and eliminates choices A and C. Ascertaining that the compound contains hydroxyl can be inferred from the name hydroxyapatite, which eliminates choice D and leaves B as the best answer.
144. **B is correct.** Spongy bone contains blood stem cells important for blood cell synthesis. Red blood cell storage is the job of the liver and spleen. Fat storage occurs is in long bones. Lymph fluid is formed from interstitial fluid and is not particularly related to bone function.

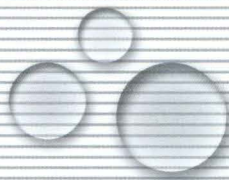


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About the Author

Jonathan Orsay is uniquely qualified to write an MCAT® preparation book. He graduated on the Dean's list with a B.A. in History from Columbia University. While considering medical school, he sat for the real MCAT® three times from 1989 to 1996. He scored in the 90 percentiles on all sections before becoming an MCAT® instructor. He has lectured in MCAT® test preparation for thousands of hours and across the country. He has taught premeds from such prestigious Universities as Harvard and Columbia. He was the editor of one of the best selling MCAT® prep books in 1996 and again in 1997. He has written and published the following books and audio products in MCAT® preparation: "Examkrackers MCAT® Physics"; "Examkrackers MCAT® Chemistry"; "Examkrackers MCAT® Organic Chemistry"; "Examkrackers MCAT® Biology"; "Examkrackers MCAT® Verbal Reasoning & Math"; "Examkrackers 1001 questions in MCAT® Physics", "Examkrackers MCAT® Audio Osmosis with Jordan and Jon".

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The following review of this book was written by Teri R— from New York. Teri scored a 43 out of 45 possible points on the MCAT®. She is currently attending UCSF medical school, one of the most selective medical schools in the country.

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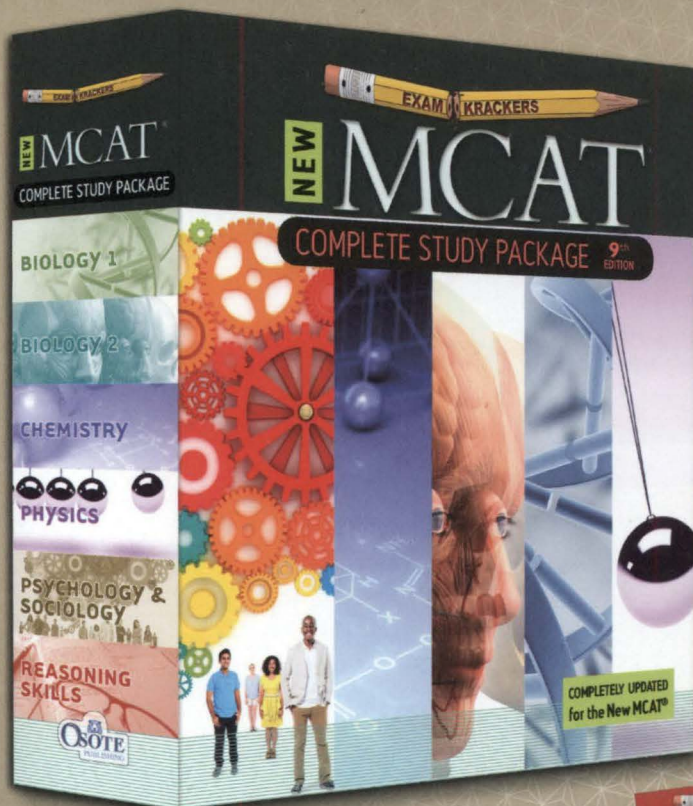
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PERIODIC TABLE OF THE ELEMENTS

1 H 1.0																	2 He 4.0
3 Li 6.9	4 Be 9.0											5 B 10.8	6 C 12.0	7 N 14.0	8 O 16.0	9 F 19.0	10 Ne 20.2
11 Na 23.0	12 Mg 24.3											13 Al 27.0	14 Si 28.1	15 P 31.0	16 S 32.1	17 Cl 35.5	18 Ar 39.9
19 K 39.1	20 Ca 40.1	21 Sc 45.0	22 Ti 47.9	23 V 50.9	24 Cr 52.0	25 Mn 54.9	26 Fe 55.8	27 Co 58.9	28 Ni 58.7	29 Cu 63.5	30 Zn 65.4	31 Ga 69.7	32 Ge 72.6	33 As 74.9	34 Se 79.0	35 Br 79.9	36 Kr 83.8
37 Rb 85.5	38 Sr 87.6	39 Y 88.9	40 Zr 91.2	41 Nb 92.9	42 Mo 95.9	43 Tc (98)	44 Ru 101.1	45 Rh 102.9	46 Pd 106.4	47 Ag 107.9	48 Cd 112.4	49 In 114.8	50 Sn 118.7	51 Sb 121.8	52 Te 127.6	53 I 126.9	54 Xe 131.3
55 Cs 132.9	56 Ba 137.3	57 La* 138.9	72 Hf 178.5	73 Ta 180.9	74 W 183.9	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.1	79 Au 197.0	80 Hg 200.6	81 Tl 204.4	82 Pb 207.2	83 Bi 209.0	84 Po (209)	85 At (210)	86 Rn (222)
87 Fr (223)	88 Ra 226.0	89 Ac* 227.0	104 Unq (261)	105 Unp (262)	106 Unh (263)	107 Uns (262)	108 Uno (265)	109 Une (267)									

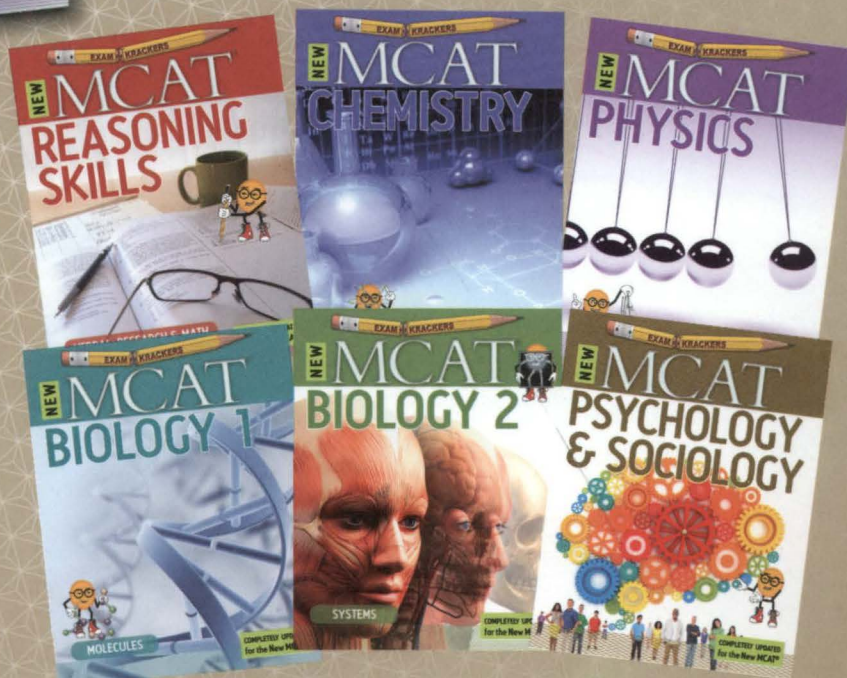
58 Ce 140.1	59 Pr 140.9	60 Nd 144.2	61 Pm (145)	62 Sm 150.4	63 Eu 152.0	64 Gd 157.3	65 Tb 158.9	66 Dy 162.5	67 Ho 164.9	68 Er 167.3	69 Tm 168.9	70 Yb 173.0	71 Lu 175.0
90 Th 232.0	91 Pa (231)	92 U 238.0	93 Np (237)	94 Pu (244)	95 Am (243)	96 Cm (247)	97 Bk (247)	98 Cf (251)	99 Es (252)	100 Fm (257)	101 Md (258)	102 No (259)	103 Lr (260)



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