CHAPTER 3

Compartmentation: Cells and Tissues

Teaching Summary

This chapter has a lot of basic cell biology review. Choose what works best for your class. Here are some ideas for teaching this chapter:

- Demonstrate how the human body is compartmentalized into internal/external and intracellular/extracellular spaces. Introduce the role of membranes, including a discussion of the fluid mosaic model and the different categories of membrane proteins.
- Categorize and distinguish the functions of organelles found in our cells. Show how the theme of compartmentation continues within the cell, and if there's time, relate this discussion to the evolution of eukaryotic cells (endosymbiont theory).
- You might consider starting with an overview of the similarities and differences between the four different types of tissue. How does the nature of the extracellular matrix change with each tissue type?
- Using structural and functional differences, distinguish between the five types of epithelial tissue, the seven types of connective tissue, the three types of muscle tissue, and the two types of neural tissue.
- Help students begin to predict physiological functions of tissues based on structural elements present (cell junctions, membrane protein composition, and membrane polarity, etc.)—and vice versa, to predict what structural elements should be expected based on tissue function.

Student Learning Outcomes

When students complete this chapter, they should be able to:

LO 3.1 Name and describe the major body cavities and compartments.

LO 3.2 Explain the four major functions of the cell membrane.

LO 3.3 Draw and label the fluid mosaic model of the cell membrane and describe the functions of each component.

LO 3.4 Compare a phospholipid bilayer to a micelle and a liposome.

LO 3.5 Map the organization of a typical animal cell.

LO 3.6 Draw, name, and list the functions of organelles found in animal cells.

LO 3.7 Compare the structure and functions of the three families of cytoplasmic protein fibers.

LO 3.8 Compare and contrast cilia and flagella.

LO 3.9 Describe five major functions of the cytoskeleton.

LO 3.10 Name the three motor proteins and explain their functions.

LO 3.11 Describe the organization and function of the nucleus.

LO 3.12 Explain how protein synthesis uses compartmentation in the cell to separate different steps of the process.

LO 3.13 Describe the structure and functions of extracellular matrix.

LO 3.14 Describe the role of proteins in the three major categories of cell junctions.

LO 3.15 Compare the structures and functions of the four tissue types.

LO 3.16 Describe the anatomy and functions of the five functional categories of epithelia.

LO 3.17 Compare the anatomy and functions of the seven main categories of connective tissue.

LO 3.18 Use structural and functional differences to distinguish between the three types of muscle tissue.

LO 3.19 Describe the structural and functional differences between the two types of neural tissue.

LO 3.20 Explain the differences between apoptosis and necrosis.

LO 3.21 Distinguish between pluripotent, multipotent, and totipotent stem cells.

LO 3.22 List as many organs as you can for each of the 10 physiological organ systems.

What's New?

- Added cerebrospinal fluid, humors of the eye, pleural and pericardial sacs to fluid compartments
- Updated Running Problem on HPV and Pap smears to reflect latest guidelines for management of abnormal tests
- New discussion of retinoids

Teaching Outline

Supplemental Material

► The American Society for Cell Biology, "Exploring the Cell," www.ascb.org/files/exploring.pdf

► Light microscopes can examine both living cells and preserved cells. A focused beam of light passes through a thin slice of tissue or thin intact cell (e.g., white blood cell), is magnified, and then is viewed through a series of lenses in the microscope. The amount of detail that can be distinguished is known as the *resolution* of the instrument. Resolution can best be thought of as the ability to see two adjacent objects as distinct points rather than a single fused entity. At 1000-fold magnification, the highest magnification usually used in light microscopy, the best resolution is 0.2 μm. This is about the size of a mitochondrion.

At the resolution of the light microscope and with the aid of colored dyes, it is possible to see the general shape and size of cells as well as the larger intracellular structures such as the nucleus.

The fine details of cell structure went undescribed until the electron microscope came into widespread use in the 1950s. In *transmission electron microscopy*, a beam of electrons is directed through an ultrathin slice of tissue onto a fluorescent viewing screen or photographic plate. The colored chemical stains of light microscopy are not effective unless viewed with a beam of visible light, so tissue for electron microscopy is prepared with stains made from heavy metals such as osmium or gold. The heavy metals scatter the electron beam so that it does not reach the photographic plate, causing those areas that absorbed the stain to appear dark in the micrograph. Electron microscopy of biological material has a resolution that is 2500 times greater than that of the light microscope, down to 0.1 nanometer (1000 nm = 1 μm). This resolution makes it possible to see details as small as large glycogen granules and the phospholipids of the cell membrane. But transmission electron microscopy, like light microscopy, has limitations. The electron beam must be passed through a vacuum, meaning that it is impossible to view living material. And the thinness of the slices makes it difficult to reconstruct the three-dimensional orientation of cellular components.

Much of our understanding of the spatial orientation of subcellular components has come from scanning electron microscopy. This instrument also utilizes an electron beam, but bounces the electrons off the exposed surfaces of intact cells or tissues. The tissue sample is coated with platinum or some other heavy metal that emits electrons onto a photographic plate. The resultant scanning electron micrograph gives a shadowed, three-dimensional view of the surface of the sample.

One of the newer techniques in microscopy is fluorescence microscopy, in which fluorescent dyes are bound to organelles, proteins, antibodies, or DNA within a cell. This allows resolution to only a few nanometers, compared to about 200 nm with optical lenses.

Functional Compartments of the Body

Fig. 3.1 (**Essentials: Levels of Organization: Body Compartments**)

Key Words: cell, cranial cavity, skull, thoracic cavity, thorax, abdomen, pelvis, abdominopelvic cavity, peritoneum, tissue membranes, diaphragm, pericardial sac, pleural sacs

The Lumens of Some Organs Are Outside the Body

Fig. 3.9b is used for the discussion of epithelia, but gives a graphical representation of how some lumens are outside of the body.

Key Word: lumen

Functionally, the Body Has Three Fluid Compartments

Fig. 3.1b

Key Words: intracellular fluid (ICF), extracellular fluid (ECF), plasma, interstitial fluid

Biological Membranes

Fig. 3.1c

Key Word: cell membrane

The Cell Membrane Separates Cell from Environment

Key Words: plasma membrane, plasmalemma, secretion, extracellular matrix

Membranes Are Mostly Lipid and Protein

Fig. 3.2 (**Essentials: The Cell Membrane**); Table 3.1

Key Word: fluid mosaic model

- The average cell membrane has a composition of 30%–50% protein, 40%–60% lipid, and up to 10% carbohydrate.
- **History notes on the evolution of the Fluid Mosaic Model:** Botanists in the early 1800s using the low resolution of a light microscope noticed a discrete layer that appeared between the cytoplasm and the rigid wall of plant cells. In 1890, the scientist Ernst Overton concluded that this layer or membrane was made of a thin layer of lipids that acted as a barrier between the aqueous interior of the cell and its watery environment. Later analysis of membranes showed that they were lipid and protein but still did not explain how the molecules were arranged in the membrane. The first theory was that the lipids of the membrane were in a single layer, similar to the oil slick formed if olive oil is poured onto the surface of a body of water. Then studies in the 1920s showed that the amount of lipid in a given area of membrane equaled a double layer of lipid surrounding the cell. This model was further modified in the 1930s to account for the presence of proteins. The protein molecules were thought to be bound to the lipids, forming a coating on both surfaces of the double lipid layer. Transmission electron micrographs showed membranes that appeared to be constructed in layers, two dark layers with a lighter layer in between. Because proteins absorb heavy metal stains used in electron microscopy and turn dark as a result, several generations of students remembered membrane structure as a "fat sandwich": two layers of protein with a layer of phospholipid sandwiched between. This model prevailed until the early 1970s. Then development of freeze-fracture techniques for the electron microscope showed that the model of the cell membrane as a uniform structure of three layers was not accurate. In freeze-fracture studies, whole cells are rapidly frozen in liquid nitrogen, placed in a vacuum, and fractured with the edge of a sharp knife. If the fracture line runs through the phospholipid layer of a membrane, it separates the membrane into two leaflets as shown in Fig. 3.4. The exposed surface is coated with layers of metal and carbon to emphasize the three-dimensional structure. Intact proteins appear as bumps in the lipid layer, while the places where they have been pulled from the lipid layer form shadowed holes.

Membrane Lipids Create a Hydrophobic Barrier

Fig. 3.2

Key Words: micelles, liposomes, sphingolipids

- One feature of cell membranes that is not apparent in the typical drawing of the fluid mosaic model is the asymmetry of the lipids in the membrane. Although the phospholipids all have a polar head and nonpolar tail, the numbers of carbons in the fatty acid chains, the numbers of double bonds between the carbons, or the molecular groups attached to the phosphate head may vary. The various types of phospholipids are not arranged evenly in the bilayer, making the membrane asymmetrical. Some of the common phospholipids found in membranes include phosphatidyl choline and sphingomyelin.

- ► The myelin membrane is about 22% cholesterol, while other mammalian cell membranes may be as much as 30% cholesterol.
- ► Membranes with higher cholesterol concentrations are less permeable to ions, water, and other small molecules. Presumably cholesterol blocks the openings between phospholipid tails through which these small molecules could otherwise pass.
- ► Because mammals maintain a relatively constant body temperature, the "plasticizing" effect of cholesterol is not as important as it is in poikilothermic animals and plants that cannot maintain a constant body temperature.
- ► In one study, liposomes loaded with antibodies against the potent anticancer drug doxorubicin (DXR) were used to prevent the drug-induced hair loss usually associated with chemotherapy. When applied to the skin of mice receiving DXR treatments, the liposomes were absorbed into hair follicles, where the antibodies protected the rapidly dividing follicle cells from DXR.

  Torchilin VP. Targeted pharmaceutical nanocarriers for cancer therapy and imaging. *The AAPS Journal* 9(2): E128–147, 2007 May 11.

Membrane Proteins May Be Loosely or Tightly Bound to the Membrane

Figs. 3.2, 3.3

Key Words: integral proteins, peripheral proteins, transmembrane proteins, lipid-anchored proteins, GPI anchor, lipid rafts, polarity

- ► The distinction is made most simply by what laboratory methods are needed to separate the protein from the membrane. To separate integral proteins, the membrane integrity must be disrupted with detergents. Peripheral proteins can be separated from their membranes without destroying the membrane.
- ► How can proteins composed of polar amino acids bind to the nonpolar lipids in the center of the phospholipid bilayer? *Some amino acids have nonpolar side chains. When these amino acids are linked to each other, they form an alpha-helix that has an exterior layer of nonpolar side groups and a central core composed of the polar amino and carboxyl groups. By putting a sequence of 20 hydrophobic amino acids in a peptide chain, the protein molecule can insert itself into the bilayer, oriented so that the nonpolar amino acid side chains interact with the nonpolar lipids. This ties the protein so firmly to the membrane that it can only be freed by disrupting the phospholipid bilayer with detergents. The sequence of 20 amino acids is significant because that is the number needed to make a helix the same length as the thickness of the membrane.*
- ► Membrane receptors, transporters, and enzymes are grouped into families according to how many membrane-spanning regions they possess. For example, the voltage-gated K^+ channel has six transmembrane segments. The related voltage-gated Na^+ and Ca^{2+} channels are made of four associated segments (domains), each with six membrane-spanning regions. The ATPase transporters of eukaryotic cells have 8–10 membrane-spanning regions. G-protein-linked membrane receptors all have seven transmembrane segments, as do the β_2 adrenergic and rhodopsin receptors.
- ► Originally it was thought that membrane proteins all floated freely within the lipid layer of the membrane.
- ► Rhodopsin, the protein pigment that absorbs light in the retina, rotates in place, somersaulting at a rate of 60° every 10 microseconds.

► Hicke L. Gettin' down with ubiquitin: Turning off cell-surface receptors, transporters and channels. *Trends in Cell Biology* 9(3): 107–112, 1999 Mar. doi: http://dx.doi.org/10.1016/S0962-8924(98)01491-3.

Membrane Carbohydrates Attach to Both Lipids and Proteins

Fig. 3.2c

Key Word: glycocalyx

► The carbohydrates of the glycocalyx play a critical role in identifying cells; for example, the carbohydrates of the glycocalyx in human blood cells differentiate the main ABO blood groups from one another.

Intracellular Compartments

Fig. 3.1b

Key Word: differentiation

Cells Are Divided into Compartments

Fig. 3.4a (**Review: Cell Structure**)

Key Words: cytoplasm, nucleus, cytosol, inclusions, organelles

► Serum is plasma from which most clotting proteins are removed. To obtain serum, allow a sample of whole blood to clot, then remove the cells of the clot and associated clotting proteins by centrifugation.

► Body fluid compartment volumes are estimated experimentally using a variety of markers. The marker must be restricted to the compartment being measured in order to give accurate results. It should also be nontoxic, not metabolized or excreted, and easily measured. Total body water is estimated using deuterium oxide (D_2O or heavy water) or tritium oxide. Calculating the volume of distribution for the extracellular fluid volume requires a molecule that can move freely between the plasma and the interstitial fluid but that cannot enter the cells. Sucrose, the disaccharide commonly known as table sugar, fits this requirement, as does a molecule called inulin. Inulin is a plant polysaccharide extracted from the roots of dahlias. It is not metabolized by humans but is excreted in the urine, so this must be taken into account when estimating ECF volume. The final compartment that can be directly measured is the plasma volume. This measurement requires a large molecule that distributes in the plasma but cannot cross the leaky epithelium to the interstitial fluid. Because endogenous plasma proteins meet this requirement, researchers found a dye, Evans blue, that binds to plasma proteins and therefore distributes only in the plasma. There are no markers for the interstitial fluid and the intracellular compartment, but we have been able to accurately estimate those volumes by subtraction.

► Ask students to brainstorm about the properties a molecule should have if it is to be used as a marker for one of the body compartments.

► Give students volumes estimated using the three markers (heavy water, Evans blue, and inulin) and ask them to determine interstitial fluid and the intracellular compartment volumes. *Interstitial = ECF – plasma; ICF = total body water – ECF.*

► *See* the Quantitative Physiology section later in this chapter for quantitative problems using the dilution technique.

► *See* a model of the evolution of eukaryotic cells: de Duve C. The birth of complex cells. *Scientific American* 274(4): 50–57, 1996 Apr.

The Cytoplasm Includes Cytosol, Inclusions, Fibers, and Organelles

Key words: cytoplasm, cytosol, inclusions, protein fibers, cytoskeleton, organelles

► Of the dissolved material in the cytosol, about 20%–30% is protein. Dissolved enzymes are among the most important cytosolic proteins.

► The membranous organelles function as semi-autonomous units within the cell, carrying out their individual functions but ultimately dependent upon the nucleus to ensure that they get replacement parts as they wear out. The membranes isolate the contents of the organelle. This allows the cell to store potentially harmful material and to control cell processes by regulating movement of material between intracellular compartments. For example, muscle cells store calcium in membranous organelles and release it into the cytosol as a signal to start contraction.

Inclusions Are in Direct Contact with the Cytosol

Fig. 3.4i

Key Words: ribosomes, fixed ribosomes, free ribosomes, polyribosomes

► Ribosomes are found in every cell at some point in their life because all cells make proteins, but they are most numerous in cells whose primary function is the synthesis of proteins for export out of the cell. Proteins that are released from cells to carry out their function elsewhere include protein hormones and digestive enzymes.

Cytoplasmic Protein Fibers Come in Three Sizes

Table 3.2

Key Words: actin fibers, microfilaments, intermediate filaments, keratin, neurofilament, microtubules, tubulin

Microtubules Form Centrioles, Cilia, and Flagella

Figs. 3.4e, 3.5; *also see* Appendix C.

Key Words: centrosome, centrioles, cilia, flagella

► Be sure to look in the text chapter at the Emerging Concepts box about the sensory functionality of primary cilia.

The Cytoskeleton Is a Changeable Scaffold

Fig. 3.4b

Key Word: microvilli

► Schwab A. Ion channels and transporters on the move. *News in Physiological Sciences* 16: 29–33, 2001 Feb. Free access *http://physiologyonline.physiology.org*

► Stidwill RP and Greber UF. Intracellular virus trafficking reveals physiological characteristics of the cytoskeleton. *News in Physiological Sciences* 15(2): 67–71, 2000 Apr. Free access *http://physiologyonline.physiology.org*

► One of the most studied examples of the cytoskeleton is that of the red blood cell (RBC)(erythrocyte). The normal flattened disk shape of the mature RBC is due to the cell's extensive cytoskeleton, composed of protein filaments just under the cell membrane that are linked to the membrane by anchoring proteins. In the inherited condition spherocytosis, some proteins of the cytoskeleton are defective, leading to red blood cells that are less flexible and spherical instead of flattened. These spherical cells rupture more easily than normal red blood cells and have a shortened life span in the body.

Motor Proteins Create Movement

Fig. 3.6

Key Words: motor proteins, myosins, kinesins, dyneins

► Mallik R and Gross SP. Molecular motors: Strategies to get along. *Current Biology* 14(22): R971–982, 2004 Nov 23.

► Hirokawa N and Takemura R. Biochemical and molecular characterization of diseases linked to motor proteins. *Trends in Biochemical Sciences* 28(10): 558–565, 2003 Oct. doi: http://dx.doi.org/10.1016/j.tibs.2003.08.006.

Organelles Create Compartments for Specialized Functions

Figs. 3.4g–i

Key words: mitochondria, Golgi apparatus, endoplasmic reticulum, vesicles

Mitochondria

Fig. 3.4g

Key Words: mitochondria, mitochondrial matrix, intermembrane space, mitochondrial DNA

► There is evidence that mitochondrial DNA can be paternally inherited, in contrast to the theory that sperm mitochondria do not survive fertilization. Schwartz M and Vissing J. Parental inheritance of mitochondrial DNA. *New England Journal of Medicine* 347(8): 576–580, 2002 Aug 22. doi: 10.1056/NEJMoa020350.

► Wallace DC. Mitochondrial DNA in aging and disease. *Scientific American* 277(2): 40–47, 1997 Aug.

The Endoplasmic Reticulum

Fig. 3.4i

Key Words: endoplasmic reticulum (ER), rough ER, smooth ER

The Golgi Apparatus

Fig. 3.4h

Key Words: Golgi apparatus, cisternae

Cytoplasmic Vesicles

Figs. 3.4c, d

Key Words: secretory vesicles, storage vesicles, lysosomes, peroxisomes

► Peroxisomes seem to be self-replicating. They do not come off the Golgi as secretory vesicles as originally thought.

The Nucleus Is the Cell's Control Center

Figs. 3.4j, 3.7 (Protein synthesis illustration)

Key Words: nuclear envelope, pores, nuclear pore complex, chromatin, nucleoli

► Most cells have a nucleus. However, the developing red blood cell loses its nucleus during the maturation process. As a result of having no DNA to direct protein synthesis, the life span of the mature red blood cell is limited to about 120 days.

Tissues of the Body

Key Word: histology

Extracellular Matrix Has Many Functions

Key Words: extracellular matrix, proteoglycans

► Weaver VM and Roskelly CD. Extracellular matrix: The central regulator of cell and tissue homeostasis. *Trends in Cell Biology* 7(1): 40–42, 1997 Jan. doi: http://dx.doi.org/10.1016/S0962-8924(97)30078-6.

► The enzymes known as matrix metalloproteinases (MMPs) are becoming known as a major player in a number of pathologies.

Cell Junctions Hold Cells Together to Form Tissues

Figs. 3.8 (**Essentials: Cell Junctions**); Table 3.3

Key Words: cell junction, cell adhesion molecules (CAMs), communicating junctions, gap junctions, occluding junctions, tight junctions, anchoring junctions, cadherins, integrins, adherens junctions, desmosomes, plaques, hemidesmosomes, focal adhesions, matrix metalloproteinases (MMPs)

► Anderson JM. Molecular structure of tight junctions and their role in epithelial transport. *News in Physiological Sciences* 16(3): 126–130, 2001 June.

► Meier T and Ruegg MA. The role of dystroglycan and its ligands in physiology and disease. *News in Physiological Sciences* 15(5): 255–259, 2000 Oct.

► Petruzzelli L, Takami M, and Humes HD. Structure and function of cell adhesion molecules. *The American Journal of Medicine* 106(4): 467–476, 1999 Apr. doi: http://dx.doi.org/10.1016/S0002-9343(99)00058-3.

► The stability of cell junctions is dependent on extracellular calcium ions; removal of calcium from the extracellular fluid will cause the cell junctions to separate.

Epithelia Provide Protection and Regulate Exchange

Fig. 3.9 (**Essentials: Epithelial Tissue**)

Key Word: epithelial tissues (epithelia)

► The constant cell division in epithelia seems to make these cells prone to genetic mutations, leading to abnormal growth patterns such as cancer or benign tumors. It has been estimated that more than 90% of all cancer in adults over the age of 45 arises in epithelial tissues.

Structure of Epithelia

Fig. 3.9c

Key Word: basal lamina (basement membrane)

► Tight junction epithelia are held together by **junctional complexes**, each consisting of a tight junction, an intermediate junction, and a desmosome, with the tight junction closest to the cell surface.

Types of Epithelia

Fig. 3.10 (**Essentials: Types of Epithelia**)

Key Words: simple, stratified, squamous, cuboidal, columnar, exchange epithelia, transporting epithelia, ciliated epithelia, secretory epithelia

Exchange Epithelia

Fig. 3.10a

Key Words: endothelium, simple squamous epithelium

Transporting Epithelia

Fig. 3.10b

Key Words: apical membrane, basolateral membrane

Ciliated Epithelia

Fig. 3.10c

Key Words: ciliated epithelia

Protective Epithelia

Fig. 3.10d

Key Words: protective epithelia, retinoids

Secretory Epithelia

Figs. 3.9b, 3.10e, 3.11

Key Words: secretory epithelia, gland, ducts, exocrine gland, serous secretions, mucous secretions (mucus), goblet cells, endocrine glands, hormones

► To differentiate between ductless endocrine and ducted exocrine glands, remember that endocrine have *no* ducts.

Connective Tissues Provide Support and Barriers

Fig. 3.12 (**Essentials: Connective Tissue**)

Key Word: connective tissues

Structure of Connective Tissue

Fig. 3.12a

Key Words: ground substance, fixed cells, mobile cells, fibroblasts, collagen, elastin, fibrillin, fibronectin

► Scientists have discovered that matrix is not simply a passive structural element in the body. Instead, it plays a key role in the specialization of cells and in cell-to-cell communication. For example, one amino-polysaccharide, hyaluronic acid, appears to have potential in medicine for improving tissue regeneration

► Examples of fixed cells include (1) fibroblasts that synthesize the fibers and ground substance that make up the matrix in most tissues, (2) chondroblasts (*chondros*, cartilage) and (3) osteoblasts (*osteo*, bone) that secrete the specialized matrix of cartilage and bone, respectively, and (4) adipocytes that store lipids as a reserve energy source, and fixed macrophages (*phagein*, to eat), also called histiocytes (*histio*-, tissue + *cyte*, cell), that ingest dead or damaged cells and pathogens such as bacteria that enter the tissue. In addition, when an infection occurs, fixed macrophages release chemical signals in order to recruit other defense cells wandering throughout the body to the infected area.

► The collagen molecule is a glycoprotein made into a characteristic triple helix called a collagen fibril. The enzymes that control collagen synthesis require vitamin C (ascorbic acid) as a cofactor. Lack of vitamin C in the diet results in inadequate collagen production, leading to poor wound healing, fragile blood vessels that bleed easily, and a decrease in bone strength. Severe vitamin C deficiency causes the disease scurvy. European explorers learned to carry lemons and limes on their long voyages in order to prevent this disease. Most collagen is made by fibroblasts in connective tissue, but some epithelial cells can also synthesize collagen. One form of collagen, type II, combines with glycoproteins to make the very thin fibers called reticular fibers. In certain types of connective tissue, collagen fibers are arranged in parallel into even larger collagen bundles.

► The Carticel website (www.carticel.com) has interesting information about autologous cartilage implants. For example, the average age of the patients is 36 and there have been few studies done in patients over 65. A single vial of the cultured chondrocytes contains about 12 million cells. One of the more significant side effects has been overgrowth of the implant. Another technique is NeoCart® (www.histogenics.com/products-platform/neocart).

Types of Connective Tissue

Figs. 3.12b, 3.13 (**Essentials: Types of Connective Tissue**)

Key Words: loose connective tissue, dense connective tissue, tendons, ligaments, cartilage, bone, adipose tissue, adipocytes, white fat, brown fat, blood, plasma

► The number of adipose cells varies from one connective tissue to another, from one region of the body to another, and from individual to individual. The nutritional state of the individual determines the size of the adipose cell. When excess fat is being stored, the cells enlarge along with the size of the fat droplet. When the body is burning fat for energy, the fat is mobilized out of the droplet into the blood and the cell shrinks accordingly. Thus, lost weight can easily be regained in the same areas of the body.

► Large numbers of mitochondria give this tissue its characteristic brown color. Adults lose most of their brown fat but some remains in the adipose tissues of the back and shoulders.

► The brown fat mitochondria metabolize fat through pathways that release the energy as heat rather than converting it to ATP. *See* Wolf G. A new uncoupling protein: A potential component of the human body weight regulation system. *Nutrition Reviews* 55(5): 178–179, 1997 May.

Muscle and Neural Tissues Are Excitable

Table 3.4

Key Words: action potentials, external lamina, muscle tissue, neural tissue, neurons, glial cells

Tissue Remodeling

Apoptosis Is a Tidy Form of Cell Death

Key Words: necrosis, apoptosis

► "Bleb" (used in the description of apoptosis) sounds like slang but actually means a blister, bubble, or vesicle. It is related to the Middle English word "blob." Pulmonologists (lung specialists) call weakened areas of lung tissue that form bubbles and rupture "blebs."

► Andreoli TE. The apoptotic syndromes. *The American Journal of Medicine* 107(5): 488, 1999 Nov. doi: http://dx.doi.org/10.1016/S0002-9343(99)00258-2.

► Saikumar P, *et al.* Apoptosis: definition, mechanisms, and relevance to disease. *The American Journal of Medicine* 107(5): 489–506, 1999 Nov. doi: http://dx.doi.org/10.1016/S0002-9343(99)00259-4.

Stem Cells Can Create New Specialized Cells

See Appendix C.

Key Words: mitosis, totipotent, differentiate, pluripotent, stem cells, multipotent, plasticity

► Marrow stem cells for cartilage repair: (literature review)

Anderson JA, *et al*. Stem cell therapies for knee cartilage repair: The current status of preclinical and clinical studies. *American Journal of Sports Medicine* 42(9): 2253–2261, 2014 Sept. doi: 10.1177/0363546513508744. Epub 2013 Nov 12.

Organs

Key Word: organs

Focus On: The Skin

► Focus On: The Skin feature in Fig. 3.15 highlights the skin as an organ. Help your students identify different tissue types, accessory structures, and cellular components they've just learned about in the chapter.

Talk the Talk

abdomen
abdominopelvic cavity
actin fibers or microfilaments
action potentials
adherin junctions
adipocytes
adipose tissue
anchoring junctions
apical membrane
apocrine glands
apoptosis
atrophy
basal lamina
basement membrane
basolateral membrane
bilayers
-blast
blood
blood plasma
bone
brown fat
cadherins
calcified
cartilage
cell adhesion molecules or CAMs
cell junctions
cell membrane
cell organelles
cell shape
cell-cell adhesions
centrioles
centrosome
chromatin
cilia

ciliated epithelia
-clast
claudins
collagen
columnar
compartmentation
connective tissues
connexins
cranial cavity
cristae*
cuboidal
-cyte
cytoplasm
cytoskeleton
cytosol
dense connective tissues
dermis
desmosomes
diaphragm
differentiation
ducts
dyneins
elastance
elastin
endocrine glands
endoplasmic reticulum or ER
epidermis
epithelial tissues or epithelia
Escherichia coli or *E. coli*
exchange epithelia
excitable tissues
external lamina
extracellular fluid (ECF)
extracellular matrix
fibroblasts
fibronectin
fixed cells
fixed ribosomes
flagella
fluid mosaic model
focal adhesions
free ribosomes
gap junctions
gland
glial cells
glycocalyx
goblet cells
Golgi apparatus
GPI anchors
ground substance
hemidesmosomes
histology
hormones
hypodermis
inclusions
integral proteins or transmembrane proteins
integrins
intermediate filaments
intermembrane space
interstitial fluid
intracellular fluid (ICF)
intracellular transport
keratin
kinesins
laminin
ligaments
lipid rafts
lipid-anchored proteins
liposomes
loose connective tissues
lumen
lysosomes
matrix
matrix metalloproteinases (MMPs)
mechanical properties
membrane
membrane modifications
micelles
microtubules
microvilli*
mitochondria*
mitochondrial DNA
mitosis
mobile cells
motor proteins
mucous membranes
mucous secretions
multipotent
muscle tissue
myosins
necrosis
nerve-cell adhesion molecules or NCAMs
neural
neural tissue
neurofilament
neurons
nonmembranous organelles
nuclear envelope
nuclear pore complexes
nucleoli*
nucleus
occluding junctions
occludins
organelles
organs
paracellular
pelvis
peripheral proteins
peritoneal membrane
peritoneum
peroxisomes
phospholipid bilayer
phospholipid matrix
plaques
plasma
plasma membrane
plasmalemma
plasticity
pleural membrane
pluripotent
polarity
polyribosomes
pores
primary cilia*
prokaryotic endosymbiont theory
protective epithelia
proteoglycans
ribosomes
rough endoplasmic reticulum (rER)
sebaceous glands
secretion
secretory epithelia
secretory vesicles
sensory receptors
serous secretions

simple squamous epithelium
smooth endoplasmic reticulum (sER)
sphingolipids
squamous
stem cells
storage vesicles
stratified
surface keratinocytes
sweat glands
Tay-Sachs disease
tendons
thoracic cavity or thorax
tight junctions
tissue membranes
totipotent
transporting epithelia
tubulin
vesicles
white fat

* These words are in the plural form. It's always good to quiz students on singular and plural forms.

Running Problem: Pap Smear

In 1988, the older Papanicolaou classification scheme for Pap smears (Class 1, Class 2, etc.) was replaced by the more detailed and clinically relevant Bethesda system. In 2001 a group of clinicians, cytotechnologists, pathologists, and patient advocates representing 45 professional societies from more than 20 countries met to review the evidence on which the guidelines for interpreting Pap smears are based. Their recommendations shaped the 2001 Bethesda system terminology guidelines (http://jama.ama-assn.org/content/287/16/2114.abstract). As a result of those recommendations, abnormal Pap smears may now be tested for the presence of DNA from the human papilloma virus (HPV). *See* Fullerton JT and Barger MK. Papanicolaou Smear: An Update on Classification and Management. *Journal of the American Academy of Nurse Practitioners*. 1(3): 84–90. 1989 July. doi: 10.1111/j.1745-7599.1989.tb00746.x.

The ThinPrep system for collection and analysis of cervical samples is now the most widely used in the United States (www.thinprep.com). This liquid-based cytology system ensures that more of a cervical sample is preserved for examination and the liquid helps remove blood, mucus, and other debris. The automated system makes better slides, and its computerized examination of about 120 fields of view on the slide selects 22 fields for the cytologist to examine. The liquid sample can also be tested for HPV and several other sexually transmitted diseases.

See also Karjane NW, *et al*. Pap Smear. 2014 Jan 22. http://emedicine.medscape.com/article/1947979-overview.

Quantitative Physiology

Volumes of Distribution

The techniques by which the volumes of the body compartments are determined provides us with interesting insight into experimental design. The determination of a volume of liquid can be estimated using a *dilution technique*. There are several requirements for this experiment. (1) The volume to be measured must be well-mixed, so that any marker that is given will distribute evenly throughout the compartment. (2) The marker must be able to be measured. If the system is a living organism, the marker must also be nontoxic, not metabolized or excreted, and must distribute only into the compartment being measured.

To carry out a dilution experiment, a known amount of marker in a known volume is administered. It is allowed to distribute; then a sample of the compartment liquid is removed and analyzed for its marker content. Because the concentration of marker in the sample is the same as the concentration throughout the compartment, the following ratio is used to calculate the compartment volume:

$$\frac{\text{amount marker in sample (known)}}{\text{volume of sample (known)}} = \frac{\text{total amount of marker (known)}}{\text{total volume of compartment (unknown)}}$$

For example, 1 gram of dye is put into a giant vat of water. The dye is stirred until it is evenly distributed throughout the vat. A 1 mL sample of water is taken out, analyzed, and found to contain 0.02 mg of dye. What is the volume of the vat?

0.02 mg dye/1 mL = 1000 mg dye/χmL

$$\chi = 1000 \text{ mg dye} \bullet 1 \text{ mL} / 0.02 \text{ mg dye}$$

$$\chi = 50{,}000 \text{ mL or } 50 \text{ L}$$

The dye distributed into a volume of 50 L. For this reason, the volumes calculated by this method are known as *volumes of distribution*.

The determination of body compartment volumes in humans has been done using a variety of markers. The marker must be restricted to the compartment being measured in order to give accurate results. *Total body water* has been estimated using water with radioactive isotopes of hydrogen. Both deuterium oxide (D_2O or heavy water) and tritium oxide can be used. Calculating the volume of distribution for the *extracellular fluid (ECF) volume* requires a molecule that can move freely between the plasma and the interstitial fluid but that cannot enter the cells. Sucrose, the disaccharide commonly known as table sugar, fits this requirement as does a molecule called *inulin*. Inulin is a plant polysaccharide extracted from the roots of dahlias. It is not metabolized by humans but is excreted in the urine, so this must be taken into account when estimating ECF volume. The final compartment that can be directly measured is the *plasma volume*. This measurement requires a large molecule that distributes in the plasma but cannot cross the leaky epithelium to the interstitial fluid. Since endogenous plasma proteins meet this requirement, researchers found a dye, Evans blue, that binds to plasma proteins and therefore distributes only in the plasma.

There are no markers for the interstitial fluid and the intracellular compartment, but we have been able to accurately estimate those volumes as well. Using the information in the paragraph above, can you explain how to calculate interstitial fluid and the intracellular volumes?

Answers:

Interstitial volume = ECF – plasma

ICF volume = total body water – ECF volume

Focus On: Physiology

1. Name the cell organelle or structure that:

a. packages protein for secretion _____

b. contains digestive enzymes _____

c. contains the information which controls all cell functions _____

d. is the site of lipid synthesis _____

e. is the main site of ATP production _____

f. is a selective barrier between the cytoplasm and the interstitial fluid _____

2. You have been doing research on the pancreatic endocrine cells that secrete insulin (a peptide) and the adrenal cortex cells that secrete aldosterone (a steroid hormone). You prepared tissue for examination under the electron microscope, but the labels fell off the jars when the fixative dissolved the glue. You sent the tissue off anyway and got back the following description for one of the tissues. Which tissue is being described? Defend your answer.

". . . cells are close to blood capillaries. Numerous dense, membrane-bounded granules throughout the cytoplasm with reduced rough endoplasmic reticulum and free ribosomes. Cells with fewer secretory granules show an increase in rough ER and ribosomes."

3. Here are some tables to have your students construct:

a. Summarize the characteristics of the inclusions.

INCLUSION	STRUCTURE	FUNCTION

b. Summarize the characteristics of the organelles.

ORGANELLE	STRUCTURE	FUNCTION

c. Complete the table below regarding characteristics of cell junctions.

TYPE OF JUNCTION	COMPOSITION	FUNCTION	WHERE OCCUR: CELL OR TISSUE TYPE

d. Complete the table below.

TYPE OF EPITHELIUM	STRUCTURAL AND FUNCTIONAL CHARACTERISTICS	LOCATIONS FOUND