1BIEN 500
Course Director: Dr. DeCoster
Textbook: Guyton and Hall (14th edition –or previous/)

FIRST TWO LECTURES:

Introduction to Physiology: The cell and General Physiology.

Chap1. Functional organization of the Human body and control of the internal environment.

Chap 2. The cell and its functions.

Chap 3. Genetic control of protein synthesis, cell function, and cell reproduction.

Chapter 1, Guyton.

- Functional organization of the Human body and control of the internal environment.

- Cells as the living units of the body.

- The basic living unit of the body is the cell. Each organ is an aggregate of many different cells held together by <u>intercellular</u> supporting structures.

- Each type of cell is specially adapted to perform ***one or a few*** particular functions.

Cells-2

- Although the many cells of the body often differ markedly from one another, all of them have certain basic characteristics that are alike. For instance, in all cells, oxygen reacts with carbohydrate, fat, and protein to release the energy required for cell function.

- Further, the general chemical mechanisms for changing nutrients into energy are basically the same in all cells, and all cells deliver end products of their chemical reactions into the surrounding fluids **(examples?).**

Cells-3

- Almost all cells also have the ability to reproduce additional cells of their own kind. Fortunately, when cells of a particular type are destroyed from one cause or another, the remaining cells of this type usually generate new cells until the supply is replenished

Symbiosis with the body

- **<u>Microorganisms living in the body outnumber Human cells</u>.**

- In addition to human cells, trillions of microbes inhabit the body, living on the skin and in the mouth, gut, and nose.

- The GI tract, for example, normally contains a complex and dynamic population of 400-1,000 species of microorganisms that outnumber our human cells.

- Communities of microorganisms that inhabit the body, often called microbiota, can cause diseases, but most of the time they live in harmony with their human hosts and provide vital functions that are essential for survival of their hosts.

- The importance of gut microbiota is digestion is widely recognized, but additional role for the body's microbes in nutrition, immunity, and other functions are just beginning to be appreciated and represent an intensive area of biomedical research. [Microbiome].

Extracellular and Intracellular Fluid

- About 60 percent of the adult human body is fluid, mainly a water solution of ions and other substances. Extracellular fluid is in constant motion throughout the body. It is transported rapidly in the circulating blood and then mixed between the blood and the tissue fluids by diffusion through the capillary walls.

- In the extracellular fluid are the ions and nutrients needed by the cells to maintain cell life.

- Cells are capable of living, growing, and performing their special functions as long as the proper concentrations of oxygen, glucose, different ions, amino acids, fatty substances, and other constituents are available. –

Differences between extracellular and intracellular fluids:

- Extracellular fluid contains large amounts of sodium, chloride, and bicarbonate ions plus nutrients for the cells such as oxygen, glucose, fatty acids and amino acids. It also contain carbon dioxide that is being transported from the cells to the lungs to be ***excreted***, plus other cellular waste products that are being transported to the kidneys for excretion (***example?***).

-     The intracellular fluid differs significantly from the extracellular fluid: specifically, it contains large amounts of potassium, magnesium, and phosphate ions instead of the sodium and chloride ions found in the extracellular fluid. Special mechanisms for transporting ions through the cell membranes maintain the ion concentration differences between the extracellular and intracellular fluids (discussed in chapter 4).

Homeostasis:

- Homeostasis is a term used by physiologists to mean maintenance of nearly constant conditions in the internal environment. Essentially all organs and tissues of the body perform functions that help maintain these constant conditions.

- For example: lungs provide oxygen to the extracellular fluid to replenish oxygen used by cells. Kidneys maintain constant ion concentrations, and the gastrointestinal system provides nutrients.

Extracellular fluid transport and mixing system- the blood circulatory system
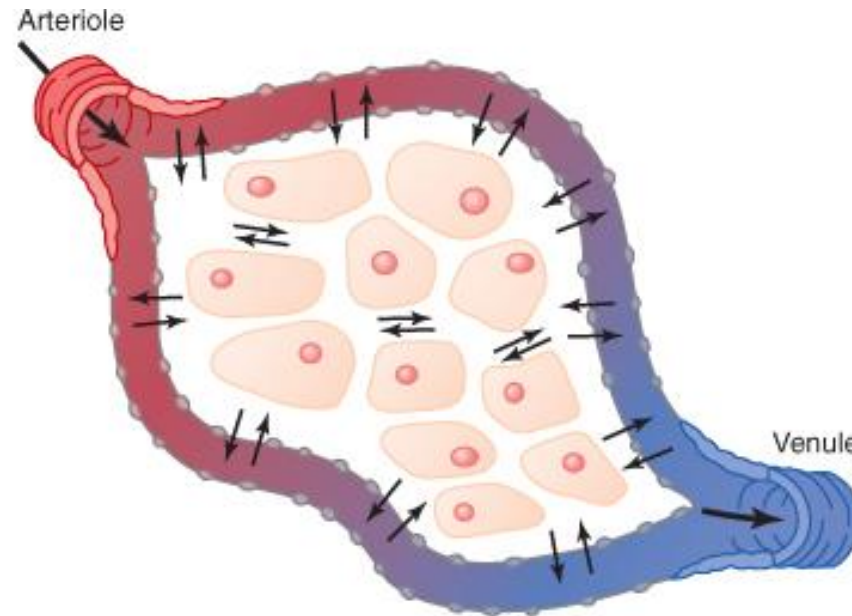
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As blood passes through the blood capillaries, continual exchange of extracellular fluid also occurs between the plasma portion of the blood and the interstitial fluid that fills the intercellular spaces. Figure (1-2). The walls of the capillaries are permeable to most molecules in the plasma of the blood, with the exception of the large plasma protein molecules. Therefore, large amounts of fluid and its dissolved constituents diffuse back and forth between the blood and the tissue spaces, as shown by the arrows (fig 1-2).

Extracellular fluid transport and mixing system- the blood circulatory system-2

- This process of diffusion is caused by kinetic motion of the molecules in both the plasma and the *interstitial fluid*. Thus, the fluid and dissolved molecules are continually moving and bouncing in all directions within the plasma and the fluid in the intercellular spaces, and also through the capillary pores. Few cells are located more than 50 micrometers from a capillary, which ensures diffusion of almost any substance from the capillary to the cell within a few seconds.

- Thus the extracellular fluid everywhere in the body- both that of the plasma and that of the interstitial fluid – is constantly being mixed, thereby maintaining almost complete homogeneity of the extracellular fluid throughout the body.

The origin of nutrients in the extracellular fluid

- Respiratory system: each time the blood passes through the body, it also flows through the lungs. The blood picks up oxygen in the aveoli, thus acquiring the oxygen needed by the cells. The membrane between the aveoli and the lumen of the pulmonary capillaries , the alveolar membrane, is only 0.4 to 2.0 micrometers thick, and oxygen diffuses by molecular motion through the pores of this membrane into the blood in the same manner that water and ions diffuse through walls of the tissue capillaries.

Homeostasis

- Gastrointestinal Tract: a large portion of the blood pumped by the heart also passes through the walls of the gastrointestinal tract. Here different dissolved nutrients, including carbohydrates, fatty acids, and amino acids, are absorbed from the ingested food into the extracellular fluid of the blood.

- Liver and other organs that perform primarily metabolic functions: not all substances absorbed from the gastrointestinal tract can be used in their absorbed form by the cells. The liver changes the chemical compositions of many of these substances to more useable forms, and other tissues of the body—fat cells, gastrointestinal mucosa, kidneys, and endocrine glands- help modify the absorbed substances or store them until they are needed.

Homeostasis-2

- Musculoskeletal system: how does the musculoskeletal system fit into the homeostatic functions of the body? -- were it not for the muscles, the body could not move to the appropriate place at the appropriate time to obtain the foods required for nutrition. The musculoskeletal system also provides motility for protection against adverse surroundings without which the entire body, along with its homeostatic mechanisms, could be destroyed instantaneously.

Removal of metabolic endproducts

- Removal of carbon dioxide by the lungs. At the same time that blood picks up oxygen in the lungs, carbon dioxide is released from the blood into the lung alveoli; the respiratory movement of air into and out of the lungs carries the carbon dioxide to the atmosphere.

- Carbon dioxide is the most abundant of all the end products of metabolism

Removal of metabolic endproducts-2

- Kidneys. Passage of the blood through the kidneys removes from the plasma (what is plasma?) most of the other substances besides carbon dioxide that are not needed by the cells. These substances include different end products of cellular metabolism, such as urea and uric acid; they also include excesses of ions and water from the food that might have accumulated in the extracellular fluid.

-     The kidneys perform their function by first filtering large quantities of plasma and then reabsorbing into the blood those substances needed by the body, such as glucose, amino acids, appropriate amounts of water, and many of the ions. Most of the other substances that are not needed by the body, especially the metabolic end products such as urea, are reabsorbed poorly and pass into the urine.

Regulation of body functions: Nervous system

- 3 major parts: sensory input portion; central nervous system (CNS= the integrative portion); and motor output portion.

- Sensory receptors detect the state of the body or the state of the surroundings such as receptors in the skin sense whenever an object touches the skin at some point.

- CNS= brain and spinal cord. A large segment of the nervous system is called the autonomic system—it operates at a subconscious level and controls many functions of the internal organs, including the level of pumping activity by the heart, movements of the gastrointestinal tract, and secretion by many of the body's glands.

Regulation of body functions

- Hormonal system of regulation. Located in the body are eight major endocrine glands that secrete chemical substances called hormones. Hormones are transported in the extracellular fluid to all parts of the body to help regulate cellular function. For instance, thyroid hormone increases the rates of most chemical reactions in all cells, thus helping to set the tempo of bodily activity. Insulin controls glucose metabolism.

- Thus, the hormones are a system of regulation that complements the nervous system. The nervous system regulates mainly muscular and secretory activities of the body, whereas the hormonal system regulates many metabolic functions.

- Reproduction

- May be considered that all body structures are organized such that they help maintain the automaticity and continuity of life (reproduction).

Control systems of the body

- Many control systems operate within the organs of the body to control functions of the individual parts of the organs.

- Others operate throughout the entire body to control the interrelations between the organs. For instance, the respiratory system, operating in association with the nervous system, regulates the concentration of carbon dioxide in the extracellular fluid (How?, breathing?-control?).

Examples of control mechanisms

- Regulation of oxygen and carbon dioxide concentrations in the extracellular fluid.

The body has a special control mechanism to maintain an almost exact and constant oxygen concentration in the extracellular fluid. This mechanism depends principally on the chemical characteristics of hemoglobin, which is present in all red blood cells. –Hemoglobin combines with oxygen as blood passes through lungs. Then, as blood passes through tissue capillaries, hemoglobin, because of its own strong chemical affinity for oxygen, does not release oxygen into the tissue fluid if too much oxygen is already there. If oxygen concentration in the tissue fluid is too low, sufficient oxygen is released to re-establish an adequate concentration. This regulation is called the oxygen buffering function of hemoglobin.

Normal ranges and physical characteristics of important extracellular fluid constituents

- mmol/L= mM; uM=?; nM=?

- Normal Calcium ion in extracellular fluid= 1.2 mM; inside cell= 120 nM—what is the gradient (fold difference between in and out?)

- Normal limits for physical and chemical components are very tight—for example temperature and pH.

Characteristics of control systems

- **Negative feedback** nature of most control systems (in physiology).

- Most control systems of the body act by negative feedback. For example, in the regulation of carbon dioxide concentration, a high concentration of carbon dioxide in the extracellular fluid increases pulmonary ventilation. This in turn decreased the extracellular fluid carbon dioxide concentration because the lungs expire greater amounts of carbon dioxide from the body.

- Thus the high concentration of carbon dioxide initiates events that decrease the concentration towards normal, which is negative to the initiating stimulus (negative feedback). –other examples throughout the course-

Positive feedback can sometimes cause _**vicious cycles**_ and death. (neuronal excitotoxicity).
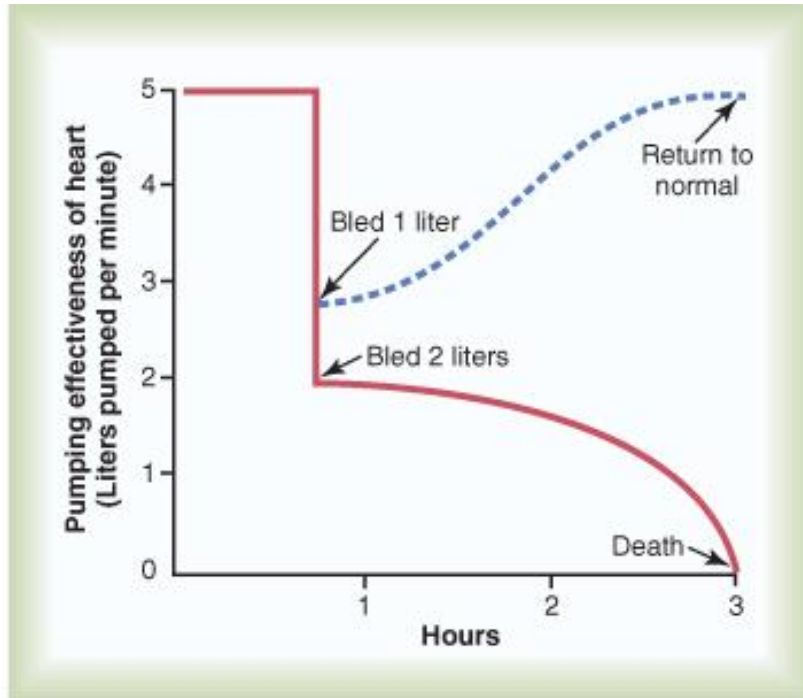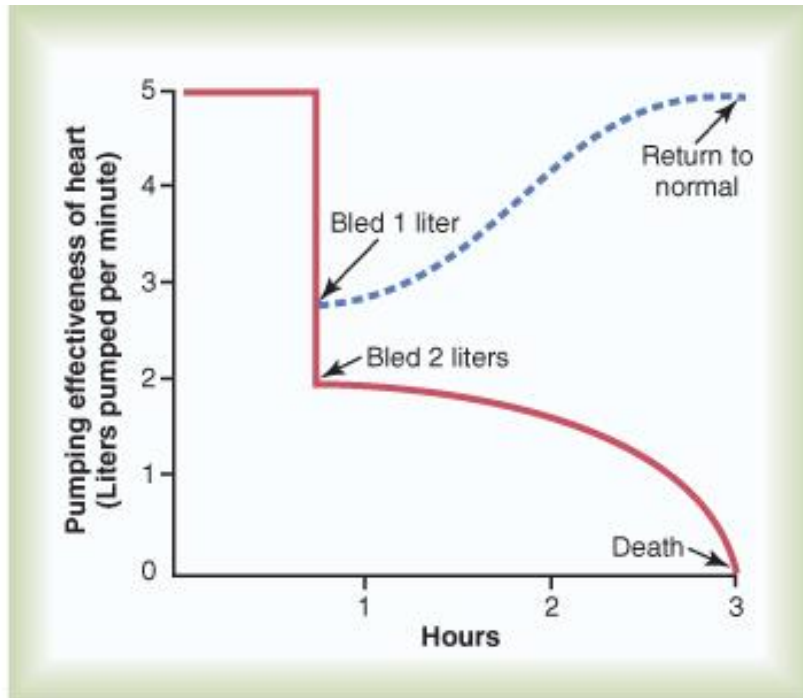

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Figure 1-3, positive feedback leading to death due to blood loss. If person is suddenly bled 2 liters, the amount of blood in the body is decreased to such a low level that not enough blood is available for the heart to pump effectively.

As a result, the arterial pressure falls, and the flow of blood to the heart muscle through the coronary vessels diminishes. This results in a weakening of the heart, further diminishing pumping, a further decrease in coronary blood flow, and still more weakness of the heart; the cycle repeats itself again and again until death occurs.
—the initiating stimulus causes more of the same, which is positive feedback (and in this case BAD!).

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Positive feedback can sometimes cause vicious cycles and death-2

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Positive feedback is also known as a vicious cycle, but a mild degree of positive feedback can be overcome by the negative feedback control mechanisms of the body, and the vicious cycle fails to develop.
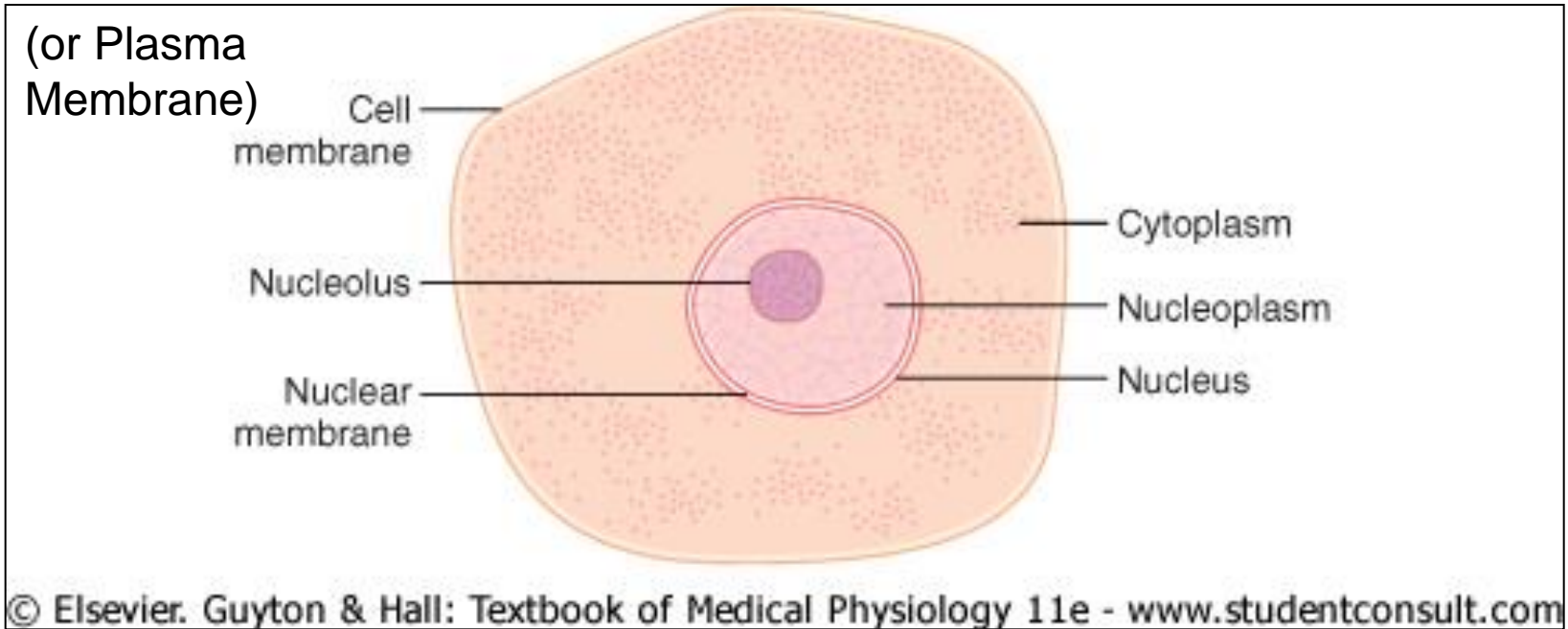
For instance, if the person in the aforementioned example were bled only 1 liter instead of 2, the normal negative feedback mechanisms for controlling cardiac output and arterial pressure would overbalance the positive feedback and the person would recover, as shown by the dashed curve of Fig. 1-3.

Positive feedback can sometimes be useful

- Example, blood clotting. When a blood vessel is ruptured and a clot begins to form, multiple enzymes called clotting factors are activated within the clot itself. Some of these enzymes act on other unactivated enzymes of the immediately adjacent blood, thus causing more blood clotting and the process continues until the hole in the vessel is plugged and bleeding no longer occurs.

-     On occasion, this process can form unwanted clots, which is in fact what explains most heart attacks, which are caused by a clot beginning on the inside surface of an atherosclerotic plaque in a coronary artery and then growing until the artery is blocked.

-   Childbirth is another example

--Chapter 2: the cell and its functions

Figure 2-1: Structure of the cell as seen with the light microscope.

(or Plasma Membrane)

Cell membrane

Nucleolus

Nuclear membrane

Cytoplasm

Nucleoplasm

Nucleus

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A typical cell, as seen by the light microscope, is shown in Fig. 2-1. Its two major parts are the nucleus and the cytoplasm. The nucleus is separated from the cytoplasm by the nuclear membrane and the cytoplasm is separated from the surrounding fluids by a cell membrane also called the plasma membrane.

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Components of the Cell (molecular)-1

- Ions. The ions provide inorganic chemicals for cellular reactions. Also, they are necessary for operation of some of the cellular control mechanisms. For instance, ions acting at the cell membrane are required for transmission of electrochemical impulses in nerve and muscle fibers.

- Proteins. These can be divided into two types—structural proteins and functional proteins.

-     Structural proteins are present in the cell mainly in the form of long filaments which themselves are polymers of many individual protein molecules. Example—microtubules within cells. Extracellularly- connective tissue of blood vessel walls, tendons, and ligaments.

Components of the Cell (molecular)-2

- Functional proteins: these proteins are for example the enzymes of the cell. Enzymes come into direct contact with other substances and thereby catalyze specific chemical reactions. For instance, the chemical reactions which split glucose to provide energy to the cell are all catalyzed by a series of protein enzymes.

- Lipids. Especially important lipids are phospholipids and cholesterol. These are significant because they are mainly insoluble in water and, therefore, are used to form the cell membrane and intracellular barriers that separate the different cell compartments.

- Triglycerides are used for energy storage.

Components of the Cell (molecular)-3

- Carbohydrates. Carbohydrates have some structural function in the cell as part of glycoprotein molecules, but they play a major role in nutrition of the cell. Carbohydrate in the form of dissolved glucose is always present in the surrounding extracellular fluid so that it is readily available to the cell.

- Also, a small amount of carbohydrate is virtually always stored in cells in the form of glycogen, which is an insoluble polymer of glucose that can be depolymerized and used rapidly to supply the cells' energy needs.

Physical structure of the cell: The cell contains highly organized physical structures called *intracellular organelles*.

Chromosomes and DNA

Centrioles

Secretory granule

Microtubules

Nuclear membrane

Golgi apparatus

Cell membrane

Nucleolus

Glycogen

Ribosomes

Lysosome

Mitochondrion

Granular endoplasmic reticulum

Smooth (agranular) endoplasmic reticulum

Microfilaments

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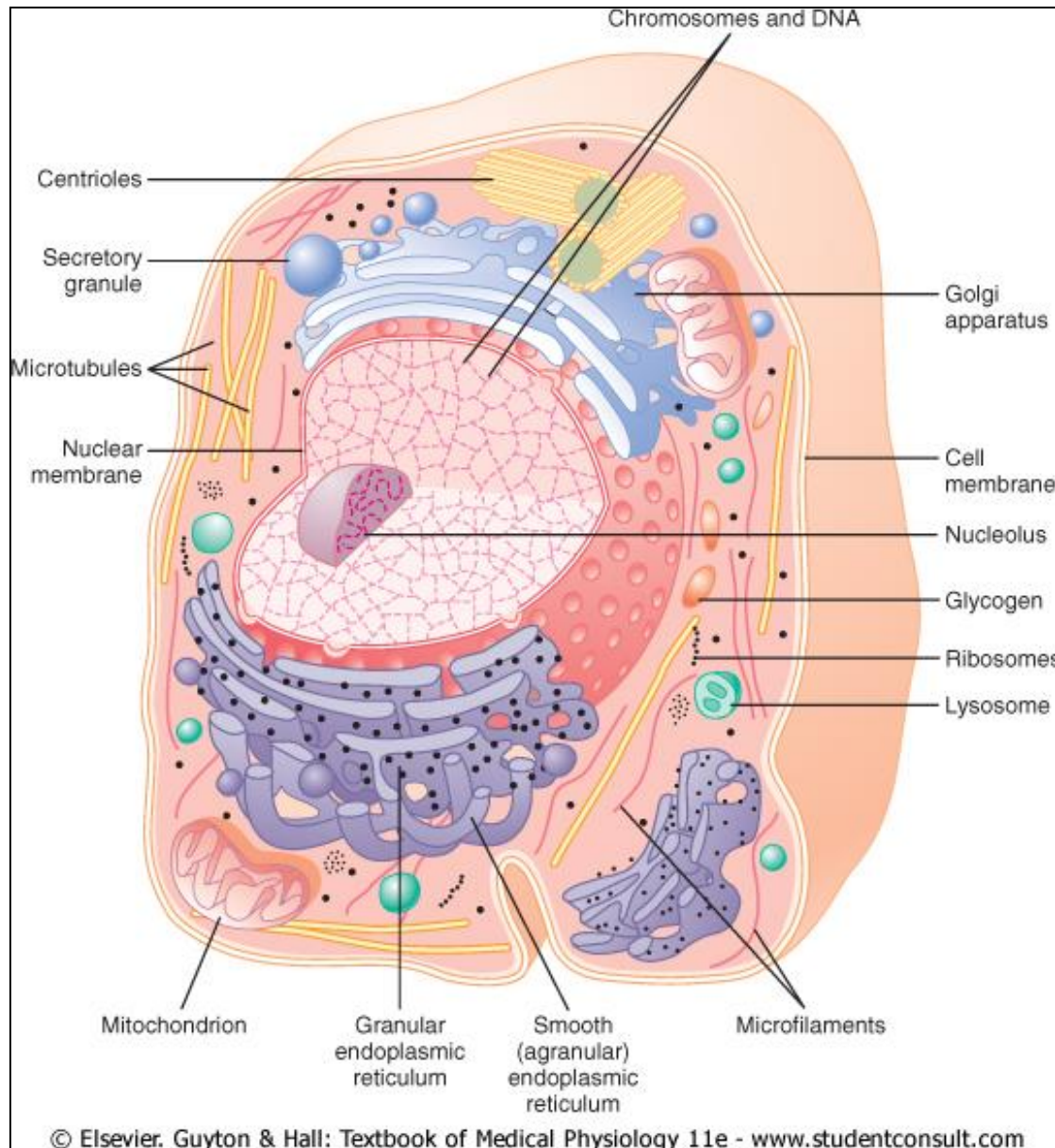
Figure 2-2: Cell Organelles

Nucleus: Chromosomes; Nucleolus; Nuclear membrane

Golgi Apparatus

Mitochondria

Endoplasmic Reticulum; rough and smooth

Ribosomes

Vesicles: Lysosomes, secretory granules

Filaments: Centrioles, microtubules, microfilaments

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Membranous structures of the cell

- Most organelles of the cell are covered by membranes composed primarily of lipids and proteins. The lipids of the membranes provide a barrier that impedes the movement of water and water-soluble substances from one cell compartment to another, because water is not soluble in lipids. However, protein molecules in the membrane often do penetrate all the way through the membrane, thus providing specialized pathways, often organized into actual pores, for passage of specific substances through the membrane.

- Cell membrane. Also called the plasma membrane. – this is a thin, pliable elastic structure only 7.5- 10 nanometers thick.
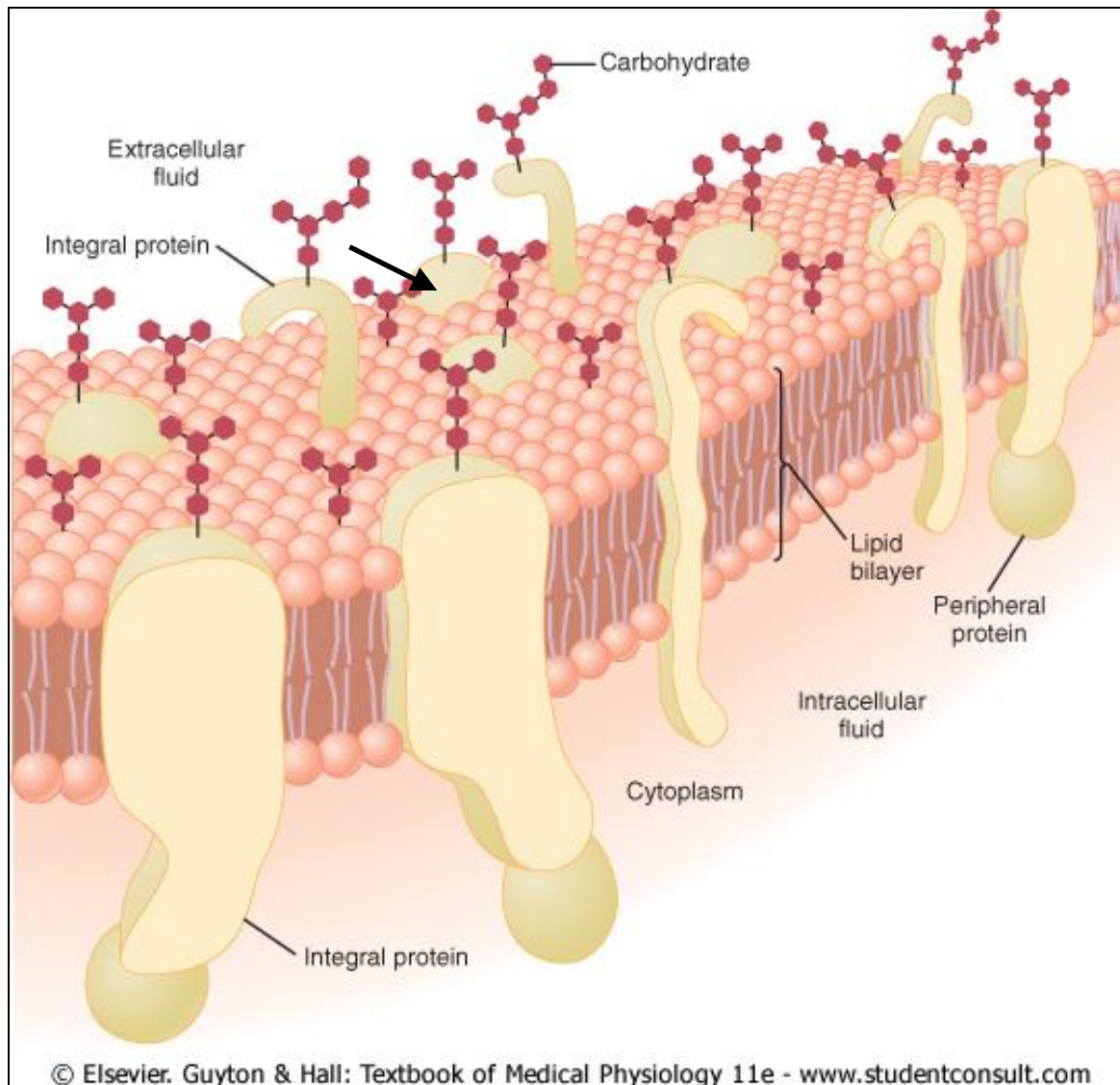
Lipid barrier of the cell membrane impedes water penetration. Figure 2-3 shows the structure of the cell membrane. Its basic structure is a lipid bilayer, which is a thin, double-layered film of lipids- each layer only one molecule thick- that is continuous over the entire cell surface. Interspersed in this lipid film are large globular protein molecules.

Figure 2-3: Cell membrane (Redrawn from Lodish HF, Rothman JE: The assembly of cell membranes. Sci Am 240:48, 1979. Copyright George V. Kevin.)

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Cell membrane-2

- The basic lipid bilayer is composed of phospholipid molecules. One end of each phospholipid molecule is soluble in water= hydrophilic. The other end is soluble only in fats= hydrophobic. Phosphate end=hydrophilic (why) and the fatty acid portion is hydrophobic.

- Like=like, so the two hydrophobic portions of the bilayer naturally tend to attach to one another in the middle of the membrane and the hydrophilic phosphate portions interact with the more aqueous environments outside and inside the cell to form the complete cell membrane.

- The lipid bilayer in the middle of the membrane is normally impermeable to the usual water-soluble substances, such as ions, glucose, and urea. Conversely, fat-soluble substances such as oxygen, carbon dioxide, and alcohol, can penetrate this portion of the membrane with ease.

Cell membrane proteins

- Two types of cell membrane proteins occur—integral proteins that protrude all the way through the membrane and peripheral proteins that are attached only to one surface of the membrane (either intracellular or extracellular) and do not penetrate all the way through.

- Many of the integral proteins provide structural channels (or pores) through which water molecules and water soluble substances, especially ions, can diffuse between the extracellular and intracellular fluids. These protein channels also have selective properties that allow preferential diffusion of some substances over others.

Cell membrane proteins-2

- Other integral proteins act as carrier proteins and others act as enzymes.

- Integral membrane proteins can also serve as receptors for water-soluble chemicals that do not easily penetrate the cell membrane. Interaction of cell membrane receptors with specific ligands that bind to the receptor causes conformational changes in the receptor protein.

- This in turn activates mechanisms leading to activation of second messengers, thereby relaying the signal from the extracellular part of the receptor to the interior of the cell.

Membrane carbohydrates

- Membrane carbohydrates occur almost invariably in combination with proteins or lipids in the form of **glyco**proteins or **glyco**lipids. The glycol portions of these molecules almost invariably protrude to the outside of the cell.

- Carbohydrate moieties attached to the outer surface of the cell have several important functions: 1) many of them have a negative electrical charge, which gives most cells an overall negative surface charge that repels other negative objects. 2) some carbohydrate moieties enter into immune reactions (more detail chapter 34).

Cytoplasm and its organelles

- The cytoplasm is filled with both minute and large dispersed particles and organelles.

- The clear fluid portion of the cytoplasm in which the particles are dispersed is called cytosol; this contains many dissolved proteins, electrolytes, and glucose.

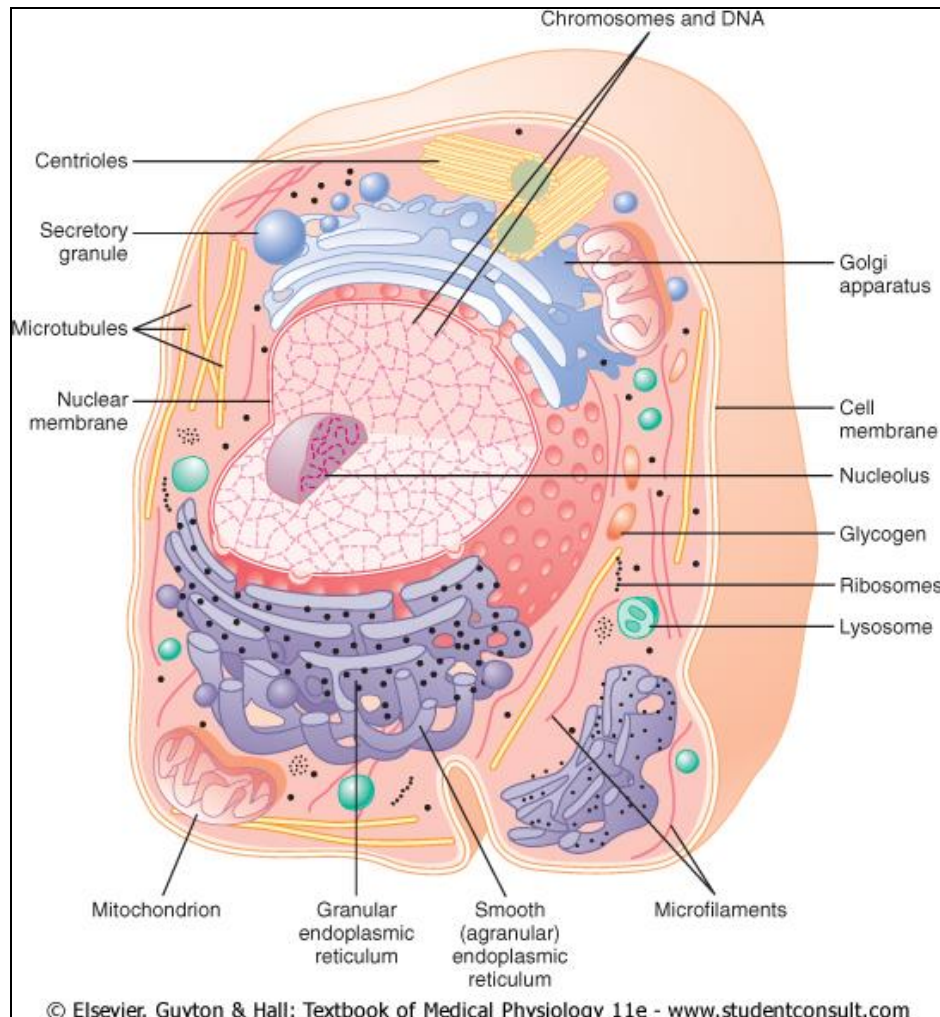# Cytoplasm and its organelles-Endoplasmic reticulum (ER)

Chromosomes and DNA

Centrioles

Secretory granule

Microtubules

Nuclear membrane

Golgi apparatus

Cell membrane

Nucleolus

Glycogen

Ribosomes

Lysosome

Mitochondrion

Granular endoplasmic reticulum

Smooth (agranular) endoplasmic reticulum

Microfilaments

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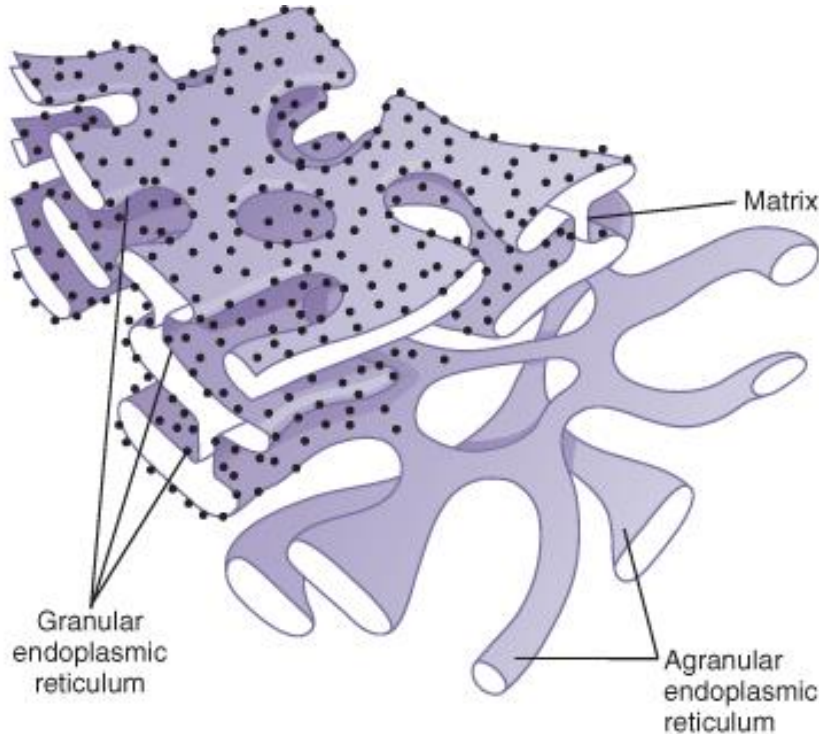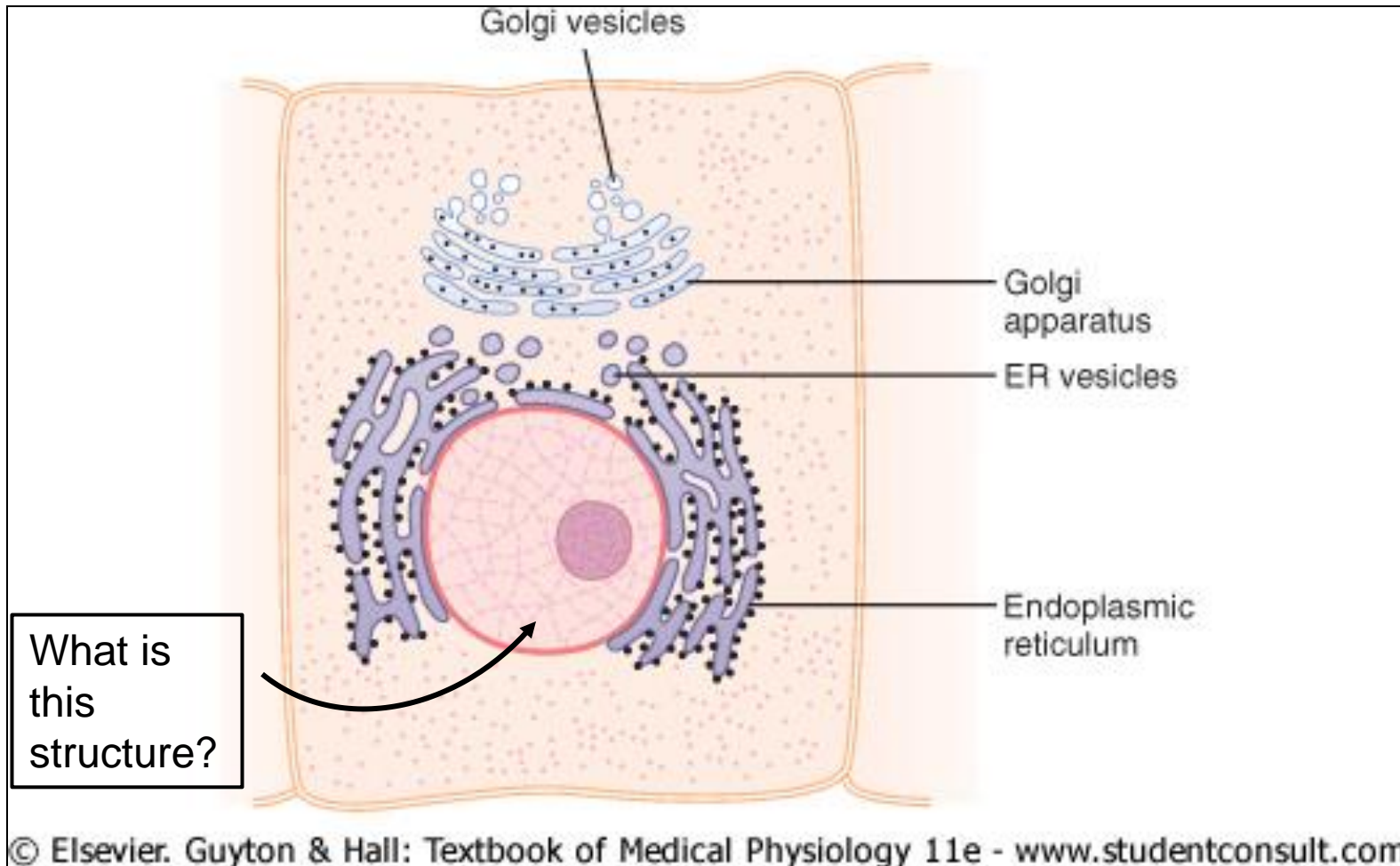
Figure 2-2 shows a network of tubular and flat vesicular structures in the cytoplasm which is known as the endoplasmic reticulum; the tubules and vesicles of the ER interconnect with one another. Electron micrographs show that the space inside the ER is *connected with* the space between the two membrane surfaces of the nuclear membrane. The vast surface area of the ER and the multiple enzyme systems attached to its membranes provide machinery for a major share of the metabolic functions of the cell.

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Ribosomes and the granular endoplasmic reticulum

Granular endoplasmic reticulum

Matrix

Agranular endoplasmic reticulum

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Attached to the outer surfaces of many parts of the ER are large numbers of minute granular particles called ribosomes. Where these are present, the ER is called the granular endoplasmic reticulum (fig. 2-4). The ribosomes are composed of a mixture of RNA and proteins, and they function to synthesize new protein molecules in the cell. Agranular or smooth ER (SER)= the part of the ER with no attached ribosomes. Functions for the synthesis of lipid substances.

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Golgi apparatus: Golgi as shown in fig. 2-5 is closely related to the ER, and has membranes similar to the SER. This organelle is prominent in secretory cells, where it is located on the side of the cell from which the secretory substances are extruded. The ER and Golgi communicate via transport vesicles which move from the ER to the Golgi

Golgi vesicles

Golgi apparatus

ER vesicles

Endoplasmic reticulum

What is this structure?

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Lysosomes

Chromosomes and DNA
Centrioles
Secretory granule
Microtubules
Nuclear membrane
Golgi apparatus
Cell membrane
Nucleolus
Glycogen
Ribosomes
Lysosome
Mitochondrion
Granular endoplasmic reticulum
Smooth (agranular) endoplasmic reticulum
Microfilaments

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Shown in fig. 2-2, are vesicular organelles that form by breaking off from the Golgi apparatus and then dispersing throughout the cytoplasm. Lysosomes provide an intracellular digestive system that allows cells to digest 1) damaged cellular structures 2) food particles that have been ingested by the cell and 3) unwanted matter such as bacteria. Lysosomes are usually 250-750 nm in diameter. It is surrounded by a typical lipid bilayer and is filled with large numbers of small granules 5 to 8 nm in diameter, which are protein aggregates of as many as 40 different hydrolase (digestive) enzymes. A hydrolytic enzyme is capable of splitting an organic compound into two or more parts by combining hydrogen from a water molecule with one part of the compound and combining the hydroxyl portion of the water molecule with the other part of the compound. For instance, protein is hydrolyzed to form amino acids, glycogen hydrolyzed to form glucose, and lipids are hydrolyzed to form fatty acids and glycerol.

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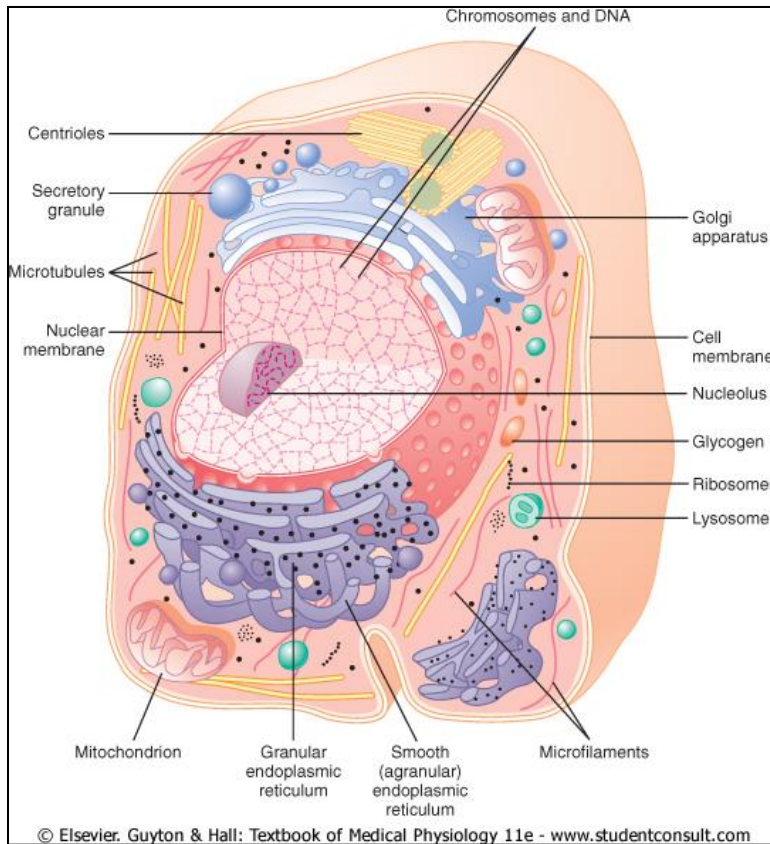
Peroxisomes

- -are similar physically to lysosomes but are believed to be formed by self-replication (or perhaps by budding off from the smooth ER rather than from the Golgi). Also different than lysosomes, peroxisomes contain oxidases rather than hydrolases. These enzymes are capable of combining oxygen with hydrogen ions derived from different intracellular chemicals to form hydrogen peroxide (H_2O_2). Hydrogen peroxide is a highly oxidizing substance and is used in association with catalase, another oxidase enzyme present in large quantities in peroxisomes, to oxidize many substances that might otherwise be poisonous to the cell. For example, about half of the alcohol a person drinks is detoxified by the peroxisomes of the liver cells in this manner.
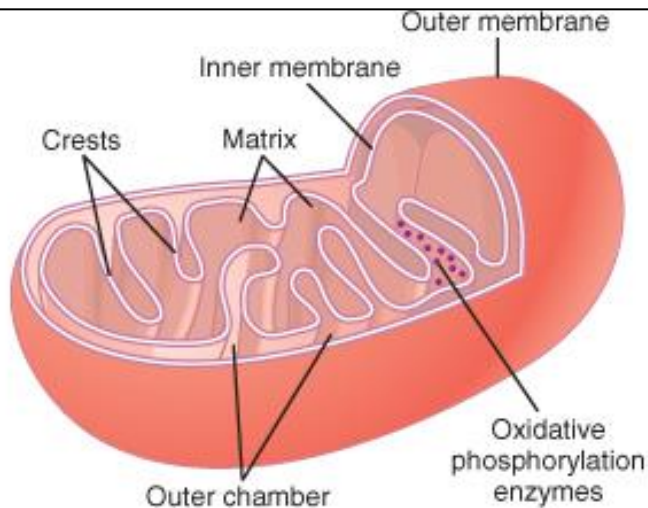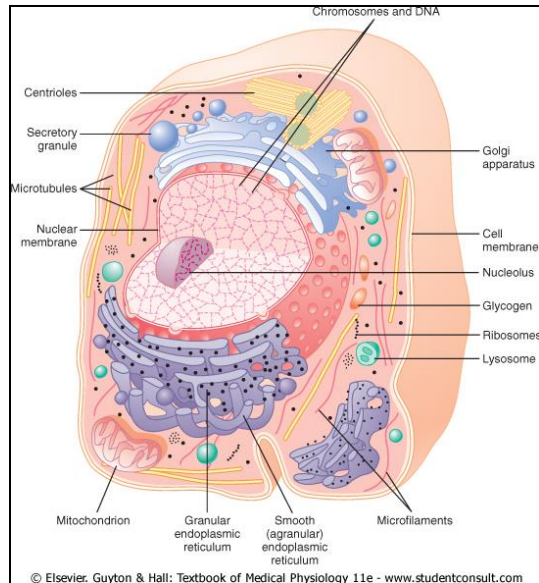
Secretory vesicles

Secretory granules
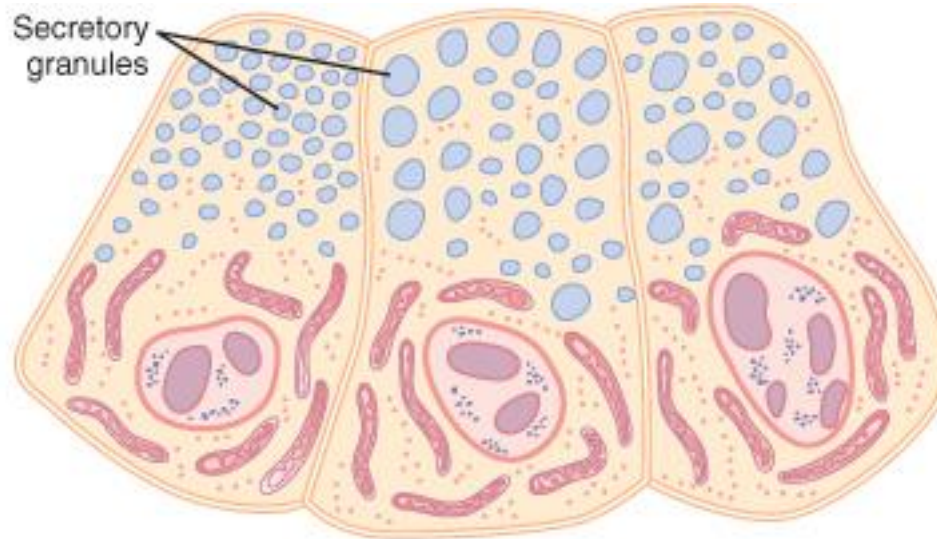
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An important function of many cells is secretion of special chemical substances. Almost all such secretory substances are formed by the ER-Golgi apparatus system and are then released from the Golgi apparatus into the cytoplasm in the form of storage vesicles called secretory vesicles or secretory granules. Fig. 2-6 shows typical secretory vesicles inside pancreatic acinar cells; these vesicles store protein proenzymes (enzymes that are not yet activated). The proenzymes are secreted later through the outer cell membrane into the pancreatic duct and become activated and perform digestive functions on food in the intestinal tract. (note the polarization of the secretory cells with vesicles facing the direction of secretion).
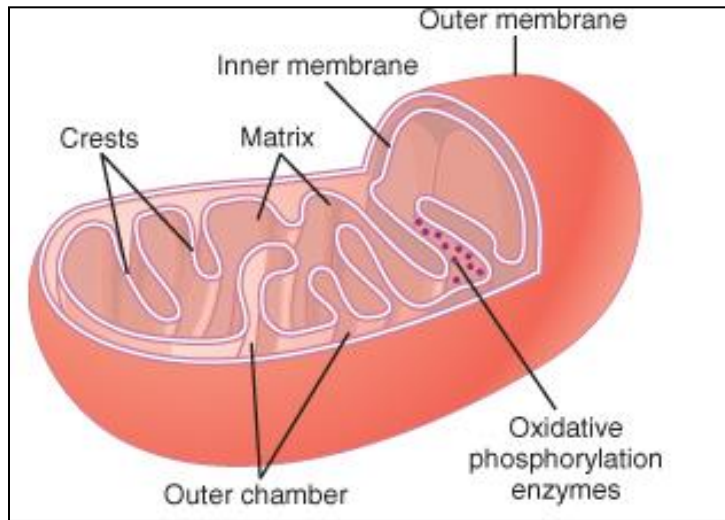
Mitochondria

Called the powerhouses of the cell, shown in fig. 2.2 and 2-7. Without mitochondria, cells would be unable to extract enough energy from nutrients taken in, and essentially all cellular functions would cease.

Mitochondria are present in all areas of each cell's cytoplasm, but the total number per cell varies from less than a hundred up to several thousand, depending on the amount of energy required by the cell. Mitochondria are also concentrated in those portions of the cell responsible for the major share of its energy metabolism. They are also variable in size and shape and *have recently been shown to fuse and split as well*. Some mitochondria are only a few hundred nanometers in diameter and globular in shape, whereas others are elongated, as large as 1 micrometer in diameter and 7 microns (micrometers) long; still others are branching and filamentous.

Chromosomes and DNA
Centrioles
Secretory granule
Microtubules
Nuclear membrane
Mitochondrion
Granular endoplasmic reticulum
Smooth (agranular) endoplasmic reticulum
Microfilaments
Golgi apparatus
Cell membrane
Nucleolus
Glycogen
Ribosomes
Lysosome

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Outer membrane
Inner membrane
Crests
Matrix
Outer chamber
Oxidative phosphorylation enzymes

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Mitochondria-2

Basic structure of the mitochondrion is shown in fig. 2-7. It is composed of two lipid bilayer-protein membranes: an outer membrane and an inner membrane. Many infoldings of the inner membrane form shelves onto which oxidative enzymes are attached (how do infoldings help?). the inner cavity of mitochondria is filled with a matrix that contains large quantities of dissolved enzymes that are necessary for extracting energy from nutrients. These enzymes operate with the oxidative enzymes on the shelves to cause oxidation of the nutrients, thereby forming carbon dioxide and water and releasing energy. The liberated energy is used to synthesize a high-energy substance called adenosine triphosphate (ATP). ATP is then transported out of the mitochondrion, and it diffuses throughout the cell to release its energy wherever it is needed for performing cellular functions—in this way ATP may be called the "energy currency" of the cell.

Mitochondria are self-replicative- thus one mitochondrion can form a second one, a third one, and so on, whenever there is a need in the cell for increased amounts of ATP. In fact, mitochondria contain their own DNA, and thus the DNA of the mitochondrion is involved in replication of the mitochondrion itself.

# Filament and tubular structures of the cell
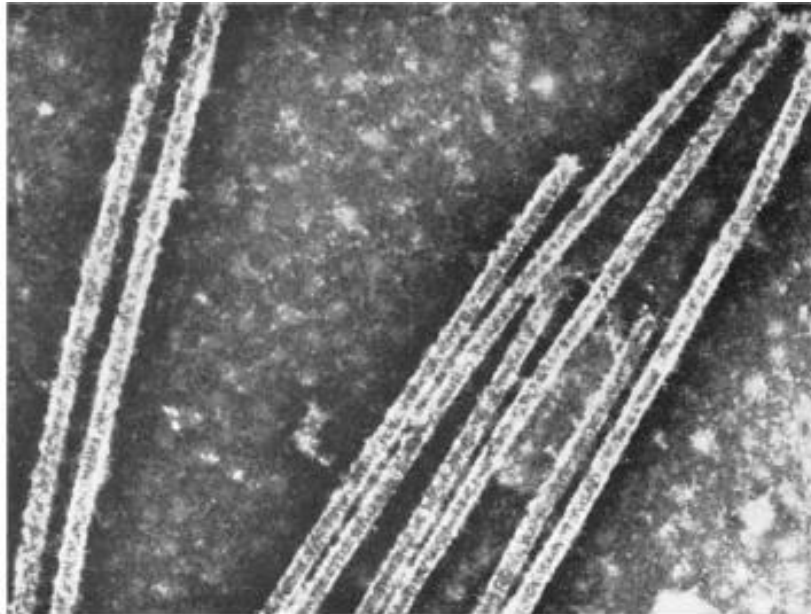
- The fibrillar proteins of the cell are usually organized into filaments or tubules. For example in muscle cells, actin and myosin filaments are organized into a special contractile machine that is the basis for muscle contraction.

  A special type of stiff filament composed of polymerized tubulin molecules is used in all cells to construct very strong tubular structures, the microtubules. Shown in fig. 2-8 are typical microtubules that were teased from the flagellum of a sperm.

  Thus a primary function of microtubules is to act as a cytoskeleton, providing rigid physical structures for certain parts of cells.

Nucleus
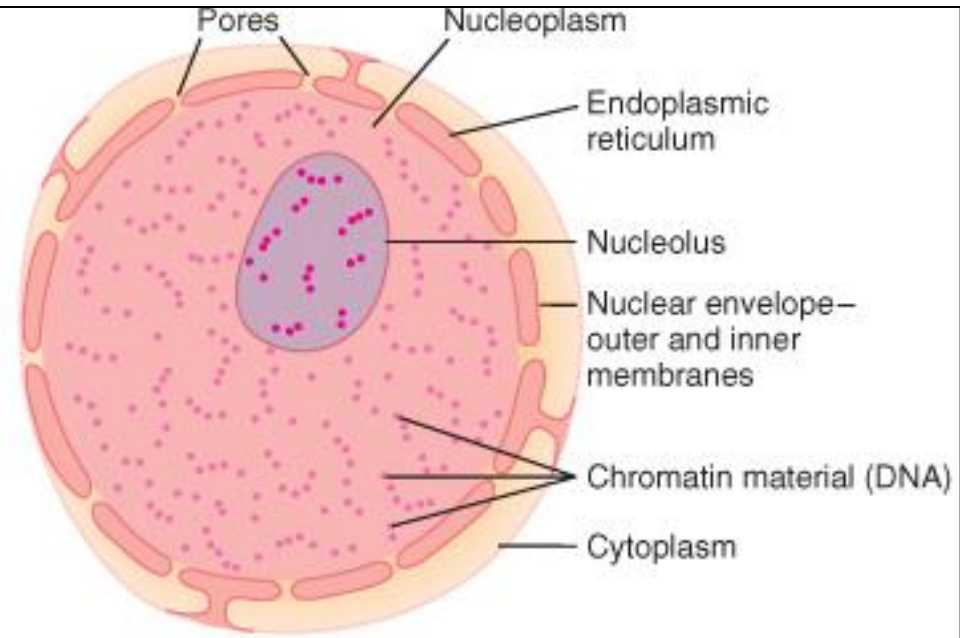
- The nucleus is the control center of the cell. It contains large quantities of DNA, which are the genes. Fig. 2-9 schematically shows the light microscope appearance of the interphase nucleus (during the period between mitoses), revealing darkly staining chromatin material throughout the nucleoplasm.

- The nuclear membrane, also called the nuclear envelope, is actually two separate bilayer membranes, one inside the other. The outer membrane is continuous with the endoplasmic reticulum of the cell cytoplasm, and the space between the two nuclear membranes is also continuous with the space inside the endoplasmic reticulum as shown in Fig. 2-9.

- The nuclear membrane is penetrated by several thousand nuclear pores. Large complexes of protein molecules are attached at the edges of the pores so that the central area of each pore is only about 9 nanometers in diameter. Even this small size is large enough to allow molecules up to 44,000 molecular weight to pass through with reasonable ease.

Nucleoli and formation of ribosomes

- The nuclei of most cells contain one or more highly staining structures called nucleoli. The nucleolus does not have a limiting membrane, instead it is simply an accumulation of large amounts of RNA and proteins of the types found in ribosomes. The nucleolus becomes considerably enlarged when the cell is actively synthesizing proteins.

A study in scale- from virus to cell:

15 nm — Small virus
150 nm — Large virus
350 nm — Rickettsia
1 µm   Bacterium
Cell
5 – 10 µm +
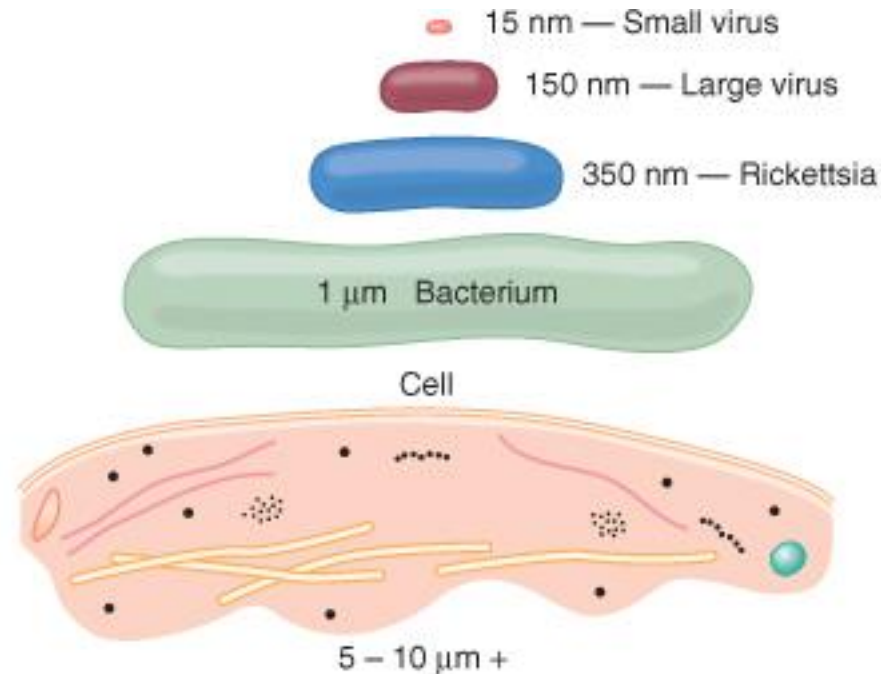
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Figure 2-10. the cell has a diameter about 1000 times that of the smallest virus, and therefore, a volume about 1 billion times that of the smallest virus. Thus the functions and anatomical organization of the cell are far more complex than those of the virus.

The virus is a living structure (book).

Functional systems of the cell Ingestion by the cell- endocytosis

- Cells must obtain nutrients from the surrounding fluids so that they can live, grow, and reproduce. Most substances pass through the cell membrane by diffusion and active transport.
- Diffusion involves simple movement through the membrane caused by the random motion of the molecules of the substance; substances move either through cell membrane pores or in the case of lipid soluble substances, through the lipid matrix of the membrane.
- Active transport involves the actual carrying of a substance through the membrane by a physical protein structure that penetrates all the way through the membrane (remember integral and peripheral membrane proteins)--.

Endocytosis-2

- Very large particles enter the cell by a specialized function of the cell membrane called endocytosis, the principal forms of which are pinocytosis and phagocytosis. Pinocytosis= ingestion of minute particles that form vesicles of extracellular fluid and particulate constituents inside the cell cytoplasm. Phagocytosis= ingestion of large particles such as bacteria, whole cells, or portions of degenerating tissue

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- Pinocytosis occurs continually in the cell membranes of most cells, but it is especially rapid in some cells such as macrophages, where about 3% of the total macrophage membrane is engulfed in the form of vesicles each minute. Pinocytosis is the only means by which most large macromolecules such as most protein molecules, can enter cells. Figure 2-11 in book shows the process of pinocytosis. –(Next slide)

Pinocytosis

Proteins   Receptors

Coated pit

Clathrin

A

B

Actin and myosin

Dissolving clathrin

C

D
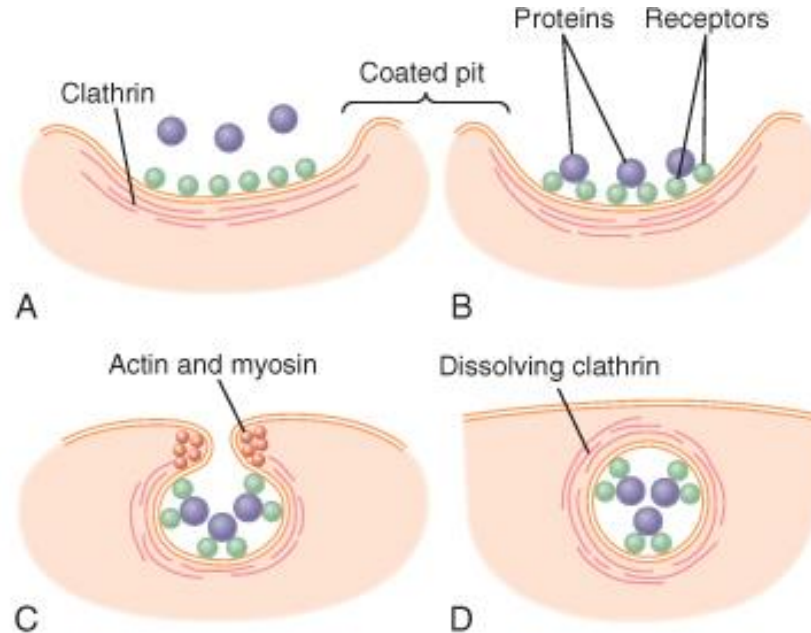
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What causes the cell membrane to go through the necessary contortions to form pinocytotic vesicles remains mainly a mystery. We do know that the process requires energy from within the cell in the form of ATP. Also, it requires the presence of calcium ions in the extracellular fluid, which probably react with contractile protein filaments beneath the coated pits to provide the force for pinching the vesicles away from the cell membrane (fig. 2-11).

Phagocytosis

- Occurs much in the same way as pinocytosis, but involves large particles rather than molecules (is a protein a particle or a molecule?). only certain cells have the ability for phagocytosis, most notably macrophages and some white blood cells.

- Phagocytosis is initiated when a particle such as a bacterium, a dead cell, or tissue debris binds with receptors on the surface of a phagocyte. In the case of bacteria, each bacterium is usually already attached to a specific antibody, and it is the antibody that attaches to the phagocyte receptors.

Digestion of pinocytotic and phagocytic foreign substances inside the cell- function of the lysosomes.

- Lysosomes
- Pinocytotic or phagocytic vesicle
- Digestive vesicle
- Residual body
- Excretion
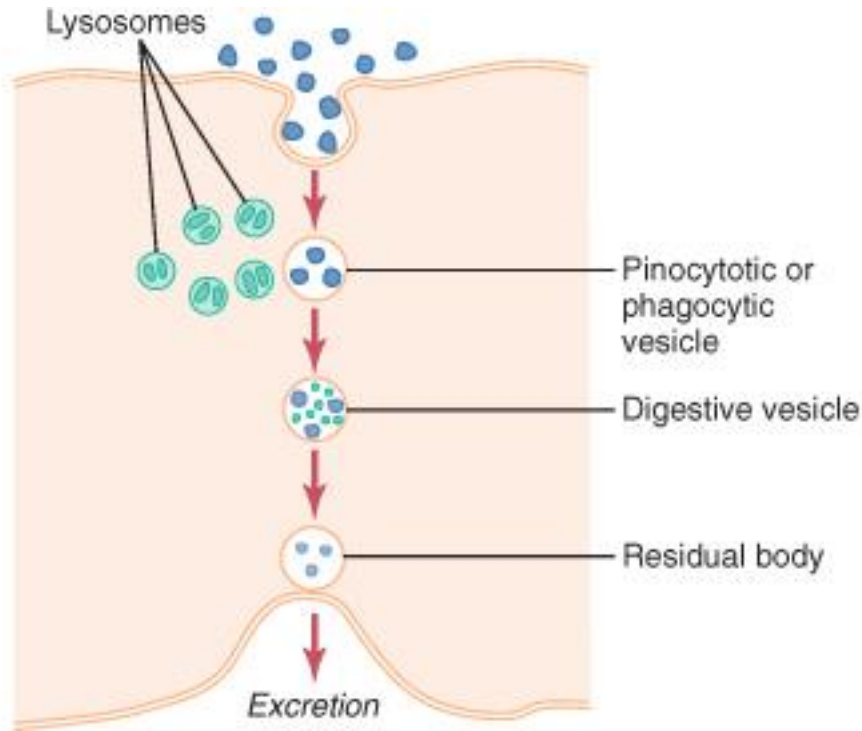
- Almost immediately after a pinocytotic or phagocytic vesicle appears inside a cell, one or more lysosomes become attached to the vesicle and empty their acid hydrolases to the inside of the vesicle (fig. 2-12). Components in the vesicle are digested and in most cases, indigestible substances are excreted through the cell membrane by a process called exocytosis, which is essentially the opposite of endocytosis.

Regression of tissues and autolysis of cells

- Tissues of the body often regress to a smaller size. For instance, this occurs in the uterus after pregnancy, in muscles during long periods of inactivity, and in the mammary glands at the end of lactation. Lysosomes are responsible for much of this regression, but the mechanism by which this process is initiated is unknown.

- Another special role of lysosomes is removal of damaged cells or damaged portions of cells caused by some type of trauma: heat, cold, physical trauma, chemicals, or other factors- these cause lysosomes to rupture. The hydrolases released from the ruptured lysosomes immediately begin to digest the surrounding organic substances; if the damage is severe, the entire cell is digested, a process called autolysis. In this way the cell is completely removed, and a new cell ordinarily is formed by mitotic reproduction of an adjacent cell to take the place of the old one.

- The lysosomes also contain bactericidal agents that can kill phagocytized bacteria before they can cause cellular damage.

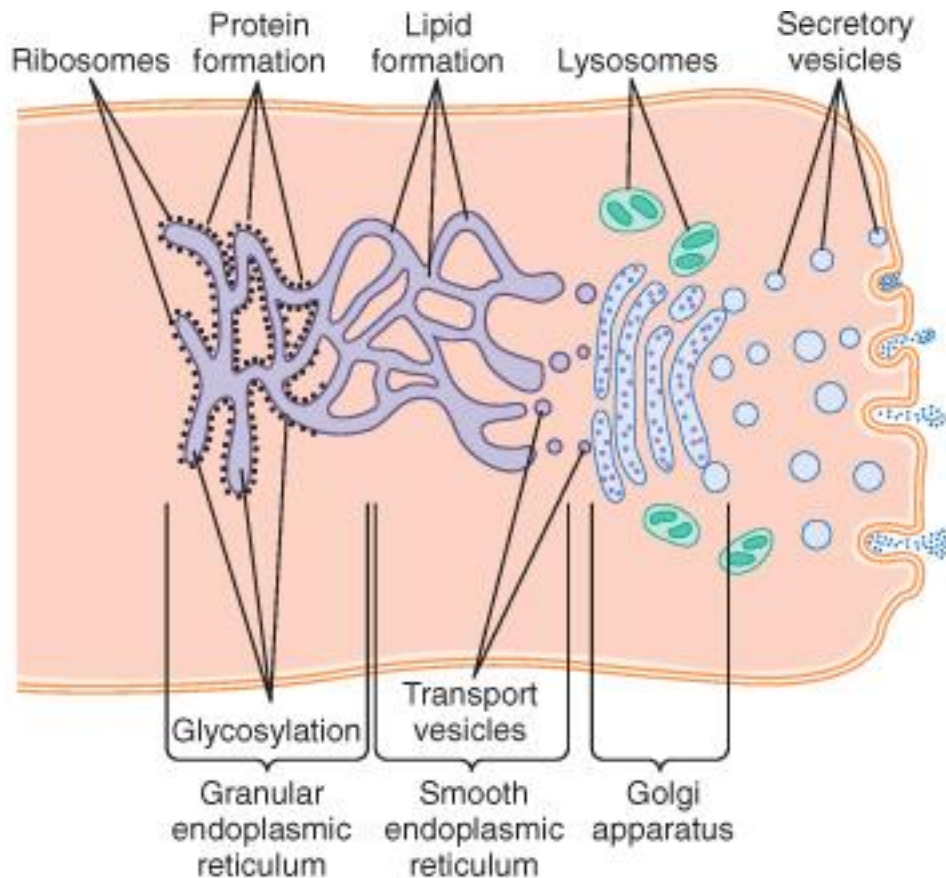# Synthesis and formation of cellular structures by ER and Golgi apparatus

- Proteins are formed by the granular endoplasmic reticulum.
- The granular portion of the ER (Rough ER) is characterized by large numbers of ribosomes attached to the outer surfaces of the ER membrane. Protein molecules are synthesized within the structures of the ribosomes. The ribosome extrude some of the synthesized protein molecules directly into the cytosol, but they also extrude many more through the wall of the ER to the interior of the ER into the ER matrix.

Synthesis of Lipids is by the smooth endoplasmic reticulum (SER).

--Synthesis of lipids, especially phospholipids and cholesterol occurs in the SER. After synthesis, the lipids are rapidly incorporated into the lipid bilayer of the ER itself, thus causing the ER to grow more extensive.
--To keep the size of the ER from growing beyond the needs of the cell, small vesicles called ER vesicles or transport vesicles continually break away from the SER; most of these vesicles then migrate to the Golgi apparatus.

Specific functions of the Golgi Apparatus

Ribosomes | Protein formation | Lipid formation | Lysosomes | Secretory vesicles

Glycosylation | Transport vesicles

Granular endoplasmic reticulum | Smooth endoplasmic reticulum | Golgi apparatus

- Although the major function of the Golgi apparatus is to provide additional processing of substances already formed in the ER, it also has the capability of synthesizing certain carbohydrates that cannot be formed in the ER.

‣ Processing of ER secretions by the Golgi Apparatus—Figure 2-13.

End!