CONCISE TEXT OF HISTOLOGY

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Preface

The reader of this text undoubtedly will be struck by its format, which departs rather considerably from that of the usual text books of histology. Overall, the text follows the traditional and logical sequence of cells to tissues to organs, but within this sequence we have elected to place the chapters on the eye and ear immediately following the coverage of nerve tissue, rather than at the end of the text. This seems a more logical arrangement since these two structures essentially are specialized nerve receptors. Similarly, it has seemed more appropriate to consider mitosis with the cell and meiosis with the reproductive organs.

However, the most obvious changes are in the organization of the material within each chapter. Here the subject matter has been broken down into smaller units, each of which is introduced by a list of key words appropriate to that unit. The key words are designed to introduce terminology and are emphasized in the text by **boldface** type; they also serve as a summary of the topic and provide a means for rapid review. Where it has been felt desirable and useful, the textual material is reinforced by line drawings. Although function is discussed and related to structure within each unit, the two again are reviewed in the functional summaries at the end of each chapter.

A second obvious departure from the usual format occurs in the treatment of the illustrative material. Rather than scattering photographs throughout the text to illustrate one or two points of description, the photographs have been collected and presented at the end of each chapter. This arrangement has allowed us to make best use of the illustrations to provide a systematic and complete pictorial review of the material already covered in narrative form and to integrate light, scanning and electron microscopy into a comprehensive study of histological structure. Although we have tried to present material of high quality, we have not searched for the ideal but have rather attempted to depict that which the student will ordinarily encounter in the usual sections. We also have used black and white illustrations rather than color. The latter, while pretty, actually present no advantage in depicting histological detail and tend to encourage the student to use color rather than form in making a histological assessment of structural details.

During preparation of the text, we have been guided by three major considerations—that most curricula place considerable constraints of time on the student, that function and structure are inextricably related and that the learning process essentially is a matter of repetition and reinforcement. We believe that the format of this text meets these criteria and, we hope, presents the vast material of histology in a concise and logical manner, without sacrificing the detail that is necessary for an understanding of the microscopic structure of the body.

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chapter 1

The Cell

Multicellular organisms are composed of two distinct structural elements: cells and those products of cells that form the intercellular substances. Cells are the fundamental units of living material and show a variety of functional specializations that are necessary for the survival of the organism. Each cell is a distinct entity, contains all the machinery for independent existence and is separated from its external environment by a limiting membrane.

PROTOPLASM

KEY WORDS—protein, carbohydrate, lipid, nucleic acids, inorganic materials, water

The living substance of a cell, the protoplasm, consists of protein, carbohydrate, lipid, nucleic acids and inorganic materials, dispersed in water to form a complex, semifluid gel. The consistency of protoplasm varies in different cells and within a cell, may change from a viscous to a more fluid state.

Protein, alone or in combination with lipid or carbohydrate, forms the major structural component of the cell and the intercellular substances. Enzymes and many hormones are proteins. The major **carbohydrates** are glucose, which provides the chief source of energy in mammalian cells, and glycogen, the storage form of glucose. Complexes of carbohydrates and proteins form the main constituents of the intercellular substances that bind cells together. Other carbohydrate-protein complexes form some enzymes and antibodies. **Lipids** not only serve as an energy source but also have important structural functions and are major components of the membrane systems of cells.

Two classes of **nucleic acids** can be distinguished. Deoxyribonucleic acid is found mainly in the nucleus where it forms the genetic material, whereas ribonucleic acid is present both in the nucleus and the cytoplasm. Ribonucleic acid carries information from the nucleus to the cytoplasm and serves as a template for the synthesis of proteins by the cell.

The **inorganic materials** are as much an integral component of protoplasm as are proteins, carbohydrates and lipids; without them physiological processes are impossible. Among the inorganic constituents are: calcium, potassium, sodium and magnesium in the form of carbonates, chlorides, phosphates and sulfates; small quantities of iron, copper and iodine; trace elements such as cobalt, manganese, zinc and other metals. The inorganic constituents have many diverse functions. Maintenance of intracellular and extracellular osmotic pressures, transmission of nerve impulses, contraction of muscle, adhesiveness of cells, activation of enzymes, transport of oxygen, and the rigidity of tissues such as bone—all depend upon the presence of inorganic materials.

Water makes up about 75% of protoplasm. Part of the water content is free and available as a solvent for various metabolic processes and part is bound to protein.

Properties of Protoplasm

KEY WORDS—irritability, conductivity, contractility, absorption, metabolism, secretion and excretion, growth and reproduction

Protoplasm is characterized by a number of physiological properties that distinguish it from inanimate material. All living cells show these properties, but in some cells a particular property may be emphasized.

Irritability is a fundamental property of all

living cells and refers to their ability to respond to a stimulus.

Conductivity refers to the ability of a cell to transmit a stimulus from the point of origin to another point on the cell surface. Conductivity also is a property of all cells but, like irritability, shows its greatest development in nerve tissue.

Contractility is the ability of a cell to change its shape in response to a stimulus and generally is manifested by a shortening of the cell in some direction. This property is especially prominent in muscle.

Absorption involves the transfer of materials across the cell membrane into the interior of the cell where it may be utilized or dealt with in some other manner. All cells show the ability to absorb materials, some very selectively.

Metabolism refers to the ability of the cell to break down absorbed materials and produce energy.

Secretion is the process by which the cell extrudes useful materials and liberates them for use elsewhere. **Excretion** on the other hand, is the elimination from the cell of the waste products of metabolism.

Growth and reproduction. Growth of an organism can occur as the result of an increase in the amount of protoplasm in existing cells or from an increase in the number of cells. There are limits to the size a cell can attain without sacrificing the efficiency with which nutrients and oxygen reach the interior of the cell. Beyond the maximum size, an increase in the amount of protoplasm is brought about by cell division.

ORGANIZATION OF CELLS

KEY WORDS—cytoplasm, nucleus, nuclear envelope, plasmalemma (cell membrane), organelles, inclusions, cytoplasmic matrix (hyaloplasm), karyolymph

Although cells differ in size, shape and function, the protoplasm of each cell consists of two major components: the **nucleus** and the **cytoplasm**. The nucleus contains the hereditary or genetic material and is completely surrounded by cytoplasm, from which it is separated by a **nuclear envelope**. The cytoplasm is limited by the **plasmalemma (cell membrane)** which separates the cell from the external environment. Contained within the cytoplasm are a number of structures that may be classified either as organelles or as inclusions. **Organelles** are highly organized, living structural units of the cytoplasm which perform specific functions in the cell. In contrast, **inclusions** generally represent cell products or metabolites that often are transitory in nature. The majority, but not all, of the organelles are membranous structures whose size and concentration varies in different cell types and with the activity of the cell. The different organelles tend to be localized within discrete areas of the cytoplasm so that they and the metabolic process associated with them remain separated from other components of the cell.

The organelles and inclusions of the cytoplasm are suspended in an amorphous medium called the **cytoplasmic matrix (hyaloplasm)**. Within the nucleus, the nuclear material also is suspended in a structureless ground material that has been called **karyolymph**. Other than differences in their locations, the karyolymph and hyaloplasm appear to be equivalent.

Cytoplasmic Organelles

Organelles are those specialized units of the cell that have the capacity to perform specific functions and therefore constitute part of the living substance of a cell. Included as organelles are cytoplasmic structures such as plasmalemma (cell membrane), granular and agranular forms of endoplasmic reticulum, ribosomes, the Golgi complex, mitochondria, lysosomes, peroxisomes, filaments, microtubules and centrioles. Many organelles are limited by membranes similar in structure to that which forms the boundary of the cell itself. These membranes, including the cell membrane, are metabolically active sheets that are essential to the life of the cell. In electron micrographs the membranes show a trilaminar structure consisting of inner and outer dense lines separated by a light zone. Because this trilaminar structure is representative of all biological membranes of a cell, it has been called a unit membrane. The unit membrane differs in thickness in different organelles and generally is greatest where it forms the plasmalemma. It must be empha-

sized, however, that although the membranes appear to show only minor variations from organelle to organelle, they may vary considerably in chemical composition, enzymatic properties and functions.

Plasmalemma (Cell Membrane)

KEY WORDS—unit membrane, phospholipid bilayer, intrinsic protein, glycocalyx, phagocytosis, pinocytosis, micropinocytosis, exocytosis

The membrane that encloses each cell, the plasmalemma or cell membrane, (Fig. 1–1) measures about 8 to 10 nm in thickness and shows the typical trilaminar appearance of the **unit membrane**. It appears as two dense lines, each approximately 3 nm in width, separated by a clear zone 2 to 4 nm wide. The cell membrane is composed primarily of proteins, lipids and carbohydrates; the lipids are mainly in the form of phospholipid with some neutral fat and cholesterol-like substances. Structurally, the cell membrane is thought to consist of a **phospholipid bilayer** in which the hydrocarbon chains are oriented inward and the polar groups are directed outward. **Intrinsic proteins** within the phospholipid bilayer may extend through the full thickness of the membrane and function as sites for transmembrane transport or may lie only partially within the bilipid layer. Other proteins are thought to be present on the external surface, which also may be coated by a polysaccharide material that forms the **glycocalyx**. This coat varies in thickness, depending upon the type of cell with which it is associated.

The cell membrane shows selective permeability and plays an active role in bringing material into the cell or discharging it from the cell. Particulate matter is taken in by the process of **phagocytosis**; the cytoplasm flows around the exogenous material, the cell membranes fuse and the material is brought into the cell in a membrane-bound vacuole. In a similar fashion, fluid may be incorporated into the cell in small cytoplasmic vesicles, and this process has been called **pinocytosis**. Both phagocytosis and pinocytosis can be observed with the light microscope. Some materials may enter the cell in even smaller vesicles that are formed by minute invaginations of the cell surface. This process, visible only with the electron microscope, has been referred to as **micropinocytosis**.

Secretory granules are discharged from the cell by **exocytosis**, a process in which the limiting membranes of the secretory granules fuse with the plasmalemma prior to the discharge of the secretory material.

Endoplasmic Reticulum

KEY WORDS—tubules, cisternae, granular endoplasmic reticulum, ribosomes, smooth endoplasmic reticulum

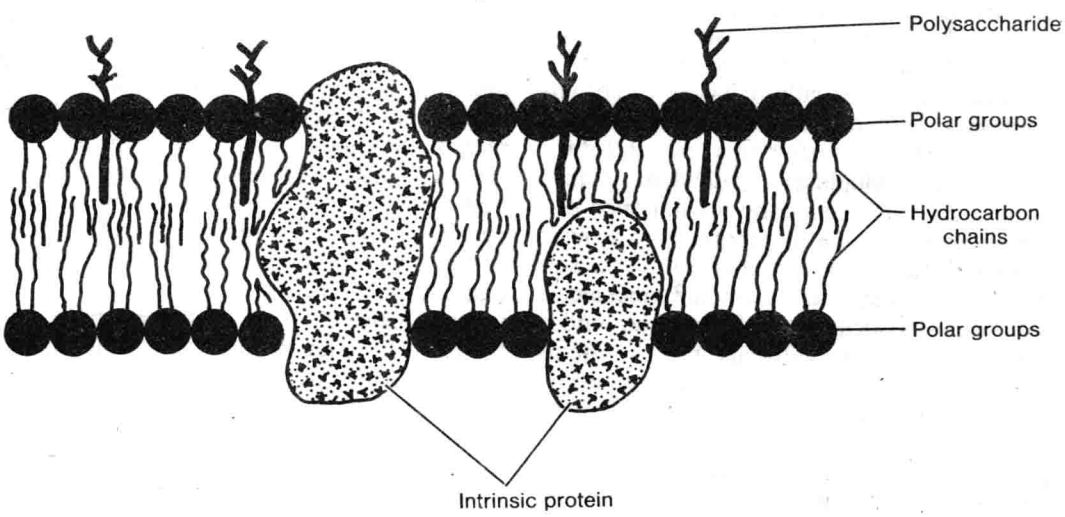

Figure 1-1 Diagrammatic representation of the structure of the plasmalemma.

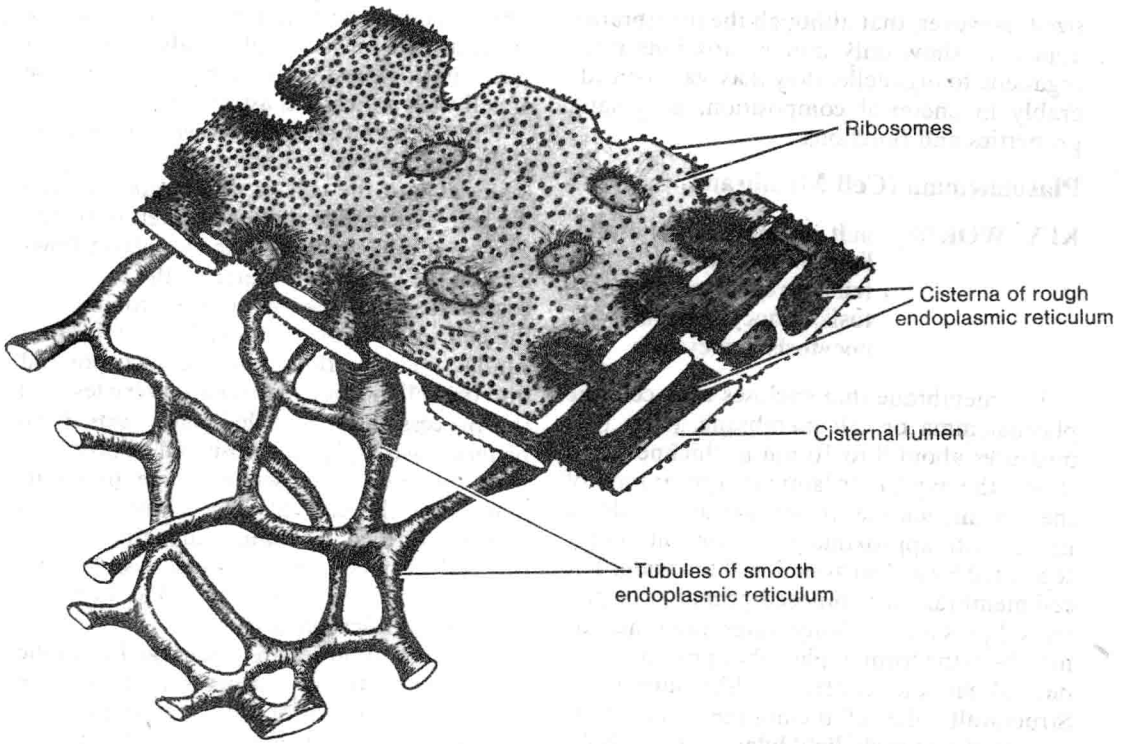

Figure 1-2 Smooth and rough endoplasmic reticulum.

The cytoplasm of nearly all cells contains a continuous, irregular network of membrane bound channels called the endoplasmic reticulum (Fig. 1–2). Typically, this organelle appears as anastomosing **tubular structures**, but the membranes also form parallel, flattened saccules known as **cisternae**. Small vesicles, not attached to tubules or cisternae, may be present also and are considered to be part of the endoplasmic reticulum. Two types of endoplasmic reticulum can be distinguished, a rough or granular form and a smooth form.

Granular endoplasmic reticulum (GER) usually consists of an array of flattened cisternae bounded by a membrane whose outer surface is studded with numerous particles of ribonucleoprotein that form the **ribosomes**. Ribosomes associated with granular endoplasmic reticulum synthesize those proteins that, for the most part, are to be secreted by the cell. The proteins are synthesized on the external surfaces of the rough endoplasmic reticulum, then cross the membrane of the reticulum to enter its lumen, where they are isolated from the surrounding cytoplasm.

Smooth endoplasmic reticulum is so named because it lacks associated ribosomes. It consists primarily of a system of interconnecting tubules and generally lacks cisternae.

In most cells, one form of endoplasmic reticulum usually predominates. Protein secreting cells such as the pancreatic acinar cells and plasma cells are characterized by an abundance of granular endoplasmic reticulum, whereas in cells that secrete steroid hormones, the smooth or agranular type predominates. In still other cells, such as liver cells, both types of endoplasmic reticulum are present in nearly equal amounts and may be continuous. Although the granular form of endoplasmic reticulum is known to be involved in the synthesis of protein materials, the exact function or functions of the smooth endoplasmic reticulum remains obscure. It has been implicated in different functions in different cells: synthesis of steroid hormones in certain endocrine cells, detoxification of drugs by the liver, metabolism of lipid and

cholesterol. It also is implicated in the release and recapture of calcium ions during the contraction and relaxation of striated muscle.

Ribosomes

KEY WORDS—**ribonucleoprotein, free ribosomes, polyribosomes (polysomes), messenger RNA, protein synthesis, transfer RNA**

Ribosomes are small, uniformly sized particles of **ribonucleoprotein**, measuring between 12 and 15 nm in diameter and composed of large and small subunits. They may be attached to the membranes of the endoplasmic reticulum or be present as **free ribosomes** suspended in the cytoplasmic matrix with no association with membranes. Free ribosomes often occur in clusters to form the **polyribosomes (polysomes)**, in which individual ribosomes are united by a thread of ribonucleic acid called **messenger RNA**.

Free ribosomes also are sites of **protein synthesis**, the protein formed being utilized by the cell itself rather than being secreted. Individual ribosomes in the cytoplasm are not active; it is only when they are attached to messenger RNA to form polysomes that ribosomes become active in protein synthesis. Similarly, ribosomes attached to endoplasmic reticulum also must be associated with messenger RNA before they become engaged in the synthesis of proteins.

Messenger RNA is formed in the nucleus on a template of uncoiled deoxyribonucleic acid (DNA). It contains a coded message that specifies the sequence in which amino acids are to be incorporated into the newly forming protein. During protein synthesis, the RNA enters the cytoplasm where it attaches to ribosomes which then move along the messenger RNA, translating the code and thereby assembling the amino acids in their proper order. Upon reaching the end of the messenger RNA, the ribosomes detach and simultaneously release the newly synthesized protein molecule. Amino acids are brought to the ribosomes for incorporation into the protein by yet another form of ribonucleic acid, the **transfer RNA**. There is a specific transfer RNA for each amino acid. Ribosomal and transfer RNA are thought to originate in the nucleolar region of the nucleus.

Golgi Complex

KEY WORDS—**negative image, saccules, forming face, maturing face, transport vesicles, condensing vacuoles, secretory granules**

The Golgi complex (Golgi apparatus; Fig. 1–3) does not stain in ordinary histological preparations, nor is it visible in living cells. However, its position in some cells may be revealed as a **negative image**—a nonstaining area of the cytoplasm usually located close to the nucleus. Its size and appearance vary with the type of cell and with the activity of a particular cell: it may be small and compact, large and net-like, or, in some cells, multiple Golgi complexes may be present.

In electron micrographs the Golgi complex is seen to consist of several flattened **saccules** or cisternae, each of which is limited by a smooth membrane. The saccules are disc-shaped, slightly curved and often appear compressed near the center and dilated peripherally. The saccules are arranged in stacks and because of their curvatures, the Golgi complex thus has a convex and a concave face. The convex surface usually is directed toward the nucleus and has been called the **forming face**; the concave or **maturing face** is oriented toward the cell membrane.

Within the Golgi stack, the saccules are separated by spaces 20 to 30 nm in width, but their cavities communicate by slender channels that extend between the adjacent saccules. The convex surface of the Golgi apparatus is associated with numerous small vesicles and at this face, the outer saccule is perforated by many small fenestrations. The saccules at the convex surface tend to be more dilated and their limiting membranes thinner than those at the concave surface.

The Golgi complex is the site of accumulation and concentration of secretory products and varies considerably in size with the activity of the cell. In protein secreting cells, peptides first accumulate within the lumen of the rough endoplasmic reticulum and then are transported to the Golgi complex in small **transport vesicles**. These vesicles are formed

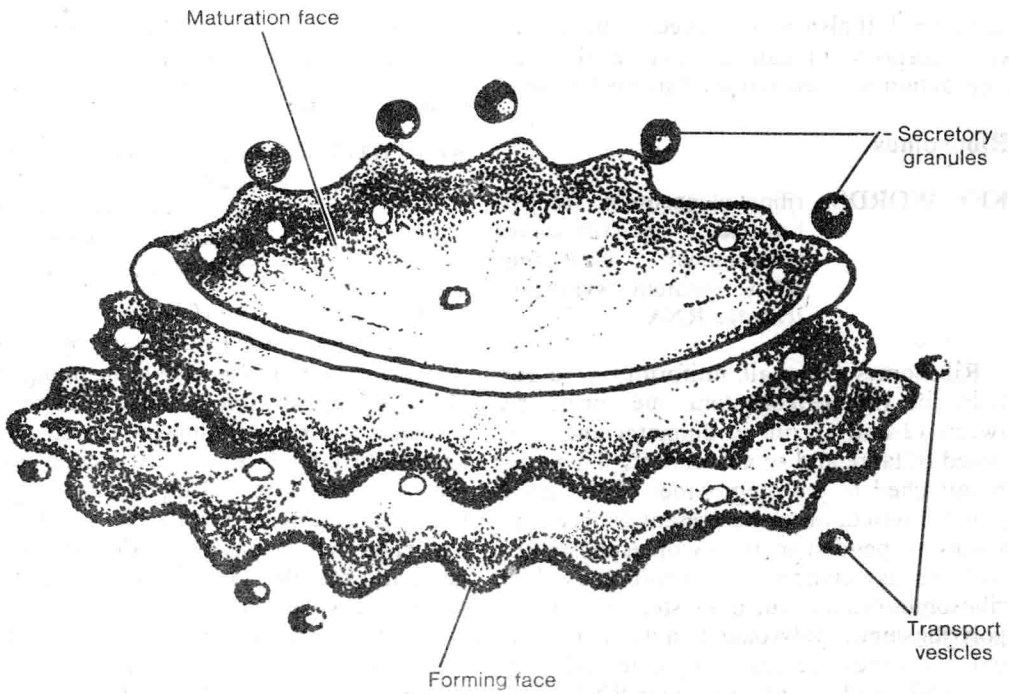

Figure 1-3 Structure of the Golgi complex.

from ribosome-free areas of the rough endoplasmic reticulum adjacent to the Golgi complex. The vesicles carry small quantities of protein to the Golgi complex where they coalesce with and contribute membrane to the developing outer saccule at the forming face. Proteins accumulate within the cisternae of the Golgi membranes and are concentrated as they pass through the Golgi complex. At the maturing face, the Golgi saccules expand and bud off to form the limiting membranes that enclose the protein material in structures known as **condensing vacuoles**. The secretory materials within the vacuoles become more concentrated and the condensing vacuoles eventually mature into the **secretory granules**. Golgi membranes also are capable of synthesizing carbohydrate and, depending upon the cell type, protein may be complexed to the newly synthesized carbohydrate to form a glycoprotein.

An equilibrium is thought to exist between the rate at which transport vesicles add new membrane to the forming face of the Golgi and the rate at which membrane is lost from the maturing face as the saccules bud off to form the limiting membranes of secretory granules. During the release of the secretory product, the membranes of the secretory granules fuse with the plasmalemma and become incorporated into the cell membrane. The membranes of the secretory granules must have some special properties since they fuse specifically with the plasmalemma and not with the membranes of other organelles.

There appears to be a continuous movement of membrane throughout the cell, from endoplasmic reticulum to transport vesicles, to Golgi complex, to secretion granules and thence to the plasmalemma. Internalization of plasmalemma occurs during phagocytosis, pinocytosis and micropinocytosis.

Lysosomes

KEY WORDS—acid hydrolases, autolysis, primary lysosomes, secondary lysosomes, phagocytosis, phagosome, heterophagic vacuole, residual body, heterophagy, autophagy, autophagic vacuole, cytolysosome, multivesicular body

Lysosomes are small, membrane-bound, dense bodies measuring 0.2 to 0.5 μm in

diameter. They contain a number of hydrolytic enzymes active at an acid pH and thus, lysosomal enzymes often are referred to as **acid hydrolases**. Demonstration of acid hydrolases within dense bodies is essential for their identification as lysosomes. The limiting membrane of the lysosomes protects the remainder of the cell from the lytic effects of the contained enzymes which, if released into the cytoplasm, would digest or lyse the cell. Such an occurrence is referred to as **autolysis** and is presumed to occur normally during resorption of tadpole tails at metamorphosis, during regression of the mesonephros during kidney development and in the regression of mammary tissue after the cessation of lactation. Increased lysosomal activity has been described during the regression of some tumors.

Lysosomes show great diversity in their morphology related to the state in which they occur and to their association with external materials incorporated into a cell or to internal structures. **Primary lysosomes** are released at the Golgi complex and are those which have not engaged in digestive activities. The enzymes of the primary lysosomes are synthesized in the granular endoplasmic reticulum, transported to the Golgi complex in transport vesicles and then released from the maturing face as membrane-bound, electron dense granules. Primary lysosomes are formed in a manner similar to the synthesis of secretory granules, but lysosomes usually are not secreted from the cell and remain within the cytoplasm.

Secondary lysosomes can be defined as vacuolar structures that are the sites of past or current lysosomal digestive activity and include a number of structures termed heterophagic vacuoles, autophagic vacuoles, and residual bodies. The relationships of these structures is best understood from a description of the processes involved in **phagocytosis**.

Some cells, such as macrophages and some of the granular leukocytes of blood, have a special capacity to engulf extracellular materials (bacteria for example) and destroy them. The process first involves invagination of the cell membrane and containment of the extracellular material in a membrane-bound vacuole. Thus, the extracellular material taken into the cell remains isolated from the cytoplasm and is sequestered in a vacuole called a **phagosome**. As the phagosome moves through the cytoplasm of the cell, it encounters a primary lysosome. The two structures fuse by coalescence of their limiting membranes, and the hydrolytic enzymes of the lysosome are discharged into the phagosome. The combined primary lysosome and phagosome now is called a **heterophagic vacuole**, a type of secondary lysosome. The material within the heterophagic vacuole is digested by the lysosomal enzymes and any useful materials are transferred into the cytoplasm for utilization by the cell. Nondegradable materials such as some dye particles, asbestos fibers, silica, carbon or other nondigestible substances may remain within the vacuole, now referred to as a **residual body**. Residual bodies are another form of secondary lysosomes which, by some, are thought to be eliminated from the cell by exocytosis. However, this concept remains controversial and in many cells the residual bodies accumulate and persist for long periods of time. The process by which substances are taken into the cell from the external environment and broken down by lysosomal activity is referred to as **heterophagy**.

In contrast, **autophagy** refers to the lysosomal breakdown of cytoplasmic organelles in normal, viable cells (Fig. 1–4). In this case the lysosomal system is involved in the destruction of aged or damaged organelles and the remodelling of the cytoplasm. During this process a portion of the cytoplasm containing aged or damaged organelles becomes surrounded by a membrane that is thought to be derived from the smooth endoplasmic reticulum. The membranous vacuole fuses with a primary lysosome to form still another type of secondary lysosome called an **autophagic vacuole** or **cytolysosome**. The fate of the materials within the autophagic vacuoles (which may be the cell's own mitochondria, ribosomes, endoplasmic reticulum, etc.) is the same as that in heterophagic vacuoles and again results in the formation of residual bodies. In many cells the indigestible components within autophagic vacuoles form a brownish material called lipofuscin pigment, the amount of which increases with aging.

Another form of lysosome is the **multivesicular body**. It is a membrane bound, vacuolar structure, 0.5 to 0.8 μm in diameter, that

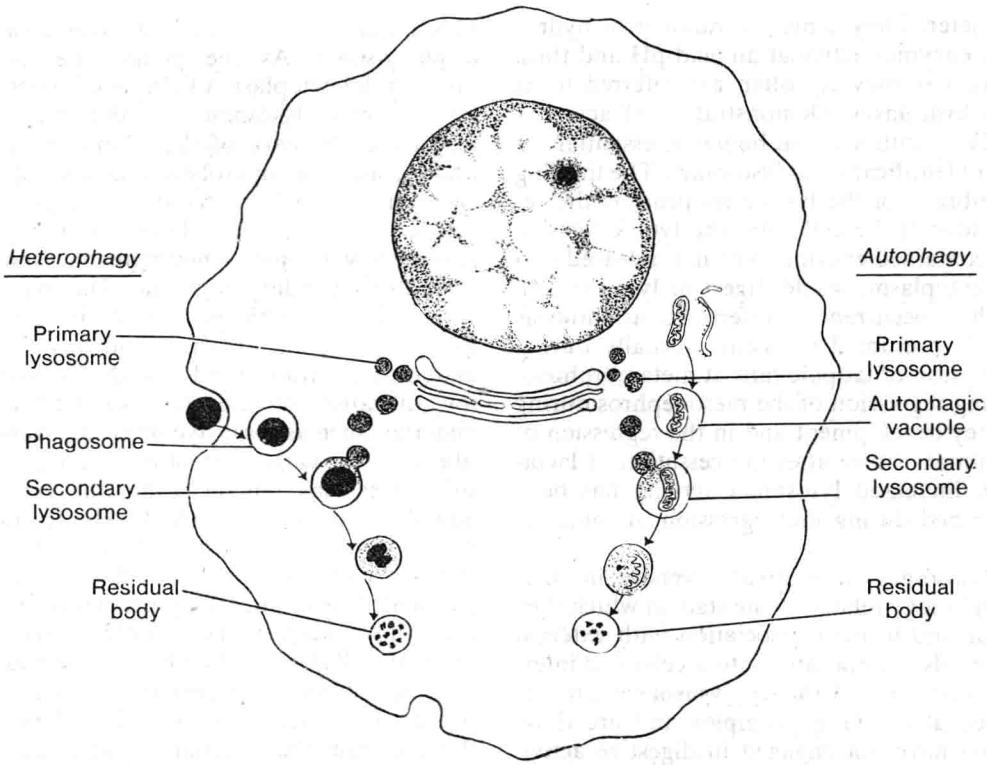

Figure 1-4 Schematic representation of autophagy and heterophagy.

contains a number of small, clear vesicles. The origin, function and exact relationship to other lysosomes is not known.

Peroxisomes

KEY WORDS—microbodies, peroxidases, glyconeogenesis

Peroxisomes, or **microbodies**, represent yet another class of membrane-bound organelles. Slightly larger than lysosomes, they show a varied internal structure that may be crystalline or dense. Peroxisomes are distinctive organelles containing the enzymes catalase, D-amino acid oxidase, urate oxidase and **peroxidases**. Because of their enzyme content, peroxisomes are able to reduce hydrogen peroxide to water and oxygen. Hydrogen peroxide is essential in a number of cell functions (such as the destruction of bacteria) but in excess is lethal to cells. Thus, peroxisomes play an important part in regulating the concentration of hydrogen peroxide within cells. Peroxisomes also have been implicated in **glyconeogenesis**, the formation of glucose from noncarbohydrate precursors.

Mitochondria

KEY WORDS—outer mitochondrial membrane, inner mitochondrial membrane, cristae, membrane space, intracristal space, intercristal space, mitochondrial matrix, Krebs cycle, elementary particle, electron transfer, deoxyribonucleic acid, matrix granule

Mitochondria are membranous structures that play a vital role in the production of the energy required by cells. They are visible in living cells examined by phase contrast microscopy and can be stained in fixed tissues where they appear as rods or thin filaments. Usually, however, they are not seen in routine tissue sections because of the lipid solvents