ESSENTIALS OF
HISTOLOGY

GERRIT BEVELANDER
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EIGHTH EDITION

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Preface

As in previous editions, our purpose in writing this book has been to provide a clear and concise introduction to the principles of histology, the microanatomy of tissues and organs. We have emphasized the relationship between structure and function to make the text more meaningful, more easily understood, and more relevant to other basic sciences. We have made the assumption that most of the people using this text intend to go into the health professions or biology, and we have attempted to lay the groundwork for the later study and recognition of differences that exist between normal and diseased or repaired tissue (pathology). Before one can understand the changes that occur during injury, healing, and disease, it is necessary to develop a clear idea of what normal tissues look like.

We have made a number of changes in this edition. In every instance our intent was to incorporate more structure-function correlations and to make clear the physiological implications of structure. Several chapters have been completely rewritten (the introduction, nervous tissue, lymphoid organs, male and female reproductive systems, and brain and special sense organs), and others have been substantially revised.

Our thanks go to the many colleagues whose micrographs appear in the text and to the many instructors and students who have given us help over the years in improving the presentation of the material. The text continues to evolve, and we are grateful for the support of our friends in this process.

Gerrit Bevelander
Judith A. Ramaley

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1

Introduction

Histology (*histos*, Gr., web) is the science that deals with the detailed structure of animals and plants and the relationships between the structural organization of cells and tissues and the functions that they perform. The smallest functional unit of living material is the cell, an organized entity capable of maintaining its own integrity, its responsiveness to the environment outside its boundaries, and its unique chemical composition. A cell is fundamentally a container for a complex, chemical organization whose properties would be seriously disrupted if the environment had free access to the interior of the cell.

Tissues are communities of cells embedded in a structural framework or *matrix*. The arrangement of cells, their interconnections, the relationship of the cells to the extracellular matrix, and the properties of the matrix must be understood to develop a concept of how the tissue performs its characteristic functions. For convenience, cell communities are divided into four classes: *nervous tissue*, *muscle*, *connective tissue*, and *epithelial tissue*. As we shall see, each of these tissues has properties that differ considerably from those of the other tissue types.

Organs are composed of tissues arranged in characteristic ways. In this text we will begin with general considerations of cell structure and then go on to tissues and finally organ systems.

PREPARATION OF TISSUE FOR STUDY

Cell and tissue structure and cell products are made visible for study by treating the cells with chemicals that *preserve* the tissue from decay, *fix* the cellular and matrix components in place to prevent distortion, and *stain* the tissue to permit the visualization of cellular and matrix elements that otherwise would lack enough contrast to be easily visible using microscopic techniques.

Living systems are so heterogeneous in composition that no single fixative will work equally well for all constitutents of a cell, a tissue, or an organ. The method of fixation commonly used for routine laboratory work is chemical fixation. In dealing with a particular tissue, an investigator will select a method that meets certain criteria:

1. There should be a minimum of distortion.

2. The fixative should not dissolve tissue components, if possible.

3. The agent should prevent decay (that is, be bactericidal) and should halt the action of cellular enzymes that can cause autodigestion.

4. The agent should help hold cells and tissue in place so that the tissue can be sliced into thin enough sections to permit the visualization of detail. Most chemical fixatives are aqueous solutions containing reagents that work either by coagulating tissue components or by establishing cross-bridges between molecules so that the latter remain in place. An example of a coagulant is ethanol. Ethanol takes up water, thus permitting active groups of protein molecules to make new chemical bonds with each other. These bonds tend to hold the proteins in position. An example of a fixative that works in

a noncoagulating way is formaldehyde. Formaldehyde (HCHO) links to a nitrogen group on a protein to form a hydroxylamine $NH \cdot CH_2OH$, which then can link with another nitrogen group to form a carbon (methylene or CH_2) bridge. The result is that the proteins are linked together. Most fixatives are a mixture of coagulant and noncoagulant chemicals.

For rapid examination of tissue—during surgery, for instance—a tissue may be frozen to harden it and fix the tissue elements and then cut *(sectioned)* immediately.

Once a tissue is preserved and fixed, thin slices *(sections)* must be prepared. It is difficult to see the arrangement of cells in thick pieces of tissue, since the dimensions of individual cells are so small (an average of 7 to 20 micrometers [μm; formerly microns]; see Fig. 1-1). For routine microscopy thin sections of tissue not more than 8 μm thick are cut with an instrument called a *microtome*. Without further treatment, the tissue organization would not be easily visible, since cellular components are nearly uniform in optical density. Special optical systems such as *phase* or *interference microscopy* can be used to visualize tissue elements without staining. Although cell components are of similar optical density, their thickness and orientation within the cell are different, thus impeding to variable extent the light passing through them. If a specimen is illuminated with polarized light in which the light waves are in phase, the light passing through certain regions of a cell or tissue will be slowed down. If the light is split into two beams, one passing through the specimen and one not, the two beams will interfere with each other when they are recombined, since they will now be out of phase. The light waves will add to or cancel out each other, making a brighter or dimmer image that accentuates the contrast and permits visualization of cell components.

More commonly in routine histology, the problem of lack of contrast is solved by treating the tissue with chemicals (stains) producing a color reaction or a precipitate that will be visible under the light microscope. Various stains combine to different extents with particular cellular components and matrix elements, and the resulting color differences serve to highlight the composition of the tissue. To accomplish this, tissues are first stabilized by fixation and then embedded in a material to hold the tissue parts in a natural relationship to each other to prevent distortion during sectioning. Embedding media are chemicals that can be converted easily from a liquid that can penetrate a tissue into a solid that can hold the tissue in place during sectioning. The hardening process or solidification may involve covalent linkages between the embedding molecules, crystallization, or polymerization (that is, formation of long chain–like molecules from shorter ones). A frequently used embedding medium in routine histology is paraffin. It has the advantage of being a quick and simple agent to use; however, it also has the disadvantage of causing considerable shrinkage, since the tissue must be dehydrated before the liquid paraffin can penetrate it. For the much thinner sections that must be made for electron microscopy (see later), various plastics are used that polymerize to form a three-dimensional spongelike framework for the tissue. After a tissue is embedded in plastic, very thin sections can be cut with a minimum of distortion.

Color can be introduced onto a thin tissue slice by treating it with dyes. Often two or more dyes are used that have a selective affinity for tissue components to further heighten the contrast. The most commonly used combination in histology laboratories is hematoxylin and eosin (H and E). In a hematoxylin and eosin section the cytoplasm of cells stains red and the nucleus blue. The cytoplasm contains an abundant protein matrix, and at the pH normally used to stain tissue, many of these proteins have enough basic (positively charged) groups to combine with eosin, an acidic dye whose color is due to its negatively charged anions. The dye hematoxylin is not itself a basic dye but can be made to attach to negatively charged sites by the use of a *mordant*, an agent that has many positive charges, which can link hema-

toxylin to acidic groups. The nucleus contains nucleic acids whose acidic phosphate groups can combine with hematoxylin with the help of a mordant.

Several other dyes can be used to stain special tissue components such as glycogen or lipids (Table 1).

Color contrast can also be added to living cells by the use of agents that can be taken up by cells. These agents are called *supravital dyes* (Table 1, Janus green B).

Major advances in the understanding of cellular function and tissue organization have been made in the last few years as a result of the introduction of new ways to reveal the structure of cells and the location of constituents of these cells. These techniques have been used to examine the growth and repair processes of cells, the mechanisms by which cells manufacture materials for use outside the cell (such as matrix components or secretory granules), and the modulations of cell structure that occur during events such as cell division or the fertilization of an egg by a sperm. What has happened is that the old stop-action view of cells based on stained dead cells is being replaced by a dynamic view of cells caught in the midst of important functions. A description of these newer techniques will be given throughout the text where appropriate.

STUDY OF TISSUES AND ORGANS

One's view of the organization of cells and tissues is dependent on the degree of detail (smallest size visible) that can be seen through the microscope. The maximum magnification possible with a light microscope is about 1,000×, and the smallest detail visible with ordinary student microscopes is about 1 μm. The latter will vary according to the properties of the optical system and the wavelength used to illuminate the tissue specimen. The limit of resolution depends directly on the minimum contrast detectable by the human eye and the wavelength of the light used, and it varies inversely with the numerical aperture of the lens system. The term *numerical aperture* (NA) is a measure of the light-gathering properties of the lens system and depends on both the light-bending (refractive) properties of the medium used to embed the specimen and the angle at which light enters the field (controlled by

Table 1. Staining characteristics of cell components

	Cell constituent	Chemical constituent	Characteristics
Nucleus	Chromatin	DNA	Purple, blue, or black with hematoxylin—basophilia Blue with toluidine blue—orthochromasia Blue-green with methyl green—pyronin
	Nucleolus	RNA	Purple, blue, or black with hematoxylin—basophilia Red with toluidine blue—metachromasia Red with methyl green—pyronin
		Deoxyribose	Red-purple with Feulgen reaction
Cytoplasm			
Organoids	Ground substance	Protein	Pink-red with eosin—acidophilia, eosinophilia
	Mitochondria	Complex	Blue with Janus green B supravital, black with iron hematoxylin, red with acid fuchsin
	Centrioles	Protein	Rarely seen in hematoxylin and eosin, black with iron hematoxylin
	Chromophil substance	RNA	Same as nucleolus
	Fibrils	Protein	Special methods, argyrophil in nerve cells
Inclusions	Lipids	Fats	Blackened by osmic acid—osmiophilia Negative image in hematoxylin and eosin removed by solvents
	Zymogen	Protein	Red with eosin—acidophilia
	Mucigen glycogen	Carbohydrate	Removed by solvents in routine hematoxylin and eosin negative image; red to purple with PAS

the condensor). It follows, then, that the resolution of the field will depend on how well the slide was prepared and how well the microscope is adjusted, as well as on several other considerations.

The best theoretical numerical aperture obtainable with the light microscope is 1.4× for oil immersion and 1.0× for high dry (40× objective). This limits resolution to a theoretical maximum of about 0.2 μm using short wavelength (blue) light. The electron microscope employs beams of electrons having properties much like light but of ultrashort wavelength. However, since the electrons in the short wavelengths of the beam can be captured by air particles in their path, the beam and the specimen must be placed in a vacuum. The electron beam is focused by magnets that serve the same function as lenses in an optical system using visible light. The first electron microscope designs required that electrons pass through the specimen to generate an image. This technique is called *transmission electron microscopy*. Within the past few years, two new techniques have been developed in which whole specimens or thick sections rather than thin sections can be bombarded with an electron beam and a three-dimensional view of the tissue surface obtained by detecting the patterns of scattered electrons. These techniques are called *scanning electron microscopy* and *high-voltage transmission electron microscopy*.

Contrast in electron microscopy is obtained by treating the tissue with heavy metals that impede the passage of electrons (that is, electron-dense chemicals) or by forming precipitates that are electron dense using antigen-antibody reactions. A new field has arisen in which tissue compounds can be identified in this manner (*immunocytochemistry*). Heavy metal salts such as osmium are often used as combined fixative and "staining" agents. Osmium is taken up to a different degree by the various cellular components. To heighten contrast, other heavy metal salts of lead and uranium are applied to thin sections *after* they are cut. This process is called *shadowing* and can be employed to show the contours of cellular elements. A commonly used technique is *freeze-fracture etching*. In this technique a tissue is frozen quickly in liquid nitrogen and then shattered along natural lines of cleavage in the tissue. The surface is then etched with metals and an image obtained of the surface texture. Freeze-fracture etching permits visualization of the location of proteins within membranes, for example.

Fig. 1-1 gives an idea of the sizes of objects normally studied in anatomy. The usual range encountered in histology varies from the limit of resolution of most student microscopes (1.0 μm) to the limit of resolution of the unaided human eye (0.1 mm or 100 μm). Cells range in size from 8 μm (red blood cells) to 150 μm (ripe ova). The size of most cells falls between these two values. For approximating cell size in a tissue sec-

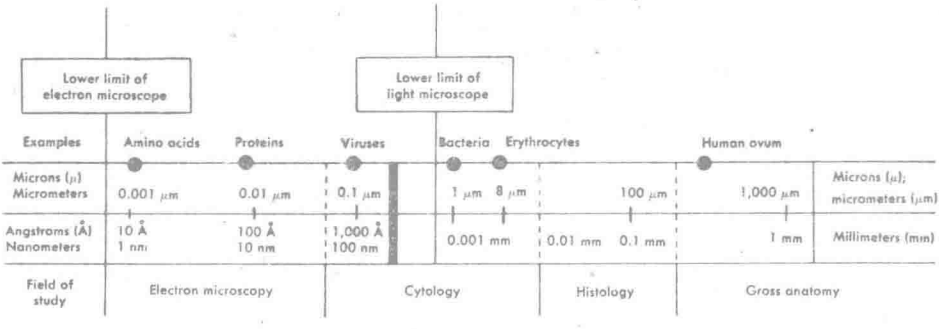

Fig. 1-1. Size of objects encountered in the study of anatomy. Note that there has been a terminology change in referring to the size of objects in histology. A micron (μ) is now a micrometer (μm), a millimicron (mμ) is now a nanometer (nm), and an Angstrom unit (Å) is now 0.1 nm. You are likely to encounter *both* sets of units, and so you should be familiar with both.

tion, the red blood cell is a useful standard. It measures approximately 8 μm in diameter and is usually present in the vasculature of most tissue. However, it must be remembered that processing tissues almost always causes some variation in the cell size.

One of the main objectives should be to develop an ability to visualize and construct a three-dimensional image of the cell or tissue from the flat, roughly two-dimensional object found on the microscope slide. To demonstrate how an object can apparently change in shape depending on how it is cut, one should consider the appearance of a simple spherical object such as an orange that has been cut in several planes (Fig. 1-2). The segments of the orange vary in shape depending on the *plane* of the section. The same kinds of variation will arise in connection with the study of cell and tissue structure.

Cellular detail visible with the light microscope is somewhat limited even when special stains are used, since most organelles are smaller than the resolution of the light microscope. For this reason it is essential to learn to recognize cells and tissues on the basis of several simple criteria. For example, one clue useful in identifying cell types is the appearance of the nucleus. In examining a slide of loose connective tissue (Fig. 3-7, for example), one can readily observe that the nuclei differ from each other in size, shape, staining intensity, presence or absence of nucleoli, degree of clumping of chromatin, and distinctness of the nuclear envelope (visible at the light microscope level only because of a rim of chromatin attached to it). Usually little if any cytoplasm is visible, and in addition the boundaries between cells may be indistinct. When cytoplasm *is* visible, the presence of variations in its staining properties (regions of basophilia, for instance) or the presence of visible inclusions (glycogen, pigment granules, vacuoles left by dissolved fats) should be noted. The identification of cells or tissues on the basis of color alone is not feasible because of

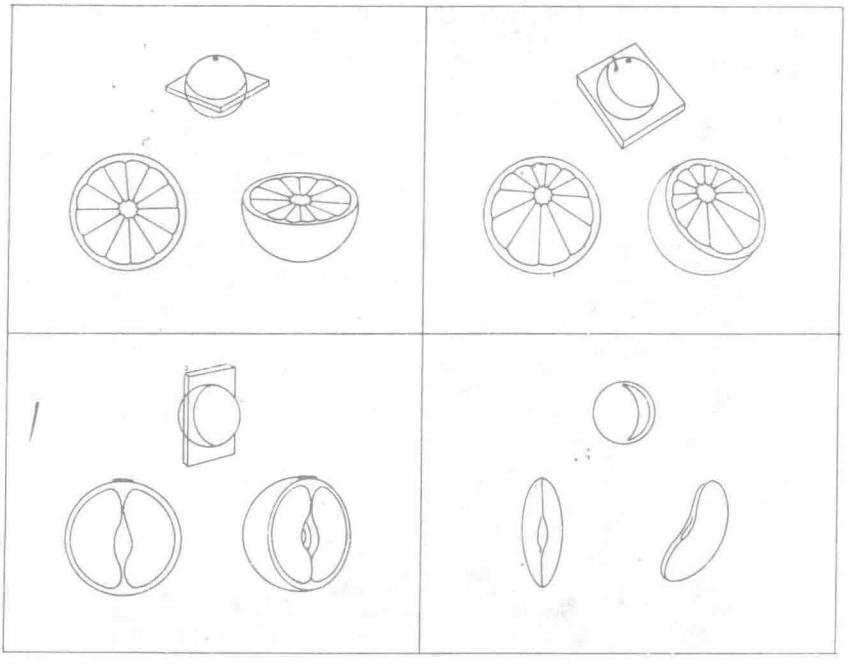

Fig. 1-2. Effects of plane of section on appearance of an object. Upper left, Orange cut perpendicular to long axis segments (cross section); lower left, orange cut parallel to long axis of segments (longitudinal section); upper right, orange cut obliquely to axis of segments (tangential); lower right, appearance of segments in space (three dimensional). (Drawing by Emily Craig.)

the diverse coloration that stained specimens may exhibit.

Another aspect of prepared specimens used in the study of histology both clinically and experimentally is the presence of *artifacts*. Poor tissue preservation or too long a delay before fixation results in autolysis (self-digestion) of the tissue and disruption and shrinkage or swelling of the cells. As slides age, the stain fades, reducing color contrast. Such distortions in the appearance of normal tissues may be present in the slides available for study.

THE CELL AND HOW ITS PROPERTIES CAN BE STUDIED

Most cells consist of a single *nucleus* embedded in *cytoplasm*. The entire unit is surrounded by a boundary called the *plasma* or *cell membrane* (Fig. 1-3). The membrane controls the movement of chemicals into and out of the cell and thus regulates the chemical environment in which cellular function takes place.

With the light microscope it is possible to see small areas of cytoplasm that differ from the rest. Early in the history of histology these regions were suspected of playing a role in cell function and were referred to as *organelles*. In the past 30 years the structure and function of these organelles, as well as other smaller cellular constituents not visible at light microscope level, have been elucidated by electron microscopy, by the study of cell fractions obtained from centrifugation, and by histochemical and autoradiographic techniques. Cellular components can be separated from each other in a centrifugal field because they differ in density, and it is possible to obtain *fractions* rich in membranes or organelles of different size and shape. The chemistry and ac-

Fig. 1-3. Liver cells of turtle showing the nucleus, cytoplasm, mitochondria, and other cell features visible at a light microscope level. (Iron hematoxylin; ×1,000.)

tivities of these fractions can then be studied.

Autoradiographic techniques can be used to mark the position of cellular components. For example, a radioactively labeled amino acid can be used to indicate where cell protein synthesis is taking place. Also, once the amino acid has been incorporated into protein, the fate of the protein can be followed. *Histochemistry* consists of identifying products of enzyme activity in a cell by looking for accumulations of a marker substance such as a colored dye. In the ovary, for example, the enzyme steroid 3-beta-ol-dehydrogenase is necessary for progesterone synthesis, and its activity changes with age and with reproductive status. The location of the enzyme activity can be visualized by a series of chemical reactions in which the hydrogen ions released from a steroid nucleus as it is metabolized by the action of the enzyme are made to react with a dye called neotetrazolium. The resulting product is purple and easily seen in the tissue.

Within the past few years it has become possible to locate specific proteins within cells by means of the technique called *immunocytochemistry*. Proteins differ from each other on the basis of size, shape, and electrical charge, and they can be used as antigens (foreign chemicals) in an antigen-antibody reaction. As part of the immune defense system, animals are able to produce antibodies to specific antigens. Once an antibody reacts with a specific tissue protein, it can be visualized in various ways by tagging it with a chemical that will fluoresce or that will produce a colored product after suitable chemical conversions are performed. Such techniques have been used, for example, to locate which cells in the pituitary produce and store specific hormones.

Cellular membranes

The three types of cellular membranes that will be considered here are the cell membrane (plasmalemma), the endoplasmic reticulum, and the Golgi apparatus. The nuclear membrane will be considered later. All these membranes serve as partitions, separating one part of the cellular environment from another. Each compartment marked off by membranes has a unique chemistry and represents a miniature space in which particular cellular reactions take place. The plasmalemma forms the interface between the cell and the outside solution in which it resides. The other membranes form intracellular compartments intimately concerned with cellular *metabolism* (the sum of the chemical processes that take place in a cell).

The molecular architecture of cellular membranes has been studied primarily in the red blood cell, a source of readily available, easy-to-isolate membrane material. According to chemical analysis, the red blood cell membrane is about 50% protein and about 50% lipid. The lipid is made up of cholesterol (one third) and polar phospholipids (the remaining two thirds) whose primary property is that they have one end soluble in aqueous solutions and one end soluble in lipid. Lipids provide the matrix of membranes. Early electron micrographs of cell membranes stained with osmium showed two thin lines of electron-dense material separated by a narrow space. On the basis of this morphology and the chemical composition of membranes, Davson and Danielli and later Robertson developed a model of membrane structure, the unit membrane hypothesis, in which it was proposed that the phospholipids are arranged in a continuous bilayer (double layer) with the nonpolar ends of the lipids facing inward and the polar ends facing toward the surface of the membrane.* The heads of the phospholipids were thought to be embedded in a surface coating of protein running in continuous sheets. In recent years it has been possible to localize proteins within the membrane, and it is now clear that the older unit membrane hypothesis cannot adequately explain the properties of membranes. A new membrane model generally known as the *fluid mosaic model* was developed by Singer and Nicolson to take the

* For a review of membrane structure, see Singer, S. J., and G. L. Nicholson. 1972. The fluid mosaic model of the structure of cell membranes. Science 175:720-731.

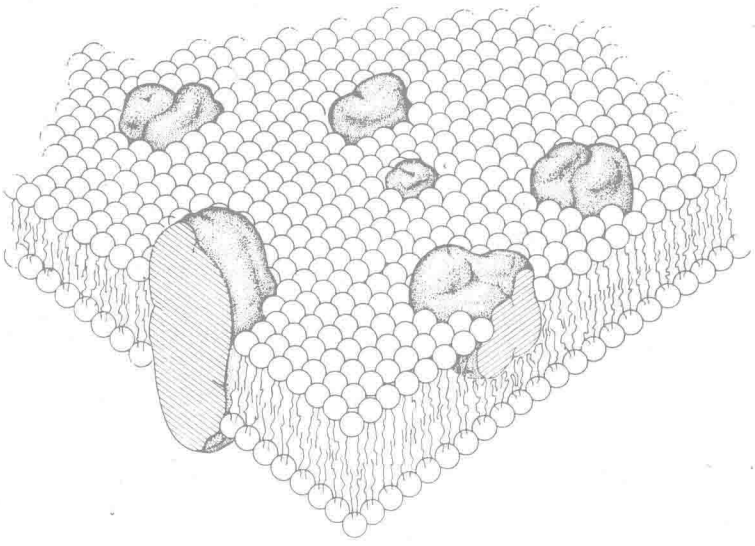

Fig. 1-4. Fluid mosaic model of cell membrane. Note lipid matrix consists of phospholipid bilayer with proteins floating in it, some passing through entire membrane, some projecting from one surface only. (From Singer, S. J., and G. L. Nicholson. 1972. Science **175**:720-731, Feb. 18; copyright 1972 by the American Association for the Advancement of Science.)

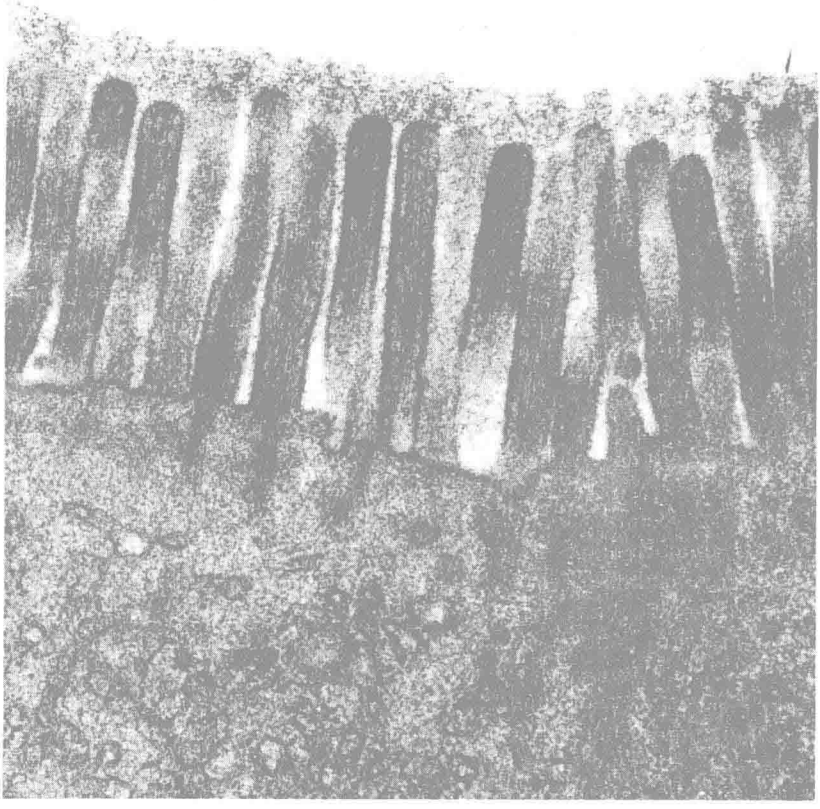

Fig. 1-5. Electron micrograph of microvilli forming striated border of small intestine of mouse and showing surface coat (glycocalyx) at periphery of microvilli. (×60,000.) (Courtesy Dr. Caramia, University of Rome.)

newer data into account. It is still suggested that the lipid forms a continuous bilayer, but it is now proposed that proteins float in this lipid, some proteins extending through the membrane and projecting onto both the intracellular and extracellular surfaces, others reaching only the inside or outside (Fig. 1-4). In this model the inner surface and the outer surface of the membrane have different properties.

Plasma (cell) membrane

The plasmalemma or cell membrane consists of two basic zones. Coating the surface of the cell membrane facing the outside world is a cell coat or glycocalyx (sweet husk) (Fig. 1-5) consisting of a fuzzy shell of carbohydrate-containing protein (glycoproteins) and lipid (glycolipids). The properties of the glycocalyx determine cell recognition, cell adhesiveness, movement, and maintenance of form. The inner zone consists of the basic fluid-mosaic membrane. Proteins projecting all the way through the membrane are probably involved in shuttle systems that move electrolytes and small metabolites such as amino acids and glucose into and out of the cell. Proteins that stud the inner surface of the membrane facing the cell cytoplasm are concerned with the regulation of cell metabolism and the initiation of cellular responses to chemical signals from outside, such as hormones.

Endoplasmic reticulum

The endoplasmic reticulum (ER) was originally named by early electron microscopists who found a series of intracellular membranes deep within the cell (the cell center was then called the endoplasm). Since that time it has become clear that the membranes are not confined to the deep parts of the cell. In all living cells, specific activities of great complexity are localized in different membrane types that channel the passage of macromolecules from one place to another within the cell. The ER consists of two basic components—granular (rough) and agranular (smooth). The rough ER consists of platelike flat channels (cisternae) stacked in piles. Studding the surface of these plates are ribosomes, the cellular organelle on which protein synthesis takes place (Fig. 1-6). The rough ER is best developed in cells that elaborate a protein-rich secretory product. When subcellular fractions of the ER are obtained, they are referred to as *microsomes*. Other cells that make protein for internal use have many cytoplasmic ribosomes alone or in clusters *(polyribosomes)* but a poor membrane system.

Smooth ER consists of a latticelike arrangement of tubules. These membranes are involved in detoxification processes in the liver and in lipid and steroid metabolism in the testes and ovaries. In skeletal muscle the smooth ER plays a role in the coupling between surface stimulation of the cell and the initiation and cessation of muscular contraction (stimulation-contraction coupling). The membranes may serve as an intracellular transport system for nascent proteins and lipids and also a communication system be-

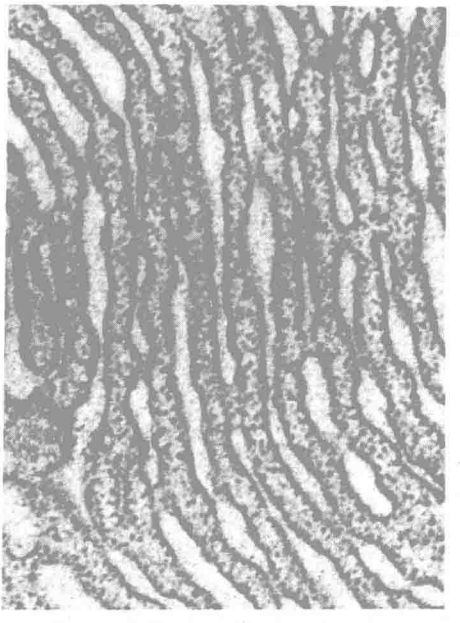

Fig. 1-6. Electron micrograph of portion of parotid gland showing profiles of the rough (granular) endoplasmic reticulum cisternae studded with ribosomes. (×50,000.) (Courtesy Dr. S. Luse.)

tween the surface and the interior of the skeletal cells, as in muscle cells.

Smooth and rough ER differ in chemical composition and enzyme content and clearly perform different functions. In the membranes from the enzyme-secreting part of the pancreas (acinar pancreas), for instance, the cholesterol-phospholipid ratio of the rough ER is about 0.02, whereas that of the smooth ER is 0.47. Differences in the lipid-protein ratio and the composition of individual lipids have also been found. The protein in rough ER is replaced every 5 days, on the average, with larger proteins being replaced more often than small proteins (an average of 4 and 28 days, respectively). The figures are dif-

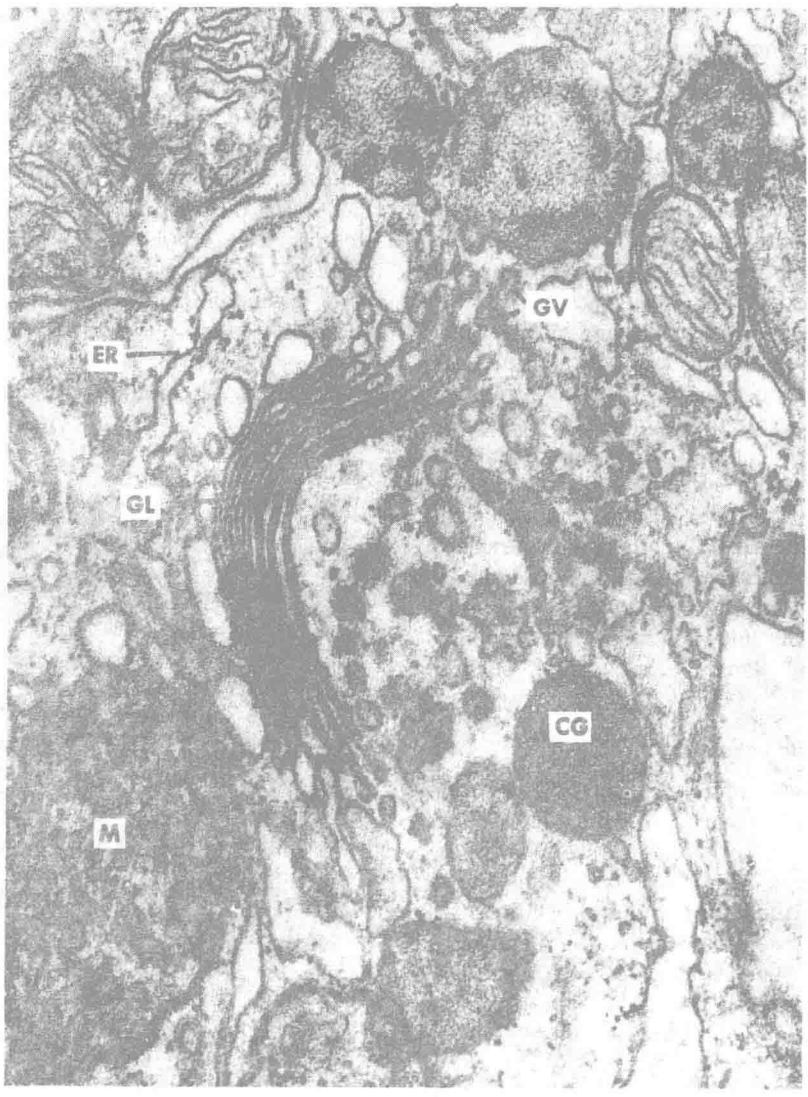

Fig. 1-7. Electron micrograph of part of the calciferous gland of *Lumbricus terrestris* showing Golgi apparatus. Note proximity of rough endoplasmic reticulum, *ER*, to stacks of Golgi lamellae, *GL*, which transmit and modify protein derived from *ER*. The material is then conveyed to the Golgi vesicles, *GV*, which undergo further changes in the cytoplasm, as represented by condensing vacuoles *(CG)*, which are eventually extruded at the free surface of the cell. *M*, Mitochondria. (×77,000.)

ferent for smooth ER, being 3 and 13 days. The need for repair and replacement of membranes should be clear when it is considered that the pancreas produces 40 mg of protein in every secreting cycle (associated with a meal) for export. There is also a lot of intracellular traffic that requires a continual replacement of membranes (see discussion on Golgi apparatus). The enzymes detected so far in smooth ER are involved in glycogenolysis and steroid production, whereas those in the rough ER are concerned with energy transfer and release, which is required to provide the energy that drives protein synthesis.

Golgi apparatus

In light microscopy the Golgi apparatus or complex appears as a clear area in actively secreting cells such as the acinar cells of the pancreas or bone-forming cells (osteoblasts). It consists of a stack of more or less flat membranous vesicles called *saccules*, which resemble a pile of hotcakes (Figs. 1-7 and 1-8). The stack is curved so that the convex surface faces the ER. This face is referred to as the *immature* face, since it seems to be receiving a shower of small vesicles that are budded off the ER. The other face is called *mature* and appears to be discharging many small vesicles. The rough ER makes two sets of proteins, one for export and one for local use within the cell. As the newly synthesized protein is released from the ER, it can follow two not necessarily related routes. In secretory cells the protein becomes concentrated within *condensing vacuoles* that, in turn, mature into *secretory granules*. These granules eventually migrate to the cell surface, perhaps moved by contractile elements with-

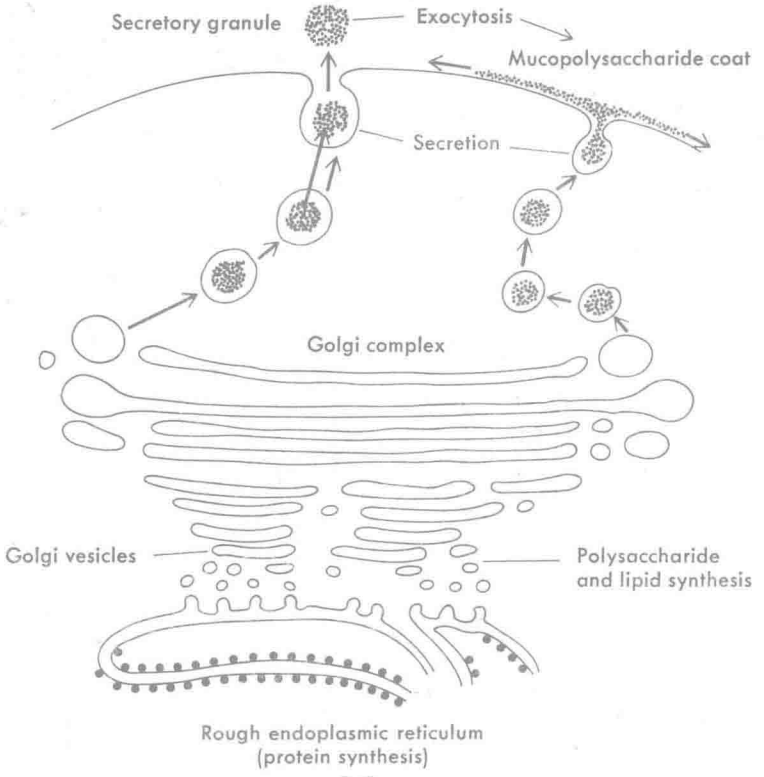

Fig. 1-8. Golgi complex showing origin from rough endoplasmic reticulum, fusion of Golgi vesicles to form stacks of smooth endoplasmic reticulum, and conveyance of product-containing secretory vesicles to cell exterior, liberating either secretory granules or extracellular coat. (From Berrill, N.J., and G. Karp. 1975. Development. McGraw-Hill Book Co., New York. Used with permission of McGraw-Hill Book Co.)

in the cell (microfilaments and microtubules, see later), and are discharged by a process called *exocytosis*. Other packets of newly manufactured protein arise from the Golgi apparatus or a complex meshwork of Golgi, ER, and enzyme-filled lysosomes (see later). This complex is referred to as GERL (an acronym formed from the words *G*olgi, *ER*, and *L*ysosome). The mature or forming face of the Golgi apparatus elaborates many *primary lysosomes* (see later).

The Golgi apparatus appears to act as a collecting system for large molecular weight (macromolecular) secretory products. Stacks of Golgi plates form clusters called *dictyosomes*, which may exist as a single large apparatus in some mammalian cells or as smaller membrane clusters scattered through the cell. Certain sugar-transferring enzymes (glycosyltransferases) are located exclusively in the Golgi membranes and serve as markers for biochemical studies of membranes. The Golgi apparatus appears to add terminal sugars to a number of glycoproteins (carbohydrate-containing proteins).

Lysosomes

A cell contains many round bubblelike vesicles sometimes with clear, homogeneous contents and sometimes with dense material or structured material within them. Some of these cell packets are concerned with intracellular functions, others with the packaging of materials for export.

The lysosome is a small, round membrane-bound organelle about 0.25 to 0.5 μm in diameter. It contains acid hydrolases, enzymes that break down proteins, nucleic acids, and carbohydrates at acidic pH. Lysosomes are found in almost all cells except red blood cells and fully keratinized skin cells. They seem to represent the "digestive system" of a cell. A freshly formed lysosome budded off the Golgi apparatus is called a *primary lysosome*. If the cell picks up foreign material (by a process called cell-eating or phagocytosis), the resulting food vacuole is called a *phagosome* (Fig. 1-9). The material in the phagosome is digested after a lysosome fuses with it and releases its digestive enzymes. The resulting packet of material, which represents a fused lysosome and phagosome, is called a *phagolysosome*. If the material inside the phagolysosome cannot be digested, usually due to a deficiency of a specific lysosomal hydrolase, lysosome storage diseases can occur. If the cell is situated along an excretory channel such as the bile

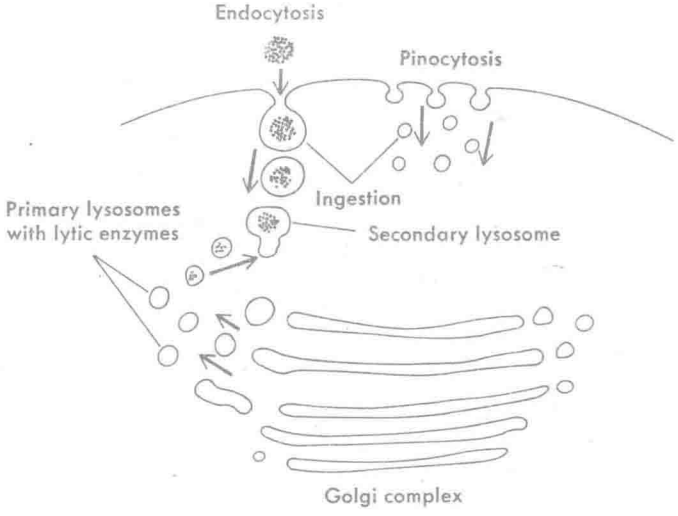

Fig. 1-9. Golgi–endoplasmic reticulum–lysosome (GERL) system is shown with primary lysosomes originating from Golgi complex and fusing with endocytic vesicles from cell surface (left) to form secondary lysosomes. (From Berrill, N.J., and G. Karp. 1975. Development. McGraw-Hill Book Co., New York. Used with permission of McGraw-Hill Book Co.)