

Atlas of HUMAN HISTOLOGY AND ULTRASTRUCTURE

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FOREWORD

The advances in the study of cellular fine structure in the past thirty years are astonishing. The electron microscope has, indeed, proved a tool of many disciplines from metallurgy to pure biological science, but perhaps it has served most significantly by bringing the disciplines of biological chemistry and morphology under one roof. Indeed, pure biological science currently is advancing primarily through the contributions of the structural and chemical disciplines interpretable as cell physiology.

Rudolph Virchow succeeded in centering the attention of investigators on the cell as the unit of life and also as the ultimate seat of diseases manifested by altered function. The problem in the late nineteenth century was, however, that reliable normal tissue histology had to be learned before pathological histology could be developed as a useful tool. The same can be said for ultrastructural morphology in the twentieth century.

The present contribution by Matthews and Martin one hundred years after Virchow advances the state of our knowledge of ultrastructure of the cell by satisfying a need. As pointed out by Keith Porter and Mary Bonneville, Johannes Rhodin, Don Fawcett and others, there is an urgent need for base-line comparative information on fine structure, specifically in the human. Many of the electron photomicrographs in prior atlases came from laboratory animals and, indeed, in many cases animal tissues were the only comparable base-line fine structure for comparison with human tissues. In this work all tissues are human, and the atlas will give all investigators an additional sense of security in the interpretation of fine structure. In addition, the comparison of thin section and light microscopy to human electron microscopy is most illuminating.

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PREFACE

With the new techniques and the constantly increasing knowledge in the field of microscopic anatomy, the student faces a continuous task in keeping up with the influx of new material. This requires surveillance of the widely dispersed sources of microscopic and especially ultrastructural anatomy in the literature. This volume was prepared in an attempt partially to alleviate this problem.

An effort has been made to produce an atlas useful both to beginning students in histology and to practicing professional microscopists, anatomists, physiologists and pathologists. To achieve this objective, human tissues were used exclusively. Recent literature references are included for further information on the subjects presented.

The transition from the viewing of conventional preparations of tissues embedded in paraffin cut at 3 to 7 microns to the viewing of tissues at the electron-microscope level has been a major obstacle to orientation. To facilitate this transition, stains effective on tissues embedded in plastic and having the character of the routine H & E are used in this atlas. Thin plastic sections (0.5 microns) provide several advantages. The optimal limit of resolution of the light microscope (0.2 microns) is realized. Preservation of cytologic detail is enhanced by the primary aldehyde fixation, postosmication, and the elimination of the need for removal of the embedding media. Reduction of several solvent stages in the preparation of tissues for thin sections further reduces the leeching out of many cellular components. Intensity of contrast has been increased over prior phase-optical preparations using monochromatic stains, but only recently has color contrast been practicable. The thin sections in this atlas were stained with a polychrome stain closely approximating the H & E differentiation familiar to most microscopists. Photomicrographs of H & E stained sections, polychrome stained thin plastic sections, "adjacent" sections, and electron micrographs of these tissues are presented sequentially in an effort to correlate microscopic structure and ultrastructure.

Specimens for this atlas were obtained from biopsy specimens, areas peripheral to surgical pathology specimens, and, in rare instances, from autopsy specimens. Several plates include electron micrographs of human tissues not previously available. It is hoped that the combination of photomicrographs and electron micrographs will provide a basis for furthering an understanding of both normal and diseased tissues.

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Special appreciation is extended to Miss Freida Carson who produced several of the blood and marrow cell micrographs and who was responsible for organizing the collection of tissues in her capacity as chief technician of the Department of Surgical Pathology; to Dr. J. A. Lynn who helped to organize the atlas; to Dr. G. J. Race for making facilities and equipment available and for his encouragement and support; to Dr. R. E. Dill for reviewing the manuscript; and to Mrs. Joan Nash for her secretarial contributions.

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The Cell

Plate 1 - CELL

Figure 1.

Electron micrograph of secretory cell of gastric glands. The cells in this figure were selected to depict several of the cellular components to be discussed in the succeeding plates. Cells vary in size, shape and content. Intracellular components and their distribution often reflect the special activities of these units. The nucleus (N) contains a nucleolus (Nu) and shows clumping of the granular chromatin, particularly adjacent to the nuclear membrane (NM). The nonclumped euchromatin is the site of genetic determination of cell morphology and function. Nuclear pores (NP) are seen in the nuclear membrane. The cytoplasm contains mitochondria (M) essential for the production of energy-rich compounds via oxygen utilization. Rough-surfaced membranes of endoplasmic reticulum (ER) ramify throughout the cell and serve as sites of protein synthesis at the ribosomes, the small granules giving the membranes their rough appearance. Ribosomes also occur free in the cytoplasm. A Golgi complex (G) consisting of flattened sacs and vesicles is interposed between secretion granules (SG), a product invested in membrane at the Golgi complex and secreted at the cell's free surface. Other organelles such as lysosomes and centrioles, and inclusions such as glycogen, pigment, etc., are not seen in this section. Electron microscopy requires that the section being viewed be very thin so that electrons can be transmitted through the cell. Hence, the same cell is cut several times in succeeding sections with the microtome and only a small part of the total cell content is included in any micrograph. The plasma membrane of these cells touches a basal lamina (BL) which is the beginning of an area of connective tissue. The plasma membrane (PM) is not straight; rather, interdigitations of adjacent cells may be seen at the arrow. These membranes are separated by at least 20 mμ. The free surfaces of cells may contain phagocytic or pinocytotic vesicles and projections in the form of microvilli. Motile structures in the form of cilia or flagella may be present. The plasma membrane is the special interface between the cell content and the environment; it thus has several features relative to permeability, dielectric properties, and systems for active and passive transport. It is a trilaminar structure consisting of two outer dense lines separated by a less dense area.

Cells and cell products serving a specific function comprise tissues, while tissues organized for a common function constitute organs; organs serving specific functions are the basis of systems. Hence, the cell is the fundamental unit of an organism. $(\times 14,700)$



Plate 2 - MITOCHONDRIA

- Figure 1. Electron micrograph of cross section of skeletal muscle. In this figure, the mitochondria are elongated branched sacs occupying the sarcoplasm between myofibrils. They are also in immediate proximity to a lipid (Li) droplet, a common relationship seen in many cell types. The mitochondria have a double-membrane arrangement. The inner membrane is infolded to form the cristae mitochondriales (Cr). Mitochondria contain all of the enzymes of the Krebs cycle, and all of the enzymes required for coupled phosphorylation and fatty-acid oxidation. They are prime users of oxygen, and have been called the "power house" of the cell because of their production of adenosine triphosphate (ATP). (×36,000)
- Figure 2. Electron micrograph of leukocyte mitochondria. These mitochondria (M) have a tubular profile in longitudinal section and a round profile in cross section. Mitochondria may attain $10 \,\mu$ in length to $5 \,\mu$ in diameter, but are usually smaller. They are well within the resolving capacity of the light microscope. Mitochondria readily change shape and size. This mitochondrion contains an electron-dense granule (MG). Analysis of these granules has shown that some of them are soluble in lipid solvents while others persist following extraction and microincineration, indicating a high mineral content. These granules contain calcium, magnesium, phosphate and a protein in bone and cartilage cells. ($\times 55,000$)
- Figure 3. Electron micrograph of salivary duct cell. The numbers of mitochondria (M) in this cell are enormous and each mitochondrion is filled with cristae. Both the number and size of mitochondria can vary in cells. Cells with large numbers of mitochondria are presumed to be active in some energy-requiring activity, such as secretion, contraction, etc. General cells have 200 to 400 mitochondria; they may, however, have very few, as in the lymphocyte, or more than 2500. This view is of one very thin section. A count of all the mitochondria of this cell sectioned serially would be enormous. The nucleus (N) and plasma membrane (PM) are indicated. (×15,000)
- Figure 4. Electron micrograph of mitochondria of secreting cell. In this view, the continuity of the inner mitochondrial membrane can be followed into the interior as it forms the cristae (Cr) membranes. Each of the membranes appears as a trilaminar unit membrane. The space between the two unit membranes is about 10 m μ . High resolution microscopy of negatively stained cristae has shown them to have small 10-m μ knobs evenly spaced along the membrane. The knobs are attached to the cristae membranes by narrow stalks. The precise localization of all mitochondrial enzymes is not yet resolved, but some enzymes appear to reside on these knobs while others occupy the matrix between cristae. ($\times 57,600$)

PLATE 2

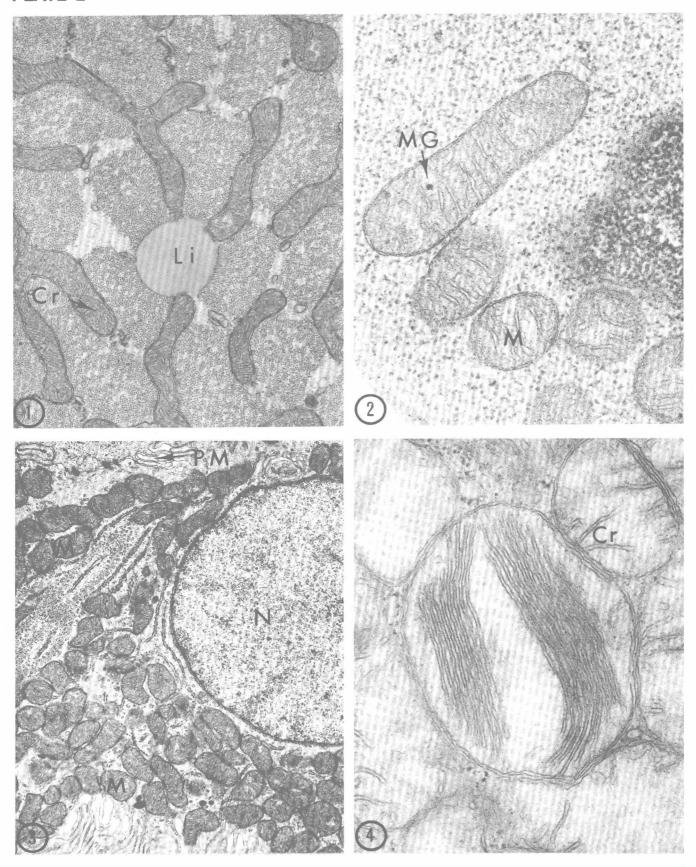


Plate 3 - LYSOSOMES

- Electron micrograph of Kupffer cell. The sinusoidal spaces (S) of the liver are lined with phagocytic Kupffer cells (KC) separated from the liver parenchyma cells (PC) by a narrow space, the space of Disse (SD). Microvilli (Mv) from both cell types project into the space. Several organelles limited by a single membrane, the lysosomes (Ly), appear as rounded bodies of varying size. These lysosomes contain electron-dense granules, lipid droplets, and myelin figures but do not have the highly organized internal structure of the mitochondria. The lysosome contains digestive enzymes capable of reducing large molecules to simpler constituents which can be used by mitochondrial enzymes. These structures are particularly rich in acid phosphatases and hydrolases and can be identified histochemically by the Gomori method. (×8,000) Electron micrograph of reticular cell in the spleen. This cell contains a nucleus
- Figure 2. Electron micrograph of reticular cell in the spleen. This cell contains a nucleus (N) in which the dispersed (euchromatin) and condensed (heterochromatin) chromatin are readily delineated. Free ribosomes (Ri), rough-surfaced endoplasmic reticulum (ER) and a mitochondrion (M) are seen in the cytoplasm. Lysosomes (Ly) containing a dense matrix and irregular dense inclusions are randomly distributed. Inspection of the mitochondrial membrane reveals a double-membrane structure with the inner membrane projecting inward forming the cristae. The lysosome is bounded by a single membrane. Erythrocytes (RBC) occupy the sinusoidal spaces between reticular cells. The reticular cells rest upon an incomplete basal lamina (BL). (×7,500)
- Electron micrograph of a macrophage in marrow tissue. In this figure, a large macrophage (Mp) has completely encompassed a neutrophil (Ne) with a several-lobed nucleus, indicative of an old leukocyte. A cytoplasmic process (P) of the macrophage extends beyond the neutrophil, which is surrounded on all sides by a thin layer of macrophage cytoplasm. Several electron-dense lysosomes (Ly) are situated at the neutrophil surface. Other lysosomes of varying sizes occupy other parts of the cytoplasm. Substances acted on by lysosomes may arise exogenously by heterophagy as seen here, or endogenously by autophagy. Some of the hydrolytic products of their action may be excreted by the cell, a process called exocytosis. These vesicles are called residual bodies (RB) before extrusion and often contain lipids in various forms. In autophagic processes, parts of cell organelles may be recognized within the autophagic vacuole or cytolysosome. An erythrocyte (E) and other leukocytes surround the macrophage. (×9,500)