TUMORS OF THE KIDNEY, RENAL PELVIS, AND URETER

by

JAMES L. BENNINGTON, M.D.
and
J. BRUCE BECKWITH, M.D.

ATLAS OF TUMOR PATHOLOGY

Second Series
Fascicle 12

TUMORS OF THE KIDNEY, RENAL PELVIS, AND URETER

by

JAMES L. BENNINGTON, M. D.

Chairman
Department of Anatomic and Clinical Pathology
Children's Hospital of San Francisco
San Francisco, California 94119
and
Associate Clinical Professor of Pathology
University of California
San Francisco Medical Center

and

J. BRUCE BECKWITH, M. D.

Professor of Pathology and Pediatrics
University of Washington School of Medicine
and
Director of Laboratories
The Children's Orthopedic Hospital and Medical Center
Seattle, Washington 98105

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ATLAS OF TUMOR PATHOLOGY

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EDITOR
HARLAN I. FIRMINGER, M. D.

Professor, Department of Pathology
University of Maryland School of Medicine
Baltimore, Maryland 21201
and
Scientist Associate, Universities Associated for
Research and Education in Pathology, Inc.
9650 Rockville Pike
Bethesda, Maryland 20014

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EDITOR'S NOTE

The Atlas of Tumor Pathology was originated by the Committee on Pathology of the National Academy of Sciences–National Research Council in 1947. The form of the Atlas became the brainchild of the Subcommittee on Oncology and was shepherded by a succession of editors. It was supported by a long list of agencies; many of the illustrations were made by the Medical Illustration Service of the Armed Forces Institute of Pathology; the type was set by the Government Printing Office; and the final printing was made by the press at the Armed Forces Institute of Pathology. The American Registry of Pathology purchased the fascicles from the Government Printing Office and sold them at cost, plus a small handling and shipping charge. Over a period of 20 years, 15,000 copies each of 40 fascicles were produced. They provided a system of nomenclature and set standards for histologic diagnosis which received worldwide acclaim. Private contributions by almost 600 pathologists helped to finance the compilation of an index by The Williams & Wilkins Company to complete the original Atlas.

Following the preparation of the final fascicle of the first Atlas, the National Academy of Sciences–National Research Council handed over the task of further pursuit of the project to Universities Associated for Research and Education in Pathology, Inc. Grant support for a second series was generously made available by both the National Cancer Institute and the American Cancer Society. The Armed Forces Institute of Pathology has expanded and improved its press facilities to provide for a more rapid and efficient production of the new series. A new Editor and Editorial Advisory Committee were appointed, and the solicitation and preparation of manuscripts continues.

This second series of the Atlas of Tumor Pathology is not intended as a second edition of the first Atlas and, in general, there will be variation in authorship. The basic purpose remains unchanged in providing an Atlas setting standards of diagnosis and terminology. Throughout the rest of this new series, the term chosen for the World Health Organization's series "International Histological Classification of Tumours" (when available) is shown by an asterisk if it corresponds to the authors' choice, or as the first synonym in bold print if it differs from the authors' heading. Hematoxylin and eosin stained sections still represent the keystone of histologic diagnosis; therefore, most of the photomicrographs will be of sections stained by this technic, and only sections prepared by other technics will be specifically designated in the legends. It is hoped that in many of the new series a broader perspective of tumors may be offered by the inclusion of special stains, histochemical illustrations, electron micrographs, data on biologic behavior, and other pertinent information for better understanding of the disease.

The format of the new series is changed in order to allow better correlation of the illustrations with the text, and a more substantial cover is provided. An index will be included in each fascicle.

It is the hope of the Editor, the Editorial Advisory Committee, and the Sponsors that these changes will be welcomed by the readers. Constructive criticisms and suggestions will be appreciated.

Harlan I. Firminger, M. D.

PREFACE AND ACKNOWLEDGMENTS

In the nearly two decades since the publication of the First Series of the Fascicle on Tumors of the Kidney, Renal Pelvis, and Ureter, there has been a virtual explosion of new information on tumors of the upper urinary tract. Many significant contributions concerning nearly all of the tumors covered in the First Series Fascicle, as well as the recognition of important new entities, have been made during this time. The authors have attempted to incorporate into this text the new well established findings in the areas of epidemiology, histogenesis, histochemistry, morphology, classification, diagnosis, treatment, and prognosis, as well as our own views on unproved and controversial theories relating to this field. While this has been largely a joint effort, Dr. Beckwith was responsible primarily for those sections relating to embryonal tumors of the kidney and Dr. Bennington for the remainder.

We wish to acknowledge the excellent First Series Fascicle by Dr. Balduin Lucké and Dr. Hans G. Schlumberger, which was such a tremendous help in the development of our manuscript and the illustrations that we have been permitted to use. They are our current figure numbers 40, 57, 58, 67, 175, 176, 201, 206, 216–218, 247, 257, and 259.

The classification and nomenclature used in this fascicle are based on our understanding of the histogenetic origin of the various tumors of the kidney, renal pelvis, and ureter. This terminology, with minor exceptions, is in general use in English speaking countries and conforms to that proposed (but not yet adopted) by the World Health Organization (WHO).

The authors wish to express their gratitude for the support in part by the U. S. Public Health Service, Grant No. R10-CA 11722, of the National Wilms' Tumor Study.

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Embryology and Anatomy of the Kidney: Our figures 1 and 4 (modified), 5, 9–11.

Histogenesis of Renal Carcinoma: Our figure 80.

Epidemiology and Etiology: Our figures 85, 86.

Morphology: Our figures 83, 87, 104–107, 109, 113, 116–118, 125, 129, 143, 144, 147, plates III-B and V, and tables V and VI (modified).

Distribution of Metastases from Renal Carcinoma: Our figures 139, 141, 155, and tables VII and VIII (modified).

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We gratefully acknowledge the secretarial assistance of Judy Fletcher and Nondis Barrett who have patiently and cheerfully carried the burden of preparing the manuscript. We also wish to thank Sheila Concannon for preparation of photographic illustrations, Dr. Michael Lagios for the original electron micrographs, Dr. John Azzopardi who kindly reviewed the manuscript and made many helpful suggestions, and the Armed Forces Institute of Pathology for the use of their facilities. Our special thanks go to Dr. Harlan I. Firminger, his editorial staff, and the reviewers chosen by the Editorial Advisory Committee for all their encouragement, kindness, and much needed patience.

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James L. Bennington, M. D.
J. Bruce Beckwith, M. D.

TUMORS OF THE KIDNEY, RENAL PELVIS, AND URETER

Contents

TUMORS OF THE KIDNEY, RENAL PELVIS, AND URETER

EMBRYOLOGY AND ANATOMY OF THE UPPER URINARY TRACT

EMBRYOGENESIS

The definitive or metanephric kidney in man has its beginnings in the second month of gestation. It is formed jointly from two different mesodermal structures; the ureteric bud, and the metanephric blastema (Hamilton et al.). The ureter, renal pelvis, renal calices, and the collecting tubules are derived from the ureteric bud, an outgrowth of the mesonephric (wolffian) duct. The nephron is composed of Bowman's capsule and glomerulus, the proximal and distal convoluted tubules and loop of Henle, all of which develop from a mesenchyme-like tissue, the metanephric blastema, located at the caudal end of the nephrogenic ridge (fig. 1).

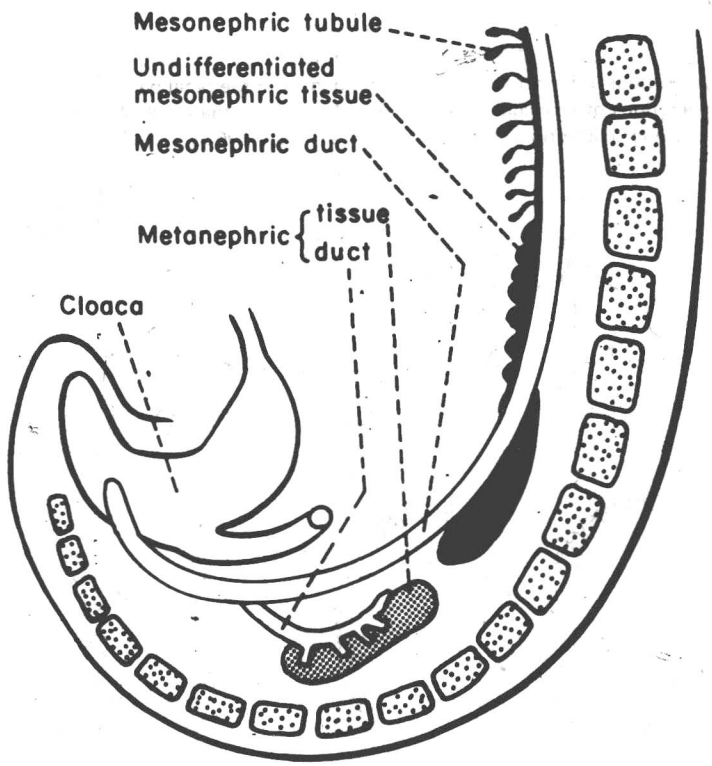

Figure 1
DEVELOPMENT OF METANEPHRIC KIDNEY
The metanephric tissue (stipple) which originates from the caudal end of the nephrogenic ridge gives rise to the nephron. The ureter, renal pelvis, and calices develop from the metanephric duct which is an outgrowth of the mesonephric duct.

The ureteric bud stretches to reach the metanephric blastema and in the process forms the ureter. The cranial end of the bud penetrates the metanephric blastema and undergoes a succession of branching. At the origin of the first several branches, a coalescence forms the renal pelvis (fig. 2) while subsequent orders of branches form the calices and collecting tubules (fig. 3; Osathanondh and Potter). Simultaneously, the metanephric blastema differentiates into two types of cells. The nephrogenic cells, characterized by scanty cytoplasm and prominent oval nuclei, orient themselves in compact masses around the growing ends of the collecting tubules, eventually differentiating into nephrons (fig. 4). Between the masses of nephrogenic cells

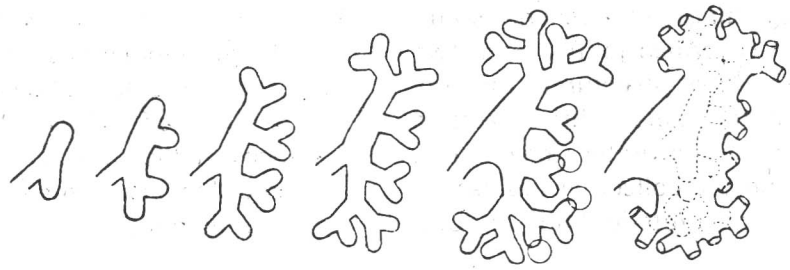

Figure 2
DEVELOPMENT OF RENAL PELVIS

Expansion of early generations of branches of the ureteral bud form the renal pelvis. The diagram represents coalescence of the third to fifth generations of branches (circled). (Fig. 9 from Osathanondh, V., and Potter, E. L. Development of human kidney as shown by microdissection. Arch. Pathol. 76:277-289, 1963.)

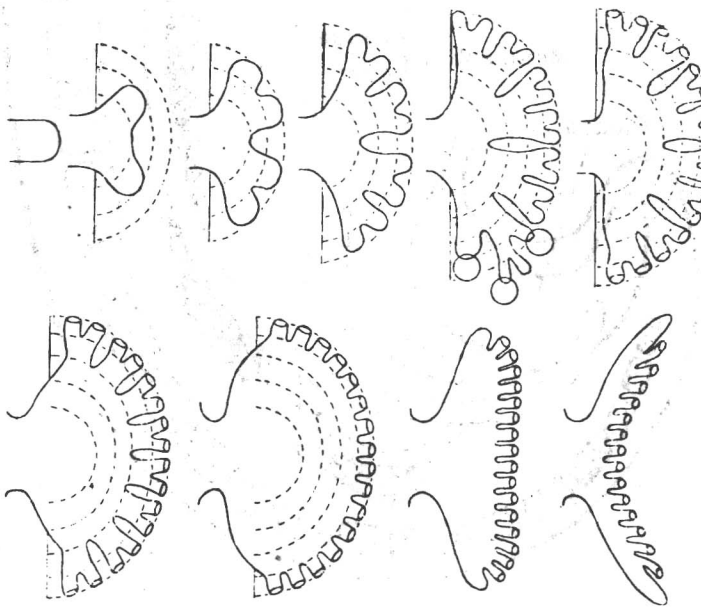

Figure 3
DEVELOPMENT OF RENAL CALICES AND PAPILLAE

Coalescence of the third to fifth generations of branches of the ureteral bud (circled) forms the primordial calix. (Fig. 10 from Osathanondh, V., and Potter, E. L. Development of human kidney as shown by microdissection. Arch. Pathol. 76:277-289, 1963.)

are widely spaced stromagenic cells with small naked-appearing nuclei, which will eventually give rise to the renal interstitial tissue. By the 36th week of gestation, nephrogenesis is usually completed and the embryonic nephrogenic and stromagenic cells are no longer recognizable.

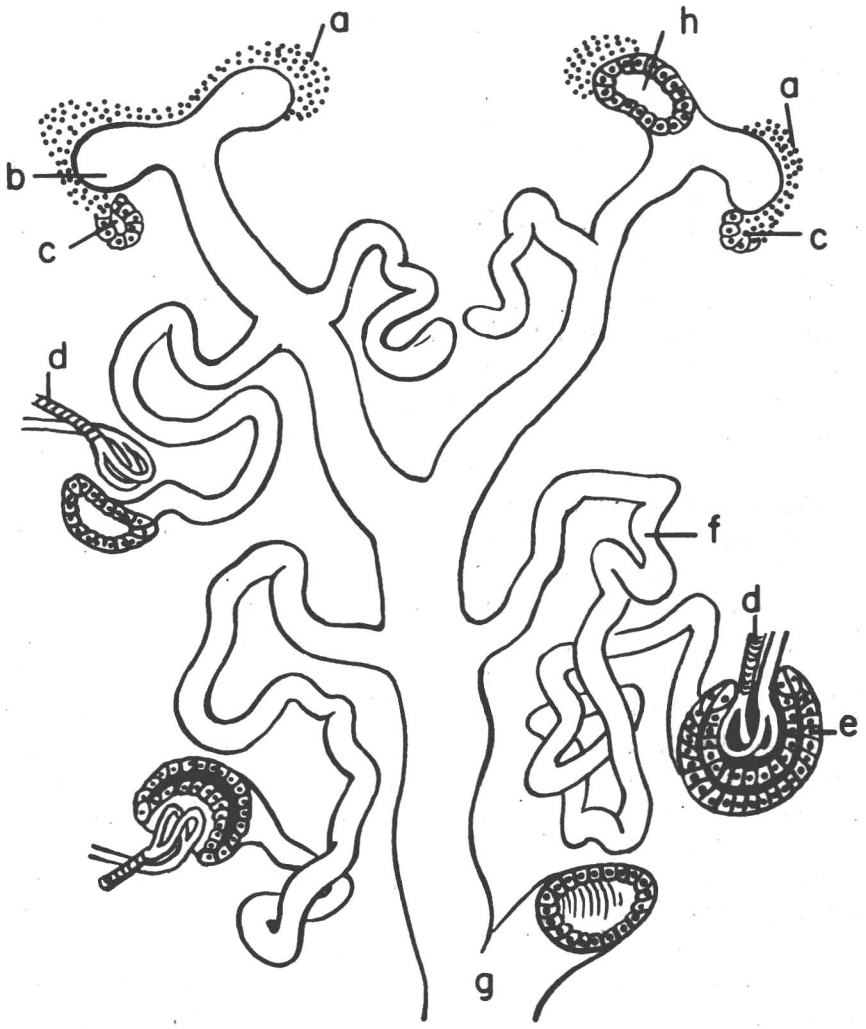

Figure 4
DIAGRAM OF DEVELOPMENT OF A METANEPHRIC KIDNEY

a. Metanephrogenic tissue capping ampulla of collecting tubule.
b. Enlarged blind end of ampulla.
c. Primordium of uriniferous tubule just formed from metanephrogenic tissue.
d. Vessel which forms the glomerulus.
e. Bowman's capsule cut open.
f. Uriniferous tubule in later stage of development.
g. Collecting tubule formed from ureteric bud of the mesonephric duct.
h. Ampulla of collecting tubule cut open. (Fig. 28-22 from Bloom, W., and Fawcett, D. W. A Textbook of Histology, 8th ed. Philadelphia: W. B. Saunders Co., 1962. [Modified from Corning])

HISTOLOGIC STRUCTURE OF THE NEPHRON

LIGHT MICROSCOPIC FEATURES. The glomerulus consists of a number of groups of capillary loops or lobules each arranged about a mesangial axis which merges with the media of the afferent arteriole at the hilum or vascular pole. Three cell types comprise the capillary loops: (1) A reflection of the visceral epithelium covers the urinary surface of the capillary loop and is arranged as short processes or podocytes which abut on the glomerular basement membrane; (2) a fenestrated endothelium which lines the vascular space; and (3) mesangial cells which are seen in the axial area where several capillaries are conjoined. The glomerular basement membrane consists of two immunochemically distinct basement membranes which are derived from the visceral epithelium and from the endothelium.

The juxtaglomerular apparatus (complex) consists of two elements: vascular and tubular (Barajas, 1970; 1971). The vascular component comprises a specialized secretory (endocrine) smooth muscle (the granular epithelioid cells) intercalated in the media of the afferent and occasionally efferent arterioles (Takeshita), and an extraglomerular mesangium, representing the polkissen of Zimmerman or lacis cells. The granular epithelioid cells have been shown by appropriate immunohistochemical technics to be the source of the protein, renin (Edelman and Hartroft; Hartroft et al.). The extraglomerular mesangium exhibits phagocytic activity similar to that of the glomerulus and in some species may contain granular epithelioid cells as well. It occupies the triangular space between the afferent and efferent arterioles and the macula densa, a specialized segment of the distal convoluted tubule. The latter represents the tubular component of the juxtaglomerular apparatus (complex).

The granular epithelioid cells of the juxtaglomerular apparatus which synthesize the protein, renin, are thought to give rise to a distinctive renin-producing tumor of the kidney resembling hemangiopericytoma (Schambelan et al.; see mesenchymal tumors of the kidney on page 201). The visceral cells of Bowman's capsule have been shown recently by in vitro and immunohistochemical studies to be the source of erythropoietin (Busuttil et al., 1971, 1972; Burlington et al.) This new evidence suggesting synthesis of erythropoietin by the glomerular epithelial cells, developmentally a tubular portion of the nephron, may account for the production of erythropoietin by renal adenocarcinomas.

Where the proximal convoluted tubule emerges from the glomerulus, the tubular cells are similar to the parietal cells lining Bowman's capsule. In the remainder of its random tortuous course through the renal cortex, the proximal convoluted tubule is lined by a single layer of long, truncated pyramidal cells containing numerous mitochondria and abundant amounts of cytoplasm. The free surfaces of the proximal convoluted tubular cells are covered by elaborate microvilli which form the brush border seen in a light microscopic section. No such brush border is evident in the distal or collecting tubules.

The proximal convoluted tubules extend deep into the medulla and terminate as the narrowed loop of Henle. The epithelial cells of Henle's loop are squamoid in the descending portion and somewhat cuboidal in the ascending limb. After Henle's loop

returns to the cortex, the nephron continues as the distal convoluted tubule which in turn subsequently empties into one of the branches of the collecting tubules. A short specialized segment of the distal convoluted tubule comprises the macula densa, which is closely applied to the afferent arteriole and the extraglomerular mesangium. Its previously described close association with the **afferent** arteriole and granular epithelioid cells has recently been shown to be a less constant feature (Barajas, 1970;1971). Relative to the adjacent segments of the distal convoluted tubule, the cells of the macula densa exhibit poorly developed basal cisternae and apical microvilli, contain fewer mitochondria, and show a more haphazard nuclear polarity. These features suggest that this specialized segment is not engaged in resorptive processes to the same degree as seen elsewhere in the distal tubule. There is a suggestion that the segment merely serves as an electrolyte leak facilitating monitoring of distal tubular sodium.

The coalescing peripheral tributaries of the collecting tubules join to form common straight collecting ducts which descend into the medulla and empty through the apex of a renal papilla into a renal calix. The microscopic appearance of the collecting tubular cells varies with the size of the tubule. In

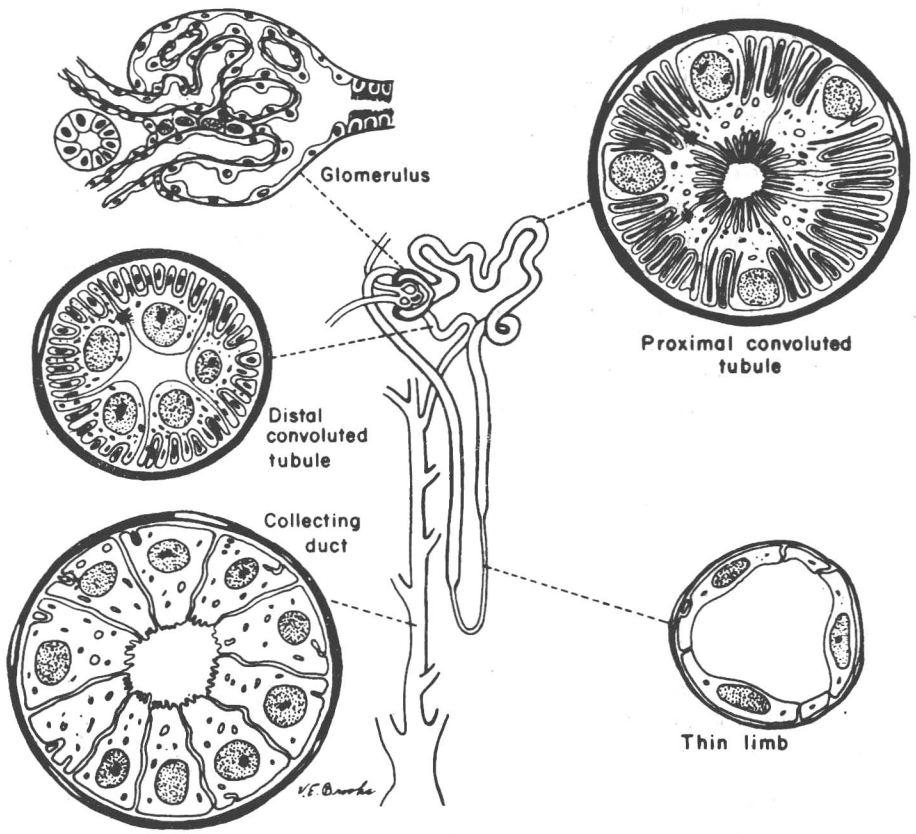

Figure 5
GENERAL HISTOLOGIC FEATURES OF THE NEPHRON

Cross sections of the various segments of the tubule roughly indicate the cellular morphologic features and the relative size of cells and tubules at these sites. (Fig. I-5 from Bennington, J. L., and Kradjian, R. Renal Carcinoma. Philadelphia: W. B. Saunders Co., 1967.)

general, the cells of the collecting tubules have sharp outlines with distinct hyperchromatic nuclei and clear pale cytoplasm. Cells of the smaller branching ducts are cuboidal, while those of the straight collecting tubules are more elongated. Surfaces of both are convex and bulge into the duct lumens (fig. 5).

ELECTRON MICROSCOPIC FEATURES. Cells of the proximal convoluted tubules have characteristic ultrastructural morphologic features which are distinctly different from those of the loop of Henle, distal convoluted tubule, and collecting ducts (Trump et al.). They are identified by their characteristic fine structure including: (1) The tall columnar shape; (2) elaborate tightly packed microvilli coated with glycocalix; (3) pinocytotic apical vesicles, vacuoles, and tubules of characteristic structure in the apical cytoplasm; and (4) abundant elongated tortuous mitochondria intimately associated with basal and lateral cisternae (elaborate invaginations of the cell membrane) (figs. 6, 7). These features are demonstrated in the three dimensional diagrammatic reconstruction of a portion of the proximal convoluted tubule (fig. 8).

In contrast, the distal convoluted tubular cells are tall and cuboidal with scattered short microvilli (fig. 9). Extensive lateral and basal cisternae are present, but they enclose several mitochondrial profiles rather than the individual mitochondria seen in the proximal convoluted tubule cells. Apical pinocytotic vesicles and vacuoles are rare.

Cells of the loop of Henle tend to be squamoid with ovoid nuclei which have folded nuclear margins (fig. 10). Basal and lateral cell interdigitations are absent and cytoplasmic organelles are scanty.

Cells of the collecting ducts (fig. 11) are cuboidal, but become more elongated in the renal medulla. Sparse microvilli are seen on cell surfaces, but no brush border is present. The elaborate system of apical pinocytotic vesicles, tubules, and vacuoles, prominent features of proximal convoluted tubules, are absent. Mitochondria are shorter and have a more rounded configuration than those of the proximal convoluted tubular cells. They are rarely associated with the infrequent basal cisternae. Droplets of membrane-bound lipid (lipofuscin) are abundant in the basal cytoplasm.

Figure 6
PROXIMAL CONVOLUTED TUBULAR CELL

The apical part of the proximal convoluted tubular cell is covered by tightly packed microvilli forming the brush border (BB). In the apical cytoplasm, apical tubules (AT), vacuoles (V), and cytosomes (C) are evident. Mitochondria (M). Tubular Lumen (TL). Nucleus (N). X9300. (Fig. 5 from Tisher, C. C. Human renal ultrastructure. I. Proximal tubule of healthy individuals. Lab. Invest. 15:1357-1394, 1966.)