

FINE STRUCTURE OF THE TRANSITIONAL EPITHELIUM OF THE DOG URETER

Hiroshi MUTO, Kumiko OHTA
and Ikuo YOSHIOKA

*From the Department of Anatomy, Aichi Medical University, Nagakute, Aichi, Japan
(Director: Prof. H. Muto)*

The fine structure of the transitional epithelium of adult dog ureter has been studied in thin sections with an electron microscope.

It is thought that the light cells represent an active stage and that the dark cells represent a less active stage of the same cell type according to the shape of nucleus and cell organelle. The dark cells are also considered as a type to be the result of pressure by adjacent cells or newly formed cells.

The free luminal surface of the cells and many cytoplasmic vesicles in these cells are bounded by a thick unit membrane. These vesicles or vacuoles are considered to function as a defense of the cytoplasm, when the epithelial cells change the form. The vesicles and the plasma membrane maintain angular conformations which suggest the membrane to be unusually rigid. It is supposed that the plasma membrane of the superficial cells is the major barrier to the free flow of water from the cytoplasm into the hypertonic urine. The possible origin of the thick plasma membrane in the Golgi apparatus was shown.

All the cells of the epithelium have a dense feltwork of tonofilaments which ramify throughout the cytoplasm. The tonofilaments connect frequently with intercellular desmosomes. Keratohyalin-like granules were seen in the tonofilaments.

INTRODUCTION

The ureter is a slightly flattened tube that extends from the end of the renal pelvis to the bladder. The ureteral epithelium is composed of the transitional one, however its function is not known. The present investigation is concerned with two aspects of a permeability barrier to the urine and a defence to the damage of the cytoplasm of the transitional epithelial cells. The transitional epithelium lining the ureters is in contact with strongly hypertonic urine. This epithelium must, therefore, have a permeability barrier to prevent a continual inflow of water and dilution of the urine from the cellular fluid of the urothelium.

It is thought that a further electron microscopic investigation of the ureteral epithelium, with special reference to a possible permeability barrier, would provide with the morphological bases for physiological studies.

MATERIALS AND METHODS

The materials used for the present study consist of 9 randomly autopsied dogs.

The ureters were removed from all cases and fixed in 10% formalin saline for the light microscopy. Paraffin sections were routinely stained with hematoxylin-eosin. For the electron microscopy, small pieces of the ureter were prepared and immediately fixed in 2% phosphate-buffered glutaraldehyde (pH 7.4) and then fixed in 2% osmium tetroxide (pH 7.4). After dehydration through a graded ethanol series, the specimens were embedded in Epon 812. These thin sections were stained with uranyl acetate and lead citrate, and observed with a Hitachi HU-12A electron microscope.

RESULTS

The ureteral epithelium of the normal adult dog has a well-developed pattern of cell differentiation, with large, squamous,

complex cells in shape at the luminal surface and smaller, more simplified cuboidal or columnar cells forming the intermediate and basal layers (Fig. 1). The cells of the basal layer are attached by half desmosomes on their basal membranes to a basement membrane. The basal and intermediate cells and the lateral and basal membranes of the squamous cells are deeply interdigitated (Fig. 2).

The epithelial cells of a ureter of the

adult dog have been divided into light cells and dark cells, primarily on difference in density of the cytoplasm. The light cells are more numerous than the dark ones and the light cells are larger than the dark cells; the former usually has larger and round nuclei and the latter has smaller and irregular ones (Fig. 3). The light cells contain a smaller Golgi apparatus, lysosomes, considerable glycogen granules, many free ribosomes, numerous cytoplas-

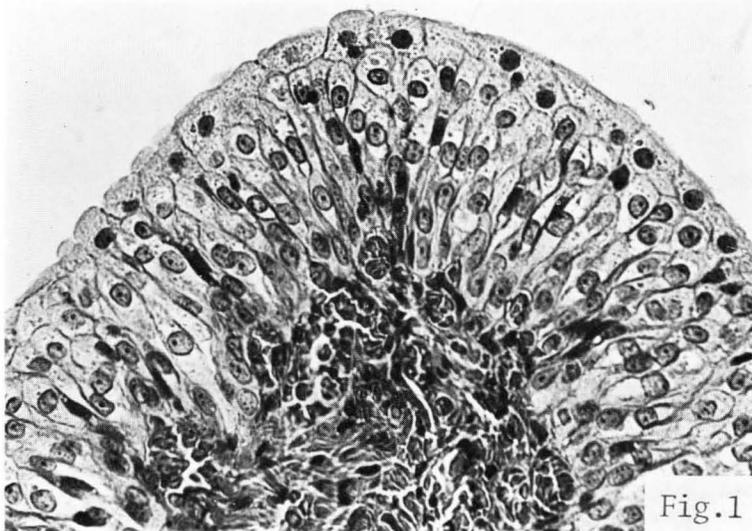


Fig. 1. The ureteral epithelium of the normal adult dog by light microscopy. $\times 400$

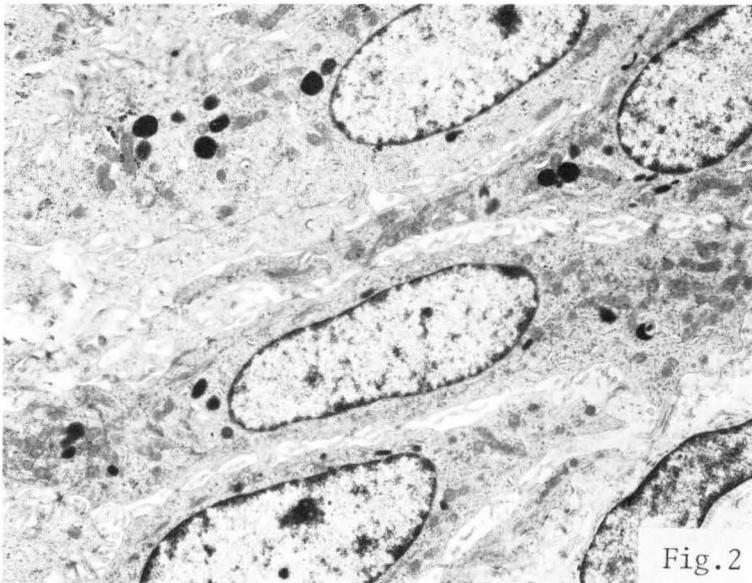


Fig. 2. The basal layer of the ureteral epithelium by electron microscopy. $\times 5,000$

mic filaments, a few mitochondria and very small endoplasmic reticulum.

The surface squamous cells at the luminal surface have several specialized features. The cells of the transitional epithelium have thick cell membrane (Fig. 4). The membrane toward the lumina of these cells is a three-layered structure, the width be-

ing greater than other cell plasma membranes. In some cases, it has a asymmetrical appearance, with the outer cell membrane being wider than the inner one (Fig. 4). The luminal membrane, when viewed by transmission electron microscopy, sometimes appeared to be raised with a pointed end as angular folds of the ure-

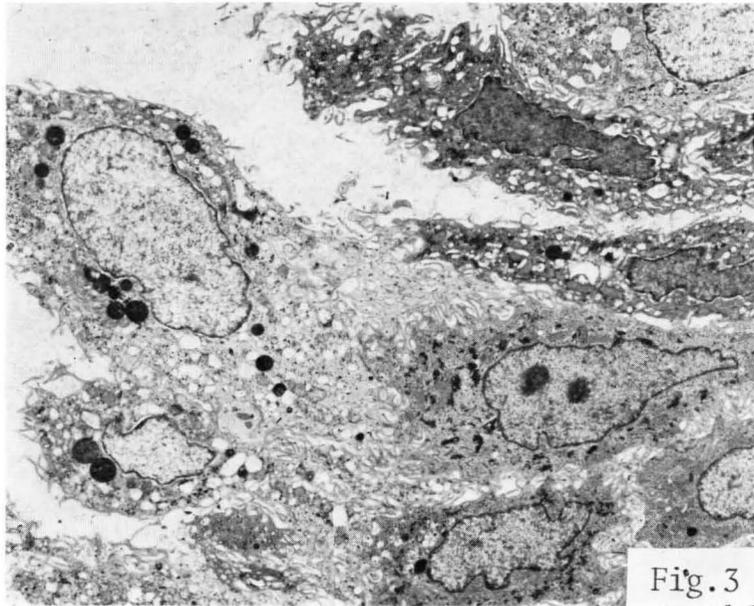


Fig. 3. Light cells and dark cells in the epithelium. $\times 1,500$

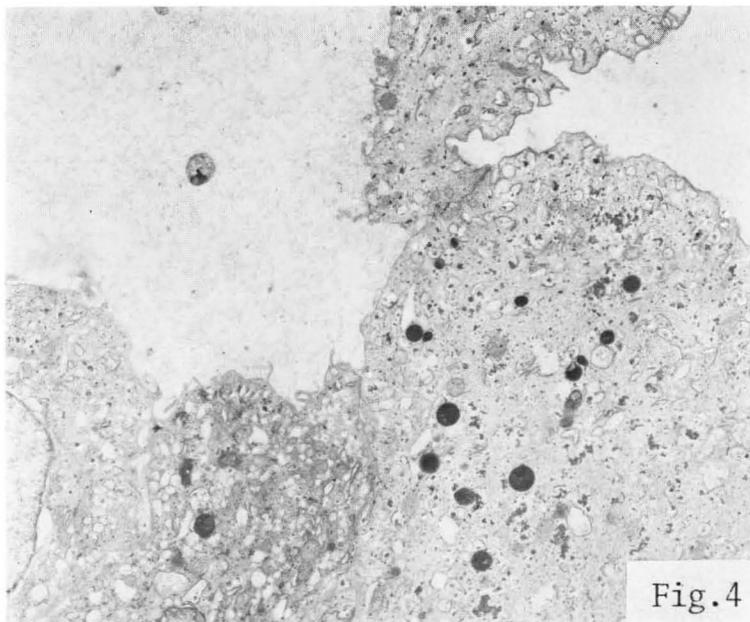


Fig. 4. The thick cell membrane of the transitional epithelial cells. $\times 4,000$

teral lumen (Fig. 4, 5).

Vesicles or vacuoles in the same type of cell membrane width may be seen in the vicinity of the Golgi apparatus within the cytoplasm of the surface squamous cells (Fig. 5). The number, size and situation of vesicles or vacuoles are variable, some

being large and approach to the luminal membrane, while others are small and isolated from there. They may be flattened or roughly spherical in shape; the large ones often contain inclusions, and the inclusion frequently seems to be a core. The specialized vesicles or vacuoles seen near

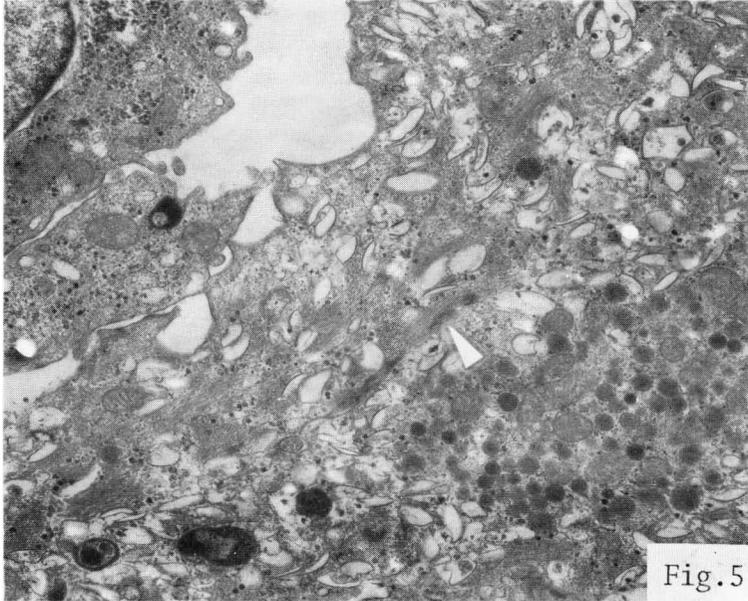


Fig. 5. The luminal cell membrane with pointed ends as angular folds of the ureteral lumen. $\times 10,000$

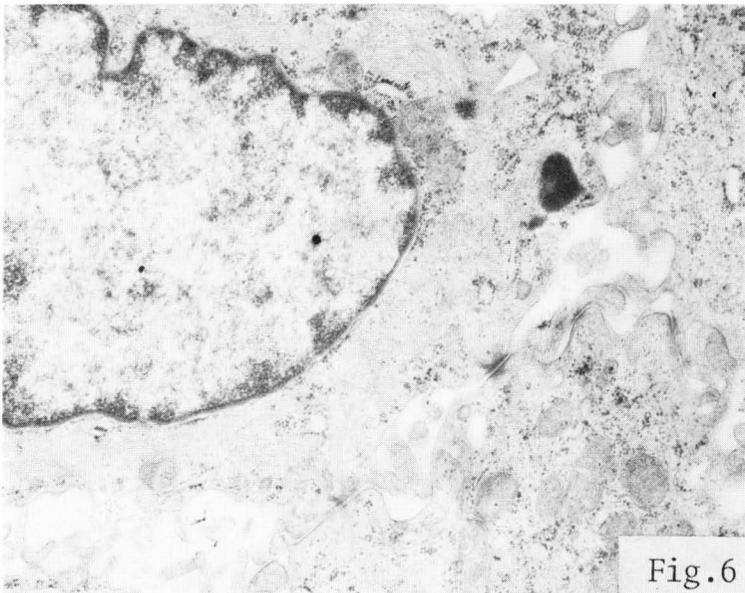


Fig. 6. Bundles of filaments terminate at desmosomes. Keratohyalin-like granules in the filaments. $\times 15,000$

the lumen were not observed in the basal cells (Fig. 5).

Contiguous surface cells are united at the lumen by a continuous tight junction, which extends about $3\ \mu\text{m}$ below the luminal surface. While these tight junctions are seen in all sections, passing through the contact between adjacent surface cells, desmosomes are frequently seen

in ureteral epithelium of adult dog, suggesting that they are arranged intermittently around the cells (Fig. 4).

Numerous filaments are observed in the cells of ureteral epithelium. Bundles of filaments in the surface cells are larger and more numerous than in the basal cells, extending in many directions, and some of them terminate at desmosomes (Fig. 6).

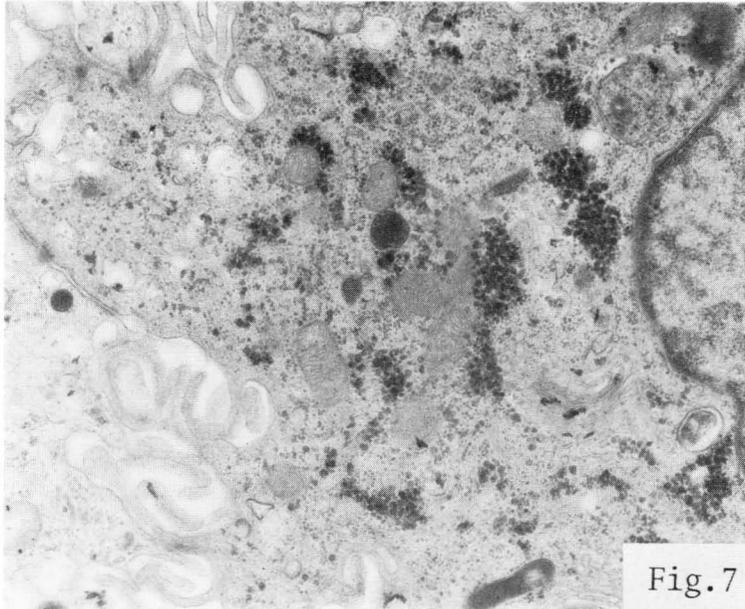


Fig. 7. Glycogen granules in the vicinity of the lysosomes or the filaments. $\times 15,000$

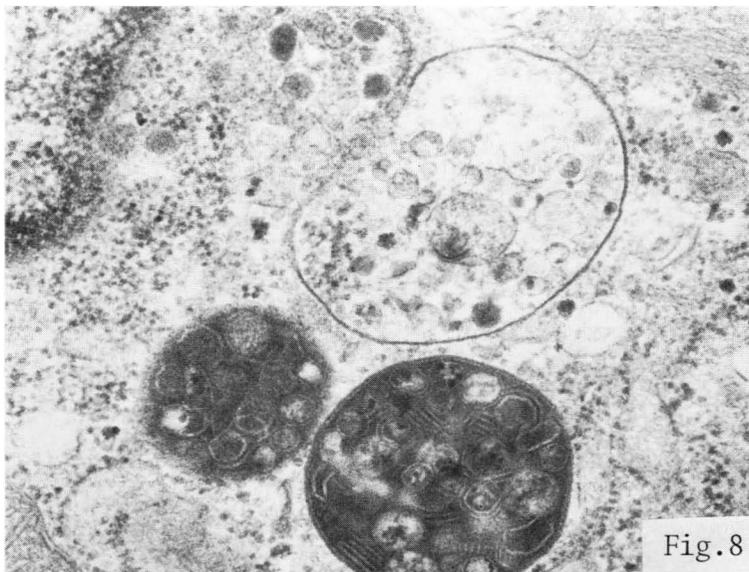


Fig. 8. Secondary lysosomes containing varied membranous or granular structures. $\times 35,000$

Keratohyalin-like granules are observed in the filaments. The granules are electron dense spherical bodies and have no limiting membrane (Fig. 5 and 6A).

Large clusters of mitochondria are present within the surface squamous cells, as well as in the deeper layer. Rough-surfaced endoplasmic reticulum is sparse in all layers though ribosomes are plentiful.

The Golgi apparatus was moderately well developed, and often associated with primary lysosomes in the surface squamous cells. The Golgi apparatus was smaller in the intermediate and basal cells. The surface cells contained patches of glycogen granules and groups of mitochondria. Glycogen granules were seen in the vicinity of the lysosomes or the filaments (Fig. 7).

Secondary lysosomes were a striking feature of the epithelium of the ureter, being most frequent in the surface and intermediate layers; in the latter, they were often clustered around the nucleus. Ultrastructurally, lysosomes within the cytoplasm of epithelial cells of the ureter have an outer limiting membrane averaging 60 Å in diameter, and a finely granular matrix which contains a multitude of varied membranous and granular structures in secondary lysosomes (Fig. 8).

The intermediate and basal cells often showed large invagination of the nuclear membrane, and also the cells were of a simpler organization. The junction of the basal cells with the submucosa was irregular in shape, giving the appearance of microprotrusions of cytoplasm dipping into the submucosa. Intercellular junctions were folded in a complex manner and, occasionally, desmosomes were seen between intermediate cells.

DISCUSSION

The epithelial cells of the ureter are divided into light cells and dark ones based on difference in density of the cytoplasm. Hayakawa observed the dark cells in the urothelial tumor of the upper urinary tract²⁾. It is considered that the light cells of the ureteral epithelium represent an active stage and that the dark

cells represent a less active stage of the same cell type in the surface squamous or intermediate layers according to the shape of the nucleus and cell organelle. The dark cells in the basal layer, however, are thought to have newly developed to have resulted. On the other hand, the dark cells are also considered as a type from pressure by adjacent cells.

The superficial cells of the transitional epithelium have thick cell membranes. Patches of similar thick membrane are found in the walls of the Golgi cisternae^{3,4)}. The cell membrane of the inner luminal surface is thicker than the other parts of the cell. This is similar to the membrane structure observed in the epithelium of the urinary bladder of the mouse, rat and human^{5,7)}. The significance of thick cell membrane is to provide the defense to the free flow of water from the cytoplasm into the hypertonic urine. Examination of the surface by scanning electron microscopy shows that these surface features are actually small ridges and sulci^{6,8-11)}. The membrane may be flat or raised into angular folds of the ureteral lumen¹²⁾.

In the Golgi area of the superficial cells numerous vesicles or vacuoles with a membrane similar to the plasma membrane can be observed¹⁾. A small sac or bladder containing fluid or substance is vesicle, and a clear sac or bladder in low density is vacuole. The substance in the vesicles seems frequently to be a core. The Golgi areas in the superficial cells may produce vesicles or vacuoles. These facts suggest that the vesicles or vacuoles are the form in which the thicker membrane is manufactured and transported. Also, these vesicles or vacuoles are considered to be a defense mechanism of the cytoplasm, when the epithelial cells change the form.

The intracellular filaments can be divided according to their function. The cytoskeletal filaments are most abundant in the cells of ureteral epithelium, where they are referred to as tonofilaments. These tonofilaments extend in many directions in the cells and some of them ter-

minate at desmosomes. The tonofilaments provide these cells with rigidity, as well as variable size and shape. On the other hand, as the keratohyalin-like granules appear in the tonofilaments, it is considered that the tonofilaments would originate in the granules (Fig. 5, 6 Δ).

Lysosomes are minute granular, membrane-bound organelles which contain enzymes for intracellular digestion. The lysosomes represent an essential part of the cellular defense and transport systems⁴. Structurally and functionally, lysosomes are divided into two categories: 1) primary lysosomes and 2) secondary lysosomes¹. Secondary lysosomes are involved in enzymatic digestive activities, and therefore contain a collection of membranous and granular structures missing in the primary lysosomes. Koss⁷) stated that the lysosomes in the cytoplasm of the ureteral epithelium store the useless or damaged asymmetric unit membrane. The vicinity of the centers of production of the lysosomes suggests the possibility of an association that is perhaps not casual but that serves the purpose of regulating the amount of production of asymmetric unit membrane by the Golgi apparatus.

REFERENCES

- 1) Fulker, M.J., Cooper, E.H., and Tanaka, T.: Proliferation and ultrastructure of papillary transitional cell carcinoma of the human bladder. *Cancer*, **27**: 71~82, 1971.
- 2) Hayakawa, M.: The clinical and cytologic studies on urothelial tumors of the upper urinary tract. *Jap. J. Urol.*, **69**: 1439~1456, 1978.
- 3) Hicks, R.M.: The fine structure of the transitional epithelium of rat ureter. *J. Cell Biol.*, **26**: 25~48, 1965.
- 4) Hicks, R.M.: The function of the Golgi complex in transitional epithelium. *J. Cell Biol.*, **30**: 623~643, 1966.
- 5) Hicks, R.M.: The mammalian urinary bladder: an accommodating organ. *Biol. Rev.*, **50**: 215~246, 1975.
- 6) Kjoergaard, J., Starklint, H., Bierring, F. and Thydo, E.: Surface topography of the healthy and diseased transitional cell epithelium of the human urinary bladder. *Urol. int.*, **32**: 34~48, 1977.
- 7) Koss, L.G.: The asymmetric unit membranes of the epithelium of the urinary bladder of the rat. *Laboratory Investigation*, **21**: 154~167, 1969.
- 8) Lloyd-Davies, R.W., Hayes, T.L. and Hinman, F.: Urothelial microcontour. I Scanning electron microscopy of normal resting and stretched urethra and bladder. *J. Urol.*, **105**: 236~241, 1971.
- 9) Lloyd-Davies, R.W. and Hinman, F.: Urothelial microcontour displayed by scanning electron microscopy. *British Journal of Urology*, **43**: 665~673, 1971.
- 10) Mooney, J.K. and Hinman, F.: Surface differences in cells of proximal and distal canine urethra. *J. Urol.*, **111**: 495~501, 1974.
- 11) Muto, H. and Yoshioka, I.: A study by scanning electron microscopy of the ureter epithelium of the black ape. *Acta Urol. Jap.*, **25**: 753~760, 1979.
- 12) Wolf, J.: Appearance, origin, causes and functional significance of the formation of surface reliefs as demonstrated on transitional epithelium. *Folia Morphologica*, **14**: 17~32, 1966.

(Accepted for publication, Jan. 17, 1980)

和文抄録

イヌ尿管移行上皮の微細構造

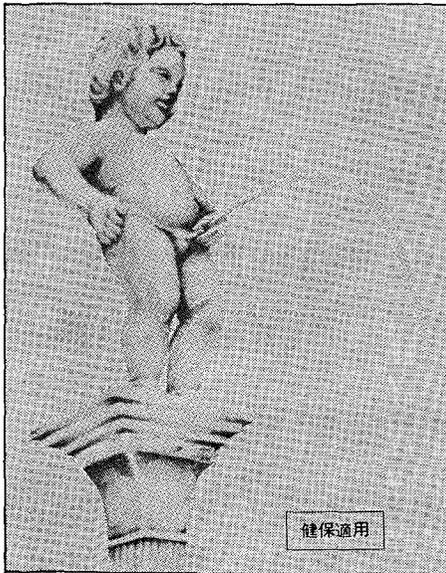
愛知医科大学解剖学教室（主任：武藤 浩教授）

武藤 浩・太田久美子・吉岡 郁夫

イヌ尿管の移行上皮を電顕で観察し、つぎのような結果を得た。上皮細胞は核の形や細胞内の小器官の状態により、機能の盛んな明細胞とそうでない暗細胞に分けられる。暗細胞はまた周囲から圧迫されたり、新生した細胞と考えられる。尿管の内腔面の細胞膜は厚く、上皮細胞内の小胞の膜も厚く、いずれも単位膜

でできている。内腔面の細胞膜は尿と上皮細胞との間の隔壁となり、浸透圧から細胞を守るものであろう。上皮細胞内には tonofilament がよく発達し、一部は desmosome に接続する。tonofilament の発生は keratohyalin 様顆粒と関係があるらしい。

ROBAVERON®



排尿障害の排尿力増強に！

ロバベロン

—排尿障害治療剤—

- 本剤は、性ホルモンおよび蛋白質を含まない成熟雄豚前立腺抽出物の水溶性注射剤です。
- 本剤は、膀胱利尿筋の筋力増強に寄与し、排尿力を高めます。
- 本剤の排尿力増強作用により、自・他覚所見の改善がみられます。

適 応 症 神経因性膀胱。前立腺肥大症による排尿困難、頻尿、尿線細小、排尿痛、残尿および残尿感。

包 装 1ml×10アンプル
使用上の注意 説明書をご参照下さい。

輸入発売元



日本商事株式会社

大阪市東区石町2丁目30番地
TEL 06-941-0301

製造元

ロバファルム社

(スイス・バーゼル)