3rd year

University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

THE GENITOURINARY SYSTEM

Anatomy

1

- [ ] Slides
- [ ] Sheet
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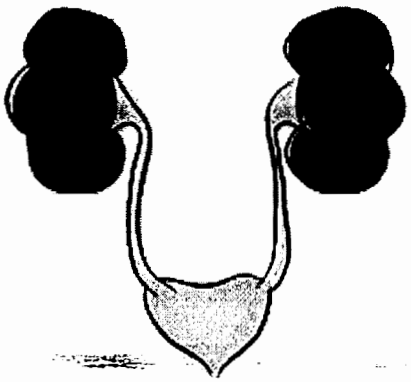
Title: _____

Professor: Dr.Faraj Bustami

Date: 30/3/2015



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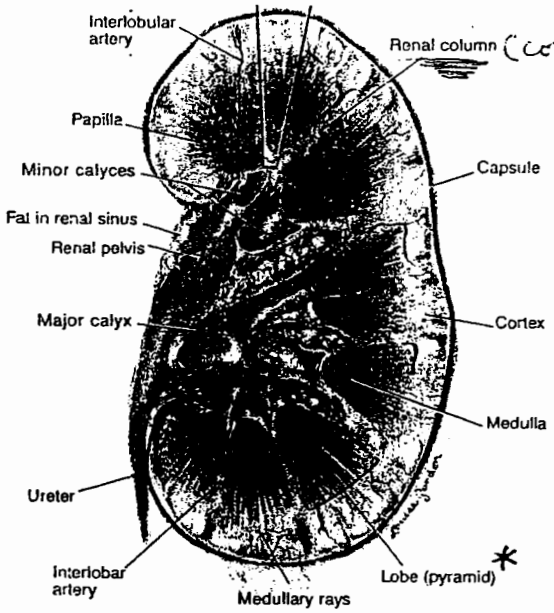
Anatomy

Urinary system
Medical
4/ 2015



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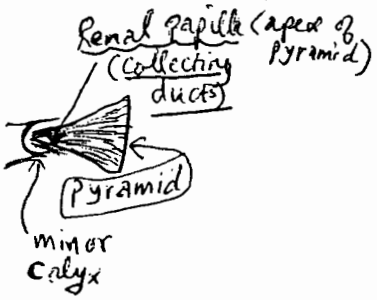
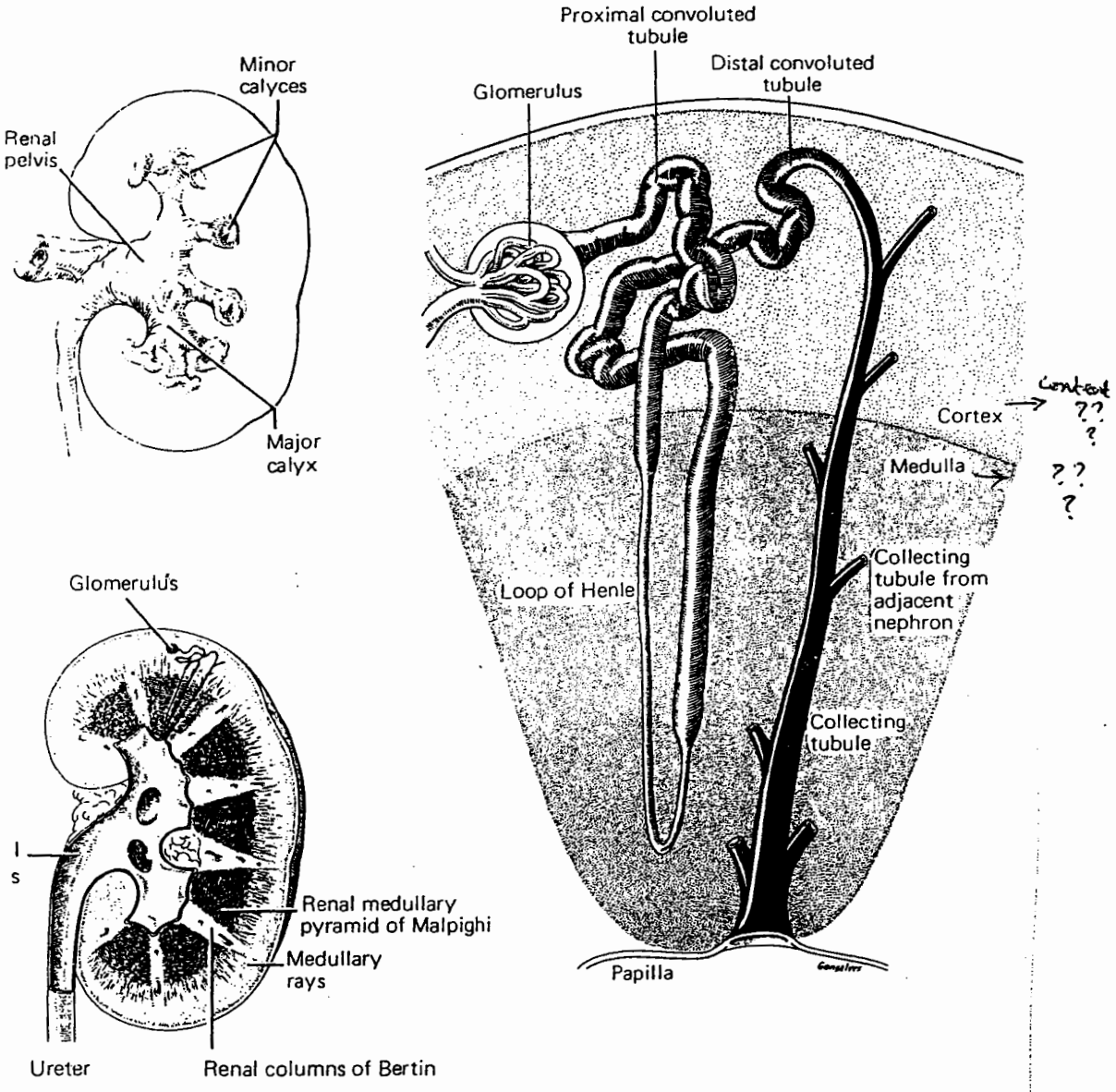
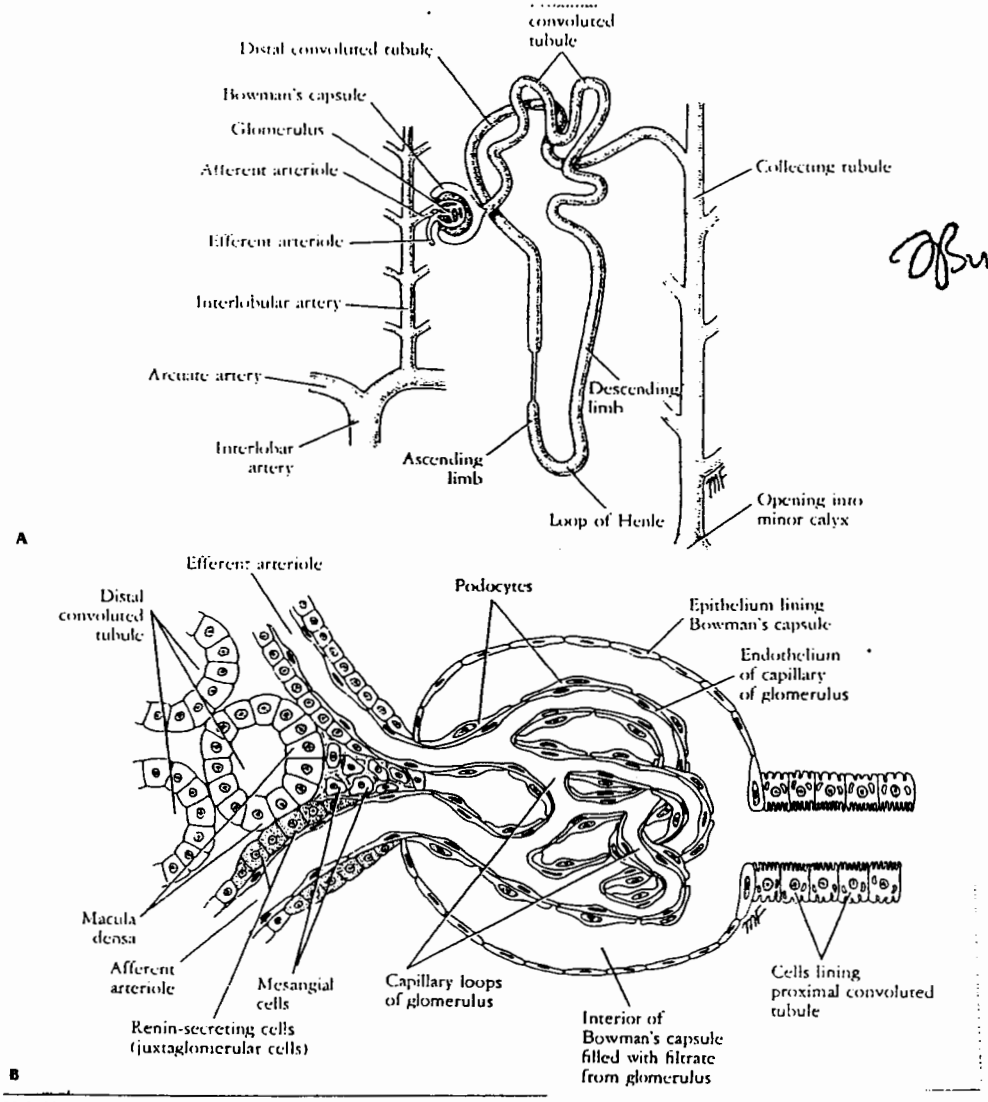


* The fresh Kidney can easily be divided into a dark reddish-brown outer cortex and a lighter-coloured inner medulla.
* The medulla → is composed of about a dozen renal Pyramids, each with its base oriented toward the cortex and its apex (the renal papilla) projecting into a minor calyx.
* The cortex → Extends into the medulla between adjacent Pyramids as the renal columns.
* Extending from the bases of the renal Pyramids into the cortex are striations known as medullary rays (400-500 in number; Each consists of a straight collecting tubule into which the distal convoluted tubules of many neighbouring nephrons empty their contents through arched collecting tubules.
* A RENAL LOBE ?? may be defined as a renal Pyramid together with the cortical tissue overlying its base and lying along its sides
* A Renal lobule ?? is a medullary ray and the associated tubules (a sleeve of nephrons draining into these tubules) and is separated from its neighbour by the interlobular arteries.


Minor calyces
Renal pelvis
Major calyx
Glomerulus
Proximal convoluted tubule
Distal convoluted tubule
Cortex
Medulla
Loop of Henle
Collecting tubule from adjacent nephron
Collecting tubule
Papilla
Glomerulus
Renal medullary pyramid of Malpighi
Medullary rays
Ureter
Renal columns of Bertin



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Uriniferous Tubules

The kidney is composed of large numbers of microscopic units called *uriniferous tubules*. Each tubule is composed of two functional regions, the *nephron*, which produces an excretion known as urine, and the *collecting tubule*, which concentrates the urine and conveys it to the calyces (Fig. 13-3).

Nephron

There are over a million nephrons in one kidney. Each consists of four distinct parts: (1) the renal corpuscle, which contains the glomerulus, (2) the proximal convoluted tubule, (3) the loop of Henle, and (4) the distal convoluted tubule (see Fig. 13-3). The parts of the nephron form a continuous tubule that measures about 50 mm in length and runs from the cortex to the medulla and then returns to the cortex

RENAL CORPUSCLE. The *renal corpuscle* is situated in the cortex. It is formed by the upper end of the uriniferous tubule, which is expanded into a structure called a *Bowman's capsule* (Figs. 13-4–13-7; see Fig. 13-3). The renal corpuscle contains the glomerulus, which is a network of capillaries into which blood enters by an *afferent arteriole* and leaves through a smaller *efferent arteriole.*

The glomerulus indents the wall of the Bowman's capsule as a fist might press into the side of a balloon (Fig. 13-8). The epithelial cells that form the wall of the Bowman's capsule also serve as a covering for the glomerulus. The renal corpuscle thus consists of the Bowman's capsule and the glomerulus (see Figs. 13-4–13-7).

The outer wall of the Bowman's capsule is lined with simple squamous epithelium that abruptly changes into cuboidal epithelium at the start of the proximal convoluted tubule. Where the capsular wall is reflected onto the glomerulus, the squamous cells change into star-shaped cells with multiple processes. These cells, called *podocytes.*

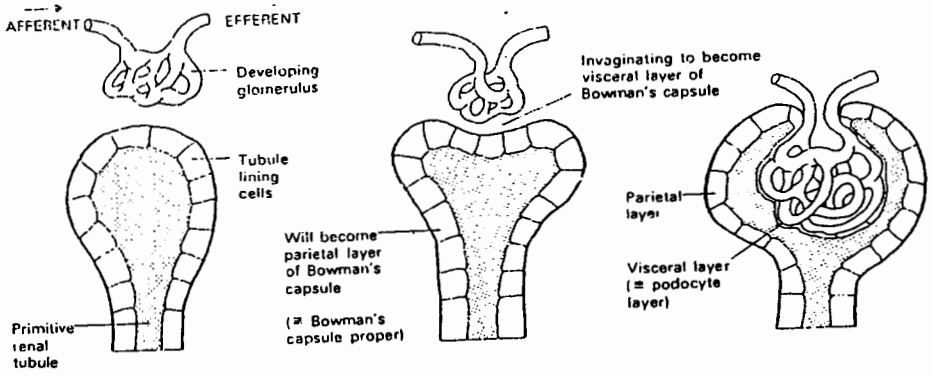


Fig. 16.8 Development of the renal corpuscle

This diagram illustrates in a highly schematic manner the mode of development of the renal corpuscle. The nephrons develop from the embryological metanephros as blind-ended tubules consisting of a single layer of cuboidal epithelium. The ends of the tubules dilate and become invaginated by a tiny mass of tissue which differentiates to form the glomerulus. The layer of invaginated epithelium flattens and differentiates into podocytes which become closely applied to the surface of the knot of glomerular capillaries. The intervening connective tissue disappears so that the basement membrane of glomerular endothelial cells and podocytes effectively fuse forming the glomerular basement membrane. A small amount of connective tissue nevertheless remains to support the capillary loops and differentiates to form the mesangium. Where the mesangium stretches between the capillary loops, its surface is directly invested by podocyte cytoplasm with podocyte basement membrane lying between the two. When examining ultra-thin light microscope specimens as in Figure 16.11 and electron micrographs as in Figure 16.14, the podocytes, endothelial cells and mesangium are identified most easily by tracing out the podocyte and endothelial cell basement membranes.

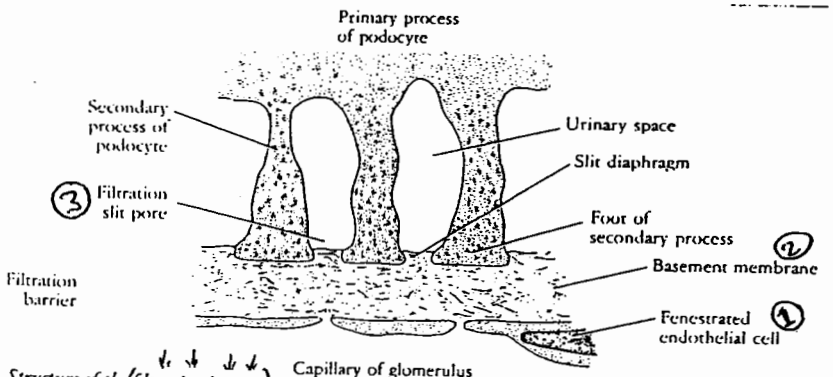
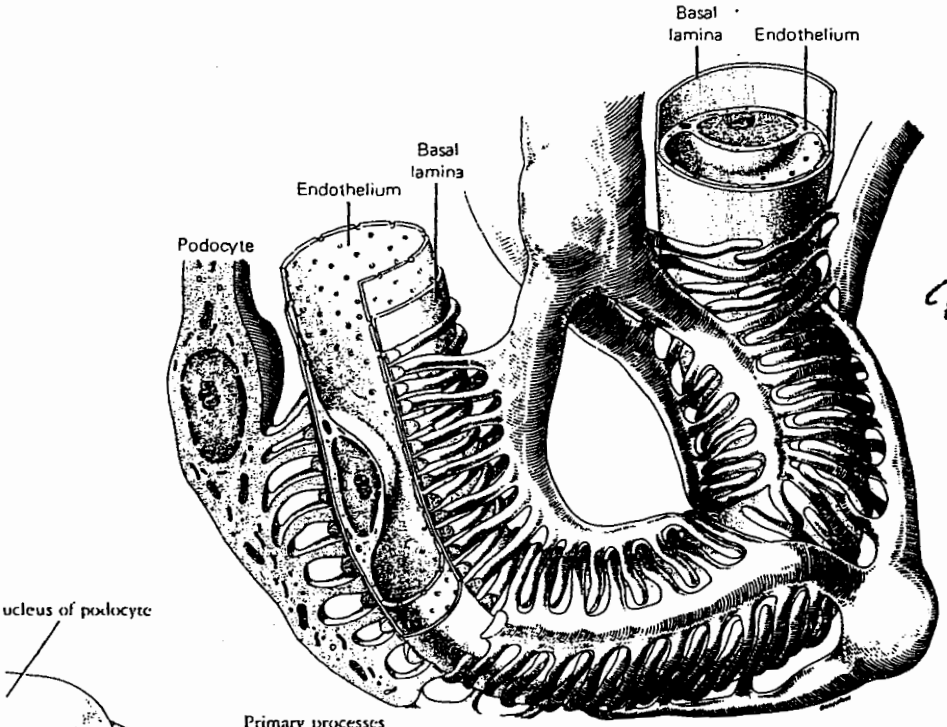


Fig. 13-11. Structure of the filtration barrier.

primary processes that tightly clasp the glomerular capillaries (Figs. 13-9 and 13-10). From the primary processes, smaller *secondary processes* arise that interdigitate with the secondary processes of other podocytes. This arrangement leaves small slitlike gaps between the processes that measure about 25 nm across and are called *slit pores* (Fig. 13-11). The secondary processes end in *feet* that are applied firmly to the basement membrane of the capillary wall of the glomerulus. Extending across the slit pores between adjacent feet is a thin *slit diaphragm* about 6 nm thick (Fig. 13-12).

The blood in the glomerular capillaries is separated from the cavity of the Bowman's capsule by: (1) the fenestrated endothelial cells lining the capillaries (Fig. 13-13), (2) a thick basement membrane (Fig. 13-14), and (3) the slit pores of the podocytes. Together these structures are known as the *filtration barrier* (see Fig. 13-11). The holes, or fenestrae, in the endothelial cells permit the passage of plasma but hold back the cells of the blood. The smaller molecules of the plasma readily pass through the basement membrane and the slit diaphragm of the podocytes to enter the cavity of the Bowman's capsule. Particles with a molecular weight greater than 160,000 are held back by the slit diaphragm. The plasma protein albumin, which has a molecular weight of 69,000, would be expected to pass through without difficulty. We know, however, that in a normal individual, it does not. The probable explanation is that the filtration mechanism is blocked by proteins with larger molecules and that the electric charge on the filter repels the albumin molecules. The fluid that finally crosses the filtration barrier and enters the capsular space is called the *glomerular filtrate.*

Lying between the glomerular capillaries are small groups of star-shaped cells that are contractile and capable of phagocytosis. These cells are called *mesangial cells* (see Fig. 13-3) and support the capillary walls by producing intercellular substance. They are also thought to remove by phagocytosis any macromolecules that escape from the capillaries into the tissue space.



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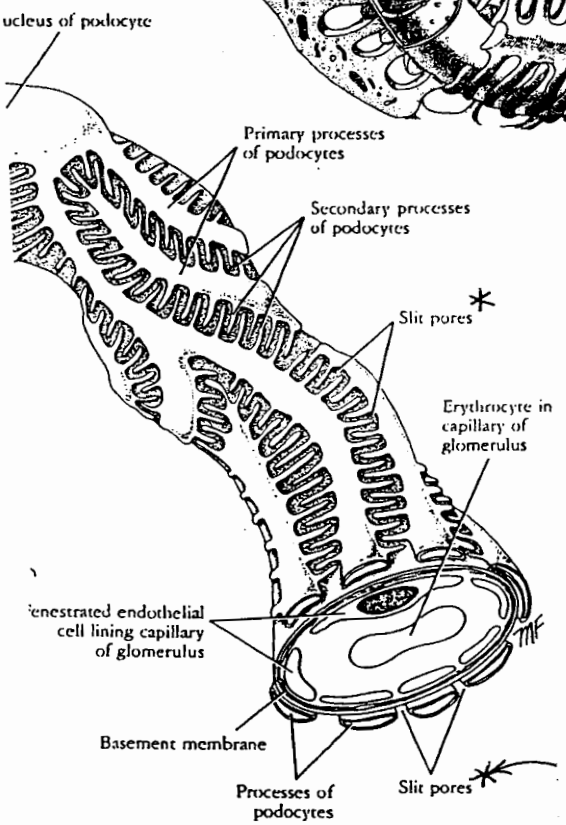
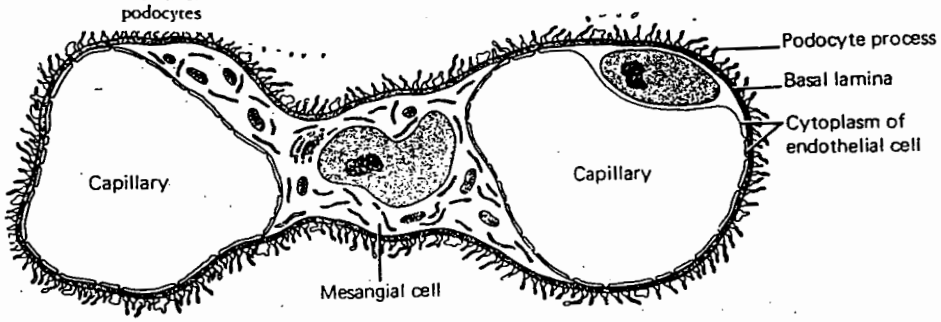


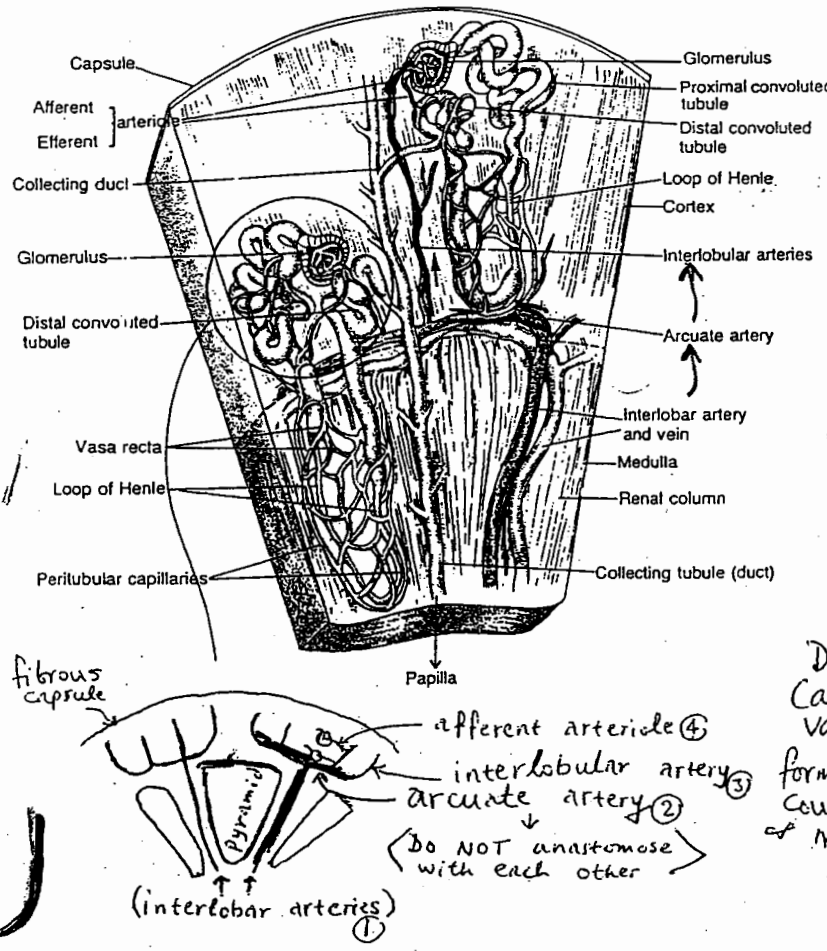
Function of the Renal Corpuscle. The rate of blood flow through both kidneys is about 1,200 ml per minute, or about 25 percent of the cardiac output. The blood enters the glomeruli under high pressure, and fluid is driven through the filter into the Bowman's capsule (see Fig. 13-3). The fenestrated capillaries of the glomeruli form the coarse filter; the basement membrane, the slit diaphragm, and the slit pores of the podocytes form the ultrafilter. The glomerular filtrate differs from the plasma in that it has almost no proteins. In 24 hours, both kidneys produce about 180 L of glomerular filtrate; about 99 percent of the filtrate is reabsorbed by the renal tubules, and only 1 percent will be excreted as urine



Mesangial cells of glomerular capillaries. They are located between 2 capillary lumens, enveloped by the basal lamina

Renal artery → anterior & Posterior divisions → 5 segmental arteries ⇒ Each segmental artery divides into LOBAR arteries (usually One for each Pyramid) ⇒ Each lobar artery divides into 2-3 INTERLOBAR arteries (which run on each side of the pyramid) ⇒ At the corticomedullary junction the interlobar arteries divide dichotomously into ARCUATE arteries which arch over the bases of the pyramids ⇒ The arcuate arteries give off INTERLOBULAR arteries which run radially into the cortex giving off AFFERENT GLOMERULAR ARTERIOLES → the EFFERENT GLOMULLAR ARTERIOLES divides soon to form Peritubular capillary plexus around the Proximal & distal convoluted tubules ← Bustami

6 A



Efferent arteriole of juxta medullary glomeruli ↓ enters a pyramid & divides into 12-24 Vasa recta ↓ breaks up to form capillary plexus around loops of Henle & collecting ducts ↓ At the venous end the C. plexus gives rise to ascending vasa recta ↓ Descending vasa recta (arterioles) ⊕ ascending vasa recta (venules) form the basis of countercurrent exchange & multiplier system

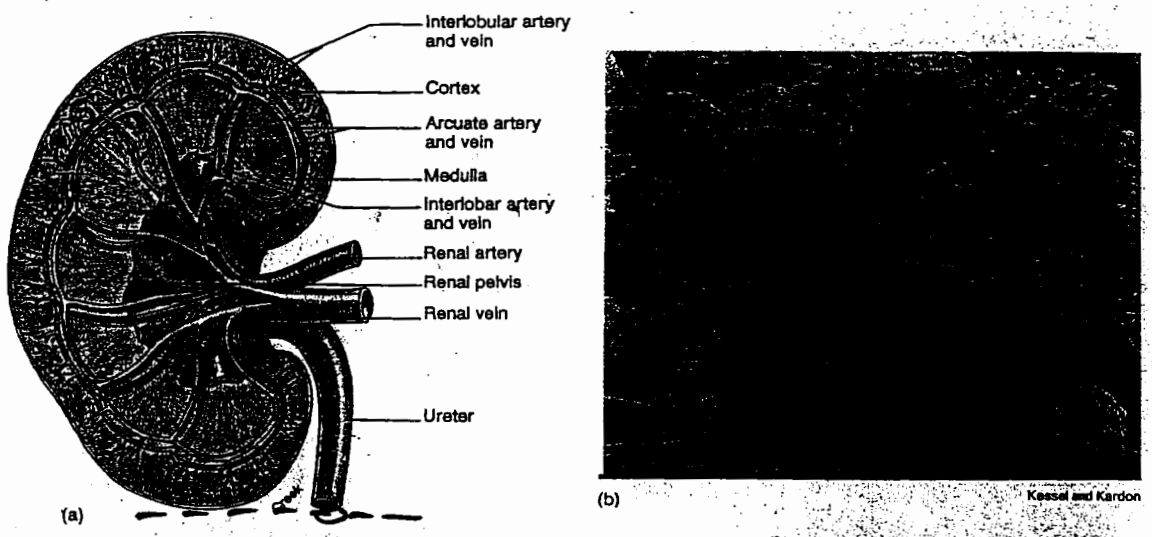


Figure 19.7 The vascular structure of the kidneys. (*a*) An illustration of the major arterial supply and (*b*) a scanning electron micrograph of the glomeruli.

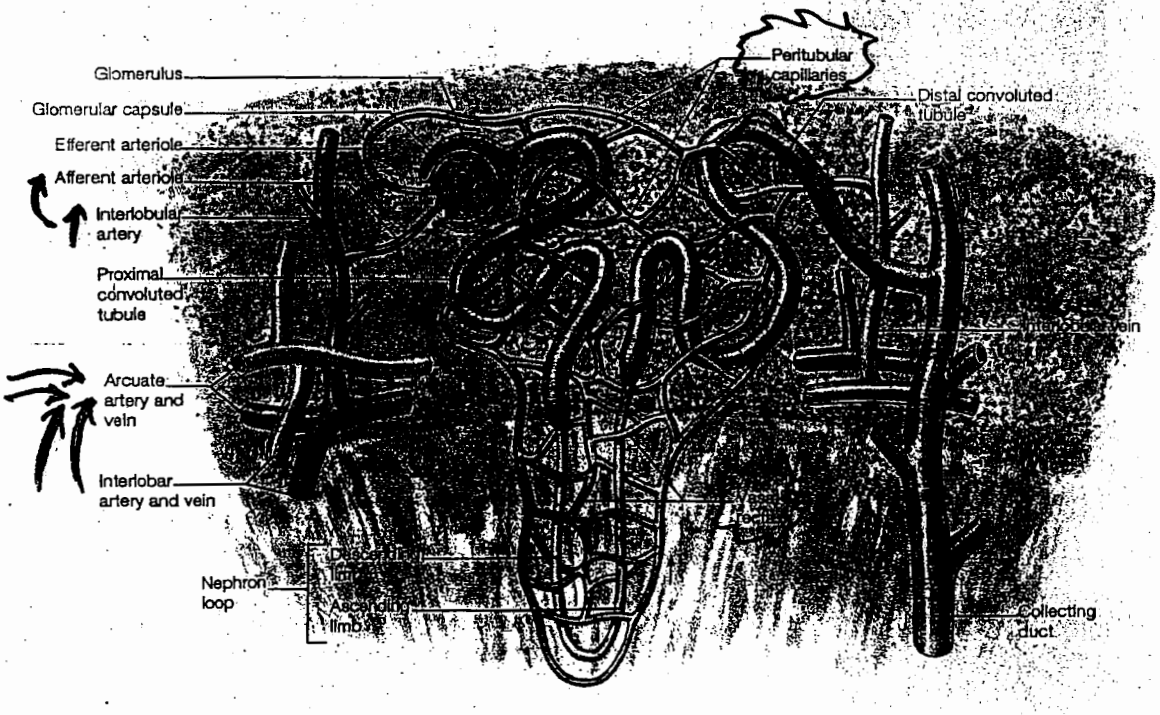
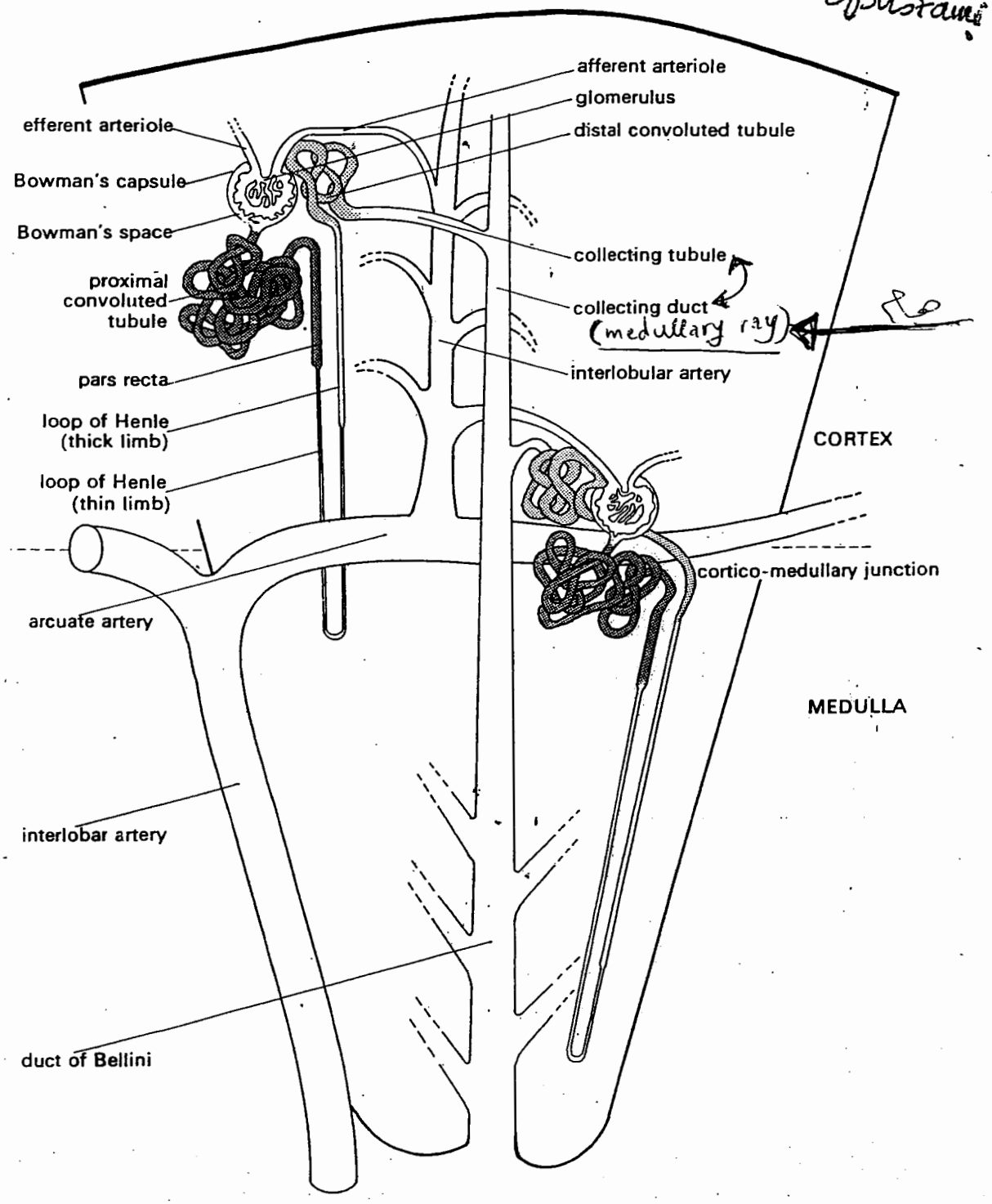


Figure 19.8 A simplified illustration of blood flow from a glomerulus to an efferent arteriole, to the peritubular capillaries, to the venous drainage of the kidneys.


afferent arteriole
glomerulus
distal convoluted tubule
efferent arteriole
Bowman's capsule
Bowman's space
proximal convoluted tubule
collecting tubule
collecting duct
(medullary ray)
pars recta
interlobular artery
loop of Henle (thick limb)
loop of Henle (thin limb)
CORTEX
cortico-medullary junction
arcuate artery
MEDULLA
interlobar artery
duct of Bellini

Renal blood flow

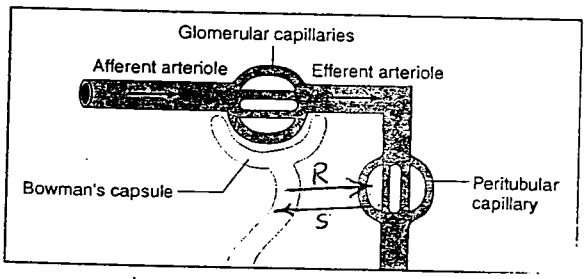
Blood entering the Kidneys passes through (2) Capillary beds in series

Because of the high glomerular capillary Pressure → only plasma filtration occurs at the glomerular capillaries

↔

The lower capillary Pressure in the Peritubular capillaries results in only Reabsorption occurring at the Peritubular capillaries

The Vasa recta arise from the Juxtamedullary glomeruli allowing a small amount (5%) of renal blood flow to Perfuse the renal medulla



Total renal blood flow averages about 1103 ml/min

(57% of it is plasma)

So Renal plasma flow is approximately 625 ml/min

About (20%) of the plasma entering the Kidney is filtered at the renal glomerulus → a glomerular filtration rate (GFR) of (125ml/min) → Between (80%) and (99%) of the glomerular filtration is reabsorped so the final urinary flow rate varies between 0.4 ml/min to 20 ml/min. and usually averages about (1 ml/min)

(9)

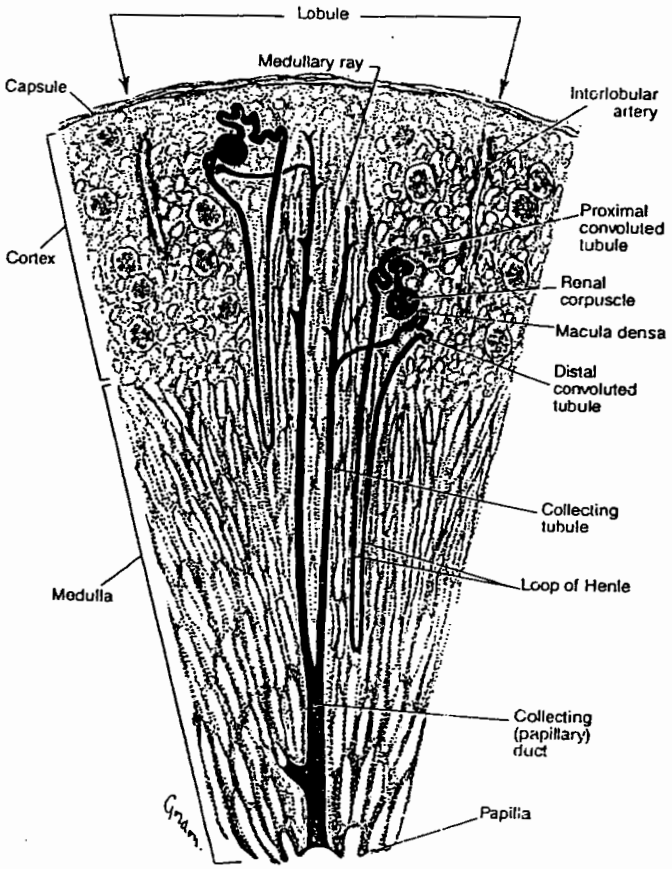


FIG. 15-2 Schematic diagram of the basic arrangement of nephrons and collecting tubules in a lobule of the kidney.

Renal terminology is imprecise and confusing. The structural unit of a kidney is a lobule. This has a central core of collecting tubules = the medullary ray of the cortex, surrounded by a sleeve of nephrons draining into these tubules. There is no line of demarcation between lobules. As the medullary rays approach the renal sinus, space between them gets less, there is no further space for the sleeve of nephrons and cortex changes to medulla. The merging of the medullary rays form the pyramids and the pyramids in turn merge to form the prominent papillae. The nephrons near the surface have short loops of Henle and are referred to as *Cortical nephrons. Those nephrons lying deeply at the bottom of the nephron sleeve are near the medulla, have long loops of Henle and are referred to as *juxta-medullary nephrons. the short loops of the Cortical nephrons do not reach into the medulla. The long loops of the juxta-medullary nephrons run into the medulla parallel to the collecting ducts and in association with the vasa recta→( )

(10)

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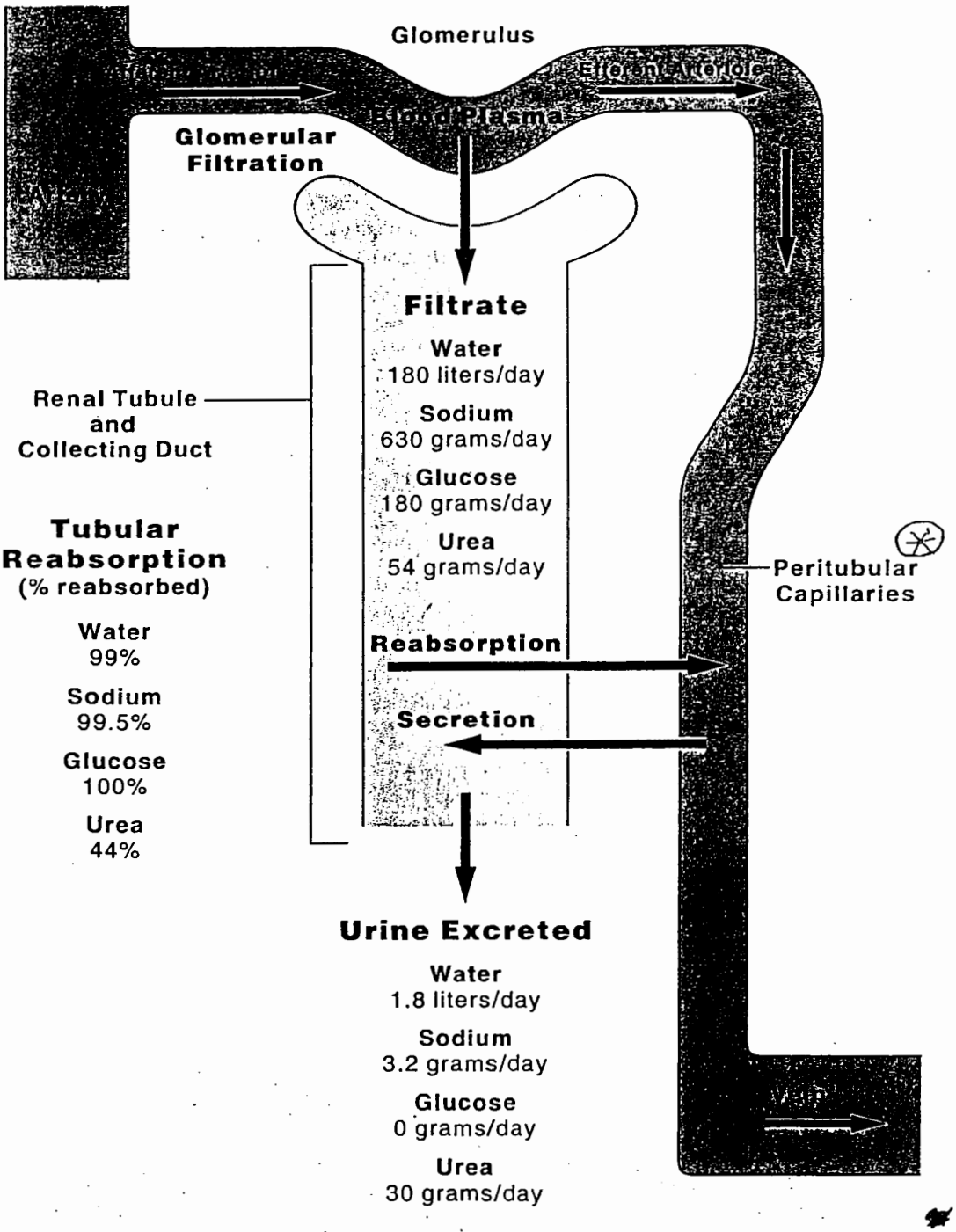
URINE FORMATION
Diagrammatic



11
A

NET FILTRATION PRESSURE

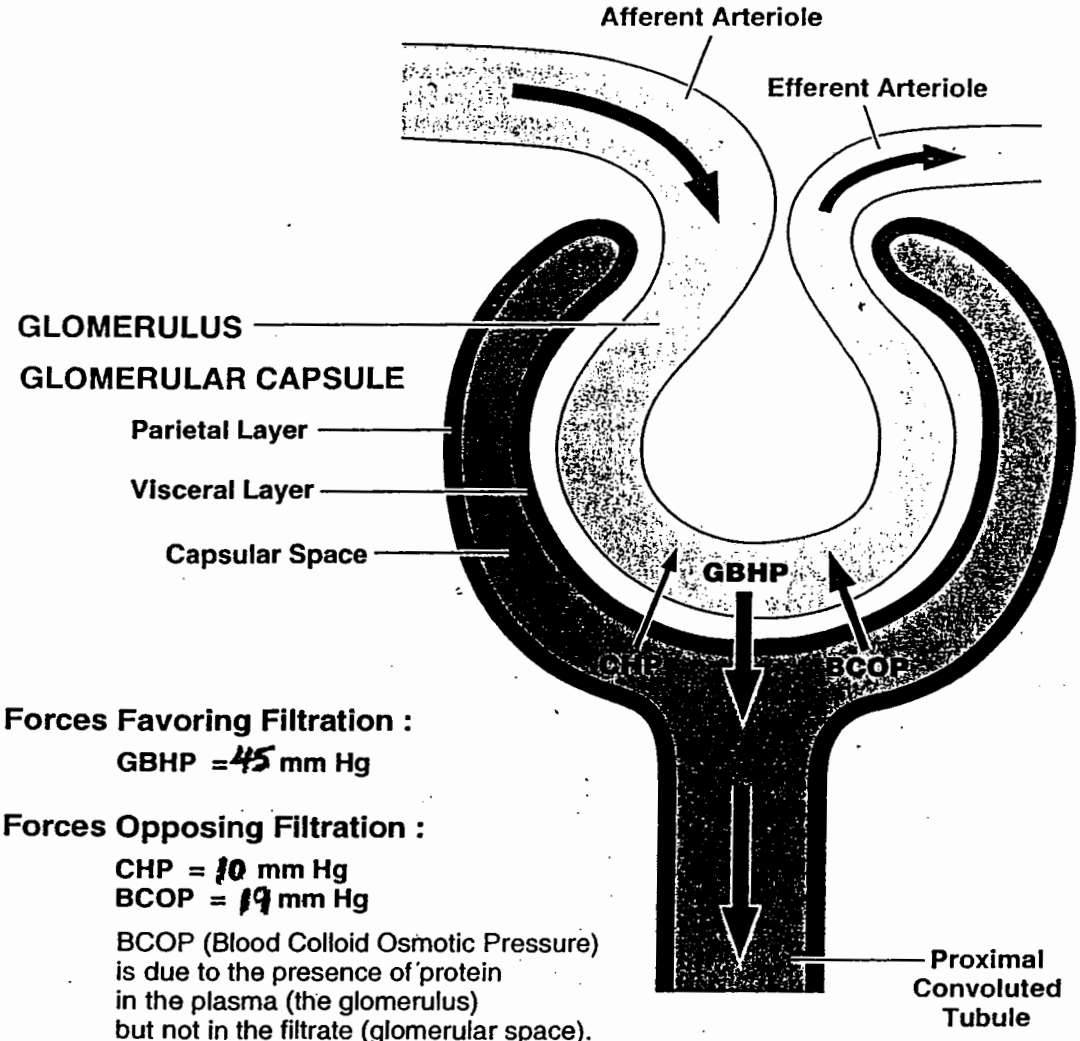
NFP = GBHP − (CHP + BCOP)

NFP = Net Filtration Pressure = 16 mm Hg

GBHP = Glomerular Blood Hydrostatic Pressure = 45 mm Hg

CHP = Capsular Hydrostatic Pressure = 10 mm Hg

BCOP = Blood Colloid Osmotic Pressure = 19 mm Hg



Forces Favoring Filtration :

GBHP = 45 mm Hg

Forces Opposing Filtration :

CHP = 10 mm Hg
BCOP = 19 mm Hg

BCOP (Blood Colloid Osmotic Pressure) is due to the presence of protein in the plasma (the glomerulus) but not in the filtrate (glomerular space).

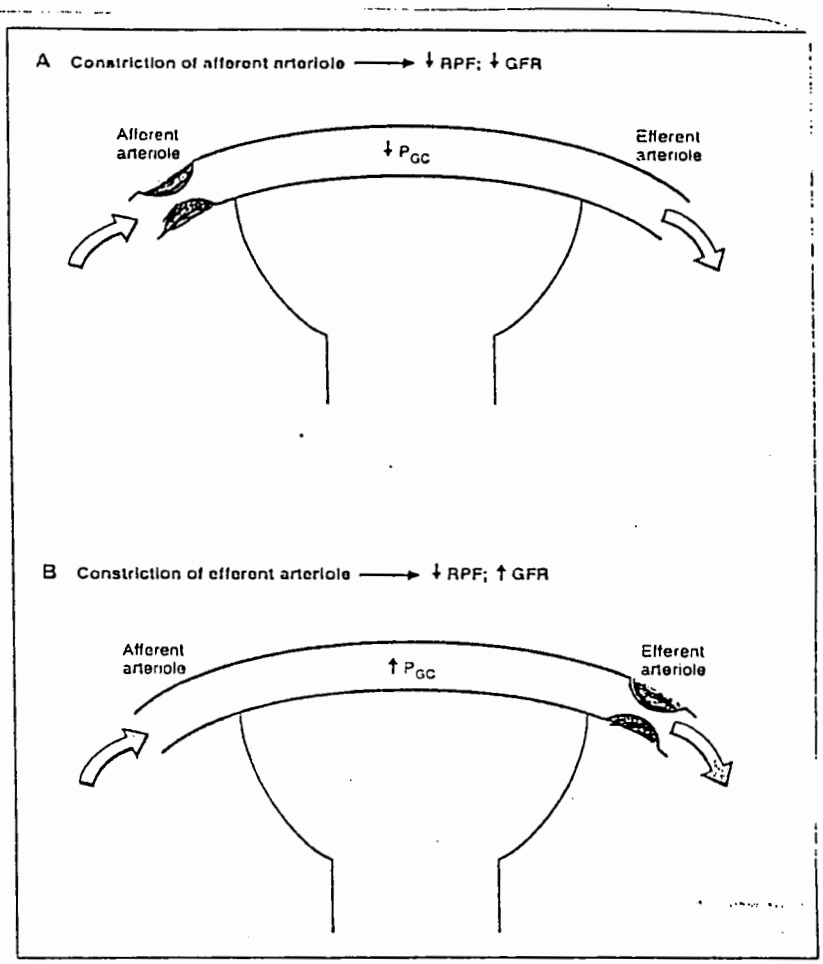
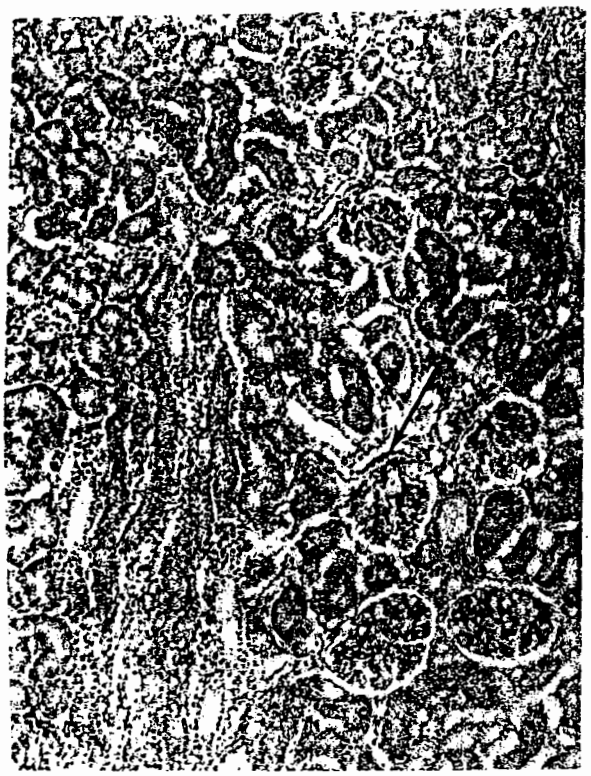


FIGURE 6–11. Effects of constricting afferent (A) and efferent (B) arterioles on renal plasma flow (RPF) and glomerular filtration rate (GFR). P_{GC}, hydrostatic pressure in the glomerular capillary.

TABLE 6–5. Effect of Changes in Starling Forces on RPF, GFR, and the Filtration Fraction

Effect	RPF	GFR	Filtration Fraction (GFR/RPF)
Constriction of afferent arteriole	↓	↓	N.C.
Constriction of efferent arteriole	↓	↑	↑
Increased plasma protein concentration	N.C.	↓	↓
Decreased plasma protein concentration	N.C.	↑	↑
Constriction of the ureter	N.C.	↓	↓

GFR, glomerular filtration rate; N.C., no change; RPF, renal plasma flow.



ig. 13-6. Photomicrograph of the cortex of the kidney, show-g several glomeruli and proxtinal and distal convoluted bules. Note a macula densa (arrow). (H&E; ×100.)

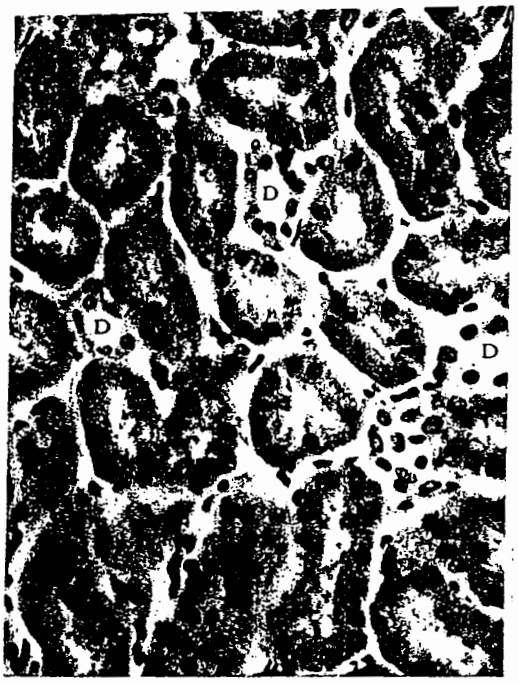
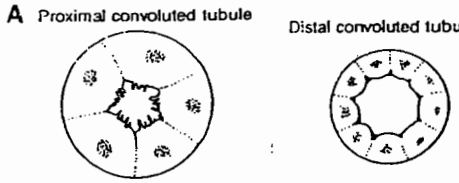
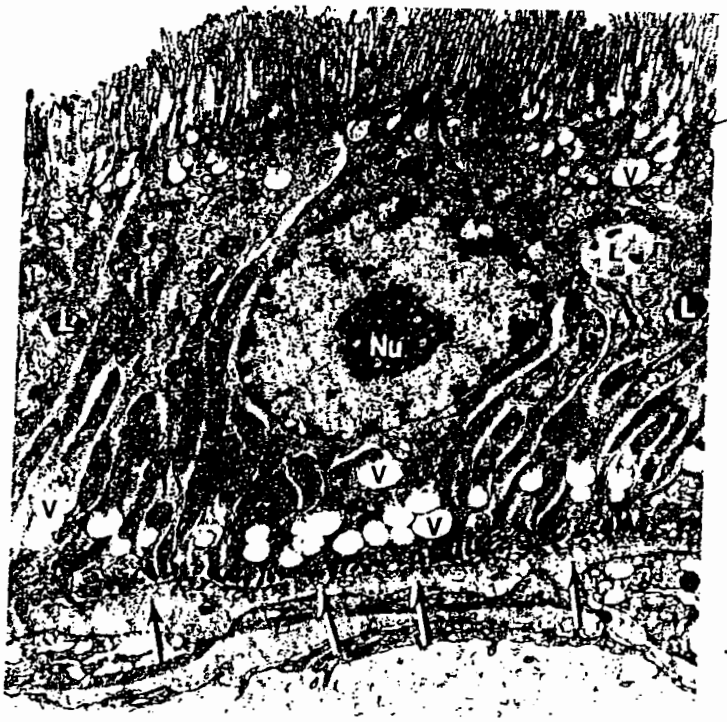


Fig. 13-17. Photomicrograph showing many proximal convoluted tubules cut in oblique and cross sections. Note that each tubule is lined with cuboidal epithelium and the cytoplasm stains strongly with eosin because of the many mitochondria (not shown). The nuclei are centrally placed, and the luminal cell surfaces have indistinct brush borders formed of microvilli. Three distal convoluted tubules are also present (D). Note that the cytoplasm of the cuboidal cells lining the distal convoluted tubules stains lighter with eosin. (H&E; ×400.)



Proximal convoluted tubules

1. Most common tubules found in the cortex
2. Have stellate-shaped lumen bounded by a distinct brush-border
3. The cells are mainly cuboidal or low columnar in shape and have indistinct lateral cell boundaries
4. Not all cells of a given tubule show a nuclear profile due to the large size of the cells
5. The cytoplasm stains intensely with eosin (due to the large number of mitochondria within the cell).
6. PAS-positive basal lamina is seen around the proximal tubules



Apical canaliculi
↓
vesicles
↓
{ vacuoles ? ⊕ lysosomes }
⇓
Proteins are reduced by acid hydrolase of lysosomes
⇓
Amino acids

Figure 20–10. Electron micrograph of a proximal convoluted tubule wall. Observe the microvilli (MV), the lysosomes (L), the vacuole (V), the nucleolus (Nu), and the mitochondria (M). The arrows point to the basal lamina. X 10,500

Electron microscopic appearance of PCT

a) a Golgi apparatus on the apical side of the nucleus
b) numerous rod-like mitochondria in the basal cytoplasm
c) The plasma membrane, especially on the base of the cell, show much INFOLDING and INTERDIGITATING with neighbouring cells
d) The microvilli are long and densely packed at the apex of the cell
e) there are small clefts between the bases of the microvilli ⟹ APICAL CANALICULI → give rise to a series of small vesicles → coalesce to form larger vacuoles
f) Endocytic Complex ← Apical canaliculi, Vesicles, Vacuoles } involved in Protein absorption
g) Vacuoles condense and fuse with lysosomes, the acid hydrolases of which reduce the absorped protein to its constituents amino acids which are then released into the blood Stream.

Other functions of Proximal convaluted tubule
- Absorption ⇒ H_2O (65% of glomerular filtrate), Na, Cl, glucose, amino acids, Vit

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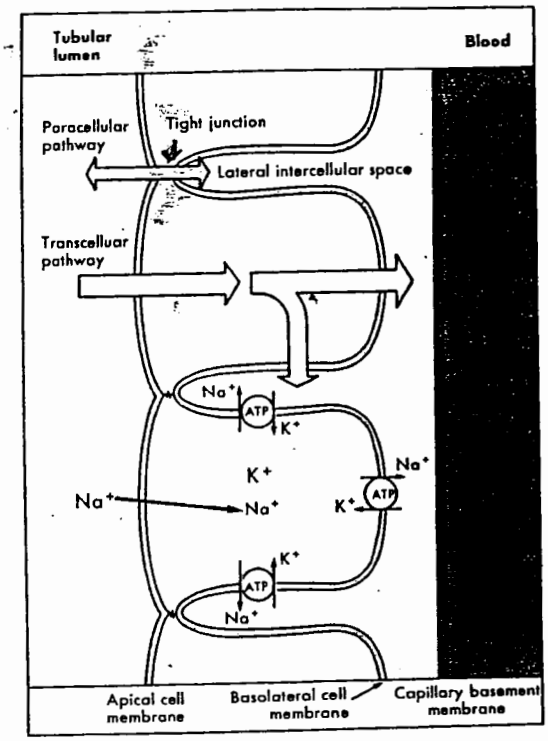


FIGURE 32-20 Schematic representation of transport pathways in an idealized proximal tubule. *ATP*, Adenosine triphosphate

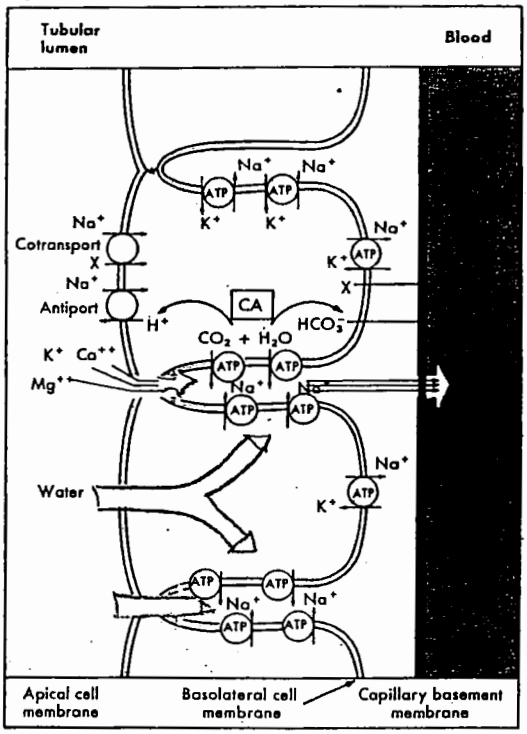


FIGURE 32-22 Schematic representation of the proximal tubule. For the Na^+-*X* co-transport protein, *X* represents either glucose, amino acids, phosphate, chloride, or lactate. CO_2 and H_2O combine inside the cells to form H^+ and HCO_3^- in a reaction facilitated by the enzyme carbonic anhydrase *(CA)*. *ATP*, Adenosine triphosphate.

Remember → the osmolarity of the glomerular filtrate is identical to that of the blood → 300 mOsm/L, BECAUSE (water) & (small solutes) are freely filtered

The osmolarity remains at 300 mOsm/L along the [entire] Proximal convoluted tubule even though a significant volume of water is reabsorbed ⇒ water is always reabsorbed in exact proportion to solute, i.e

the process is isosmotic

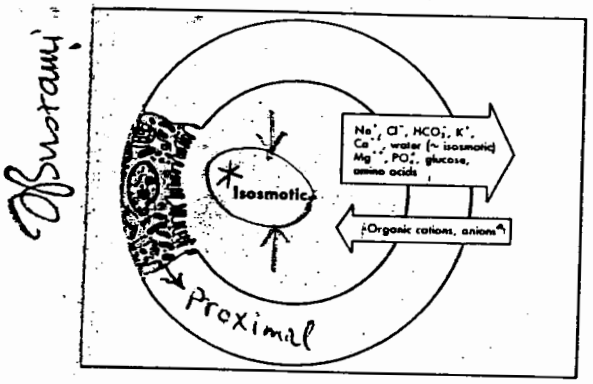


FIGURE 32-21 Schematic representation of a cell in the proximal tubule and the primary transport characteristics. Tubular fluid is isosmotic.

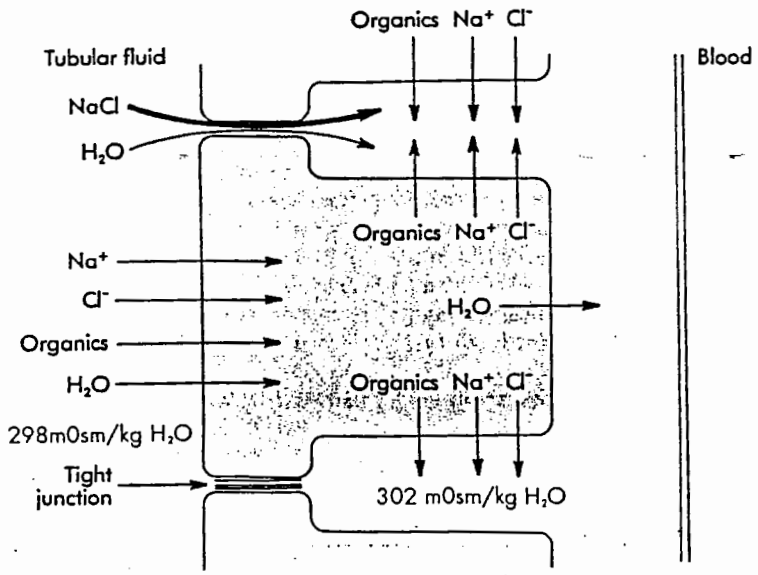


FIGURE 36-5 Routes of water reabsorption across the proximal tubule. Transport of Na^+, Cl^-, and organic solutes into the lateral intercellular space increases the osmolality of this compartment, which establishes the driving force for osmotic water reabsorption across the proximal tubule. An important consequence of osmotic water flow across the proximal tubule is that some solutes, especially K^+, Ca^{++}, and Mg^{++}, are entrained in the reabsorbed fluid and are thereby reabsorbed by the process of solvent drag.

Absorption of K^+ at PCT?

↓

largely passively

↓

Reabsorption of H_2O → leaves high tubular concentration of K^+ → creates a concentration gradient for K^+

Renal tubular epithelial cells

Can transport **Solutes** & **water** from one side of the tubule to the other → **Reabsorption** / **Secretion**

- **held together** by **tight junctions**
- & **separated** by **intercellular spaces**

Secretion / Reabsorption
- across cells → **transcellular pathway**
- OR
- between cells → **paracellular pathway**

Na^+ Reabsorption by transcellular pathway
- depends on the operation of **Na^+-K^+-ATPase**
- 2-step process
  - → Movement across apical membrane **down** an electrochemical gradient established by the Na^+-K^+-ATPase
  - → movement across the basolateral membrane **against** an electrochemical gradient via the Na^+-K^+-ATPase

Proximal tubule → **Reabsorbs** **67%** → water, Na^+, Cl^-, K^+
- **ALL** → glucose, amino acids

Key element in reabsorption → Na^+-K^+-ATPase
- In 1st half → Na^+ ⊕ glucose ⊕ aminoacids ⊕ **bicarbonate**
- In 2nd half → Na^+ ⊕ **Cl^-**

During the 1st phase

Na^+ entry into the cell across apical membrane mediated by → Specific transport Proteins (Not by simple diffusion)

* Couple movement of Na^+ with movement of other Solutes
* Each transp. protein → Uses the potential energy released by downhill movement of Na^+ to POWER the uphill movement of other solutes

Co-transport protein (Symporters)

Na^+ Na^+ Na^+ Na^+ — glucose, amino acid, phosphate, Cl^-

leaves across basolat. memb. by Na^+-K^+-ATPase

Antiporters

Na^+-H^+ antiporter

its secretion results in HCO_3^- reabsorption

leave down their electrochemical gradient

* Reabsorption of Na^+ & other solutes.

↑ osmolality of the lateral intercellular space

Water will flow by osmosis across both the tight junctions & apical membrane → tubular cell

- Accumulation of fluid within the lateral intercellular space → ↑ hydrostatic pressure in this compartment
- Absorbed fluid → {Isosmotic to plasma} Drives fluid into the capillaries

2nd phase of Proximal tubular Reabsorption

Reabsorption of **Na^+ with Cl^-** in 2nd half of Prox. tubule

In 1st half of Proximal tubule → **Na^+ Reabsorbed & HCO_3**

leaves behind a Solution Rich in Cl^-

→ Rise of Cl^- concentration in tubular fluid CREATES A GRADIENT that favours the diffusion of Cl^- from tubular lumen ACROSS TIGHT junctions into the lateral intercellular space

Movement of negatively charged Cl^- attracts the positively Na^+

→ Na^+ & Cl^- reabsorption by 2nd half of Proximal tubule also occurs by transcellular route → pathway is unknown

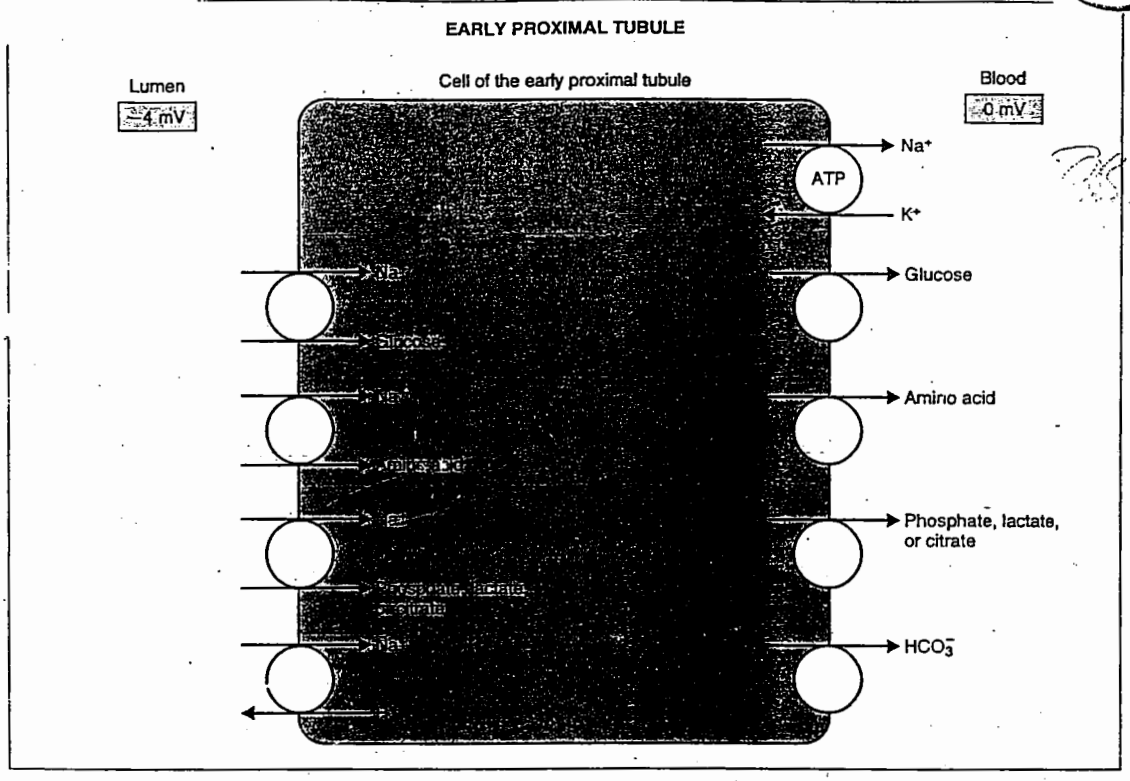
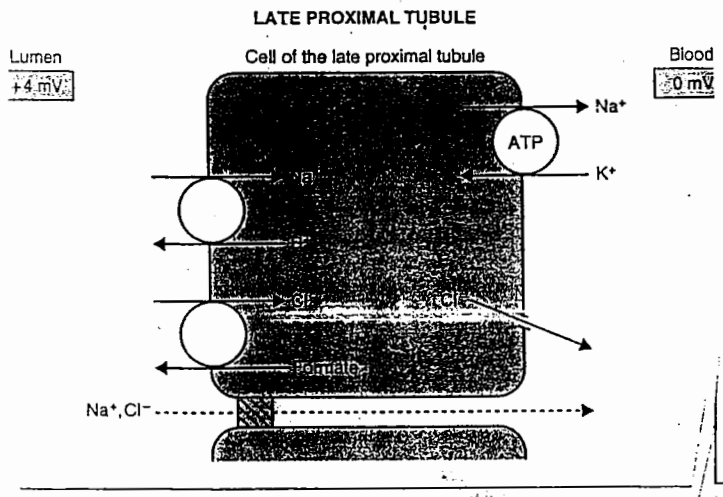


FIGURE 6–18. **Cellular mechanisms of Na^+ reabsorption in the early proximal tubule.** The transepithelial potential difference is the difference between the potential in the lumen and the potential in blood, −4 mV. ATP, adenosine triphosphate.



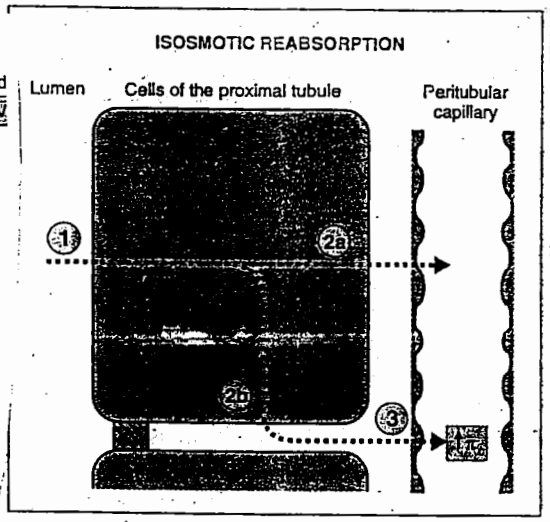
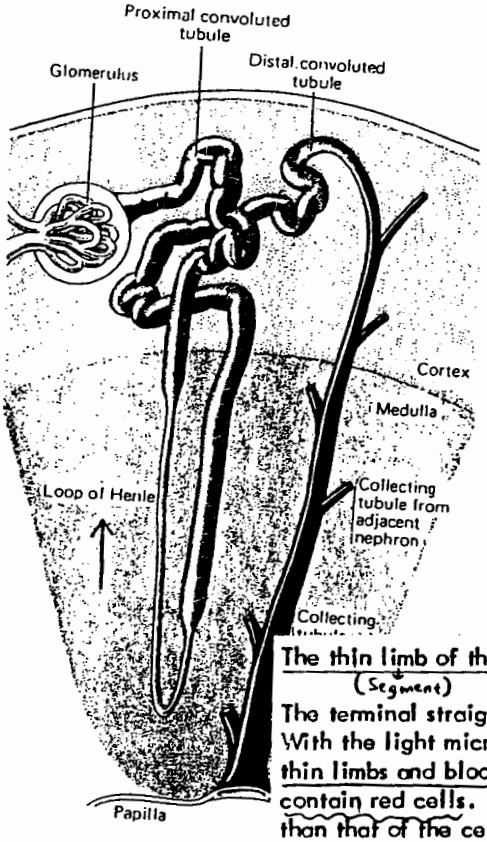
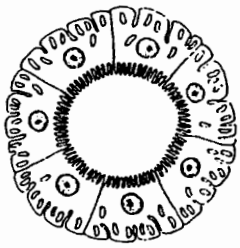


FIGURE 6–20. Mechanism of isosmotic reabsorption in the proximal tubule. Dashed arrows show the pathways for reabsorption; circled numbers correspond to the text. π_c, peritubular capillary colloid osmotic pressure.



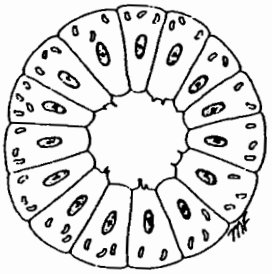


Proximal convoluted tubule

Thin segment of loop of Henle

16 B

Distal convoluted tubule



Collecting tubule

Dfarrami

The thin limb of the Loop of Henle
(Segment)

The terminal straight portion of the PCT suddenly changes to the descending thin limb. With the light microscope, it is usually difficult to distinguish the difference between thin limbs and blood capillaries, even when they are side by side, unless the capillaries contain red cells. When empty, the cytoplasm of the capillaries is slightly thinner than that of the cells lining the thin limbs, while the nuclei of the thin limb cells are slightly more prominent in that they bulge into the lumen. The difference is quite marked on examination with the EM, since the cytoplasm of the cells of the thin limb not only have microvilli on their surfaces, but are at least twice as thick as those of the capillaries. The nuclei appear almost uniformly round, while those of the capillaries are usually oval or irregular in shape.

The loop of Henle → interposed between the proximal and distal convoluted tubules & has descending and ascending limbs which lie together inside the Renal medulla (close to the Vasa recta & the collecting tubules)

① → thin descending limb (structure ⋮)
→ quite long in juxtamedullary nephrons
→ the cells show high water permeability → Reabsorp water from the tubular fluid (equilibration between the tubular fluid & the surrounding renal interstitium takes place by water extraction) → (hypertonic tubular fluid)

② → thin ascending limb (structure as above)
→ impermeable to H_2O + highly permeable to NaCl → NaCl passively diffuses into the renal interstitium but H_2O cannot follow → (hypotonic tubular fluid)

③ → thick ascending limb → impermeable to H_2O
Cotransport of $Na^+ K^+ 2Cl^-$
(more hypotonic tubular fluid)

① → Concentrating segment
②+③ → diluting segment

* Similar in structure to early distal tubule (lined by eosinophilic cuboidal epithelium)

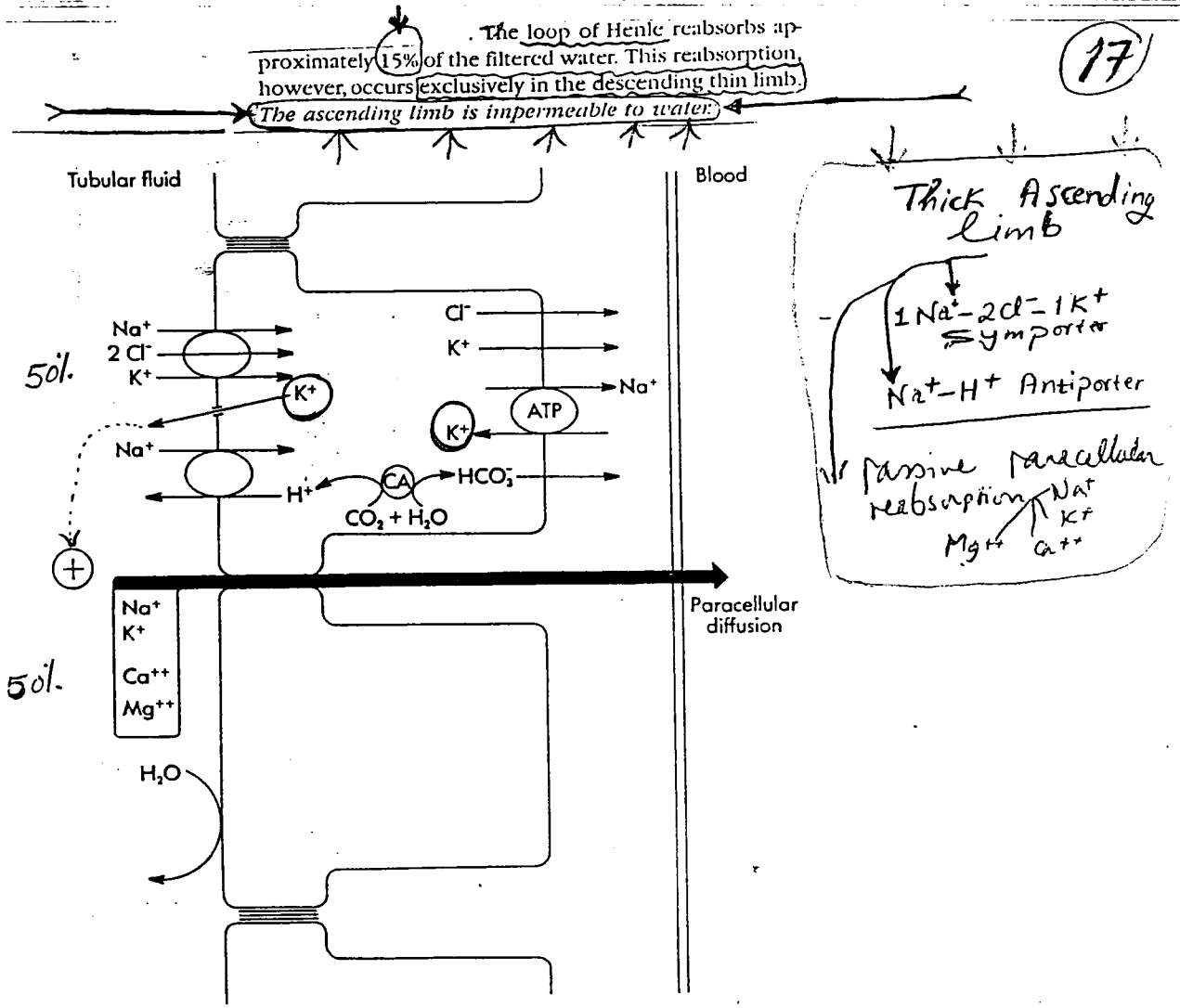


FIGURE 36-7 Transport mechanisms for NaCl reabsorption in the thick ascending limb of Henle's loop. The lumen positive transepithelial voltage results from the diffusion of K^+ from the cell into the tubular fluid, and plays a major role in driving passive paracellular reabsorption of cations.

The key element in solute reabsorption by the thick ascending limb is the Na^+-K^+-ATPase pump in the basolateral membrane (Figure 36-7). As with reabsorption in the proximal tubule, the reabsorption of every solute by the thick ascending limb is linked to the Na^+-K^+-ATPase pump. The operation of the Na^+-K^+-ATPase pump maintains a low cell $[Na^+]$. This low $[Na^+]$ provides a favorable chemical gradient for the movement of Na^+ from the tubular fluid into the cell. The movement of Na^+ across the apical membrane into the cell is mediated by the $1Na^+$-$2Cl^-$-$1K^+$ symporter, which couples the movement of $1Na^+$ with $2Cl^-$ and $1K^+$. This symport protein uses the potential energy released by the downhill movement of Na^+ and Cl^- to drive the uphill movement of K^+ into the cell. An Na^+-H^+ antiporter in the apical cell membrane also mediates Na^+ reabsorption as well as H^+ secretion (HCO_3^- reabsorption) in the thick ascending limb (Figure 36-7). Na^+ leaves the cell across the basolateral membrane via the Na^+-K^+-ATPase pump, and K^+, Cl^-, and HCO_3^- leave the cell across the basolateral membrane by separate pathways.

The voltage across the thick ascending limb is positive in the tubular fluid relative to the blood because of the unique location of transport proteins in the apical and basolateral membranes. *The important points to recognize are that increased salt transport by the thick ascending limb increases the magnitude of the positive voltage in the lumen, and that this voltage is an important driving force for the reabsorption of several cations, including Na^+, K^+, Ca^{++}, and Mg^{++}, across the*

paracellular pathway

Because the thick ascending limb is very impermeable to water, reabsorption of NaCl and other solutes reduces the osmolality of tubular fluid to less than 150 mOsm/kg H_2O. → HYPO.....

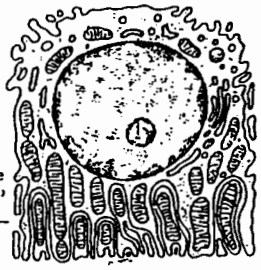
Distal convoluted tubule (DCT)

consists of 3 parts:

① Early DCT → the continuation of the thick segment of Henle's loop and has the same histological structure (lined by Eosinophilic cuboidal epithelium)
- → Reabsorbs 5% of the filtered Na^+ (Na^+–Cl^- cotransporter at the luminal membrane)
- → impermeable to H_2O (like the thick segment)
- → called the cortical DILUTING segment

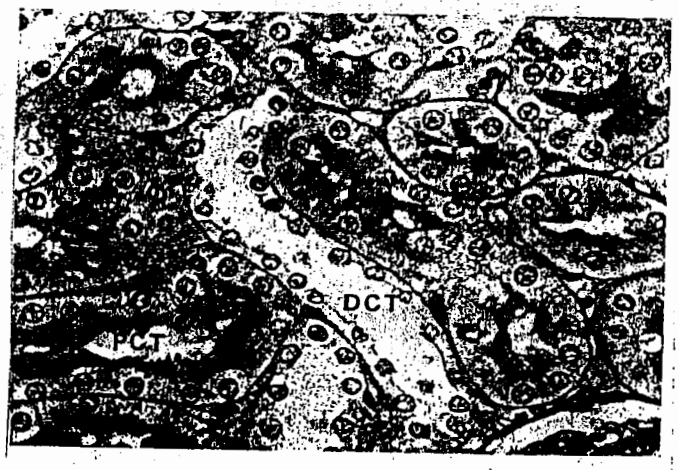
② The macula densa: ↘
Columnar closely packed cells
- may function to sense Na^+ / Cl^- ?? concentration in DCT
- part of J-G apparatus

EM → Early Distal convoluted tubule and ascending thick limb of Henle's loop



Ofurstrami

③ The late or convoluted portion: Can be distinguished from PCT by the following criteria →



1) The lumen of the DCT is generally WIDER
2) The cells are Shorter and lighter staining
3) Nuclear profiles are usually seen in each cell (in part because many are binucleate)
4) a brush border is lacking

Anatomically & functionally the late distal tubule & collecting ducts (tubules) are similar → 2 major cell types interspersed along these segments:
- Principle cells (light cells) → involved in Na^+ reabsorption (3% of filtered Na^+) & K^+ secretion → have VERY DISTINCT CELL BOUNDARIES
- intercalated cells (dark cells) → involved in K^+ reabsorption (in low dietary K^+ content) & H^+ secretion → have a greater No. of mitochondria

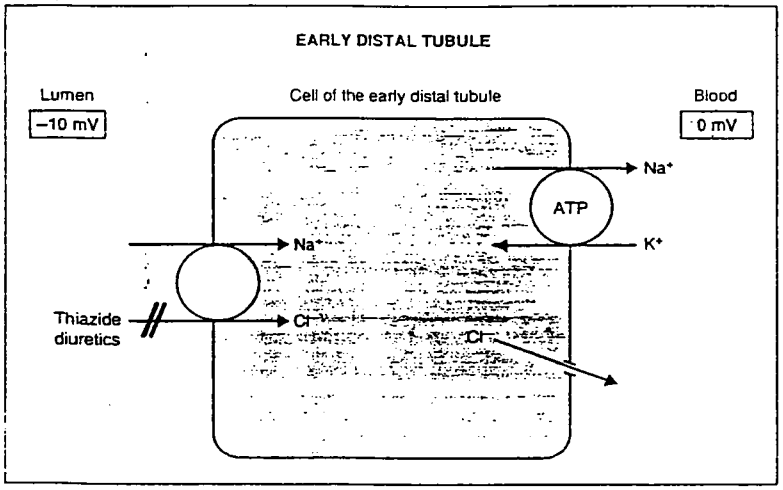
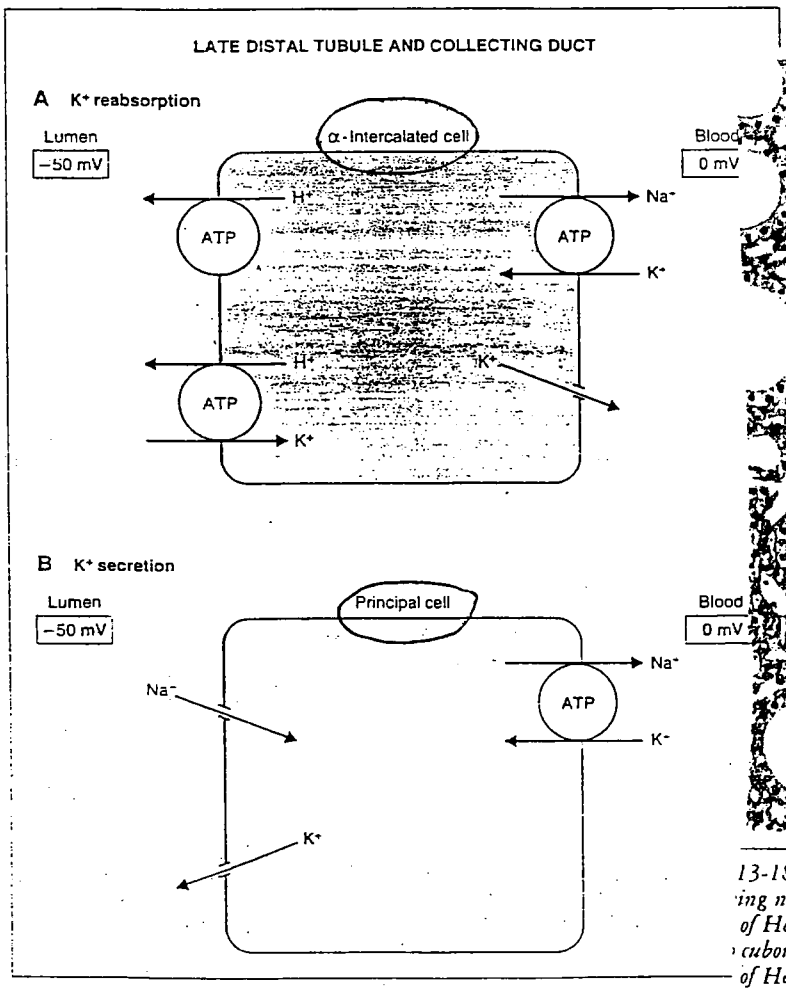
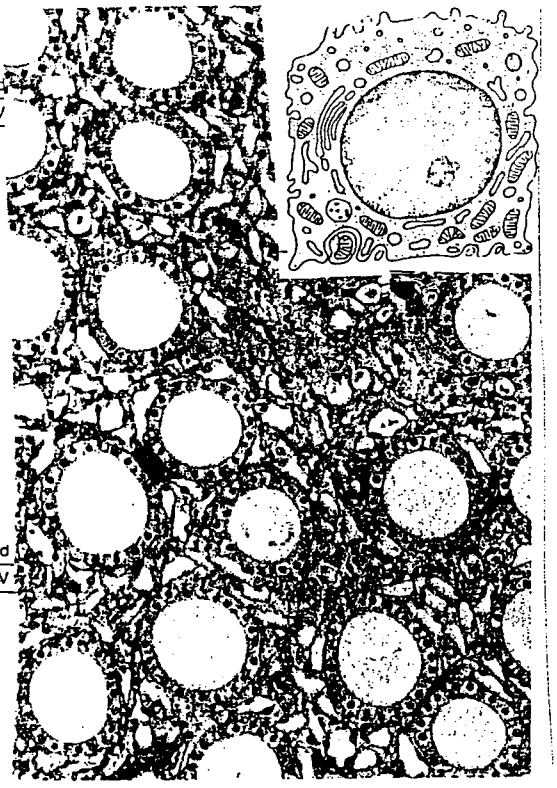


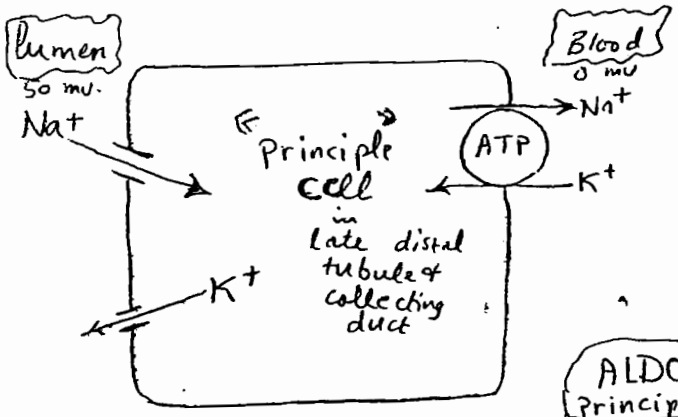
FIGURE 6–23. Cellular mechanism of Na^+ reabsorption in the early distal tubule. The transepithelial potential difference is −1(mV. ATP, adenosine triphosphate.

Cortical diluting Segment





13-18. Photomicrograph of the medulla of the kidney, ing numerous collecting tubules and thin segments of the of Henle in cross section. The collecting tubules are lined cuboidal epithelial cells, and the thin segments of the of Henle are lined with flattened cells. (H&E; ×200.)



The mechanism for Na^+ reabsorption in the principle cells of the late distal tubule + collecting duct

The luminal membrane of the principle cells contains Na^+ channels → Na^+ diffuses through these channels down its electrochemical gradient from the lumen into the cell → Na^+ then is extruded from the cell via the Na^+-K^+ ATPase in the basolateral membrane

ALDOSTERONE acts directly on the principle cells to → ↑ Na^+ reabsorption
↑ K^+ secretion

* Aldosterone increases Na^+ reabsorption in the principle cells by inducing synthesis of the luminal membrane Na^+ channels & the basolateral membrane Na^+-K^+ ATPase ⟹ ↑ Na^+ entry into the cell & provides more Na^+ to Na^+-K^+ ATPase ⟿ more Na^+ is pumped out of the cell & more K^+ pumped into the cell → ↑ intracellular K^+ concentration → ↑ the driving force for K^+ secretion from the cell into the lumen

Collecting Tubules

(a) is the most distal part of the Uriniferous tubule and is NOT part of the nephron

(b) Each DCT of a nephron becomes continuous with a collecting tubule that runs a short arched course and ENTERS a MEDULLARY RAY → Here a number of short collecting tubules join a main collecting tubule as side tributaries.

↓ (Low water permeability in the presence or absence of ADH)

The main collecting tubule then passes down in the medullary ray to enter the medullary pyramid

↓

When the collecting tubules reach the inner zone of the pyramids group of them join at acute angles to form straight papillary ducts that open on the apex of the renal papilla into a minor calyx

* (High water permeability in the presence of ADH)

The cells lining the collecting tubules are at first CUBOIDAL, later in the straight papillary duces they are TALL COLUMNAR

(d) The cell borders are regular with few interdigitations
(e) The nuclei are dark staining but the cytoplasm is pale staining because there are relatively few cytoplasmic organelles
(f) on the apex of the renal papilla, the columnar epithelium changes to the transitional epith. lining the minor calyx.

Functions → The collecting tubules (ducts) function in the **Conservation of Water** and the **production of hypertonic Urine**. As the ducts pass through the medulla to the tips of the papillae, they pass through the INCREASINGLY HYPERTONIC ENVIRONMENT ESTABLISHED AND MAINTAINED BY THE LOOPS OF HENLE. The permeability of collecting ducts to water is controlled by antidiuretic hormone (ADH). In the presence of this hormone, the collecting ducts become permeable to water which is drawn from the tubules (ducts) by OSMOSIS as the result of the hypertonic environment maintained in the medullary interstitium. The Loss of Water from the tubules (ducts) results in a concentrated hypertonic urine. In the absence of ADH → the kidney cannot concentrate or form hypertonic urine. This condition is known as Diabetes insipidus (production of large amounts of dilute urine → Severe dehydration of the individual.

How does the kidney produce urine that is more concentrated than blood & what determines how high the urine osmolarity will be ??

⇓

Remember the {4 partners} within the RENAL MEDULLA

Collecting tubules & ducts (1) | Loop of Henle (2) | Vasa Recta (3) | ADH (4)

⇓

- Urine becomes hyperosmotic, in the presence of ADH
- As the tubular fluid flows down the collecting tubules & ducts → it is exposed to interstitial fluid with increasingly hyperosmolarity (i.e the corticopapillary osmotic gradient 300 mosm/L. → 600 → 900 → 1200) → water will be reabsorbed until the tubular fluid equilibrates osmotically with surrounding interstitial fluid → The final urine osmolarity, in the presence of ADH will be equal to the osmolarity at the bend of the loop of Henle (1200 mOsm/L)

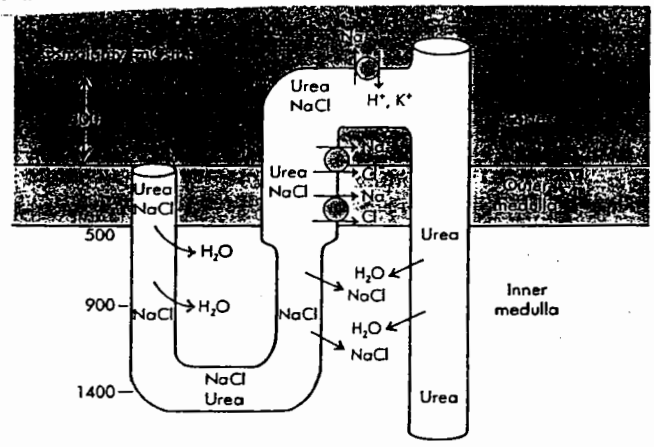
	Na+ reabsorption %	H2O reabsorption %
Proximal c. tubule (PCT)	65% ~ 67% (2/3)	65% (2/3)
Thin descending Segment of Henles loop	X (impermeable to Na+)	15%
Ascending limb of Henle's (thin, thick)	25%	X (impermeable to H2O)
distal convoluted tubule (early & late)	5%	10% {ADH needed in late dct}
Collecting tubules & duct	4%	9% {ADH needed}

Remember
- NaCl → is a major solute of tubular fluid in the thin ascending limb
- Urea → is a major solute of tubular fluid of the medullary collecting duct

the thin ascending limb is more permeable to NaCl than to urea → NaCl gradient across the thin ascending limb

the collecting duct is more permeable to Urea than to NaCl → Urea gradient across the collecting duct

both gradients are created by active reabsorption of NaCl by the THICK ASCENDING LIMB



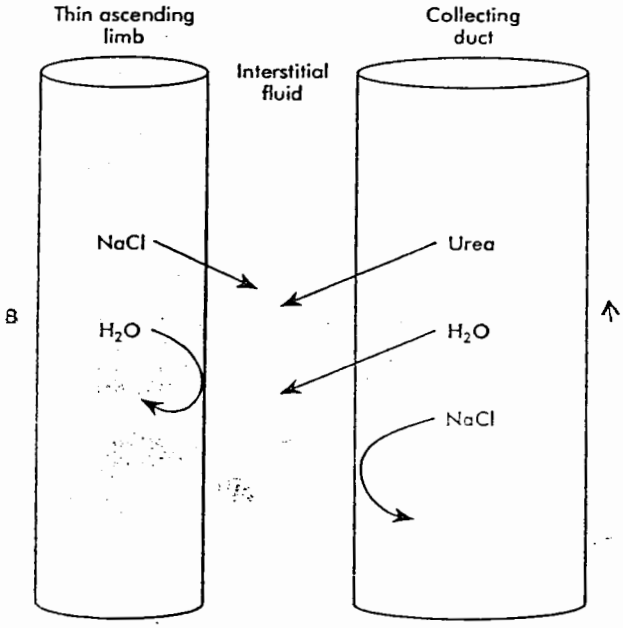


FIGURE 19-18
Mechanism of formation of concentrated urine according to the two-solute hypothesis.
A Overall view of the loop of Henle, distal tubule and collecting duct: The osmolarity of the interstitial fluid at different levels of the medulla is shown on the scale at the left. The tubular fluid leaving the proximal tubule is isotonic. As the tubular fluid travels through the descending limb of the loop of Henle, water leaves the descending limb, drawn by the increasing osmotic pressure of interstitial fluid in the medulla. As a result, the tubular fluid in the descending limb becomes progressively more concentrated. As the tubular fluid passes through the thin ascending limb, NaCl, but not water, diffuses out, so that the osmotic pressure of interstitial fluid decreases. In the thick ascending limb, more salt is removed by active reabsorption. The tubular fluid entering the distal tubule is more dilute than plasma with respect to NaCl, while urea has been concentrated by the reabsorption of water. Urea and water diffuse down their concentration gradients as tubular fluid passes through the collecting duct. The remaining solutes in the tubular fluid are concentrated further by the water reabsorption, and a urine as concentrated as the interstitial fluid at the innermost part of the medulla may be formed if ADH levels are high. If ADH levels are low, a final urine similar to the dilute urine in the distal tubule is excreted.
B The two driving forces that generate a high solute concentration in the medullary interstitial fluid are the NaCl gradient between ISF and thin ascending limb, and the urea gradient between collecting duct and ISF. Water cannot leave the thin ascending limb in response to the osmotic gradient, but can be reabsorbed from the collecting duct in the presence of antidiuretic hormone.

Currently the most plausible hypothesis is the two-solute hypothesis (see Figure 19-18). This hypothesis builds on the finding that, along with NaCl, urea makes up a large fraction of the total solute of the medullary interstitial fluid. The high concentrations of NaCl and urea in the medullary interstitial fluid result because (1) NaCl is the major solute of tubular fluid in the thin ascending limb, and urea is a major solute in the tubular fluid of the medullary collecting duct; and (2) the thin ascending limb is more permeable to NaCl than to urea, and the collecting duct is more permeable to urea than to NaCl.

In summary, two driving forces are at work in the two-solute hypothesis (Figure 19-18, *B*): the NaCl gradient across the thin ascending limb and the urea gradient across the collecting duct. Both of these gradients are created by the active reabsorption of NaCl by the thick ascending limb. Both gradients drive solute into the medullary interstitial fluid, concentrating both NaCl and urea in the interstitial fluid. The high osmotic concentration of solute in the medulla provides the driving force for water recovery from the medullary collecting duct.

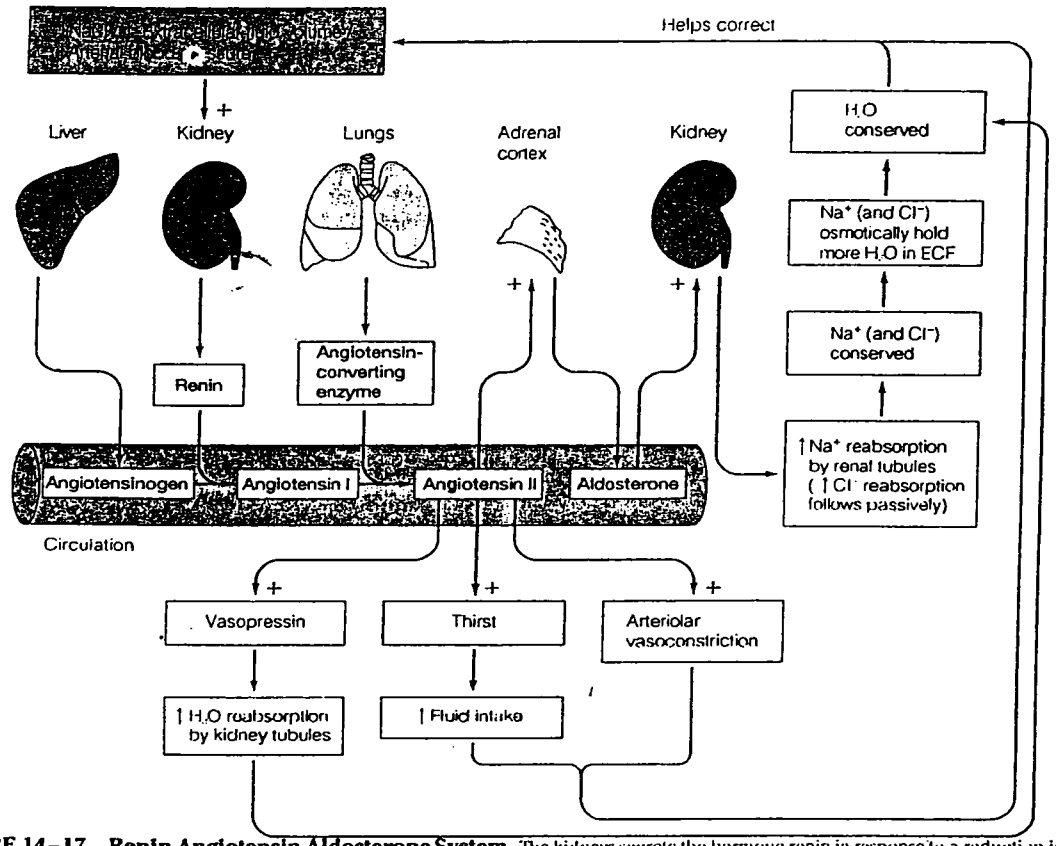
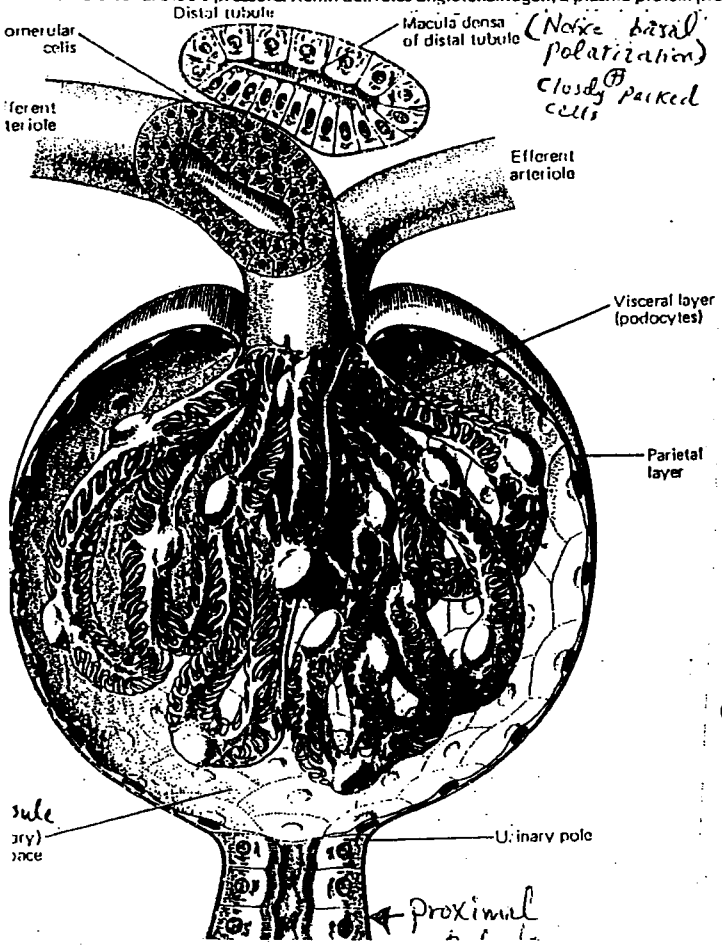


FIGURE 14–17 Renin-Angiotensin-Aldosterone System The kidneys secrete the hormone renin in response to a reduction in NaCl/ CF volume/arterial blood pressure. Renin activates angiotensinogen, a plasma protein produced by the liver, into angiotensin I. Angiotensin I is



Juxta-glomerular apparatus

(1) Juxtaglomerular cells in the wall of the Afferent arteriole → modified smooth muscles in the media of the afferent arteriole, contain secretory granules (Renin)

(2) macula densa : Columnar closely packed cells in the wall of the distal tubule → may function to sense < Na^+ / Cl^- ?? Concentration in the distal tubule

(3) Extra-glomerular mesangial cells (Polkisen) → forms a loose mass of cells between aff. & eff. arterioles, of unknown function

TABLE 19–2 Effects of Angiotensin II

FUNCTION	RESULT
Acts as a potent vasoconstrictor	Increased blood pressure
Facilitates synthesis and release of aldosterone	Resorption of sodium and chloride from lumen of distal convoluted tubule
Facilitates release of ADH	Resorption of water from lumen of collecting tubule
Increases thirst	Increased tissue fluid volume
Inhibits renin release	Feedback inhibition
Facilitates release of prostaglandins	Vasodilation of afferent glomerular arteriole, thus maintaining glomerular filtration rate

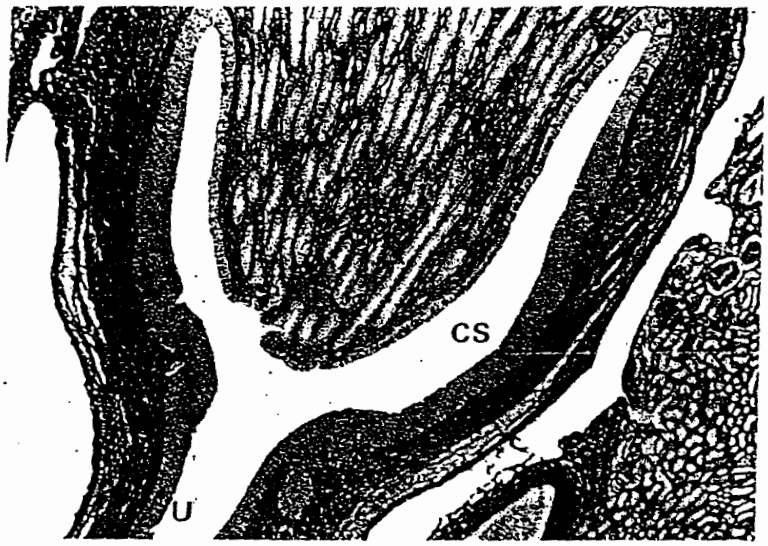


Fig. 16.26 Renal papilla

(Monkey: Azan × 30)

The renal papilla forms the apex of the medullary pyramid where it projects into the calyceal space. The ducts of Bellini DB, the largest of the collecting ducts, converge in the renal papilla to discharge urine into the pelvicalyceal space CS. The renal pelvis is lined by urinary epithelium E, and the wall of the pelvis contains smooth muscle SM which contracts to force urine into the ureter U.

Very small central cavity with short cleft radiating from it

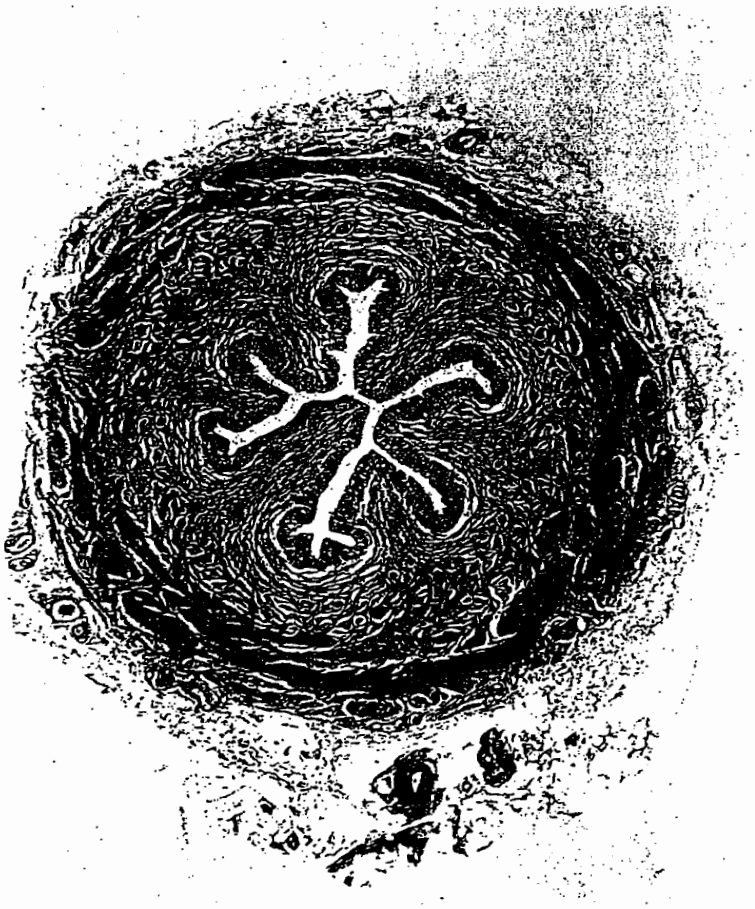


Fig. 16.27 Ureter

(TS: Masson's trichrome × 18)

The ureters are muscular tubes which conduct urine from the kidneys to the bladder. Urine is conducted from the pelvi-calyceal system as a bolus which is propelled by peristaltic action of the ureteric wall. Thus the wall of the ureter contains two layers of smooth muscle arranged into an inner longitudinal layer L and an outer circular layer C. Another outer longitudinal layer is present in the lower third of the ureter. The lumen of the ureter is lined by urinary epithelium which is thrown up into folds in the relaxed state allowing the ureter to dilate during the passage of a bolus of urine. Surrounding the muscular wall is a loose connective tissue adventitia A containing blood vessels, lymphatics and nerves.

1. Mucosa → thrown into folds
   lined by transitional epith over a lamina propria of C-T.
2. Muscularis
   - in upper 2/3 → 2 layers of smooth muscle (I.L, O.C)
   - in lower 1/3 (L-C-L) (I.L, O.C, Outermost Longitudinal)
3. Adventitia → C-T

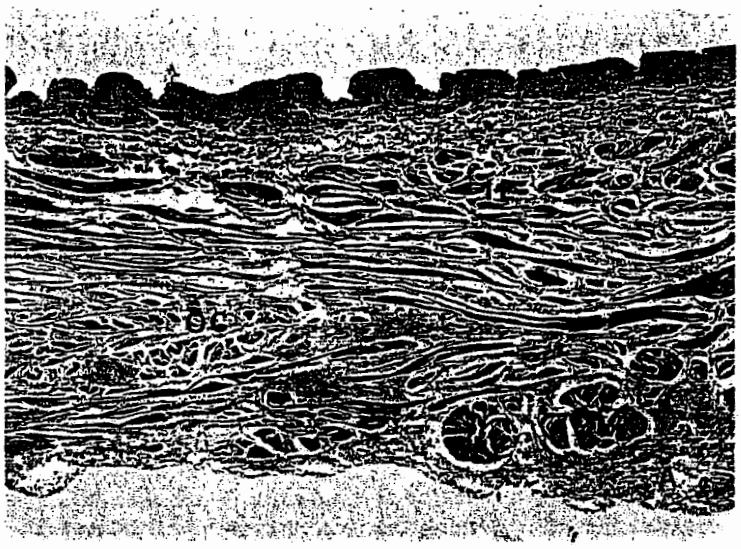


Fig. 16.28 Bladder

(TS: Masson's trichrome × 12)

The general structure of the bladder wall resembles that of the lower third of the ureters. The wall of the bladder consists of three loosely arranged layers of smooth muscle and elastic fibres which contract during micturition. Note the inner longitudinal IL, outer circular OC and outermost longitudinal OL layers of smooth muscle. The urinary epithelium lining the bladder is thrown into many folds in the relaxed state. The outer adventitial coat A contains arteries, veins and lymphatics.

The urethra, the final conducting portion of the urinary tract, is discussed as part of the male reproductive tract in Chapter 18.

Fig. 16.29 Urinary epithelium

(H & E × 480)

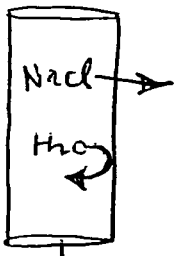
Urinary epithelium, also called transitional epithelium or urothelium, is found only within the conducting passages of the urinary system for which it is especially adapted. The plasma membranes of the superficial cells are much thicker than most cell membranes and have a highly ordered substructure, thus rendering urinary epithelium impermeable to urine which is potentially toxic. This permeability barrier also prevents water from being drawn through the epithelium into hypertonic urine. The cells of urinary epithelium have highly interdigitating cell junctions which permit great distension of the epithelium without damage to the surface integrity (see also Figs. 5.16 and 5.17).

Urinary epithelium rests on a basement membrane which is often too thin to be resolved by light microscopy and was formerly thought to be absent. The basal layer is irregular and may be deeply indented by strands of underlying connective tissue containing capillaries. This unusual feature led early histologists to believe, mistakenly, that urinary epithelium contradicted the principle that epithelium never contains blood vessels.

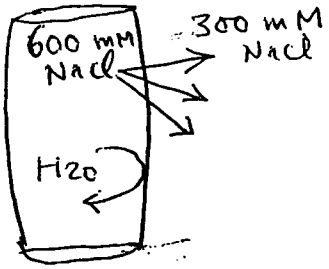
Thin Ascending limb of Henles loop

- impermeable to H_2O
- highly permeable to NaCl (by facilitated diffusion of Cl^-)
- moderately permeable to urea

No active transport



Hypotonic relative to renal interstitium



Descending limb

There is favourable NaCl gradient between the tubular lumen (600 mM NaCl) & renal interstitium (300 mM NaCl)

NaCl PASSIVELY diffuses into renal interstitium

H_2O CANNOT follow (this segment is always impermeable to H_2O)

fluid inside tubule becomes hypotonic relative to renal interstitium

Thick Ascending limb → impermeable to H_2O; large amount of Solute transport

Na^+–K^+–$2Cl^-$ cotransport → inhibited by loop diuretics (ethacrynic acid, furosemide)

initiate medullary osmolar gradient

Distal convoluted tubule → low (H_2O, urea) permeability in both presence or absence of ADH

- cortical collecting duct
- outer medullary collecting duct

→ low (urea) permeability in the presence or absence of ADH

H_2O permeability depends on presence or absence of ADH

inner medullary collecting duct

- H_2O permeability (Regulated by ADH)
- Variable urea permeability
  - high in presence of ADH
  - low = absence = =