بسم الله الرحمن الرحیم

The kidney

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outlines

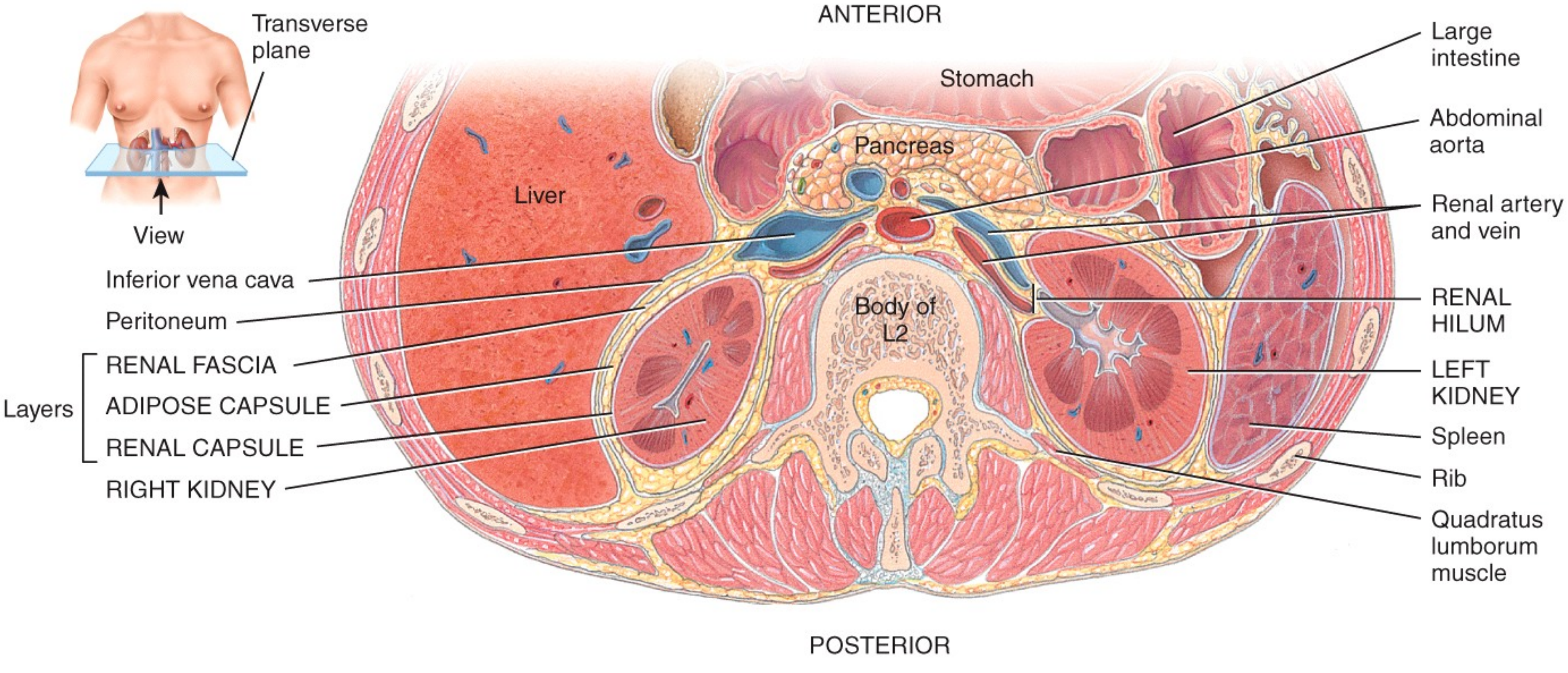
Renal anatomy

Renal physiology

Evaluation of kidney function

Renal Anatomy

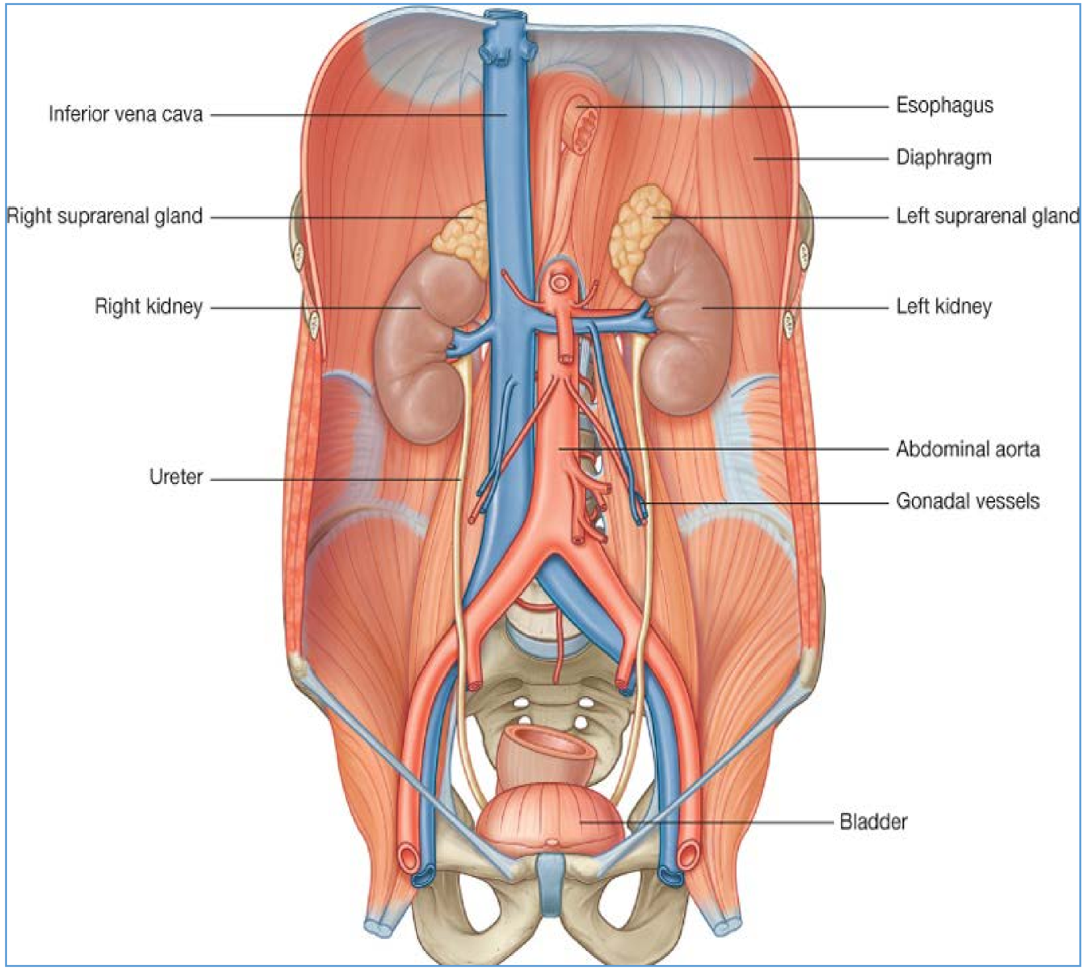
The kidneys are retroperitoneal, partly protected by the lower ribs.



(a) Inferior view of transverse section of abdomen (L2)

Position of the kidneys

- *Kidneys are* retroperitoneal paired organs.
- Each kidney lies , on the posterior abdominal wall, lateral to the vertebral column
- In the supine position, the kidneys extend from approximately T12 to L3.
- *The right kidney is slightly lower than the left kidney* because of the large size of the right lobe of the liver.
- With contraction of the diaphragm during respiration, both kidneys move downward in a vertical direction (high of one vertebra, 1 inch, 2.5 cm).

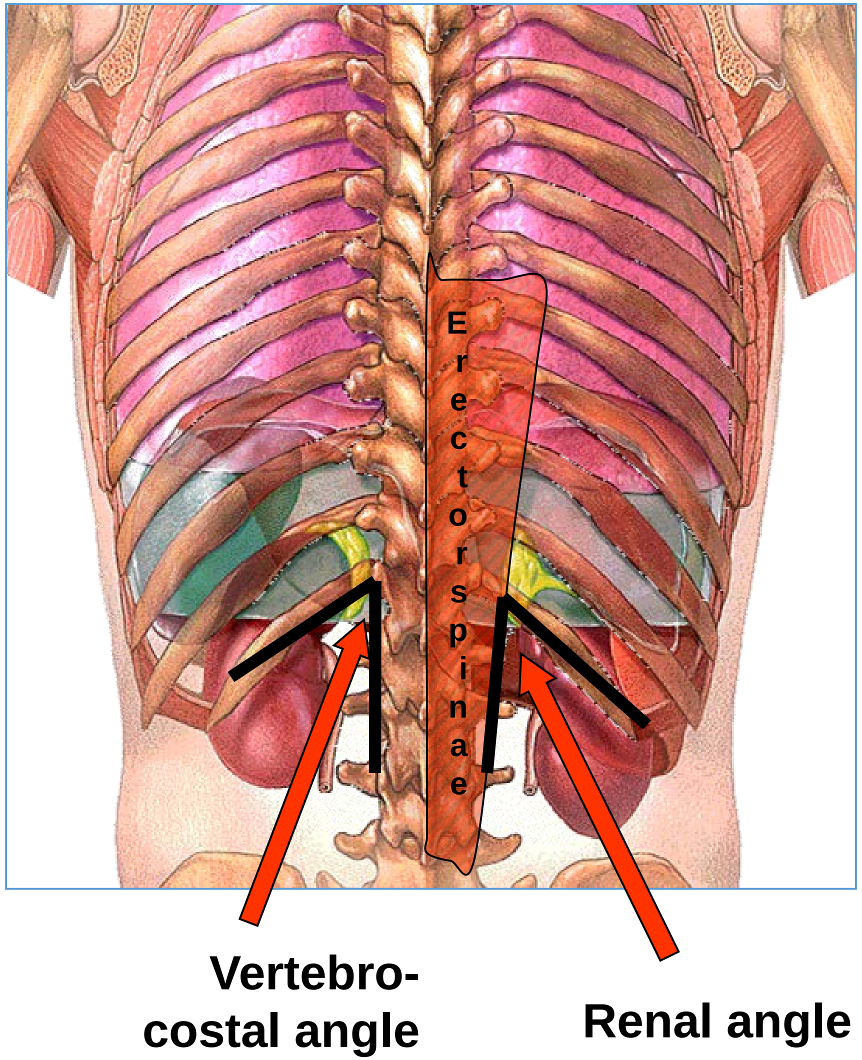



gettyimages

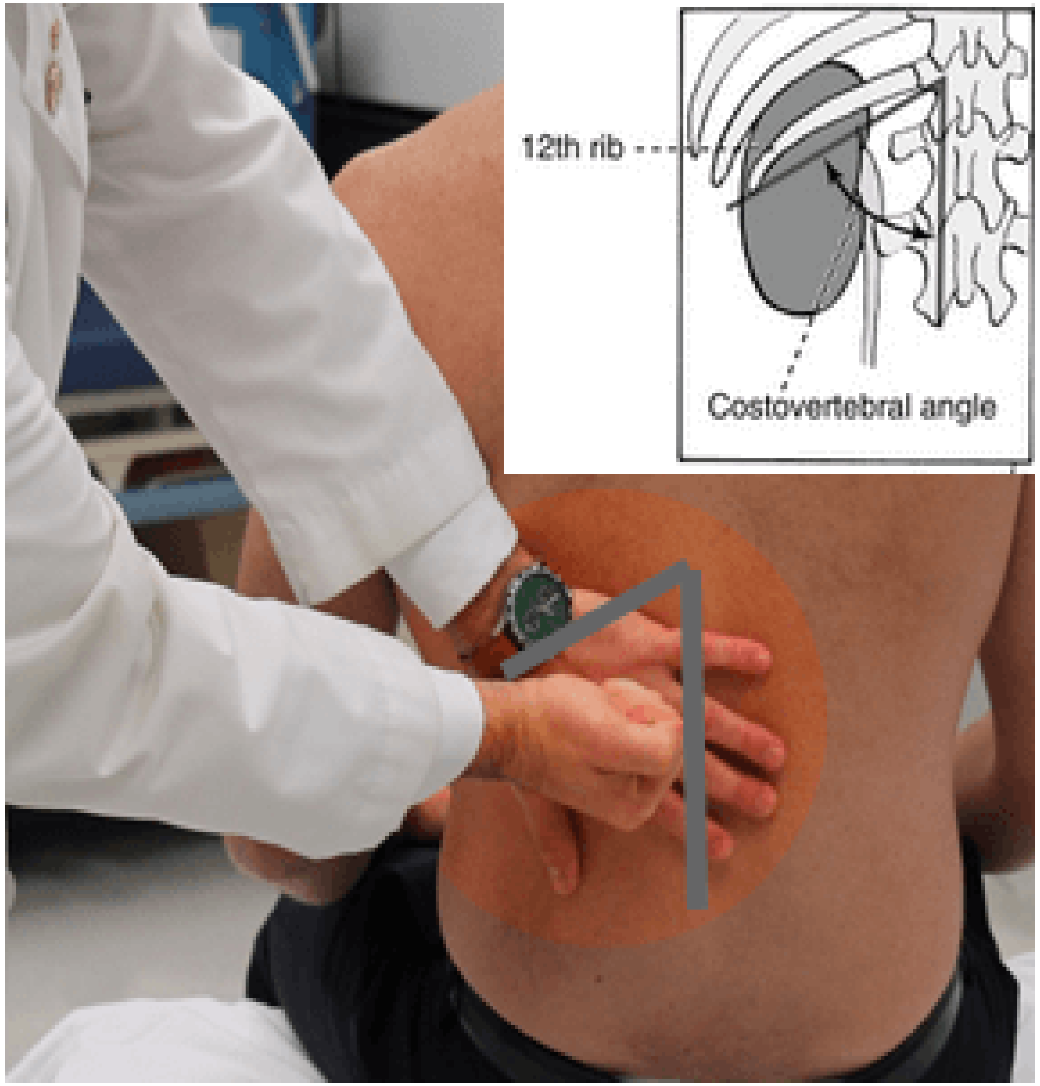
12-8cm	Lenght
7-5 cm	Width
5-3 cm	Depth

Vertebrocostal & Renal Angles

- The angle between the **last rib** and the lateral border of **erector spinae muscle** is occupied by kidney and is called the **<u>'Renal angle'</u>**
- The **<u>Vertebrocostal angle</u>** is occupied by the lower part of the pleural sac.

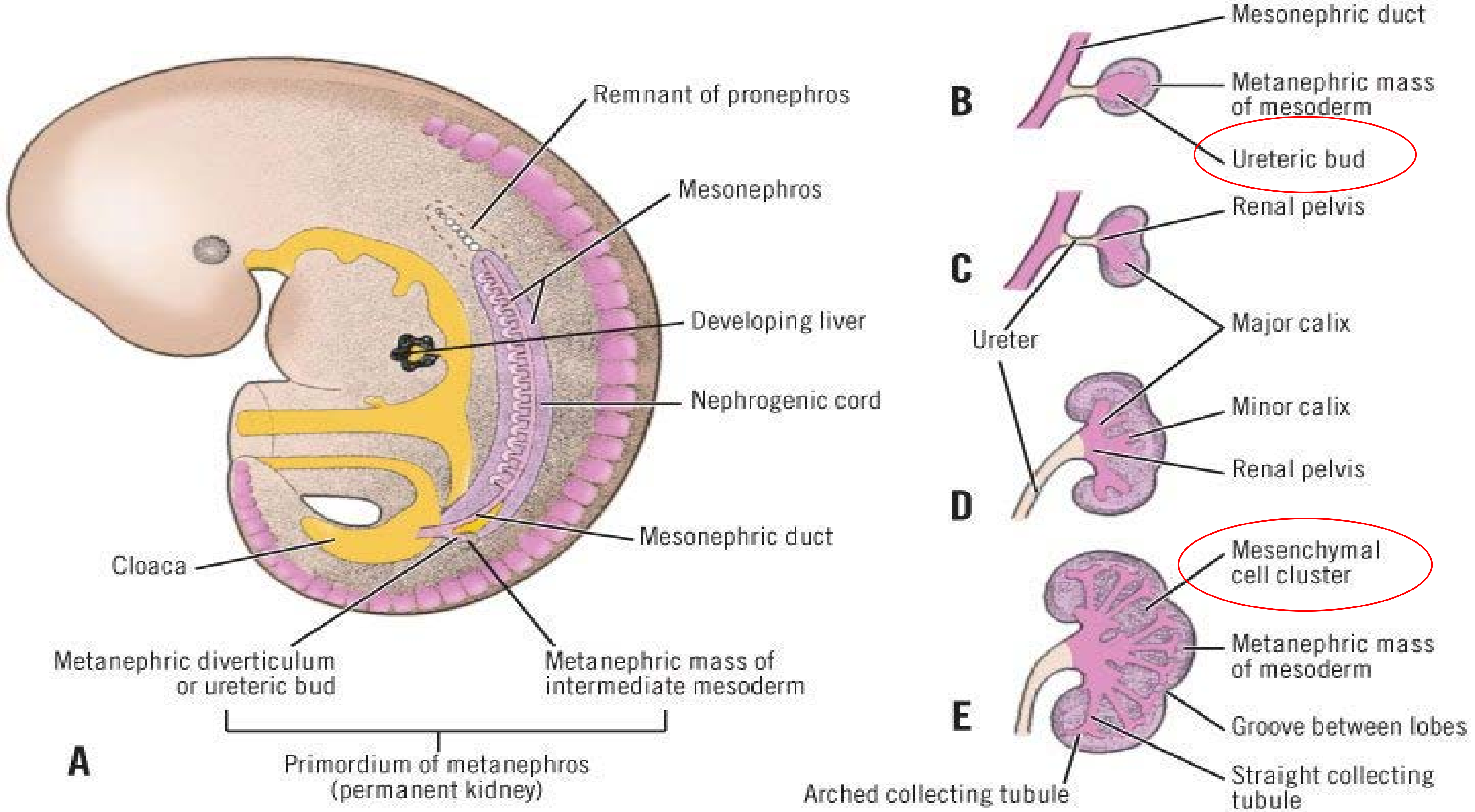



Costovertebral Angle
RegisteredNurseRN.com


12th rib
Costovertebral angle

Timeline of Kidney Embryology

- Week 4 : appearance of Wolffian or Mesonephric Duct
- Day 28 : formation of Ureteric Bud (UB)
- Week 4-8 : Initial MM induction and UB branching
- Week 8 : First nephrons are formed
- Week 6-8 : kidneys ascend from pelvis to lumbar location
- Week 8-15 : Period of UB branching with stochastic formation of UB ampulla and nephron units
- Week 10 : filtration begins
- Week 32-36: End of Nephrogenesis


Remnant of pronephros
Mesonephros
Developing liver
Nephrogenic cord
Mesonephric duct
Cloaca
Metanephric diverticulum or ureteric bud
Metanephric mass of intermediate mesoderm
Primordium of metanephros (permanent kidney)
A
B
Mesonephric duct
Metanephric mass of mesoderm
Ureteric bud
C
Renal pelvis
Ureter
Major calix
D
Minor calix
Renal pelvis
E
Mesenchymal cell cluster
Metanephric mass of mesoderm
Groove between lobes
Straight collecting tubule
Arched collecting tubule

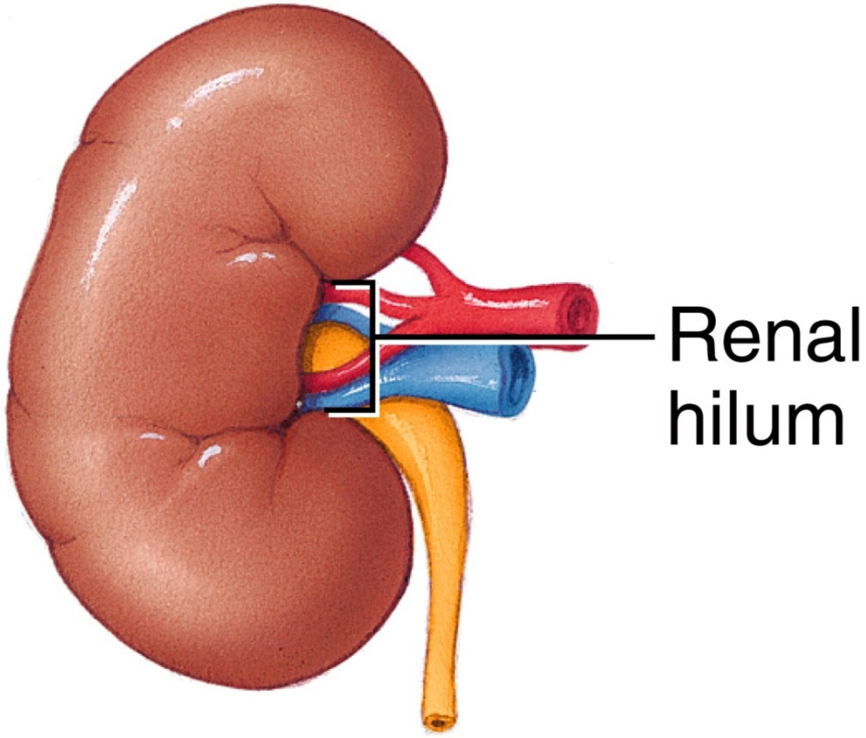
Each kidney in adults:900000 nephrones

Low birth weights: 225000

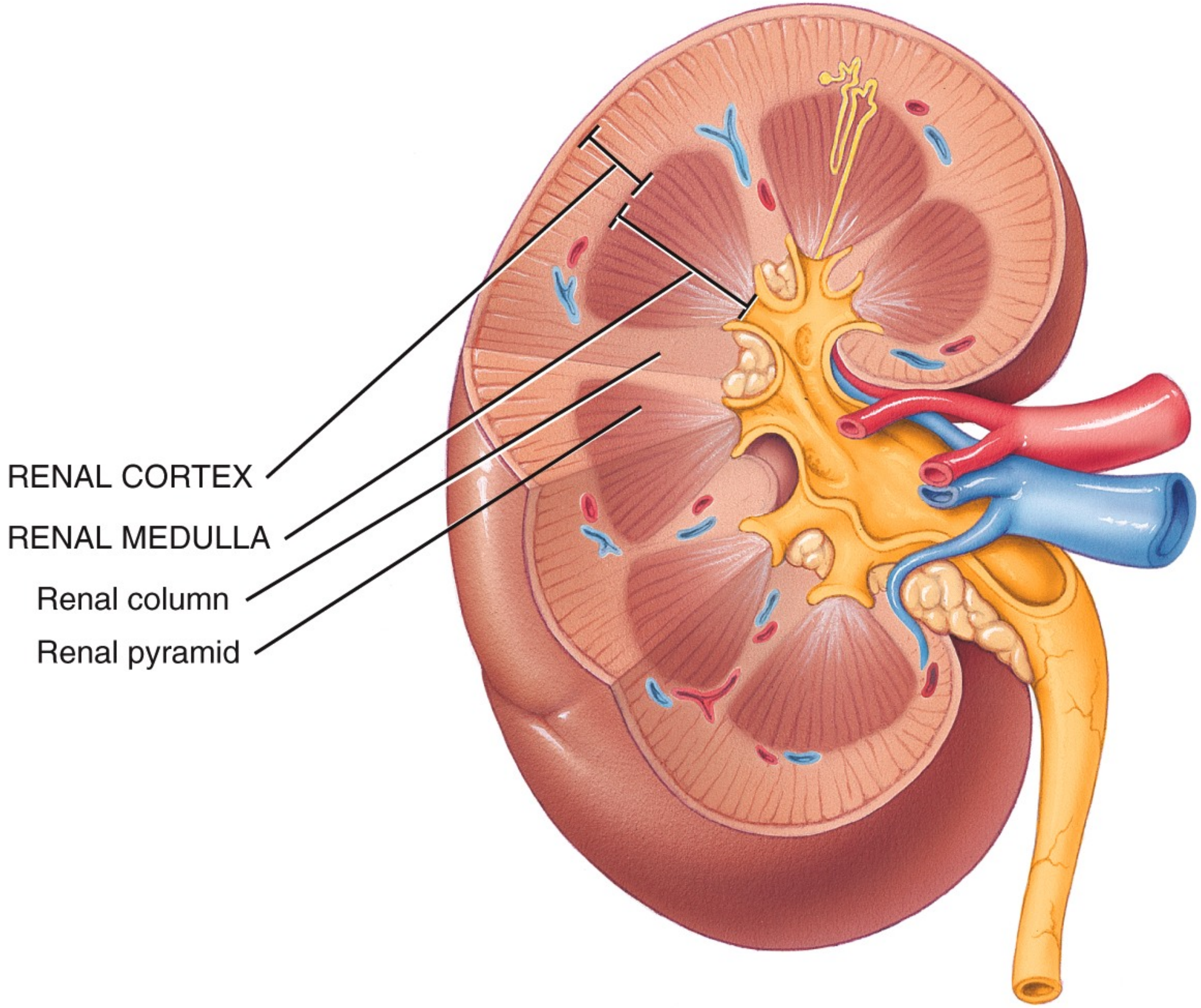
Renal Anatomy

The indented area is called
the Hilum.

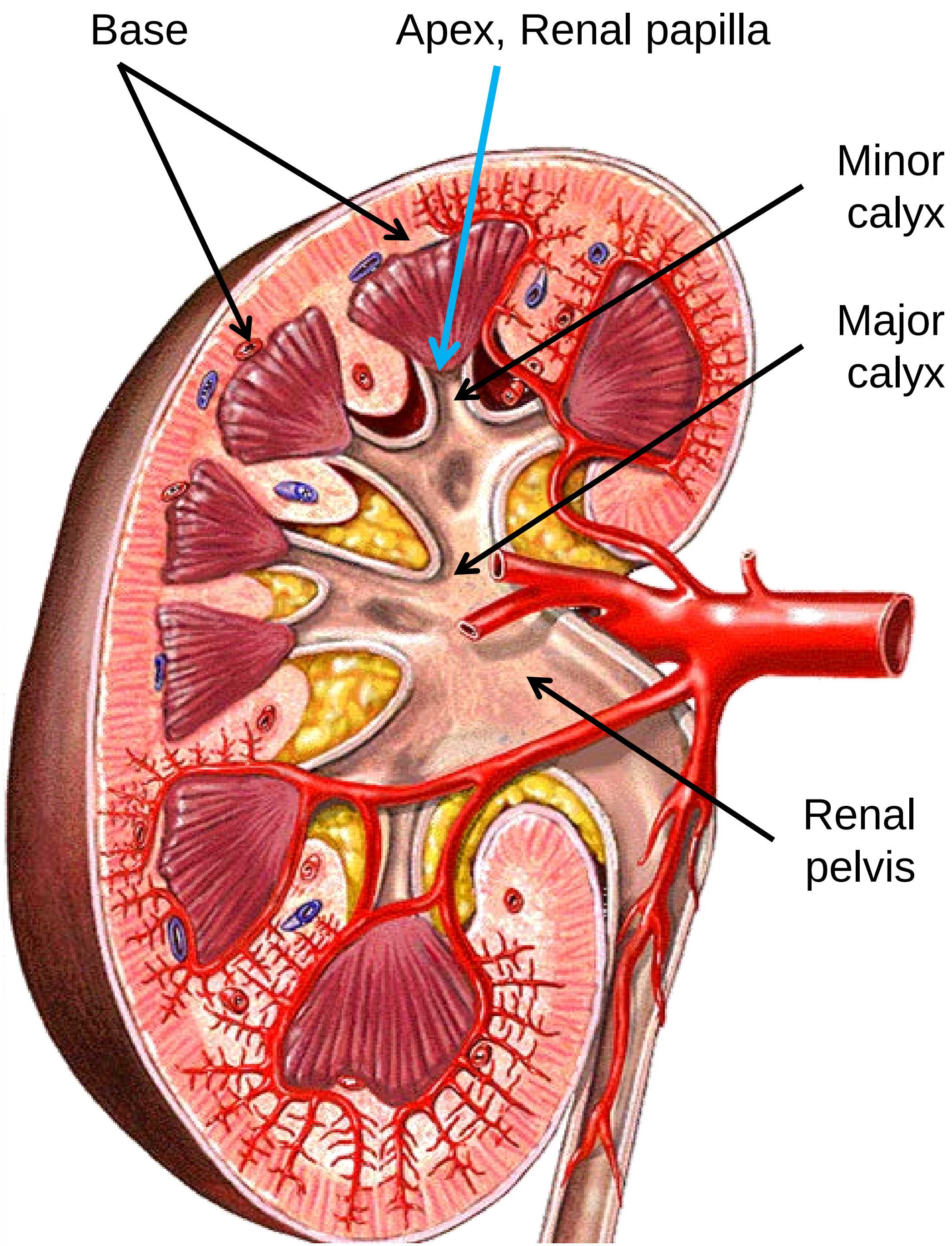
This is the entrance for:
Renal Artery
Renal Vein
Ureter
Nerves
Lymphatics



Internal Renal Anatomy



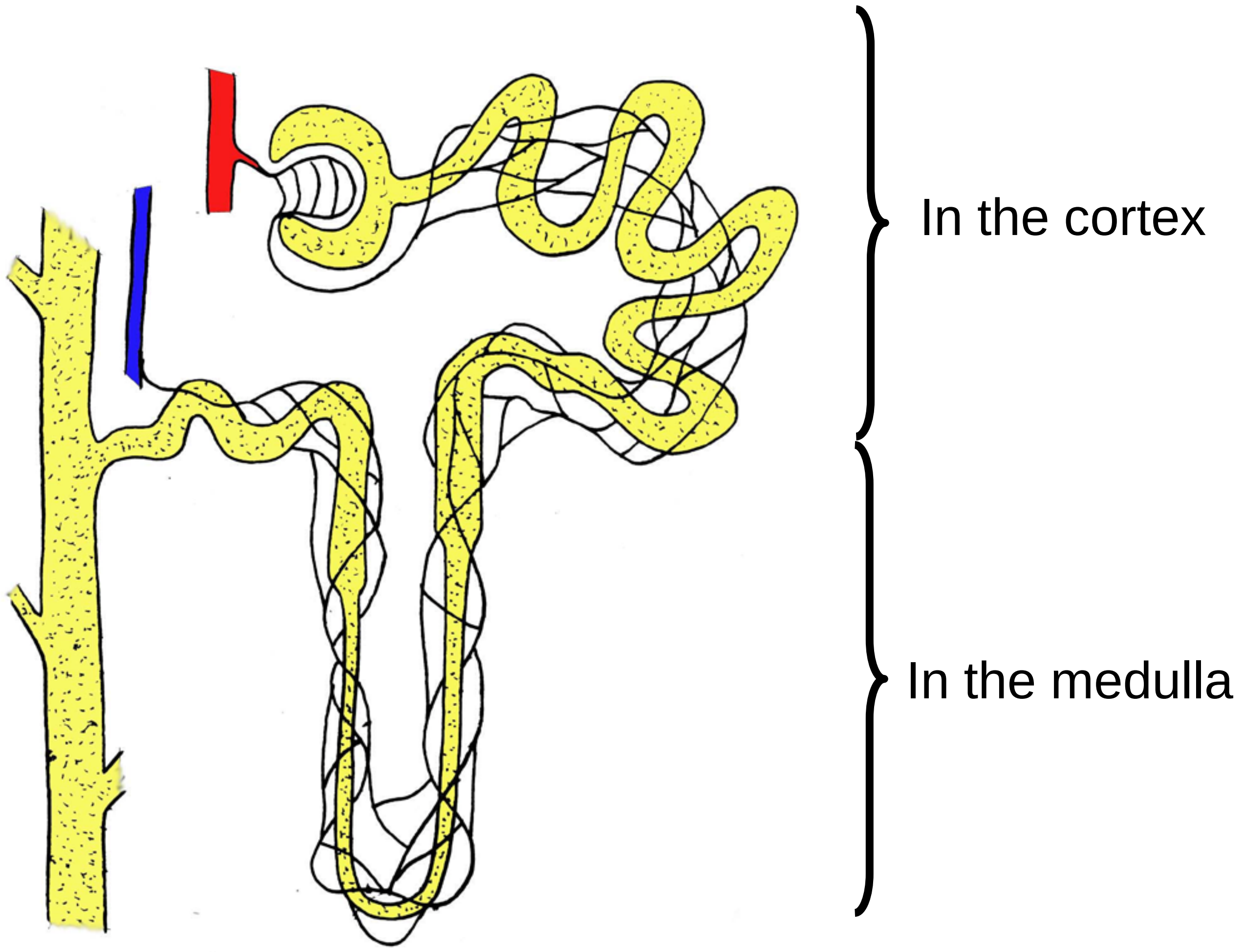
- The **bases** of the renal pyramids are directed outward, toward the cortex, while the **apex** of each renal pyramid projects inward, toward the **renal sinus**.
- The apical projection (**renal papilla**) is surrounded by a **minor calyx**
- In the renal sinus, several minor calices unite to form a **major calyx**, and two or three major calices unite to form the **renal pelvis**, which is the funnel-shaped superior end of the ureters.



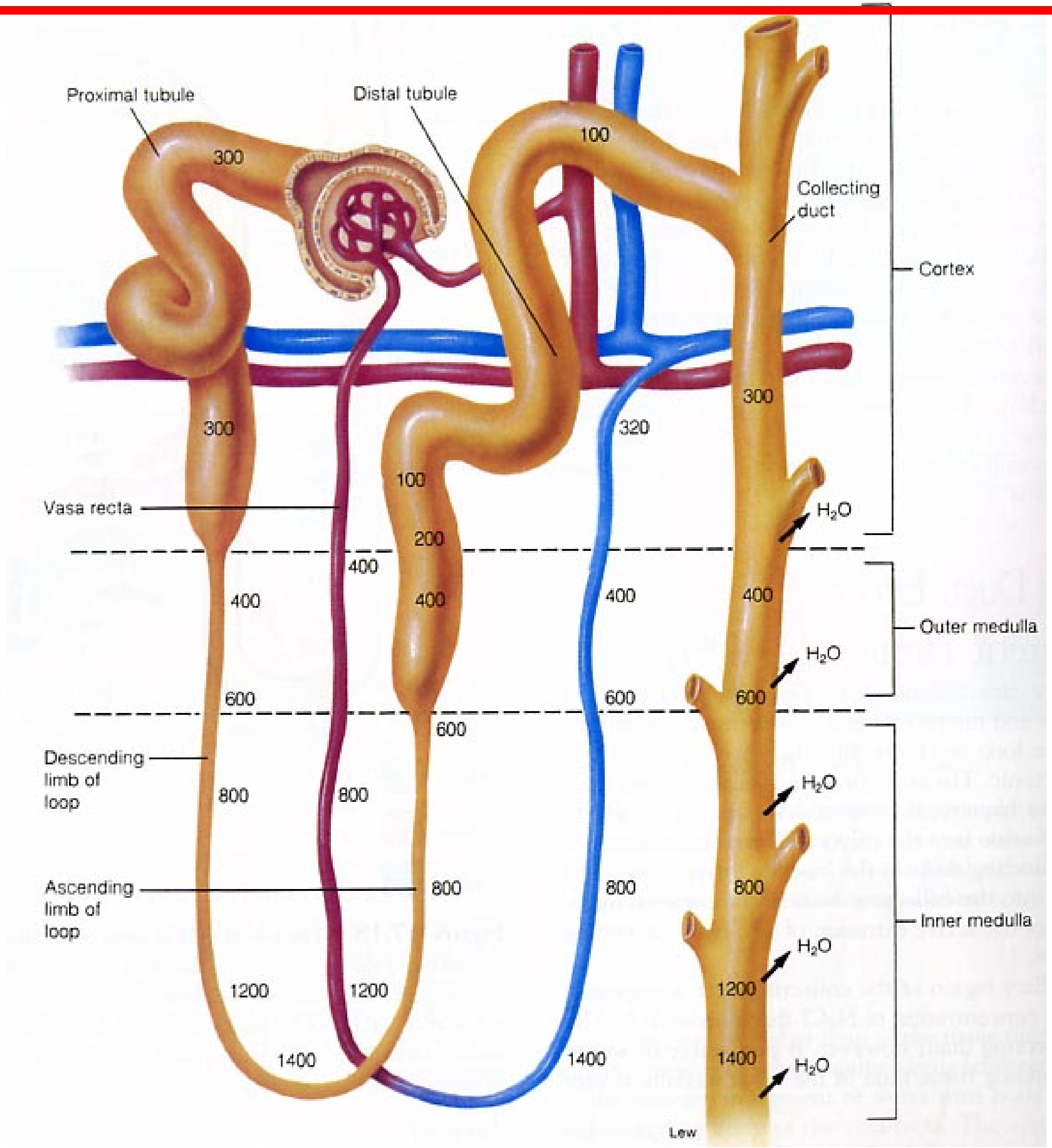
Renal blood flow normally drains approximately 20% of the cardiac output, or 1000 mL/min.

Microscopic anatomy

The nephron



Functional Unit of the Kidney is the NEPHRON



Glomerulus

Bowman capsule

Proximal Tubule

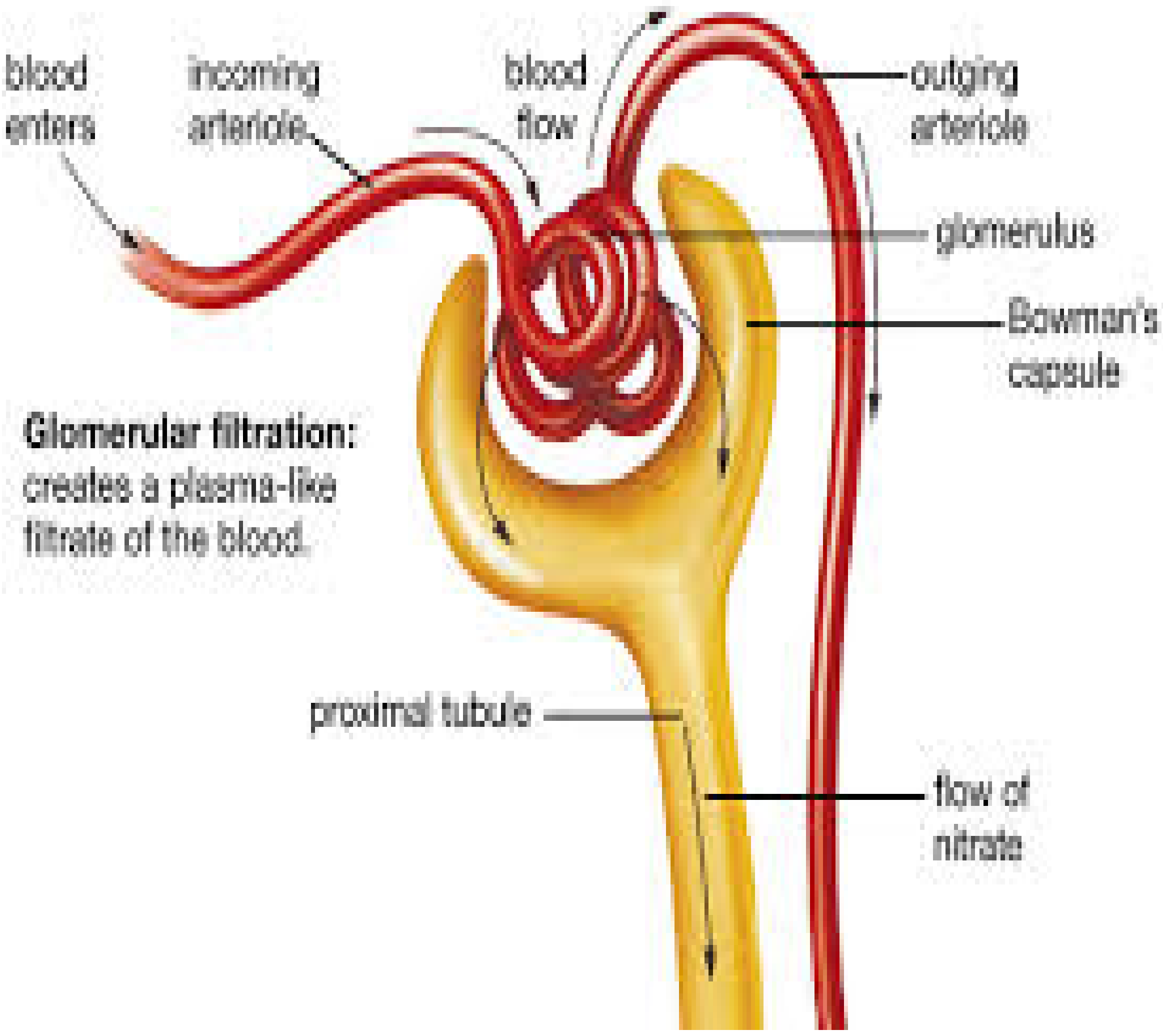
Loop of Henle

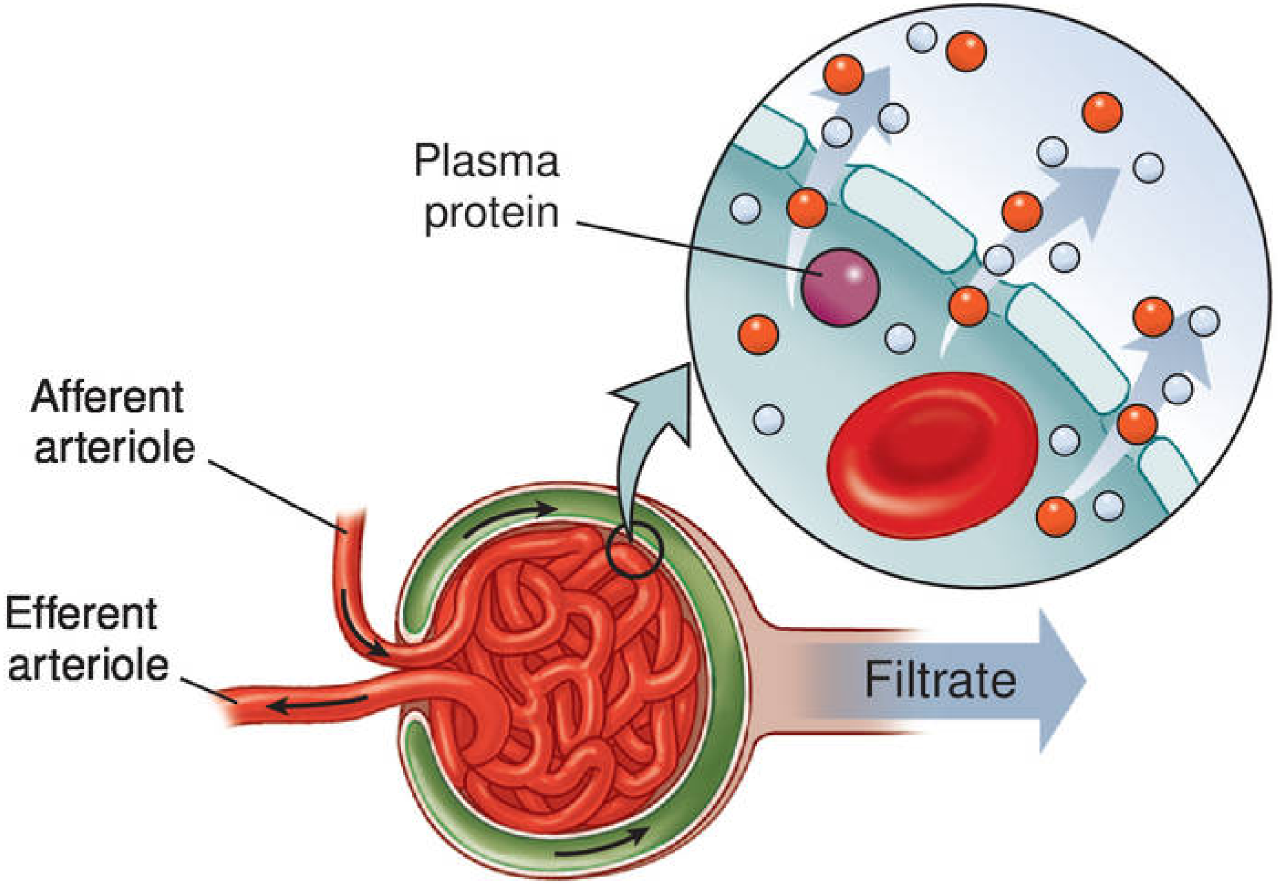
Distal Tubule

Collecting Duct

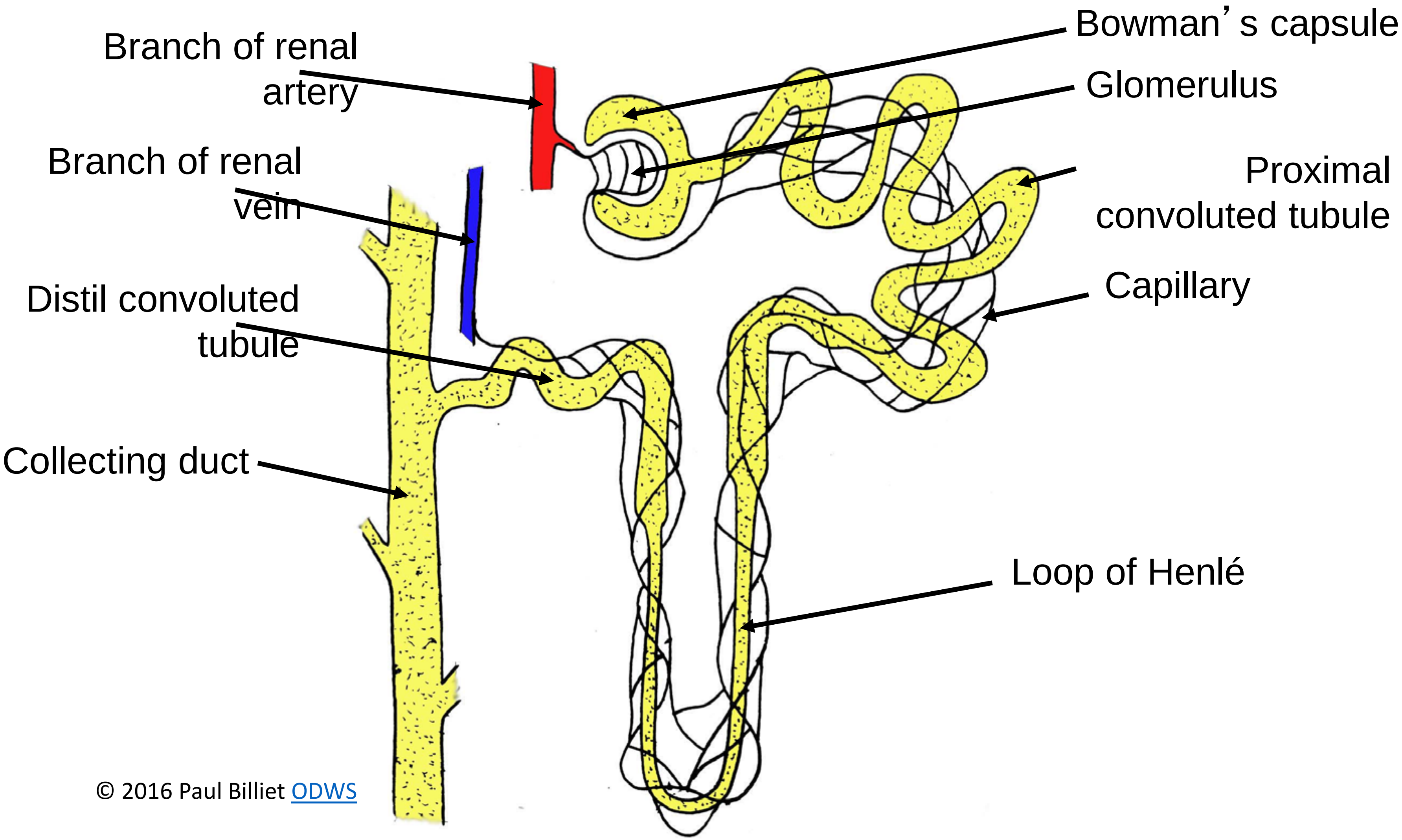
GLOMERULUS

- کلافه عروقی
- مواد زاید را به توبولها می رساند


blood enters
incoming arteriole
blood flow
outging arteriole
glomerulus
Bowman's capsule
Glomerular filtration:
creates a plasma-like filtrate of the blood.
proximal tubule
flow of nitrate


Plasma protein
Afferent arteriole
Efferent arteriole
Filtrate

The nephron



Branch of renal artery
Branch of renal vein
Distil convoluted tubule
Collecting duct
Bowman's capsule
Glomerulus
Proximal convoluted tubule
Capillary
Loop of Henlé

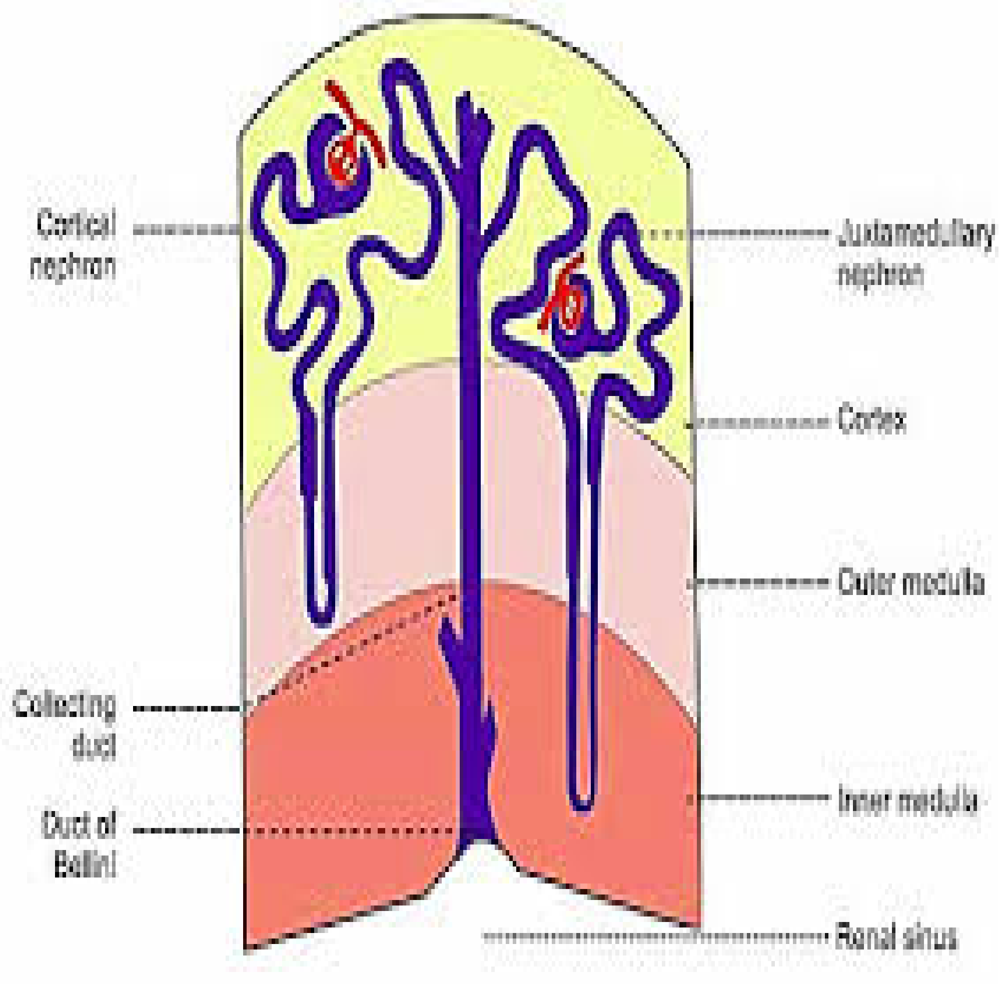
Two Kinds of Nephrons

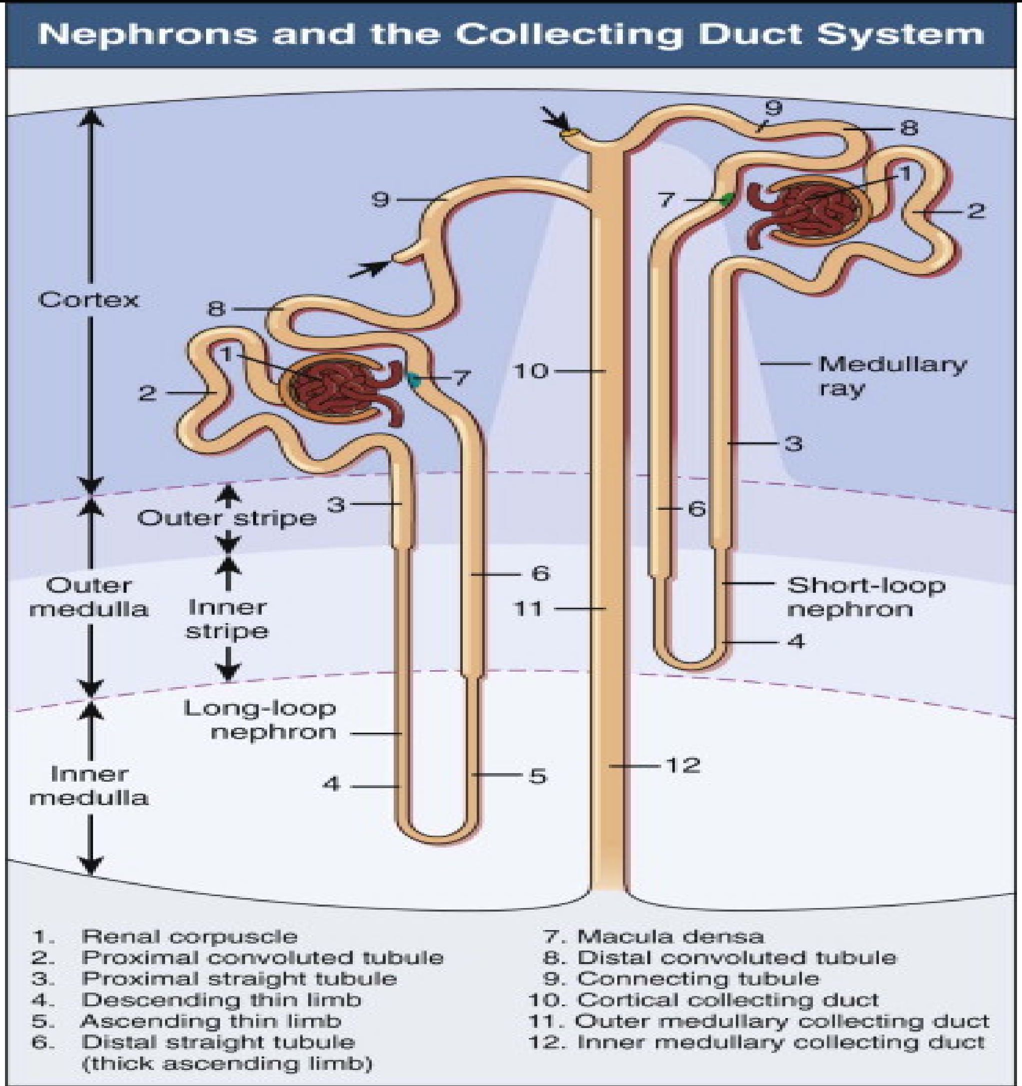
Cortical nephrons : 80-85% of nephrons

Renal corpuscle in outer portion of cortex

Short loops of Henle extend only into outer region of medulla Create urine with osmolarity similar to blood.

Cortical nephrones





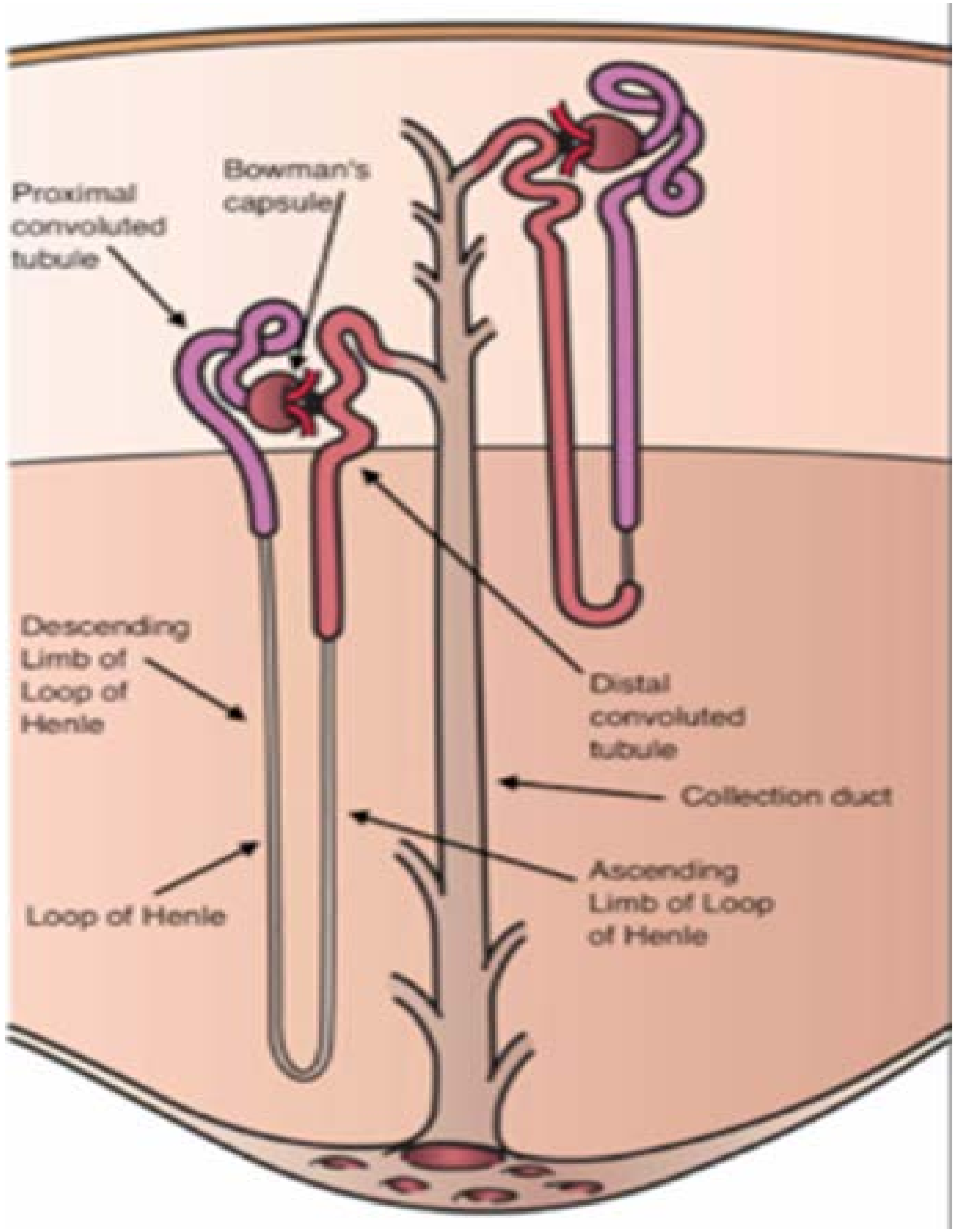
Juxtamedullary Nephrons

Renal corpuscle deep in cortex with long nephron loops

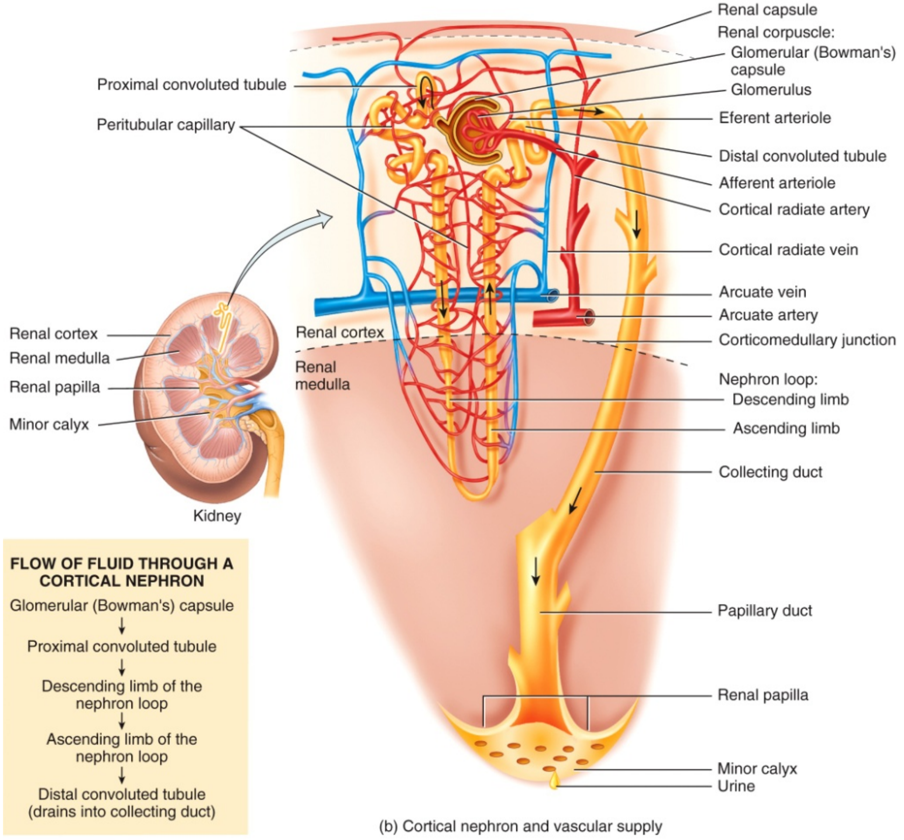
Receive blood from peritubular capillaries and vasa recta

Ascending limb has thick and thin regions

Enable kidney to secrete **very concentrated urine.**

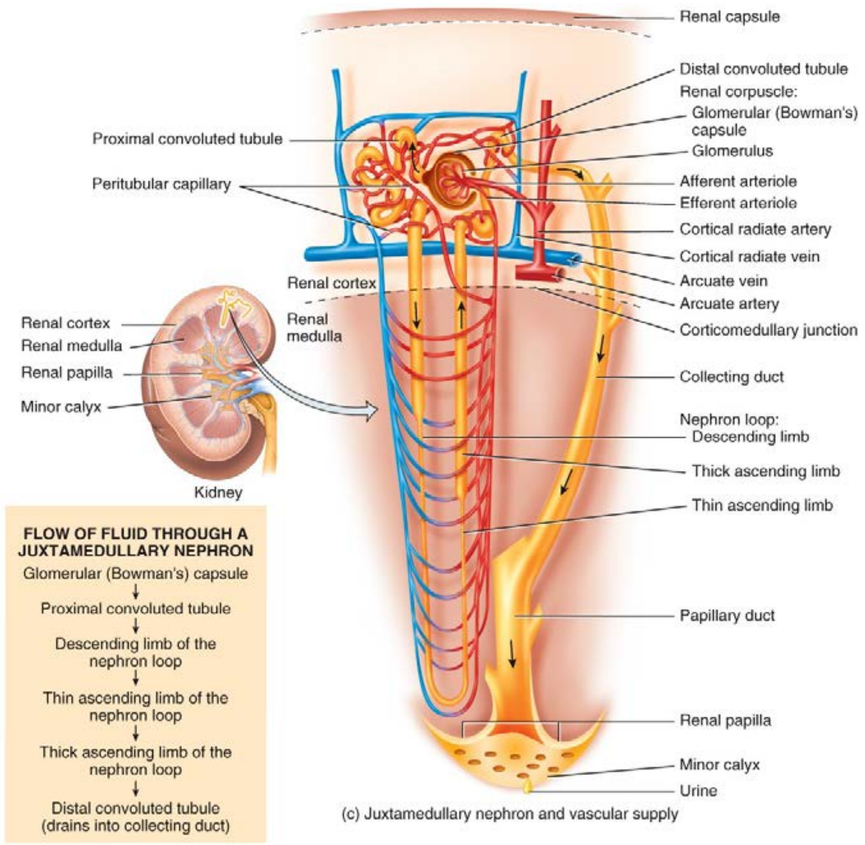

Proximal convoluted tubule
Bowman's capsule
Descending Limb of Loop of Henle
Loop of Henle
Distal convoluted tubule
Collection duct
Ascending Limb of Loop of Henle

Cortical



(b) Cortical nephron and vascular supply

Juxtamedullary



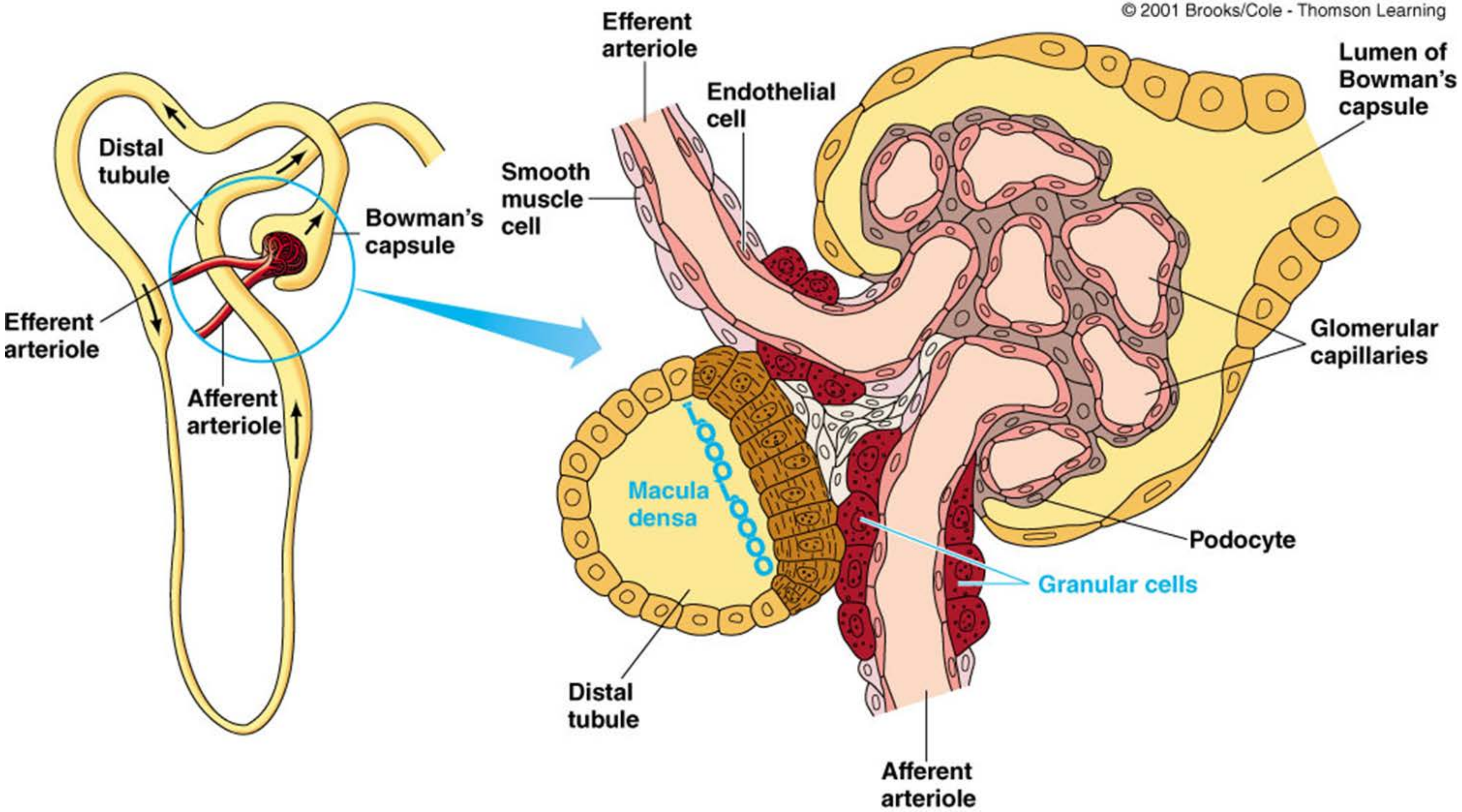
(c) Juxtamedullary nephron and vascular supply

The Juxtaglomerular Apparatus

The ascending loop contacts the afferent arteriole at the macula densa.

The wall of the arteriole contains smooth muscle cells; juxtaglomerular cells.

The apparatus regulates blood pressure in the kidney.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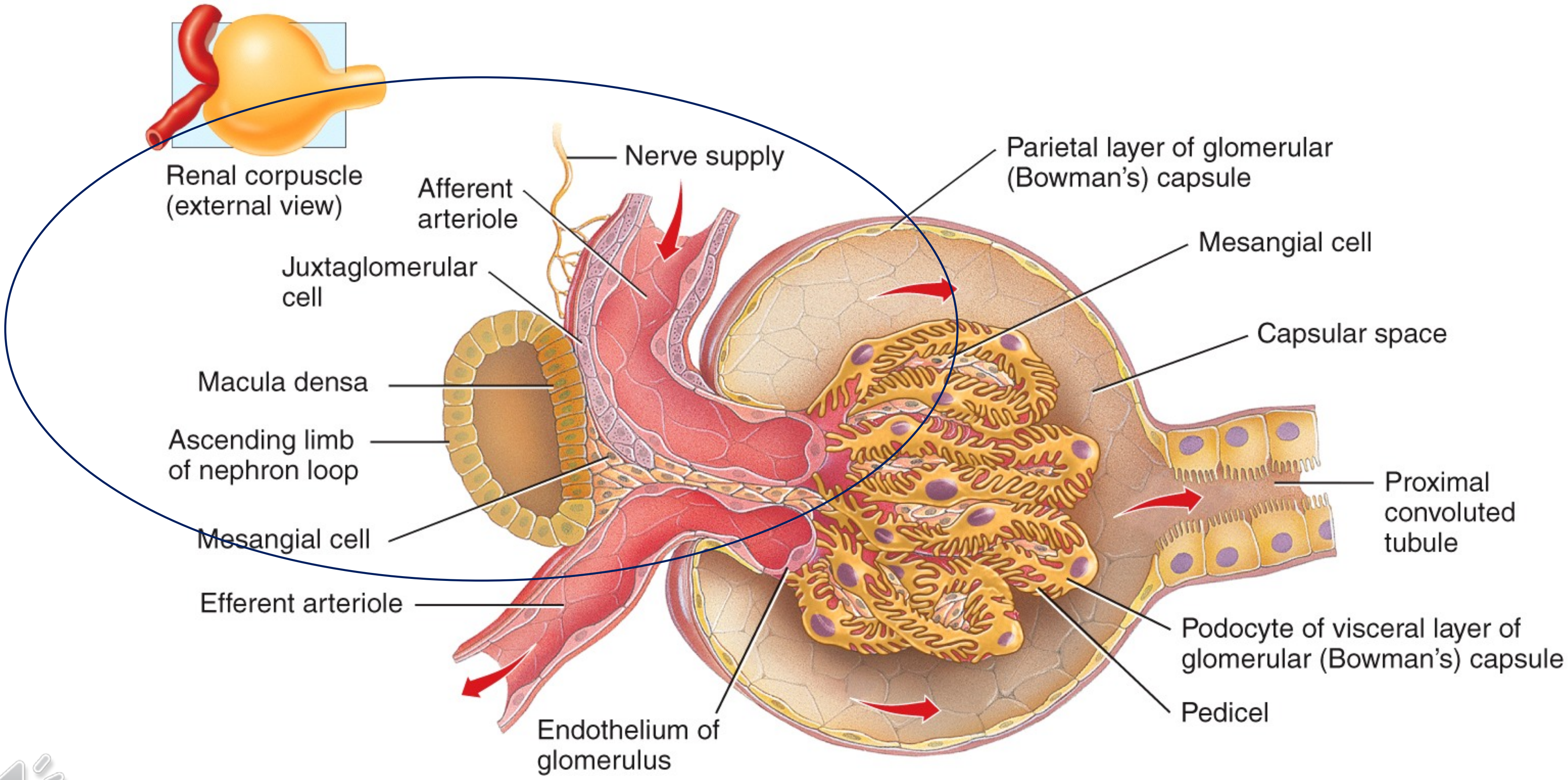
Distal tubule
Bowman's capsule
Efferent arteriole
Afferent arteriole
Efferent arteriole
Endothelial cell
Smooth muscle cell
Lumen of Bowman's capsule
Glomerular capillaries
Macula densa
Podocyte
Granular cells
Distal tubule
Afferent arteriole

Histology of a Renal Corpuscle

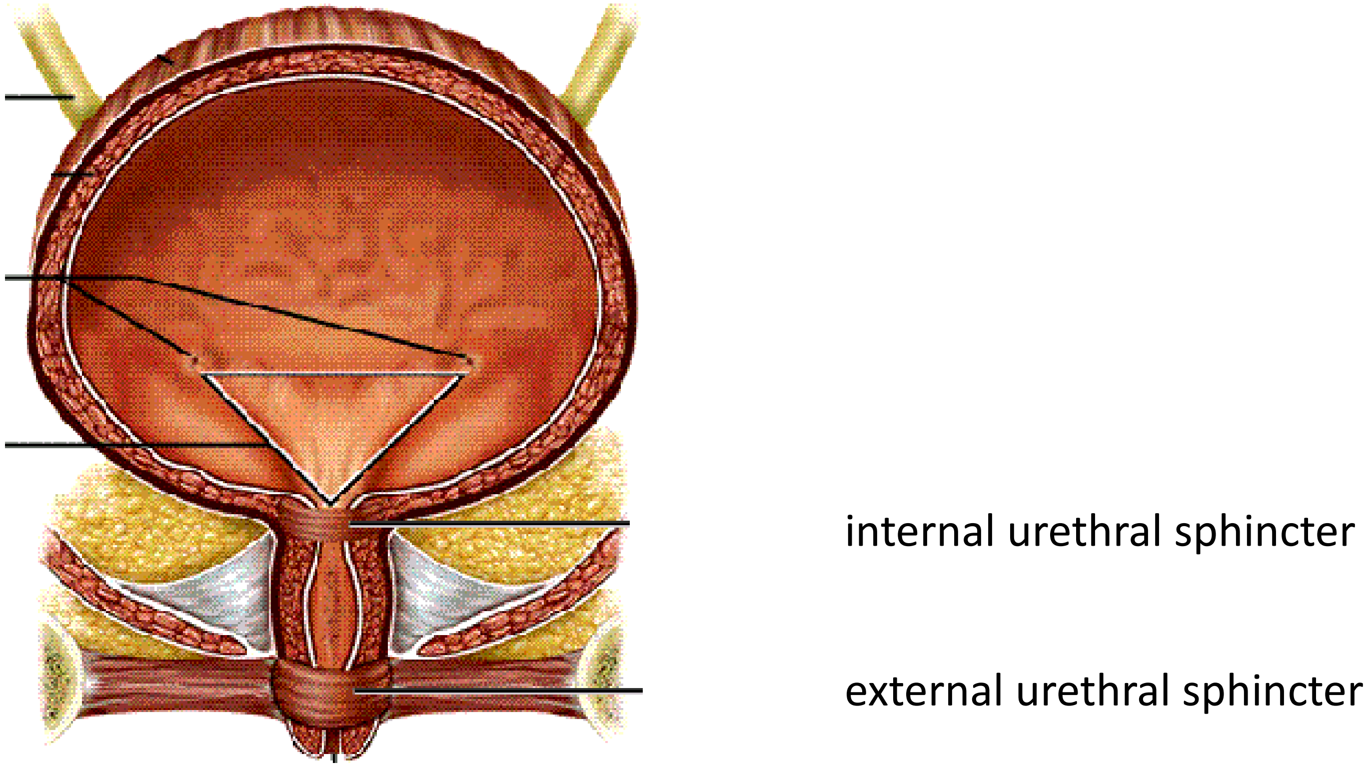


(a) Renal corpuscle (internal view)

Urination

In both sexes:

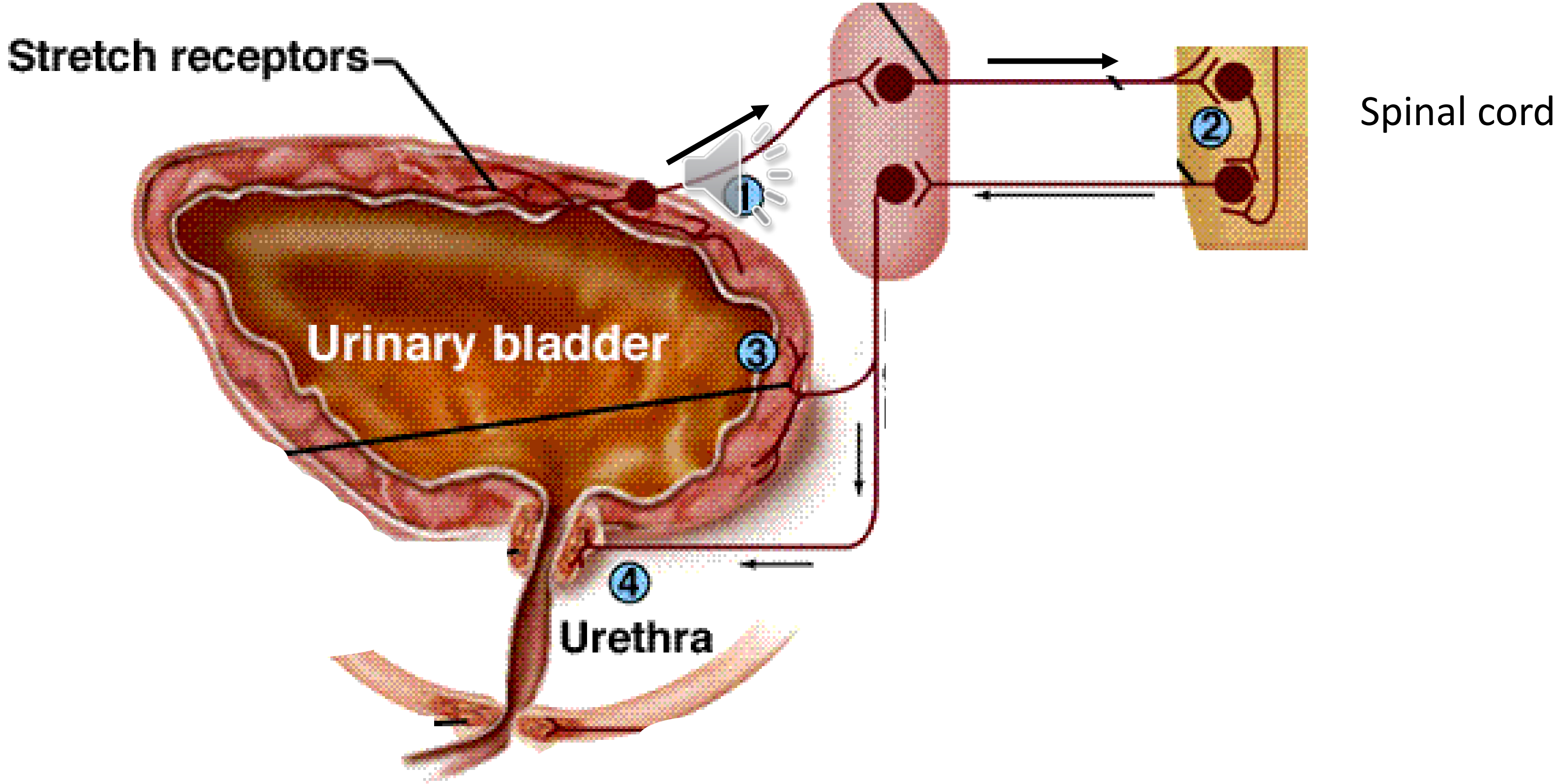
- internal urethral sphincter- under involuntary control.
- external urethral sphincter - under voluntary control



Voiding Urine in infants

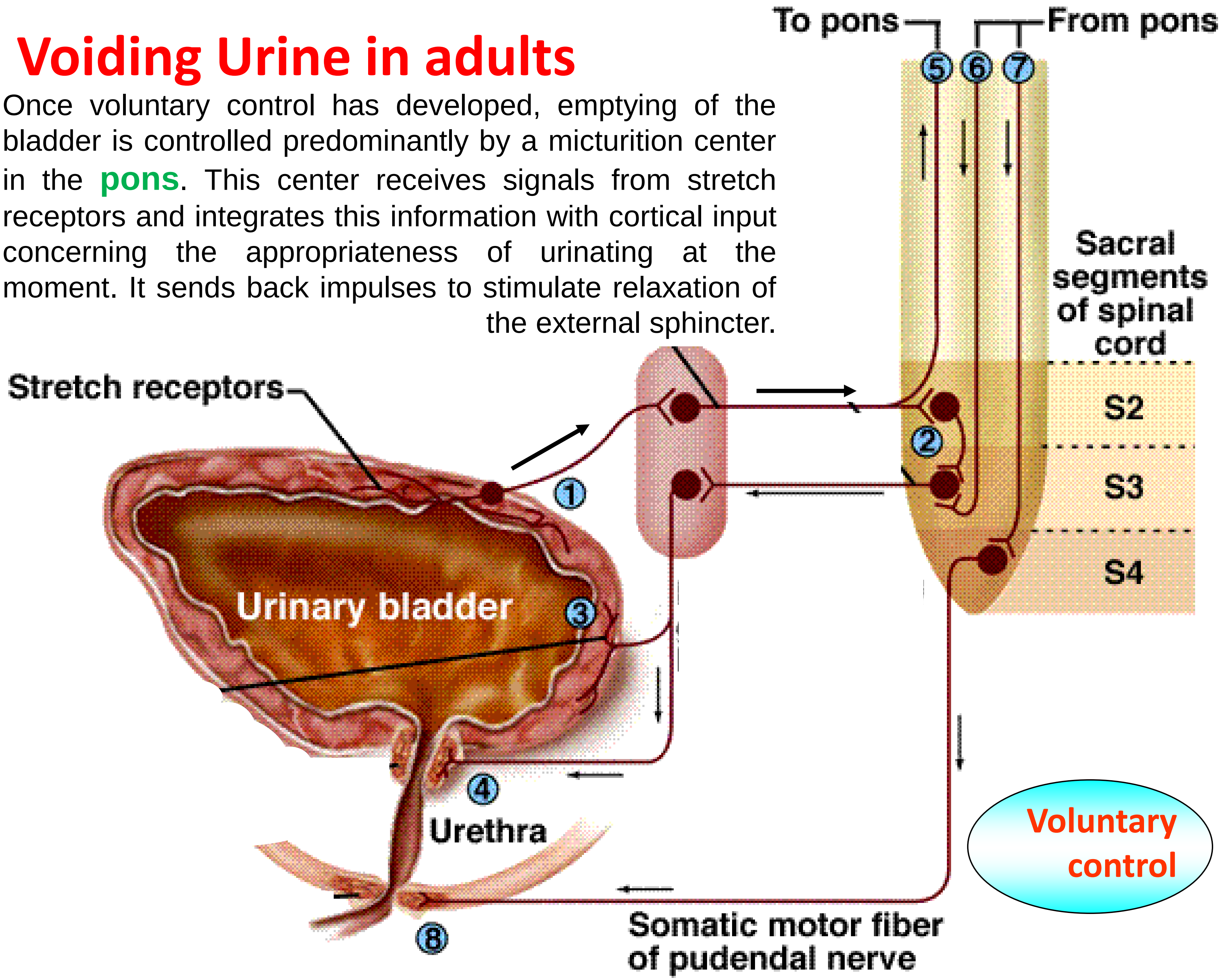
micturition reflex

When the bladder contains about 200 ml of urine, stretch receptors in the wall send impulses to the spinal cord. Parasympathetic signals return to stimulate contraction of the bladder and relaxation of the internal urethral sphincter.



Voiding Urine in adults

Once voluntary control has developed, emptying of the bladder is controlled predominantly by a micturition center in the **pons**. This center receives signals from stretch receptors and integrates this information with cortical input concerning the appropriateness of urinating at the moment. It sends back impulses to stimulate relaxation of the external sphincter.



Voluntary control

Kidney

Kidney only 1% of total body weight, despite it

The renal blood flow= 20% of cardiac output

Kidney Functions

Regulation of water, electrolyte balance, pH .1

Removal of waste from blood and excretion of urine .2

Secretion of hormones .3

Erythropoietin

Renin

Activated vitamin D

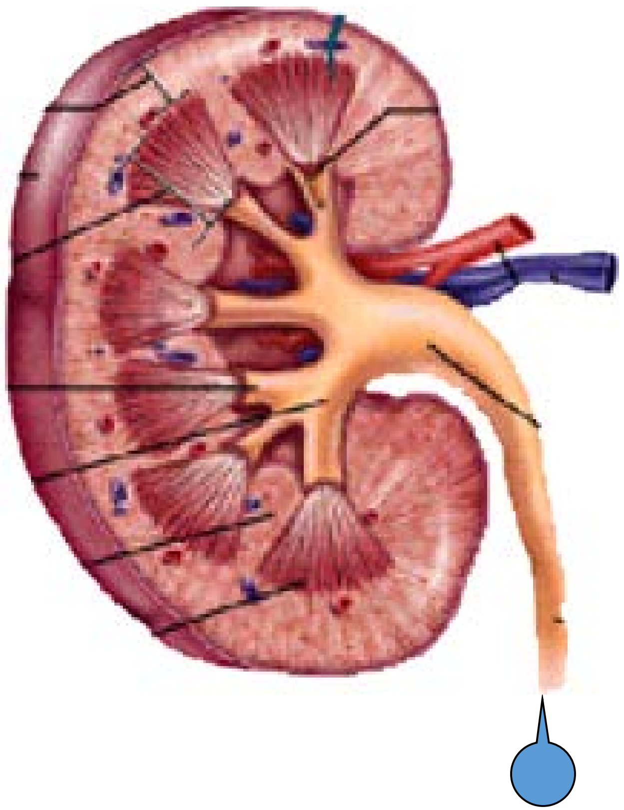
Other functions

4.free radicals & drugs detoxification

5.glucose synthesis

Functions of the Kidneys

1) filter blood plasma, separate wastes, return useful materials to the blood, and eliminate the wastes.



Toxic ***nitrogenous wastes***

- **ammonia, urea, uric acid, creatine, and creatinine**

- **cause diarrhea, vomiting, and cardiac arrhythmia,weakness,neuropathy, convulsions, coma, and death.**

Renal failure

Acute kidney injury

Chronic kidney injury

Glucose Synthesis

The kidneys synthesize glucose from amino acids and other precursors during prolonged fasting, a process referred to as **gluconeogenesis**.

The kidneys' capacity to add glucose to the blood during prolonged periods of fasting rivals that of the liver.

Renal physiology

Nephron Functions

Filtration

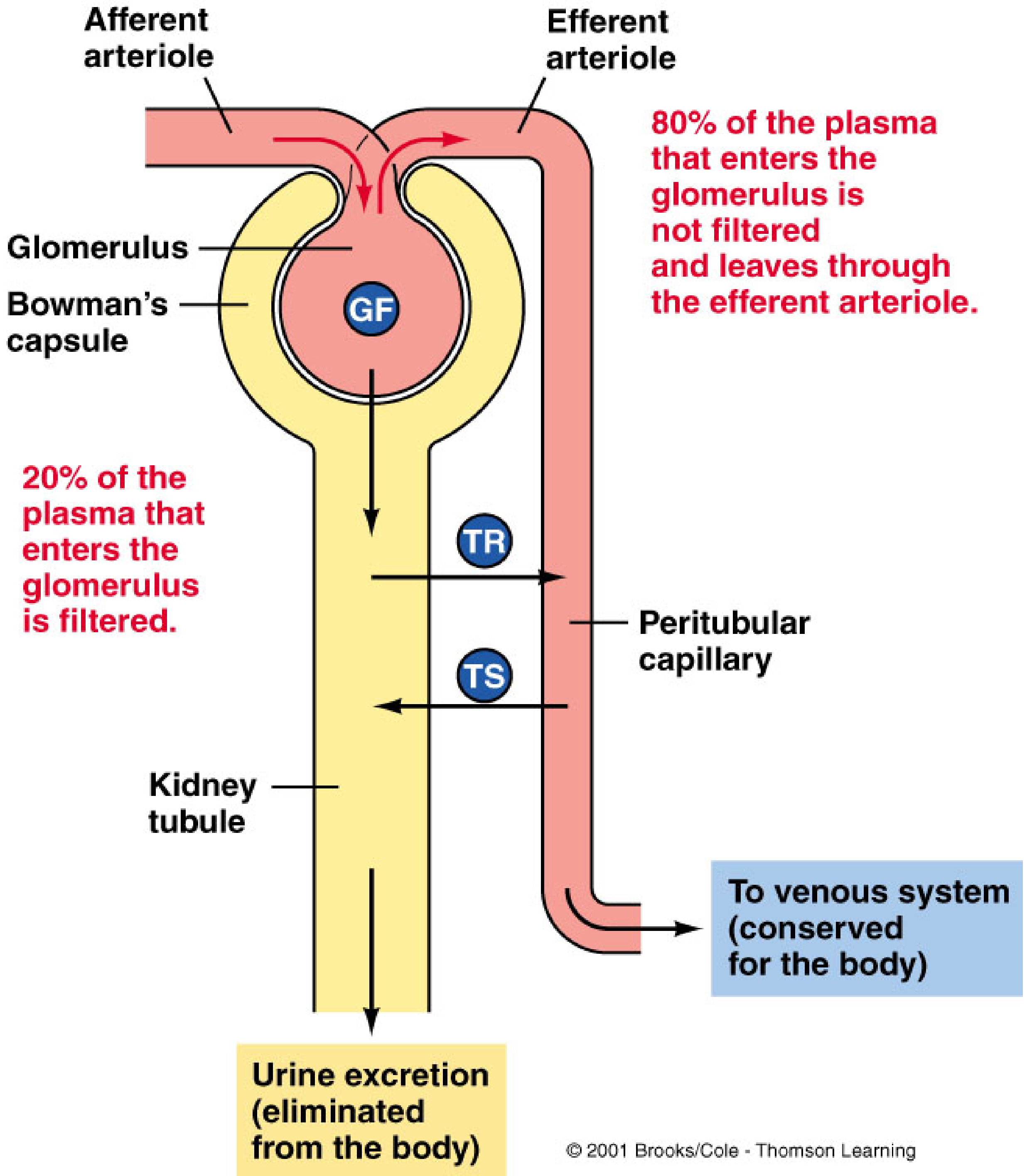
Selective Reabsorption

Tubular Secretion

concentration

تشکیل ادرار=

(فیلتراسیون+ترشح)-بازجذب


Afferent arteriole
Efferent arteriole
80% of the plasma that enters the glomerulus is not filtered and leaves through the efferent arteriole.
Glomerulus
Bowman's capsule
GF
20% of the plasma that enters the glomerulus is filtered.
TR
Peritubular capillary
TS
Kidney tubule
To venous system (conserved for the body)
Urine excretion (eliminated from the body)

Glomerular filtration rate (GFR)

represents the flow of plasma from the glomerulus into Bowman's space over a specified period and is the chief measure of kidney function

Glomerular Filtration Rate

GFR averages 130mL/min in males and 120mL/min in females

Controlled by:

Renal Autoregulation

Neural Regulation

GFR is approximately 120 ml per min (180 L per day). Average urine output, on the other hand, averages only about 1.5 L daily. The reabsorption of 178.5 L requires a sophisticated tubular network

Glomerular Filtration Rate

Although glomerular filtration is affected by **renal artery pressure**,

this relationship is not linear across the range of physiologic blood pressures due to **autoregulation** of GFR

Renal Autoregulation

Myogenic reflex

Tubuloglomerular feedback

Ag II vasoconstriction

Renal Autoregulation

Myogenic Mechanism

Smooth muscle cells in afferent arterioles contract in response to elevated blood pressure

Tubuloglomerular Feedback

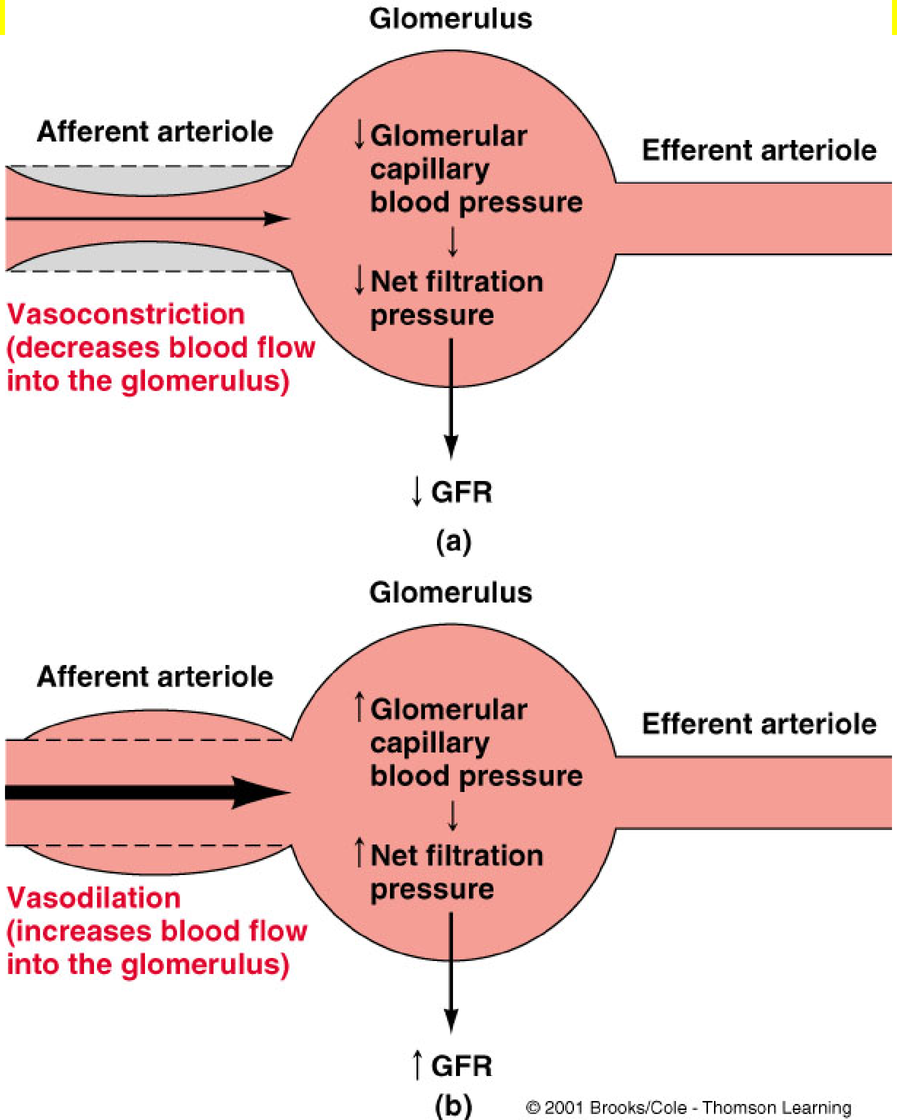
High GFR diminishes reabsorption

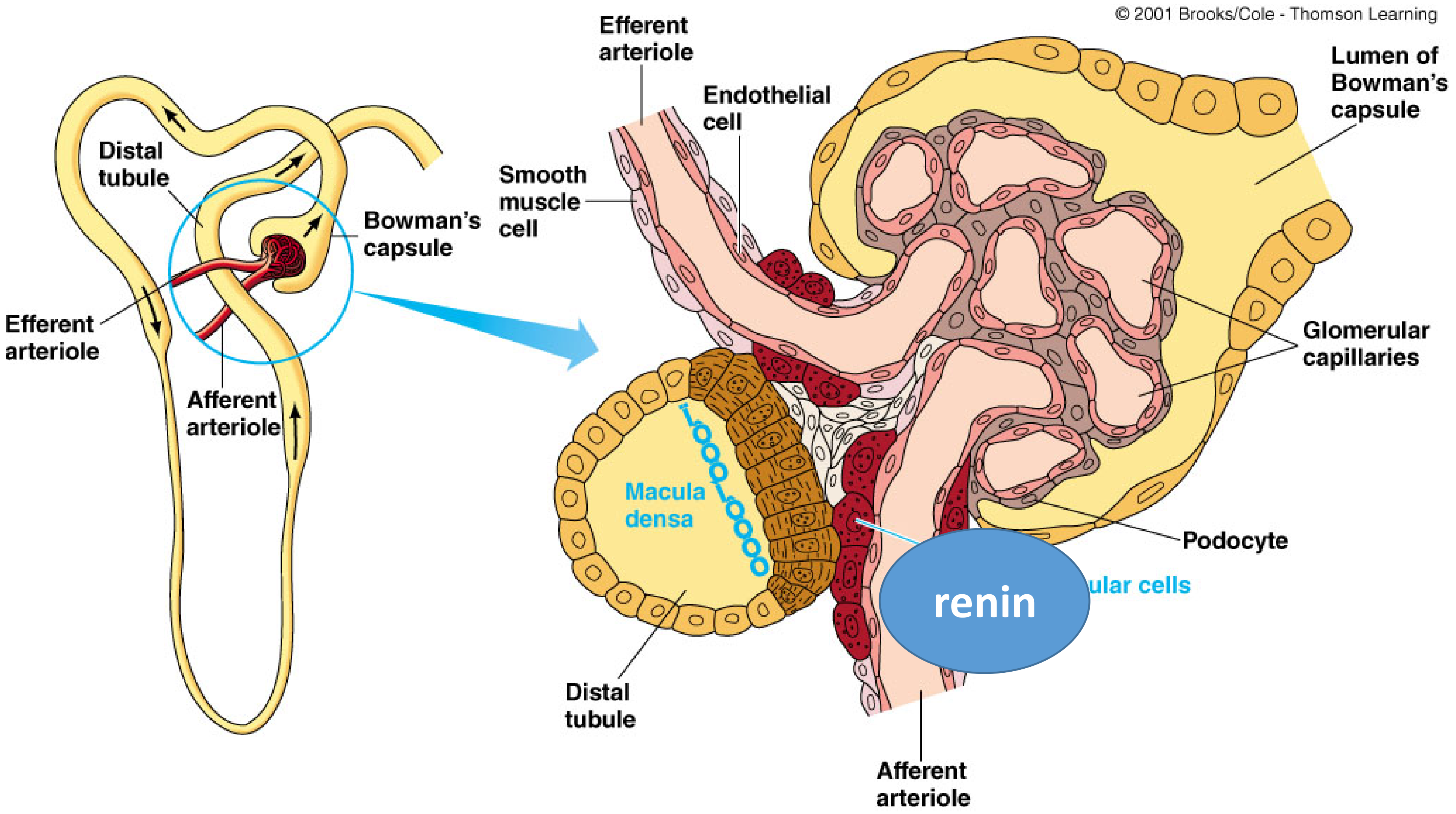
Macula Densa inhibits release of nitric oxide

Afferent arterioles constrict

ATP is important

Regulation of Filtration Pressure





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Distal tubule
Bowman's capsule
Efferent arteriole
Afferent arteriole
Efferent arteriole
Endothelial cell
Smooth muscle cell
Lumen of Bowman's capsule
Glomerular capillaries
Macula densa
Podocyte
renin
ular cells
Distal tubule
Afferent arteriole

Renin

Ag I

Ag II

Hormonal Regulation

Angiotensin II

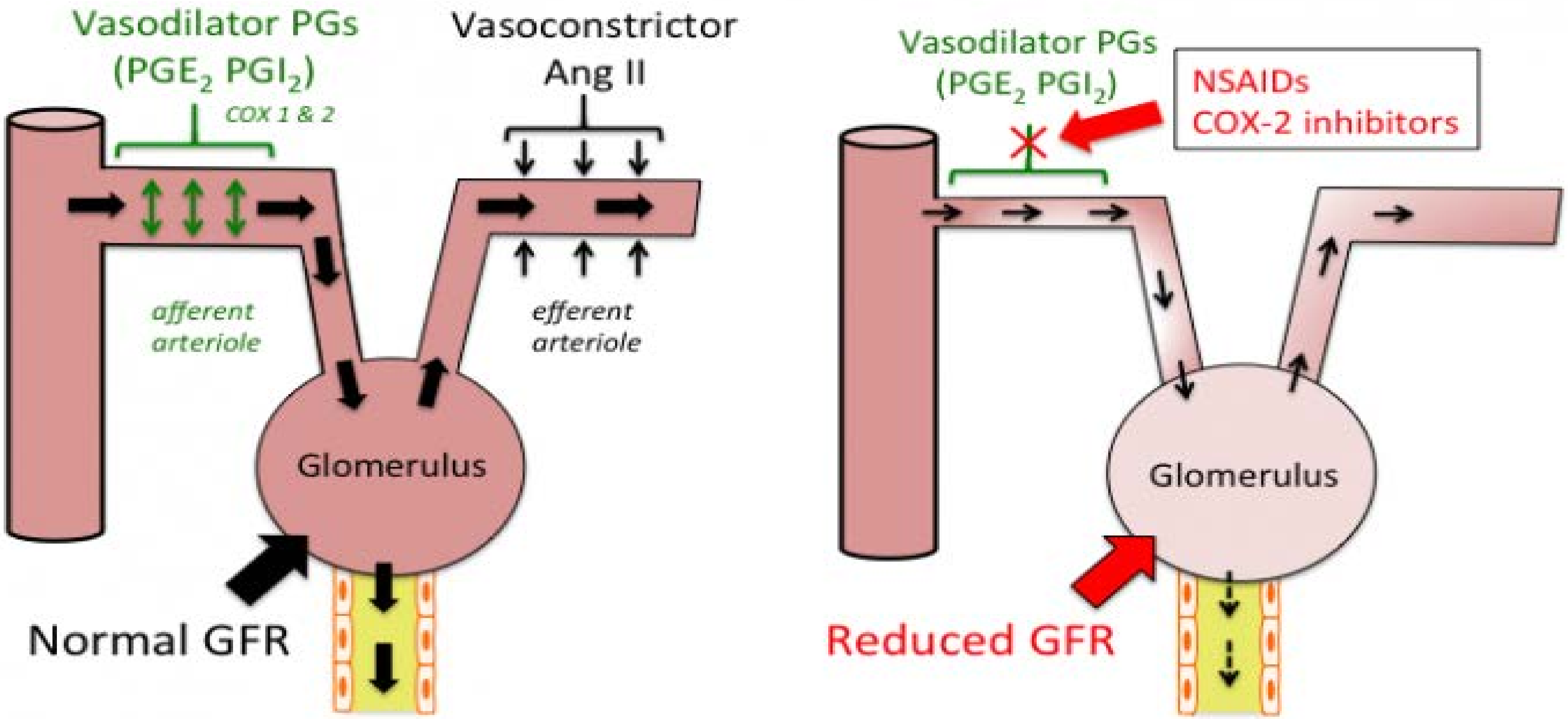
During states of reduced renal blood flow, renin is

released from granular cells within the wall of the afferent arteriole

near the macula densa in a region called the juxtaglomerular apparatus.

Ag II

Angiotensin II evokes <u>vasoconstriction of the efferent arteriole</u>, and the resulting increased glomerular hydrostatic pressure elevates filtration to normal levels.



Vasodilator PGs
(PGE2 PGI2)
COX 1 & 2
Vasoconstrictor
Ang II
afferent
arteriole
efferent
arteriole
Glomerulus
Normal GFR
Vasodilator PGs
(PGE2 PGI2)
NSAIDs
COX-2 inhibitors
Glomerulus
Reduced GFR

Atrial Natriuretic Peptide

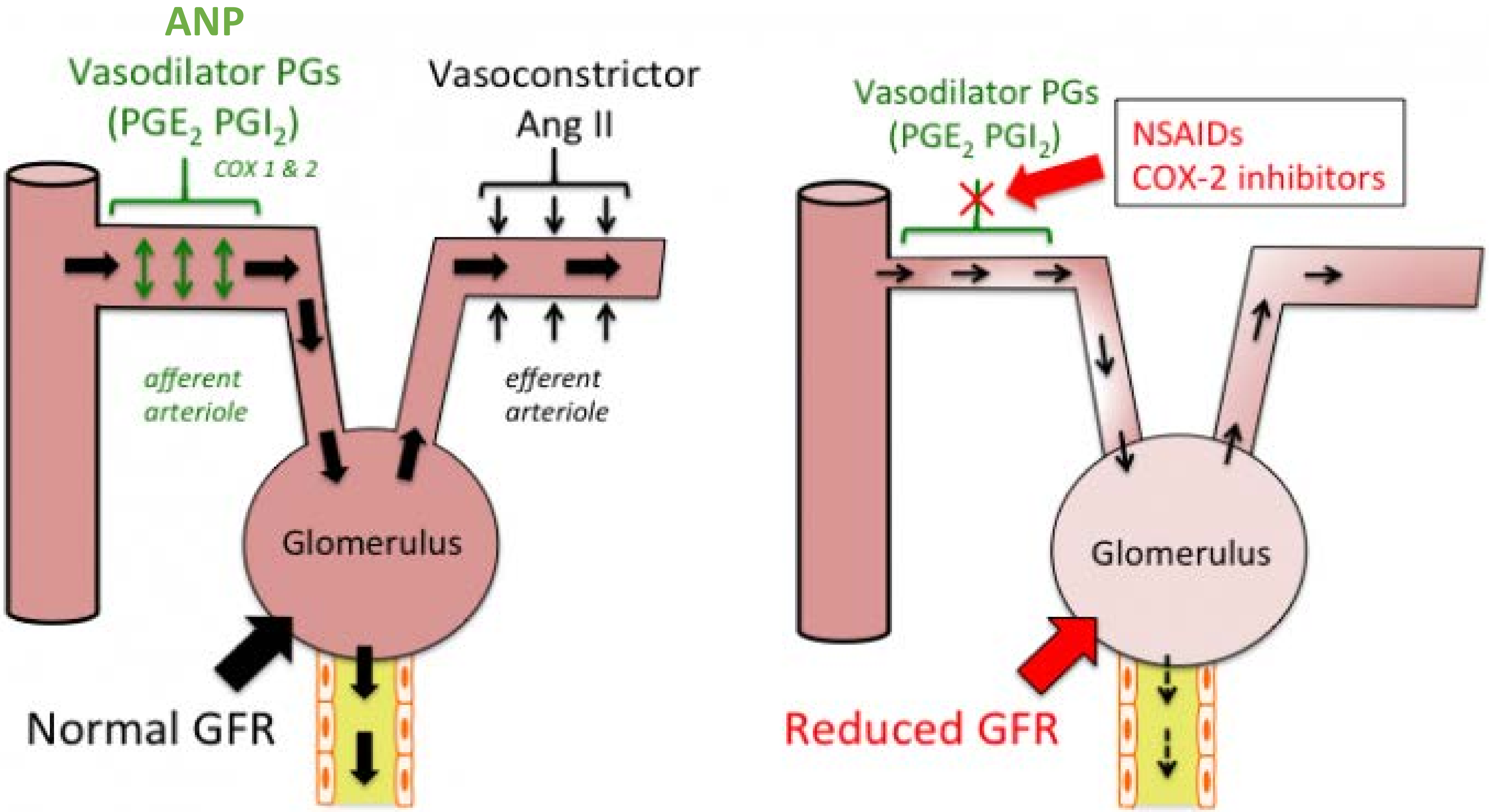
relaxes mesangial cells, increasing capillary surface area and GFR.

ANP is secreted in response to stretch of the cardiac atria.

HORMONAL

PROSTAGLANDINE

Dilatation of afferent arteriol



ANP
Vasodilator PGs
(PGE$_2$ PGI$_2$)
COX 1 & 2
Vasoconstrictor
Ang II
afferent arteriole
efferent arteriole
Glomerulus
Normal GFR
Vasodilator PGs
(PGE$_2$ PGI$_2$)
NSAIDs
COX-2 inhibitors
Glomerulus
Reduced GFR

Neural Regulation

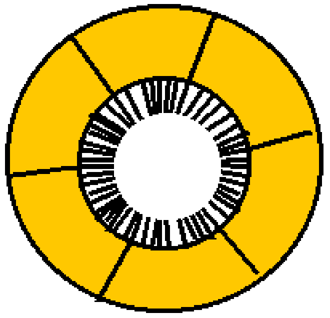
Kidneys are richly supplied by **sympathetic fibers**.

Strong stimulation (exercise or hemorrhage)–afferent arterioles are constricted.

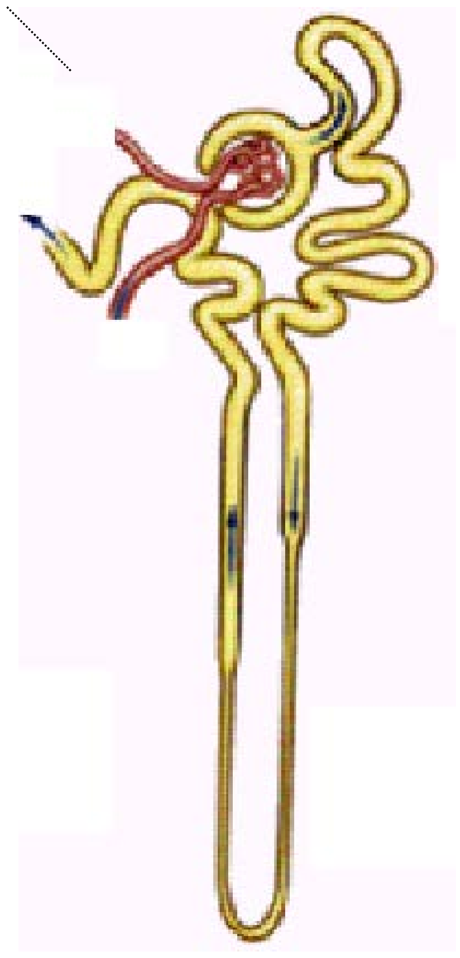
Urine output is reduced, and more blood is available for other organs.

Reabsorption

- The **proximal** convoluted tubule (PCT) is formed by one layer of epithelial cells with long apical microvilli.

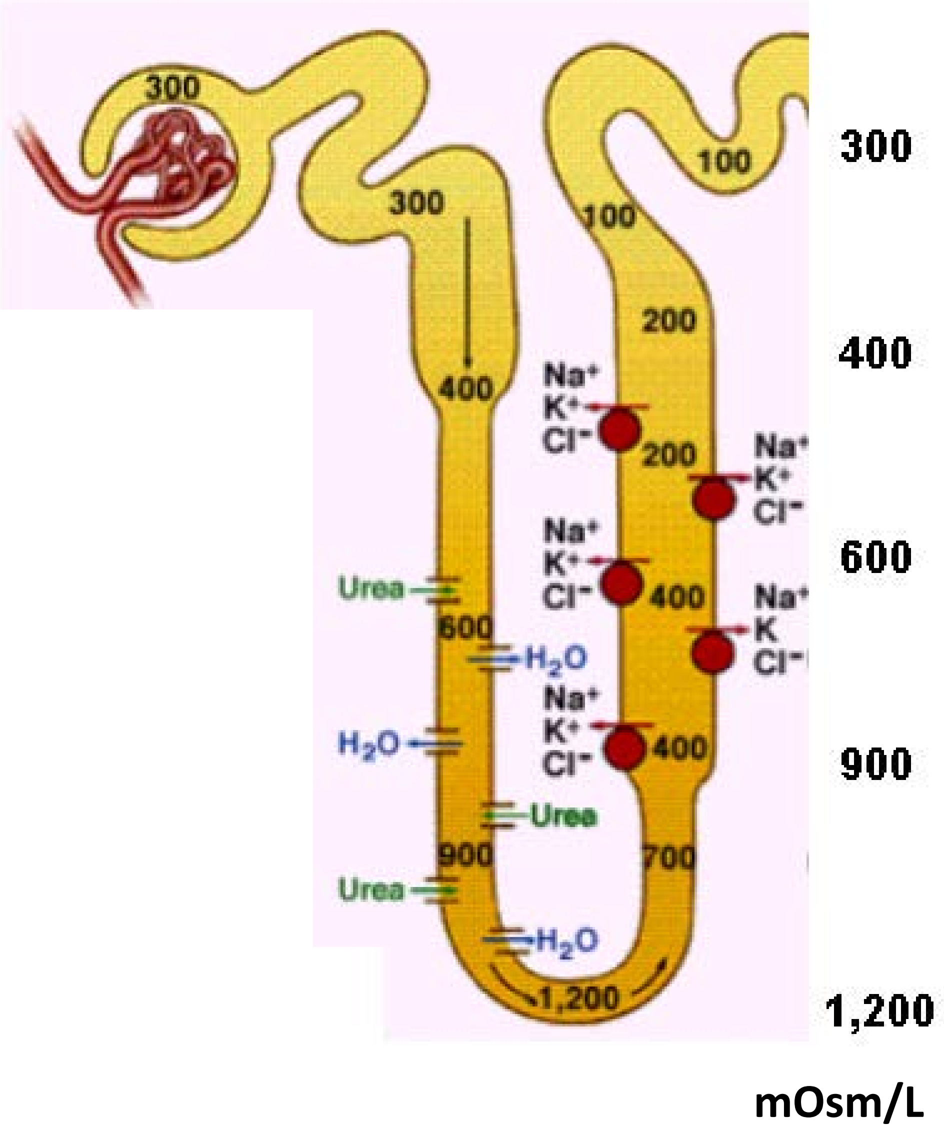


- **The proximal tubule is responsible for reabsorbing ~60% of filtered NaCl and water, as well as ~90% of filtered bicarbonate and most critical nutrients such as glucose and amino acids. The proximal tubule uses both cellular and paracellular transport mechanisms . The apical membrane of proximal tubular cells has an expanded surface area available for reabsorptive work created by a dense array of microvilli called the brush border, and leaky tight junctions enable high-capacity fluid reabsorption.**

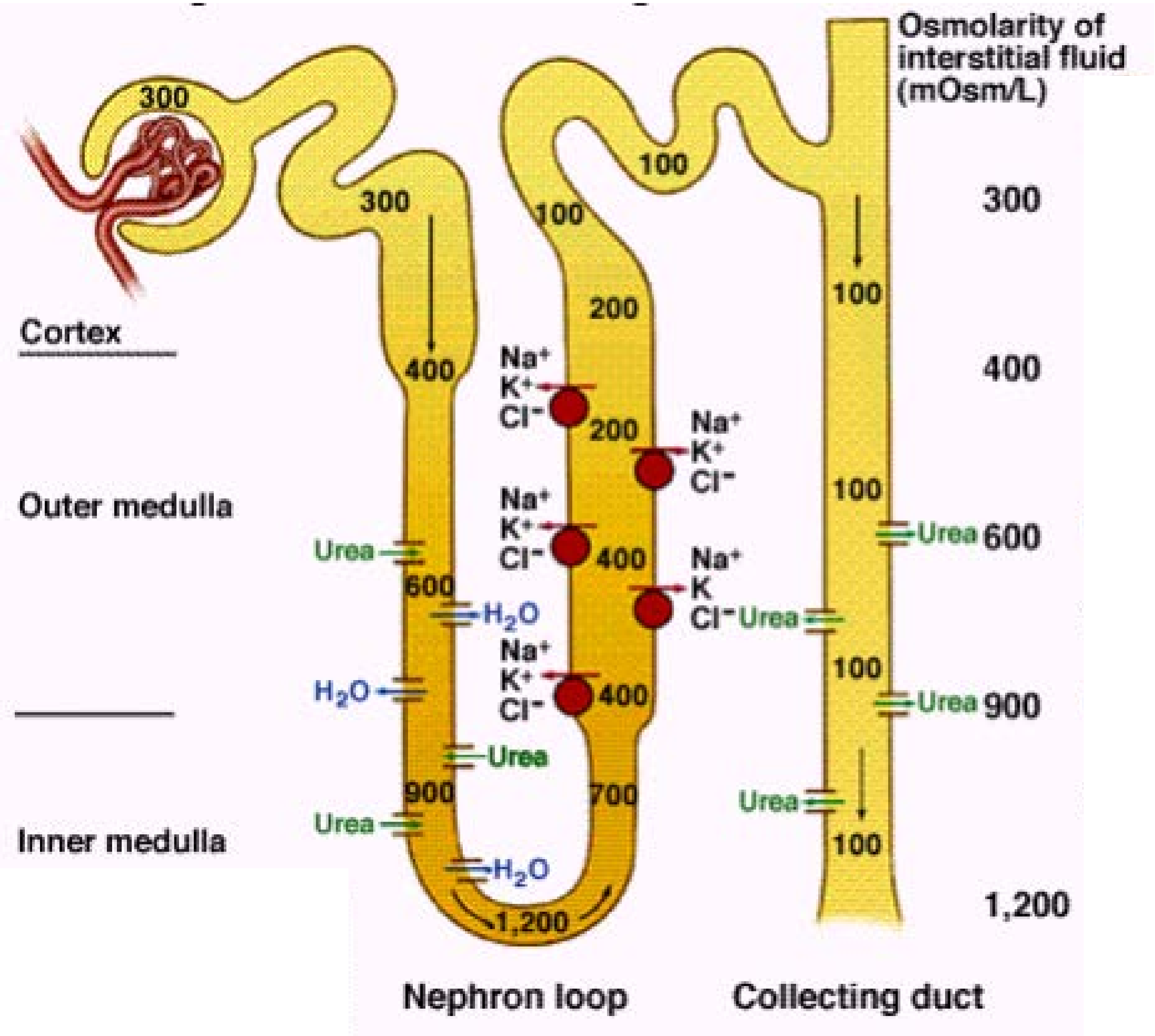


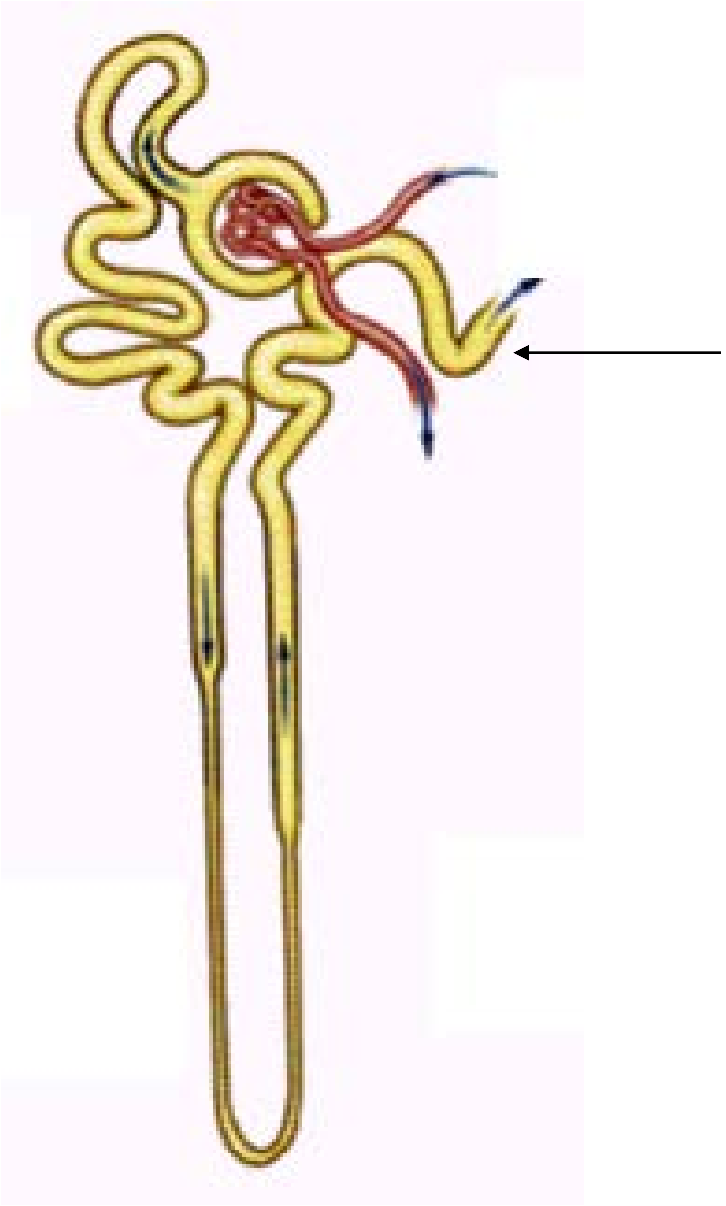
- Approximately **15–25% of filtered NaCl** is reabsorbed in the loop of Henle, mainly by the thick ascending limb. The loop of Henle has an import role in urinary concentration by contributing to the generation o hypertonic medullary interstitium in a process called countercurrent multiplication. The loop of Henle is the site of action for the mos potent class of diuretic agents (loop diuretics) and also contribut to reabsorption of calcium and magnesium ions.

- The **thick ascending limb** reabsorbs solutes but is impermeable to water. Thus, the tubular fluid becomes very diluted while extracellular fluid becomes very concentrated with solutes.

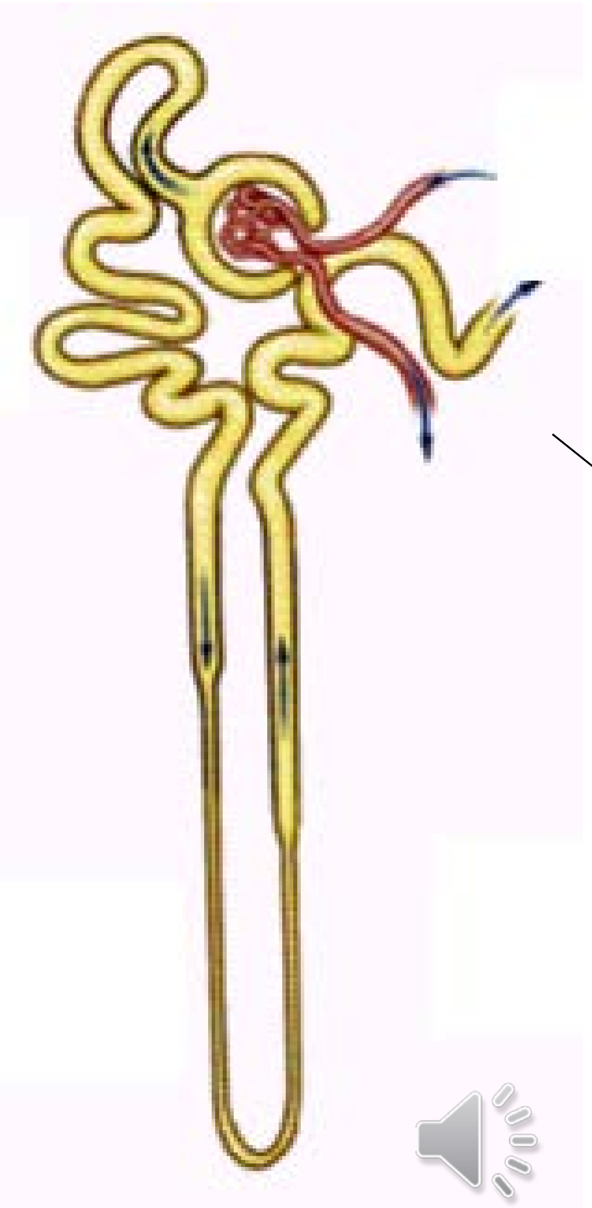


The high osmolarity enables the collecting duct to concentrate the urine later.



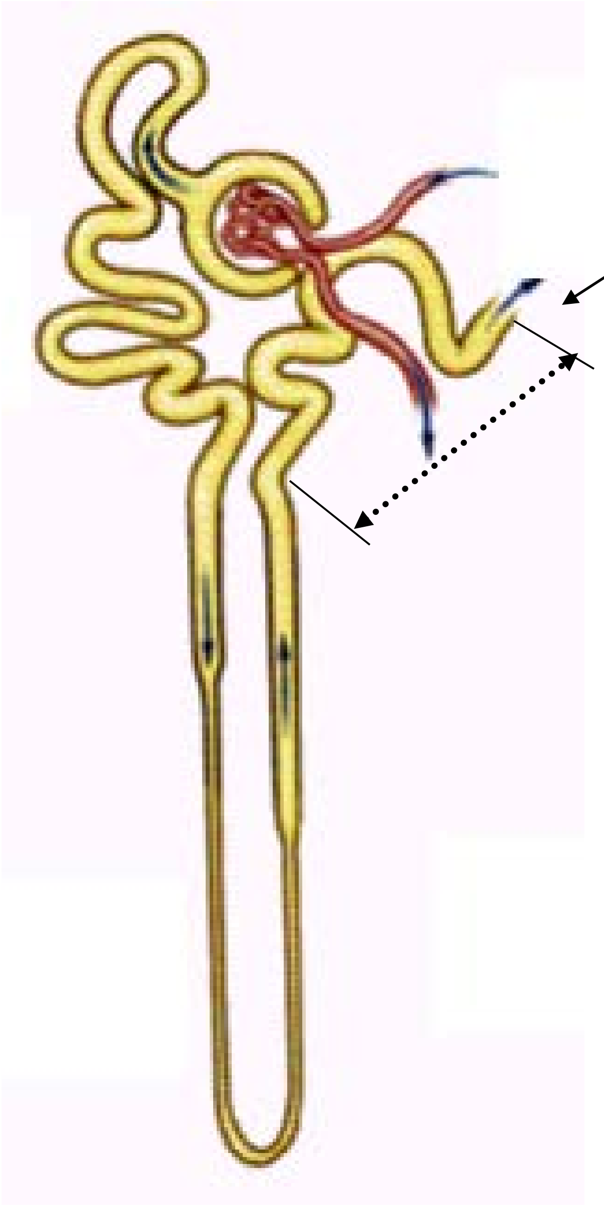


Reabsorption in Distal Convoluted Tubules



The distal convoluted tubule reabsorbs ~5% of the filtered NaCl. This
segment is composed of a tight epithelium with little water permeability.
The major NaCl-transporting pathway uses an apical membrane, electroneutral thiazide-sensitive Na+/Cl– cotransporter in tandem with basolateral Na+/K+-ATPase and Cl– channels .
Apical
Ca2+-selective channels (TRPV5) and basolateral Na+/Ca2+ exchange
mediate calcium reabsorption in the distal convoluted tubule. Ca2+ reabsorption is inversely related to Na+ reabsorption and is stimulated by parathyroid hormone

A molecular complex of TRPM6 and TRPM7 proteins is critical for
Mg2+ reabsorption in the distal convoluted tubule.



Collecting duct Aldosterone

The collecting duct modulates the final composition of urine. The two major divisions, the cortical collecting duct and inner medullary collecting duct, contribute to reabsorbing ~**4-5% of filtered Na+** and are important for hormonal regulation of salt and water balance

COLLECTING DUCT

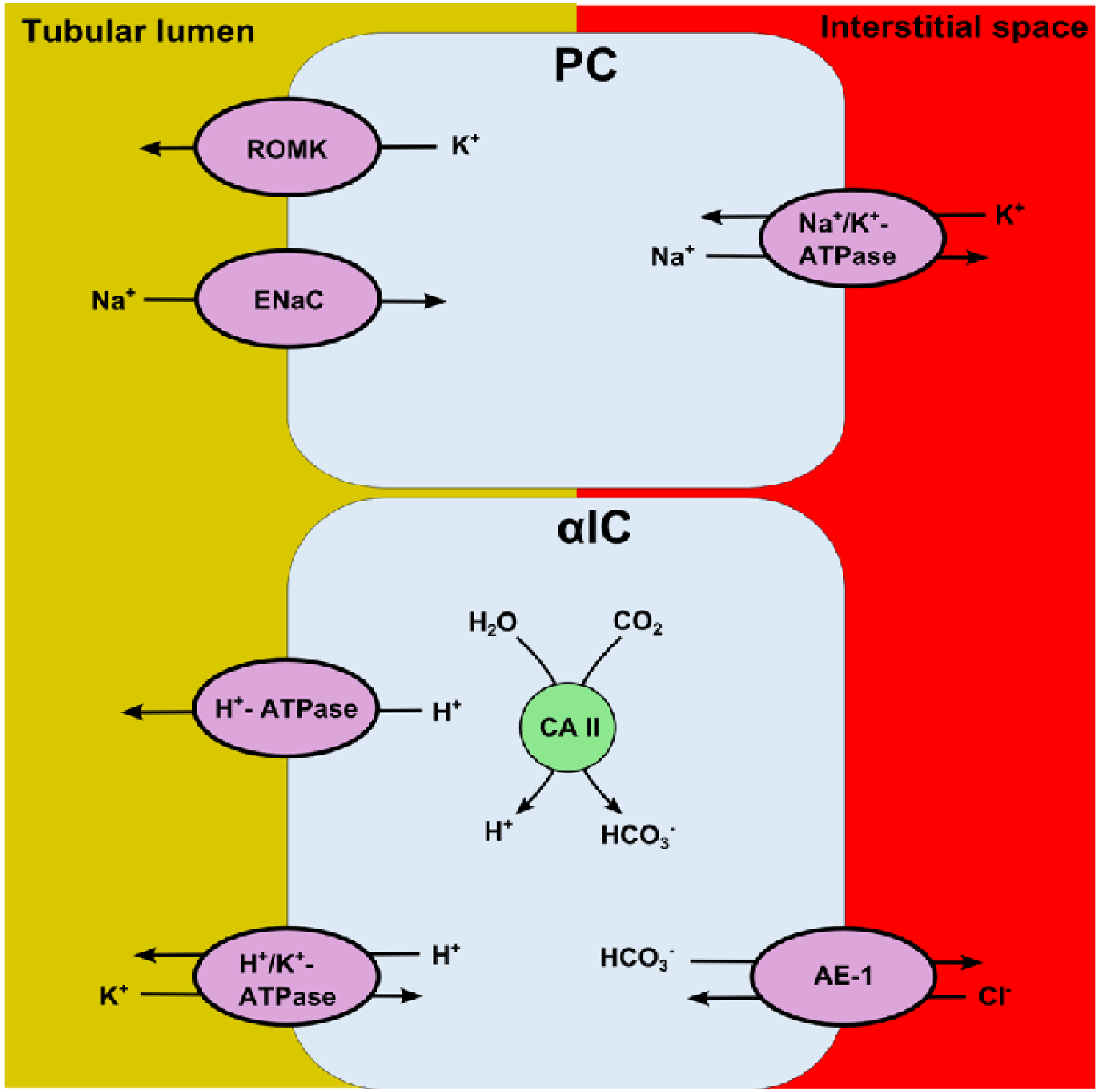
1-K SECRETION

2-PH REGULATION

3-URINE CONCENTRATION

Principal cells are the main water, Na^+-reabsorbing, and K^+-secreting cells, and the site of action of aldosterone, K^+-sparing diuretics, and mineralocorticoid receptor antagonists such as spironolactone.

The other cells are **type A and B intercalated cells**. Type A intercalated cells mediate acid secretion and bicarbonate reabsorption also under the influence of aldosterone. Type B intercalated cells mediate
bicarbonate secretion and acid reabsorption.


Tubular lumen
Interstitial space
PC
ROMK
K+
Na+/K+-ATPase
K+
Na+
Na+
ENaC
αIC
H2O
CO2
H+- ATPase
H+
CA II
H+
HCO3-
H+/K+-ATPase
H+
K+
HCO3-
AE-1
Cl-

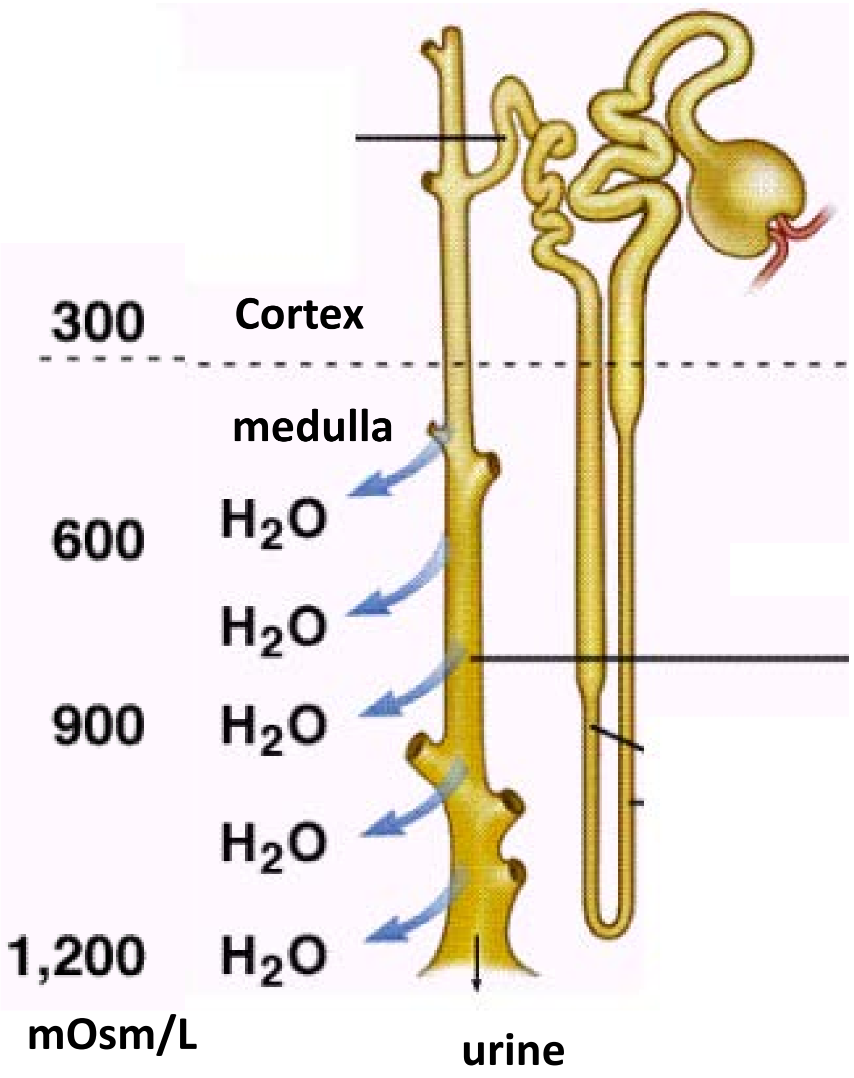
Inner medullary collecting duct cells also

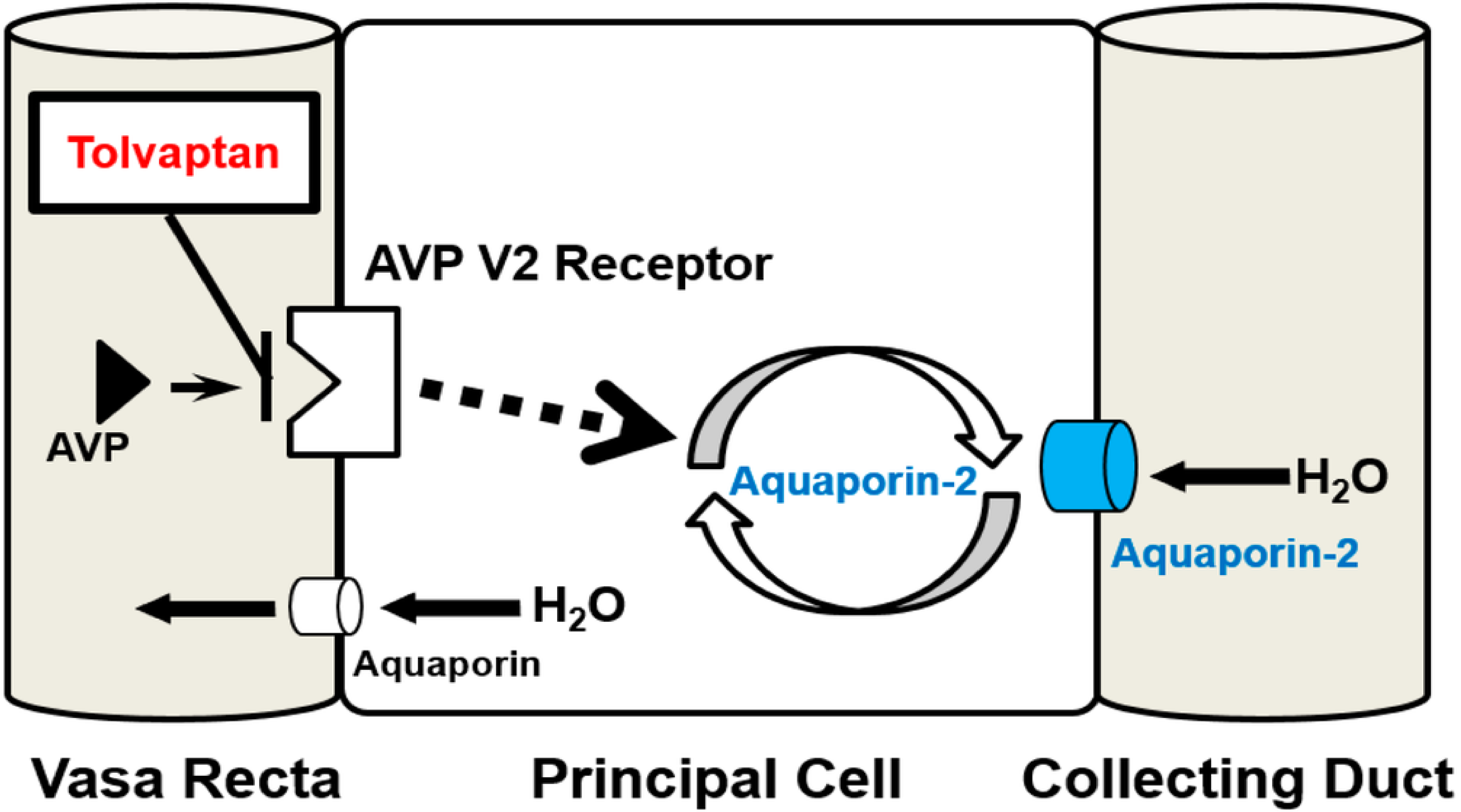
have vasopressin-regulated water channels (aquaporin-2 on the apical membrane, aquaporin-3 and -4 on the basolateral membrane). The antidiuretic hormone vasopressin binds to the V2 receptor on the basolateral membrane and triggers an intracellular signaling cascade through G-protein-mediated activation of adenylyl cyclase, resulting in an increase in the cellular levels of cyclic AMP. This signaling cascade stimulates the insertion of water channels into the apical membrane of the inner medullary collecting duct cells to promote increased water permeability. This increase in permeability enables water reabsorption and production of concentrated urine. In the absence of vasopressin, inner medullary collecting duct cells are water impermeable, and urine remains dilute.

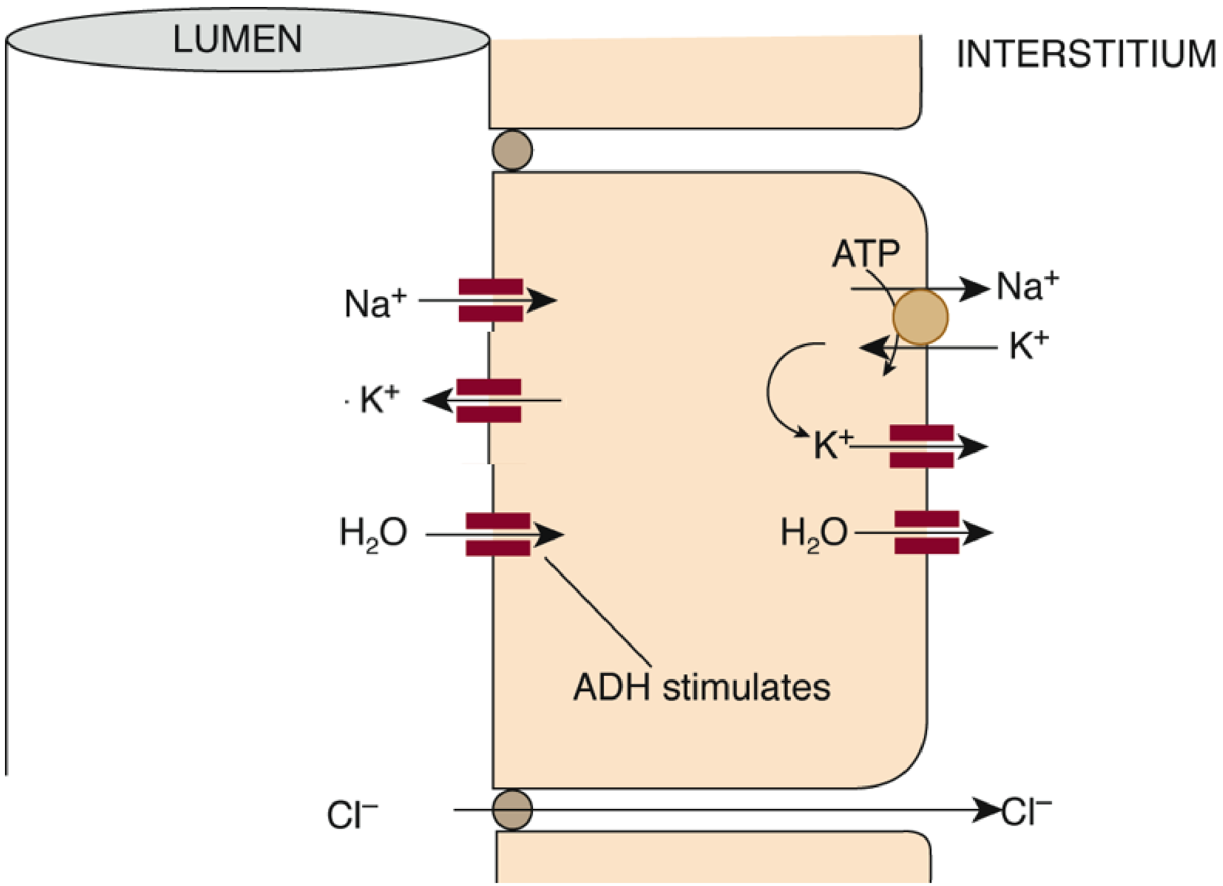
Control of Urine Concentration depends on the body's state of hydration.

In a state of ***full hydration***, a. antidiuretic hormone (ADH) is not secreted and the CD permeability to water is low, leaving the water to be excreted.

b. In a state of ***dehydration***, ADH is secreted; the CD permeability to water increases. With the increased reabsorption of water by osmosis, the urine becomes more concentrated.




Tolvaptan
AVP V2 Receptor
AVP
Aquaporin-2
H_2O
Aquaporin-2
H_2O
Aquaporin
Vasa Recta
Principal Cell
Collecting Duct


LUMEN
INTERSTITIUM
ATP
Na+
Na+
K+
K+
K+
H2O
H2O
ADH stimulates
Cl−
Cl−

1) Glomerular Filtration

2) Tubular Reabsorption

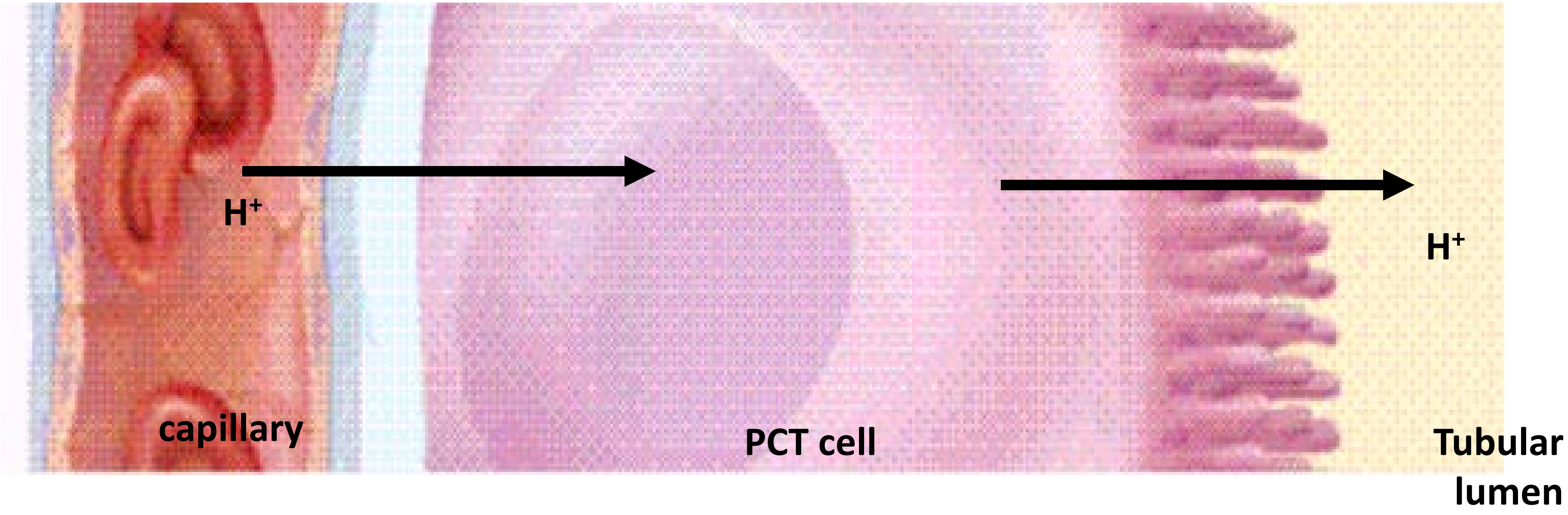
3) Tubular Secretion

4) Concentrating Urine by Collecting Duct

Tubular Secretion

Renal tubule extracts chemicals from the blood and -secretes them into the tubular fluid.

serves the purposes of waste removal and **acid--base balance.**



1) Glomerular Filtration

2) Tubular Reabsorption

3) Tubular Secretion

4) Concentrating Urine by Collecting Duct

Urine Volume

An average adult produces ***1-2 L*** of urine per day.

Excessive urine output is called ***polyuria***.

Scanty urine output is ***oliguria***. An output of less than ***400 mL/day*** is insufficient to excrete toxic wastes.

TRANSPORTERS

1-Transcellular different

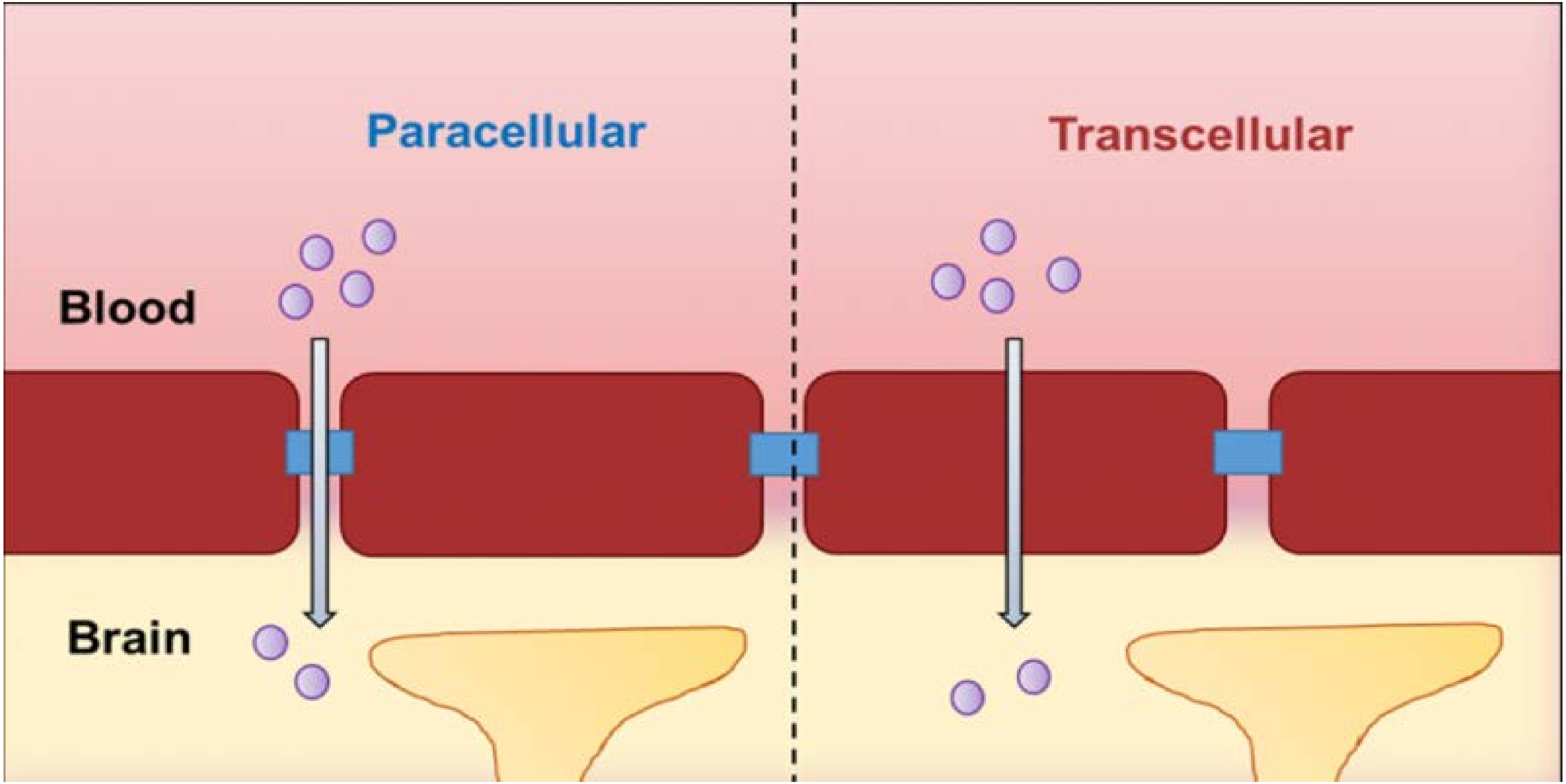
mechanisms mediate specific types of transport activities, including

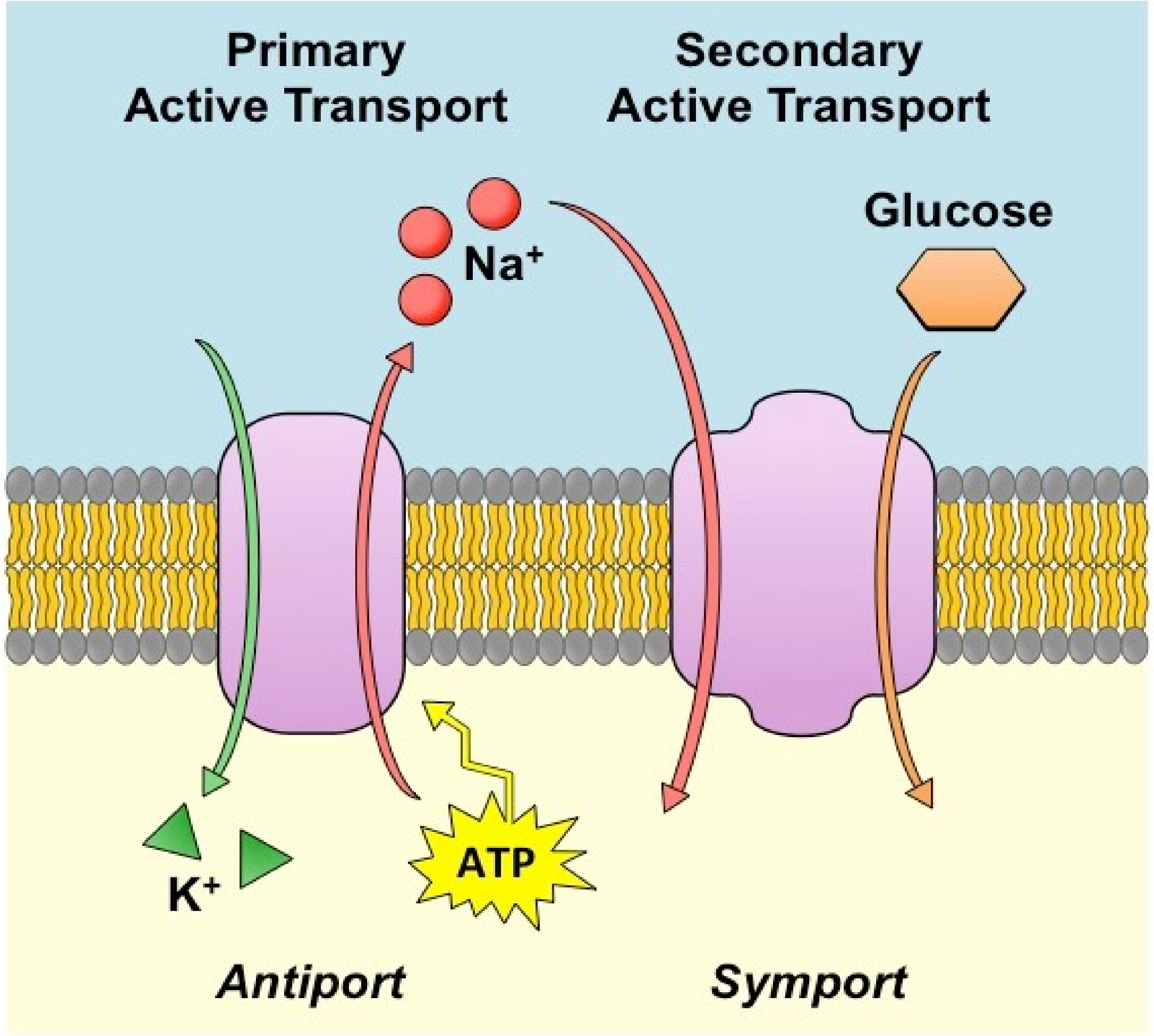
active transport (pumps)

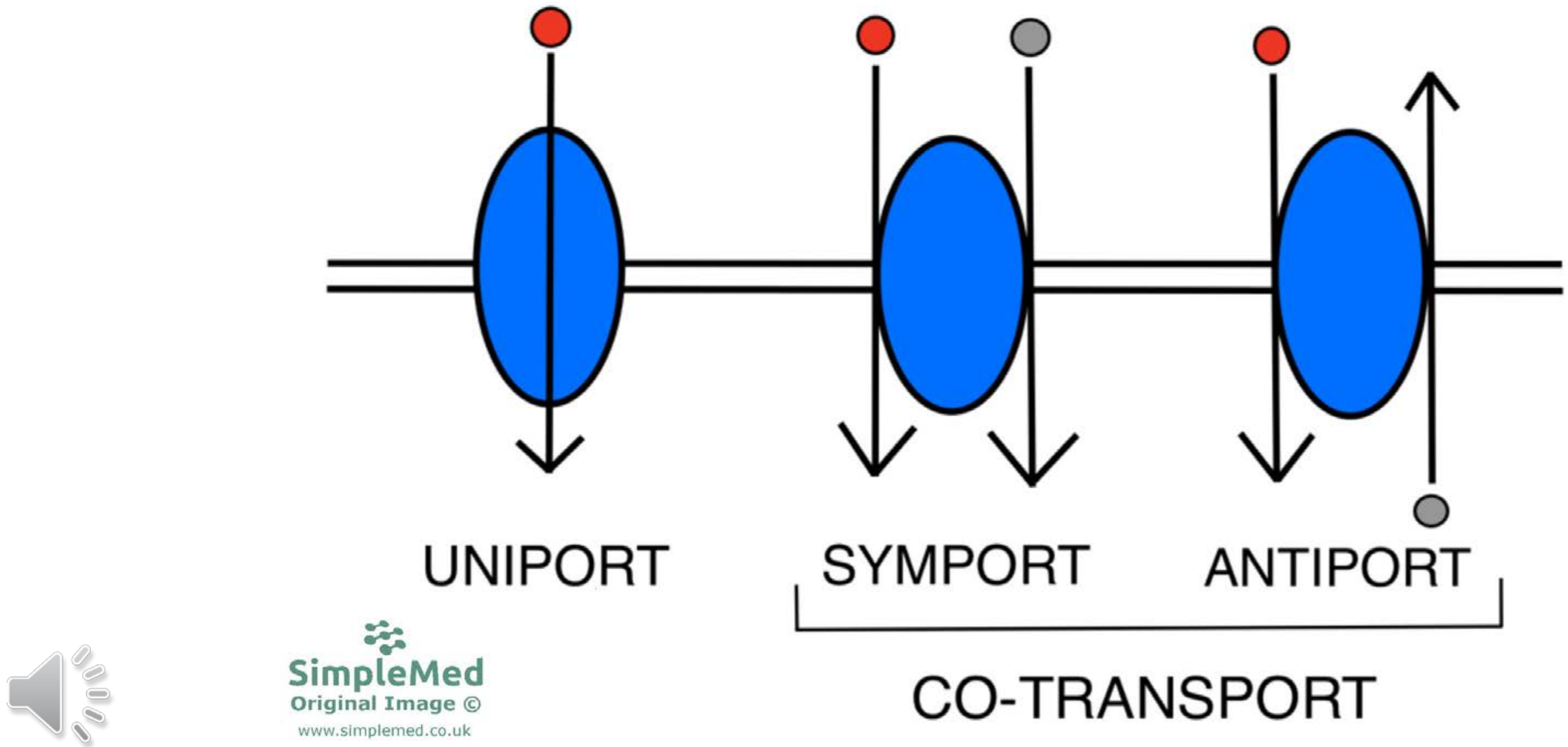
passive transport (channels) or uniporters or carriers or simple transporters , facilitated diffusion (transporters).

Many other transporters operate by translocating two or more ions/solutes in concert either in the same direction (symporters or cotransporters) or in opposite directions (antiporters or exchangers) across the cell membrane

2-paracellular(tight junctions)


Paracellular
Transcellular
Blood
Brain


Primary
Active Transport
Secondary
Active Transport
Na+
Glucose
ATP
K+
Antiport
Symport


UNIPORT
SYMPORT
ANTIPORT
CO-TRANSPORT
SimpleMed
Original Image ©
www.simplemed.co.uk

Renal Function Tests

Assessment of Renal Function

Creatinine(Cr)

A naturally occurring amino acid, predominately found in skeletal muscle

Freely filtered in the glomerulus, excreted by the kidney and readily measured in the plasma

As plasma creatinine increases, the GFR exponentially decreases.

Limitations to estimate GFR:

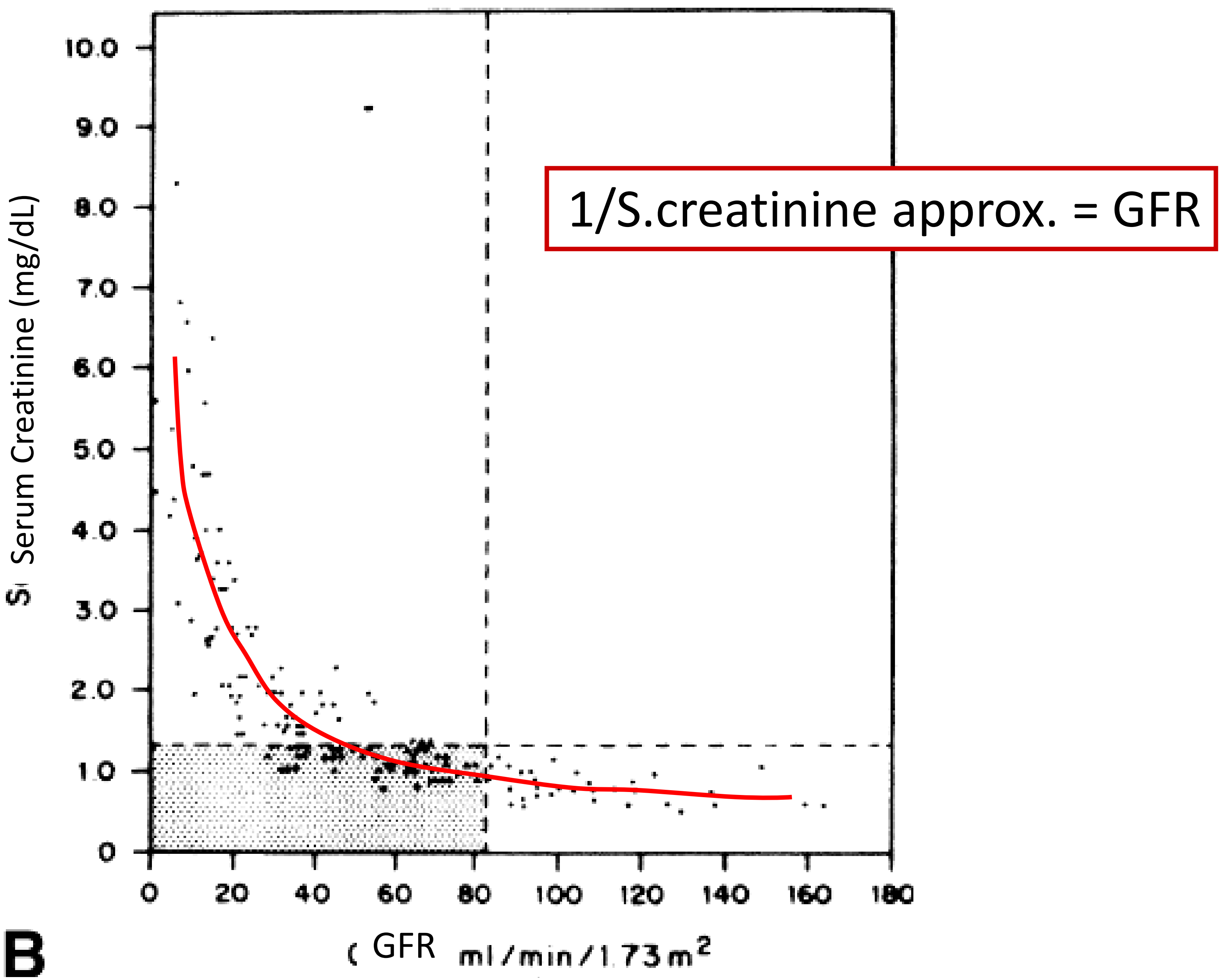
Patients with decrease in muscle mass, liver disease, malnutrition, chronic use of glucocorticoids ,advanced age, may have low/normal creatinine despite underlying kidney disease

15-20% of creatinine in the bloodstream is not filtered in glomerulus, but secreted by renal tubules (giving **overestimation of GFR**)

Medications may artificially elevate creatinine:

Trimethroprim (Bactrim)

Cimetidine


1/S.creatinine approx. = GFR
Serum Creatinine (mg/dL)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0
20
40
60
80
100
120
140
160
180
GFR ml/min/1.73 m2
B

Cystatin C

a member of the cystatin superfamily of cysteine protease inhibitors, is produced at a relatively constant rate from all nucleated cells.

Serum cystatin C has been proposed to be a more sensitive marker of early GFR decline than is PCr.

however, like serum creatinine, cystatin C is influenced by the patient's age, race, and sex and also is associated with diabetes, smoking, and markers of inflammation.

Best substance for evaluation of GFR HAS :

No secretion

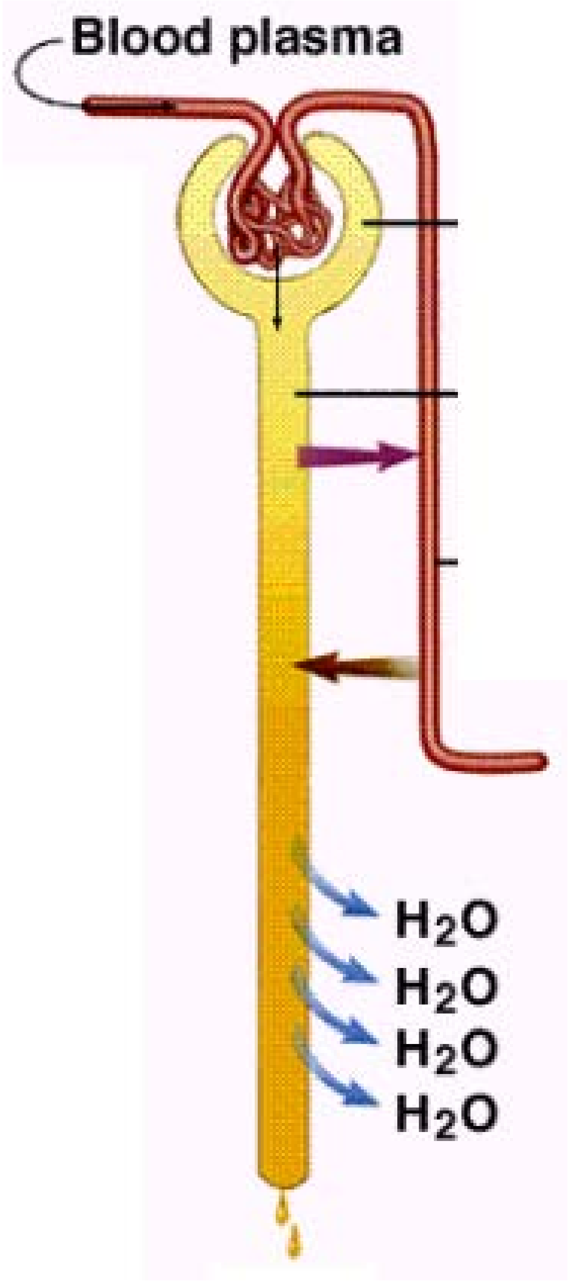
No reabsorption

2.Glomerular Filtration Rate .2

Measuring GFR requires a substance that is not secreted or reabsorbed at all. iothalamate

Inulin, a polymer of fructose, is suitable.

Inulin filtered by the glomeruli remains in the b. renal tubule and appears in the urine; none is reabsorbed, and the tubule does not secrete it. For this solute, GFR is equal to the renal clearance.



CALCULATING OF GFR

1-Average of urea and cr cl

2-COCKROFT GAULT

3-MDRD

4-CKD-EPI

$$\text{Creatinine Clearance} = \frac{\text{Creatinine}_{\text{urine}} \times \text{Volume}_{\text{urine}}}{1{,}440 \times \text{Creatinine}_{\text{serum}}}$$

Cr clearance(cc/min)

$$\frac{\text{urine cr(mg/dl)*urine volume in 24 hrs(cc)}}{\text{Plasma cr(mg/dl)*1440}}$$

مثال

- آقای 24 ساله با حجم ادرار 24 ساعته 2 لیتر و سطح کراتینین سرمی 3 میلیگرم بر دسی لیتر وسطح کراتینین ادراری 900 میلی گرم بر دسی لیتر به شما مراجعه کرده است.
- میزان کلیرانس کراتینین چقدر است؟

UREA CLEARANCE

$$Cu = \frac{Uu \times V}{Pu}$$

where, Cu = urea clearance in ml/minute

Uu = urine urea in mg/ml

V = volume of urine in ml

Pu = urea in mg per ml of plasma

AVERAGE OF UREA & CR CL IS MORE ACCURATE

Cl cr+cl urea/2

GFR Estimating Equations

Cockcroft-Gault formula

$$C_{cr}\ (\text{ml/min}) = \frac{(140-\text{age}) \times \text{weight}}{72\ S_{cr}} \ {}^{*}0.85 \text{ if female}$$

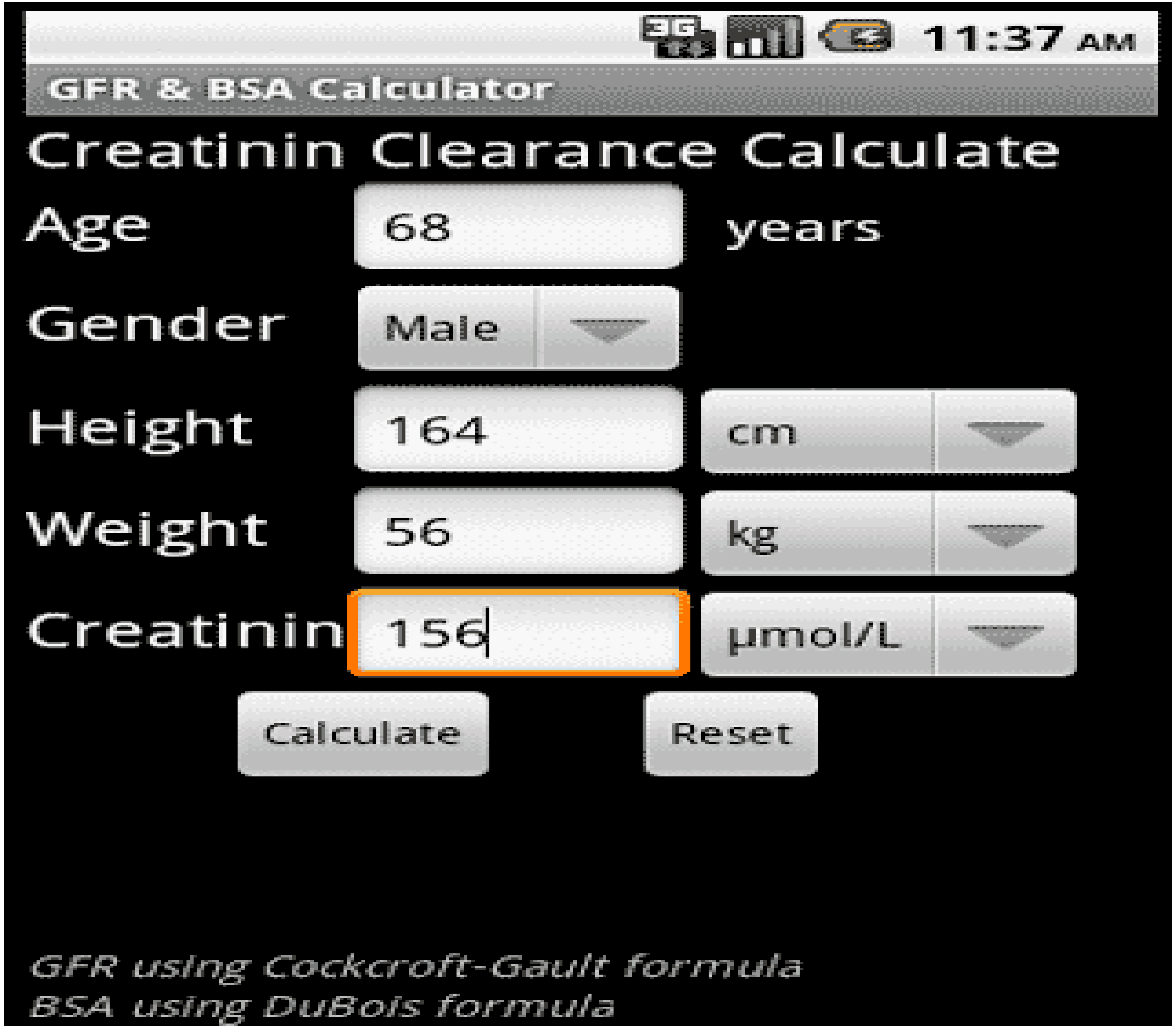
MDRD Study equation

$$\text{GFR}\ (\text{ml/min/1.73 m}^2) = 186 \times (S_{cr})^{-1.154} \times (\text{age})^{-.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$$

All labs will be reporting GFR within a few years

On Line Calculator: www.kidney.org

$$eGFR\ (CKD\text{-}EPI) = 141 \times \min(\text{creatinine}/k,\ 1)^{\alpha} \times \max\ (\text{creatinine}/k,\ 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018\ [\text{if female}] \quad (2)$$


11:37 AM
GFR & BSA Calculator
Creatinin Clearance Calculate
Age
68
years
Gender
Male
Height
164
cm
Weight
56
kg
Creatinin
156
µmol/L
Calculate
Reset
GFR using Cockcroft-Gault formula
BSA using DuBois formula

Cockroft-Gault formula

- **Creatinine clearance (men) =**

$$\frac{(140 - \text{age}) \times \text{body weight in kgs}}{\text{Plasma creatinine in mg\%} \times 72}$$

This value should be multiplied 0.85 for women, since a lower fraction of the body weight is composed of muscle

مثال

خانم 40 ساله با وزن 60 کیلوگرم و آزمایشات زیر میزان GFR را محاسبه کنید:

Cr:3 mg/dl

Urea:70

$$(140-40)*60/72*3*0.85=23.6$$

Common Causes of Kidney Disease

The two most common causes of kidney disease are

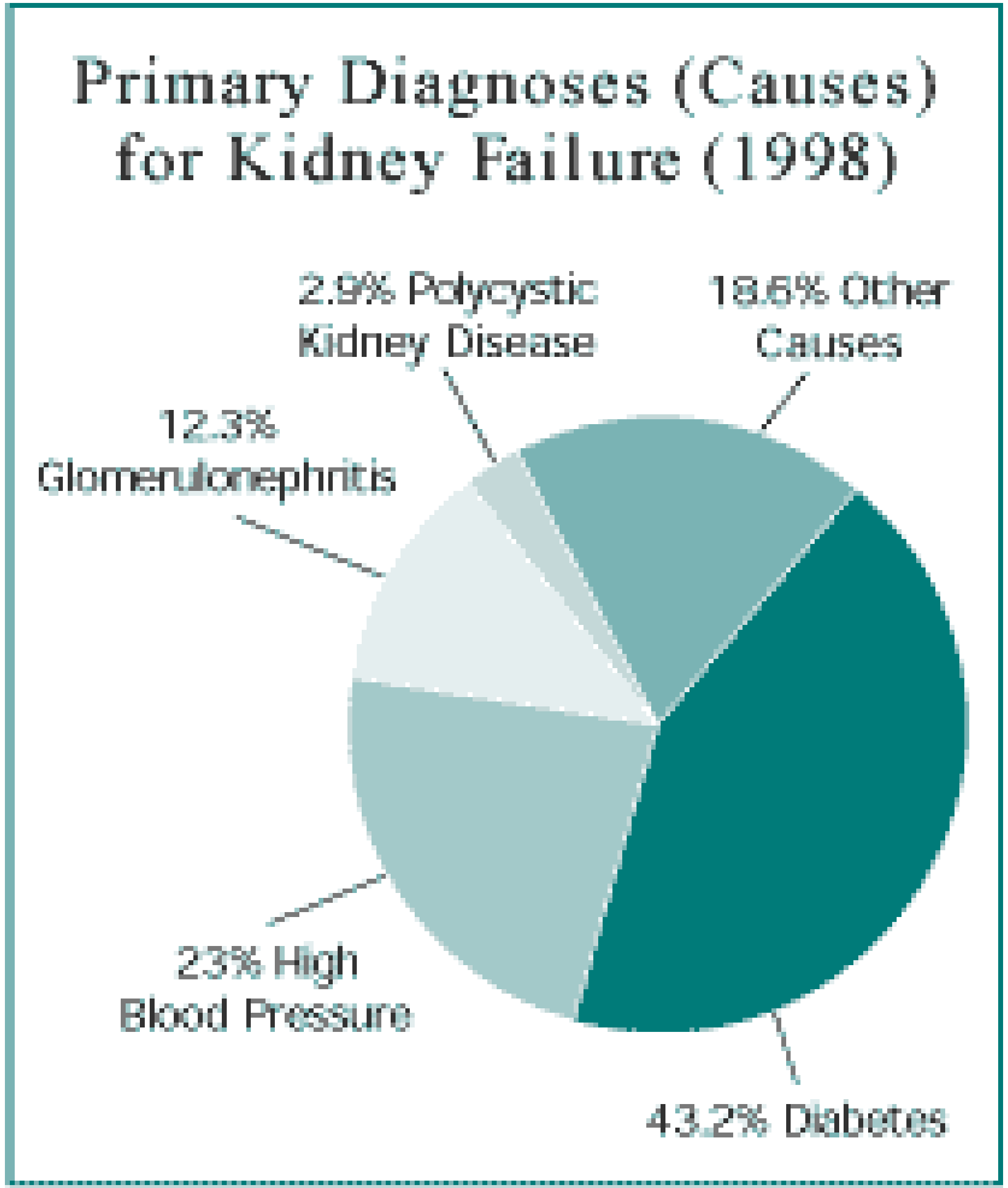
diabetes

high blood pressure

glomerulunephritis

Hereditary also plays a role

infections


Primary Diagnoses (Causes) for Kidney Failure (1998)
2.9% Polycystic Kidney Disease
18.6% Other Causes
12.3% Glomerulonephritis
23% High Blood Pressure
43.2% Diabetes

Types of kidney disease

1-AKI

2-CKD

3-UTI

4-ELECTROLYTE ABNORMALITY

5-NEPHROLITHIASIS

6-ACD-BASE DISTURBANCE

7-CYSTIC & INHERITED

“Renal Failure”

Chronic

CKD: Chronic Kidney Disease

Acute

AKI: Acute Kidney Injury

Approach to acute Kidney Disease

Diagnostic Categories

Prerenal disease

Postrenal disease

Intrinsic renal disease

Glomerular

Tubular

Interstitial

Vascular

reference

- 332 e
- 61