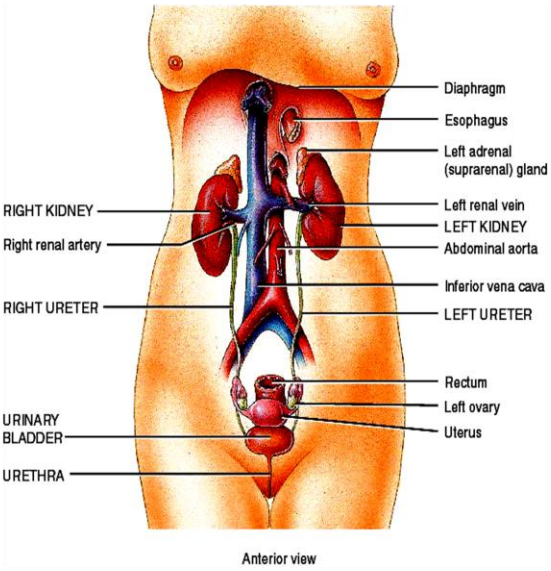
Chapter 25
The Urinary System

- Kidneys, ureters, urinary bladder & urethra
- Urine flows from each kidney, down its ureter to the bladder and to the outside via the urethra
- Filter the blood and return most of water and solutes to the bloodstream

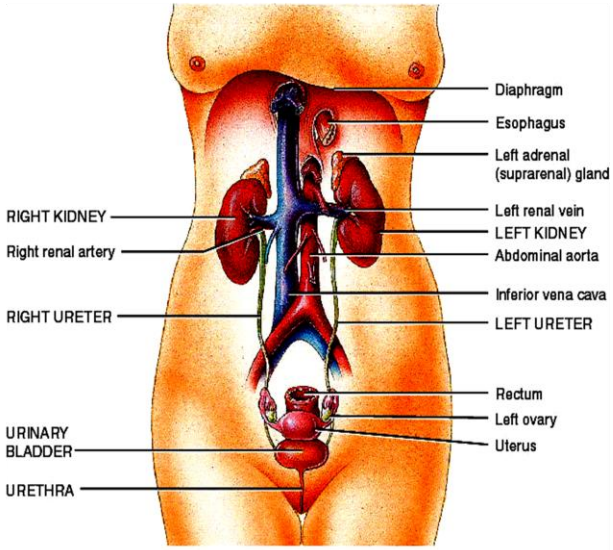


Overview of Kidney Functions

- Regulation of blood ionic composition
  - Na+, K+, Ca+2, Cl- and phosphate ions
- Regulation of blood pH, osmolarity & glucose
- Regulation of blood volume
  - conserving or eliminating water
- Regulation of blood pressure
  - secreting the enzyme renin
  - adjusting renal resistance
- Release of erythropoietin & calcitriol
- Excretion of wastes & foreign substances

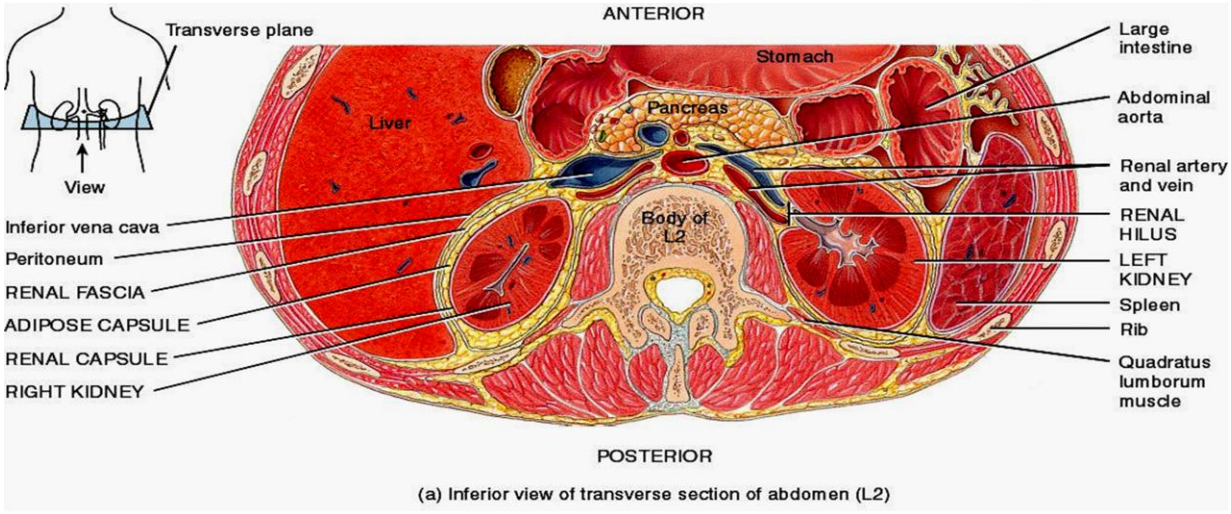
External Anatomy of Kidney

- Paired kidney-bean-shaped organ
- 4-5 in long, 2-3 in wide, 1 in thick
- Found just above the waist between the peritoneum & posterior wall of abdomen
  - retroperitoneal along with adrenal glands & ureters
- Protected by 11th & 12th ribs with right kidney lower



Anterior view

External Anatomy of Kidney



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

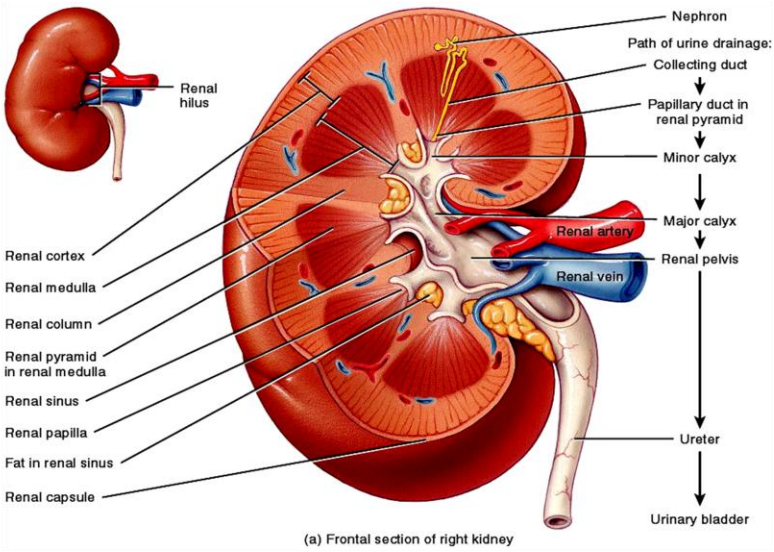
- Blood vessels & ureter enter hilus of kidney
- Renal capsule = transparent membrane maintains organ shape
- Adipose capsule that helps protect from trauma
- Renal fascia = dense, irregular connective tissue that holds against back body wall

Internal Anatomy of the Kidneys

- **Parenchyma of kidney**
  - **renal cortex = superficial layer of kidney**
  - **renal medulla**
    - **inner portion consisting of 8-18 cone-shaped renal pyramids separated by renal columns**
    - **renal papilla point toward center of kidney**
- **Drainage system fills renal sinus cavity**
  - **cuplike structure (minor calyces) collect urine from the papillary ducts of the papilla**
  - **minor & major calyces empty into the renal pelvis which empties into the ureter**

Internal Anatomy of Kidney

- What is the difference between renal hilus & renal sinus?
- Outline a major calyx & the border between cortex & medulla.

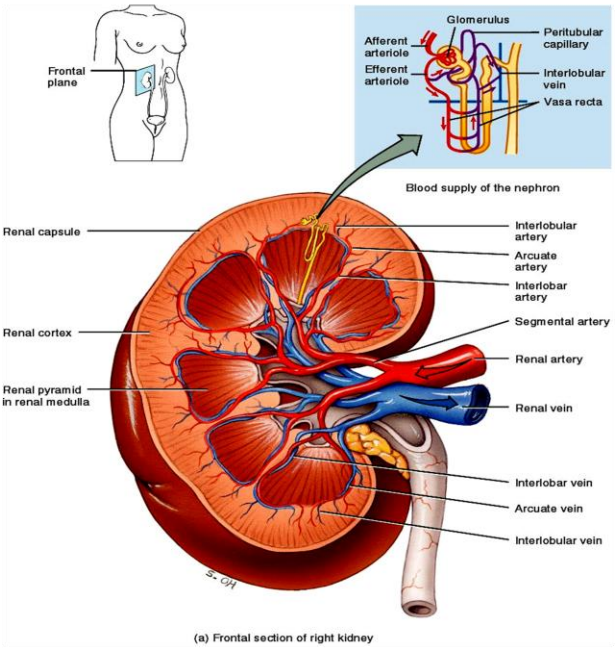


(a) Frontal section of right kidney

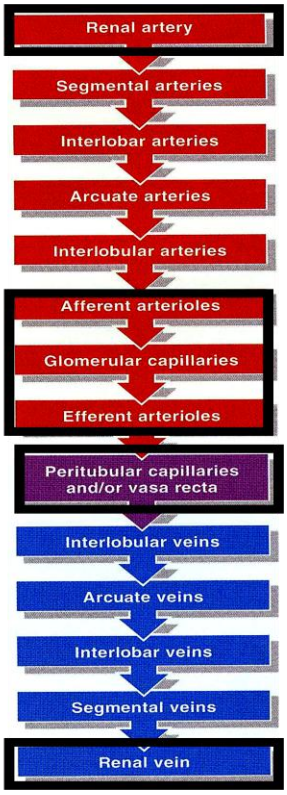
Blood & Nerve Supply of Kidney

- Abundantly supplied with blood vessels
  - receive 25% of resting cardiac output via renal arteries
- Functions of different capillary beds
  - glomerular capillaries where filtration of blood occurs
    - vasoconstriction & vasodilation of afferent & efferent arterioles produce large changes in renal filtration
  - peritubular capillaries that carry away reabsorbed substances from filtrate
  - vasa recta supplies nutrients to medulla without disrupting its osmolarity form
- Sympathetic vasomotor nerves regulate blood flow & renal resistance by altering arterioles

Blood supply of the kidneys

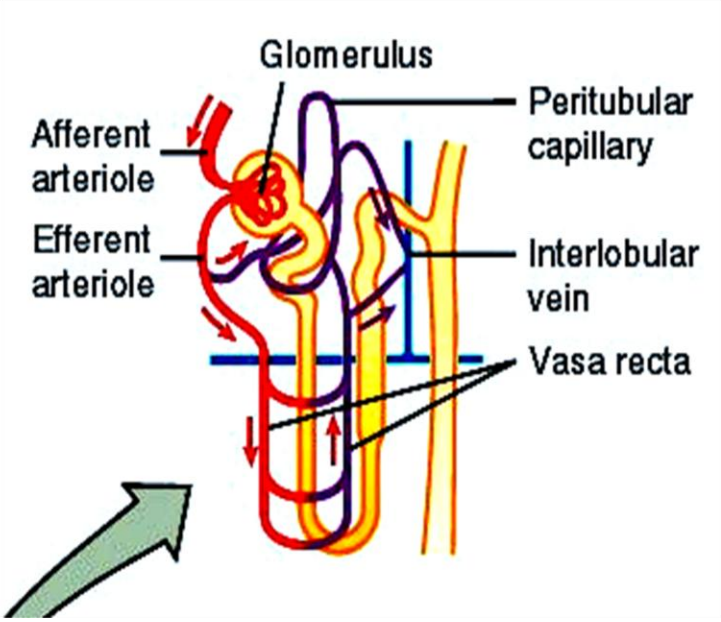


- Each nephron has the following blood supply:
  - Afferent arteriole
  - Glomerular capillaries
  - Efferent arteriole



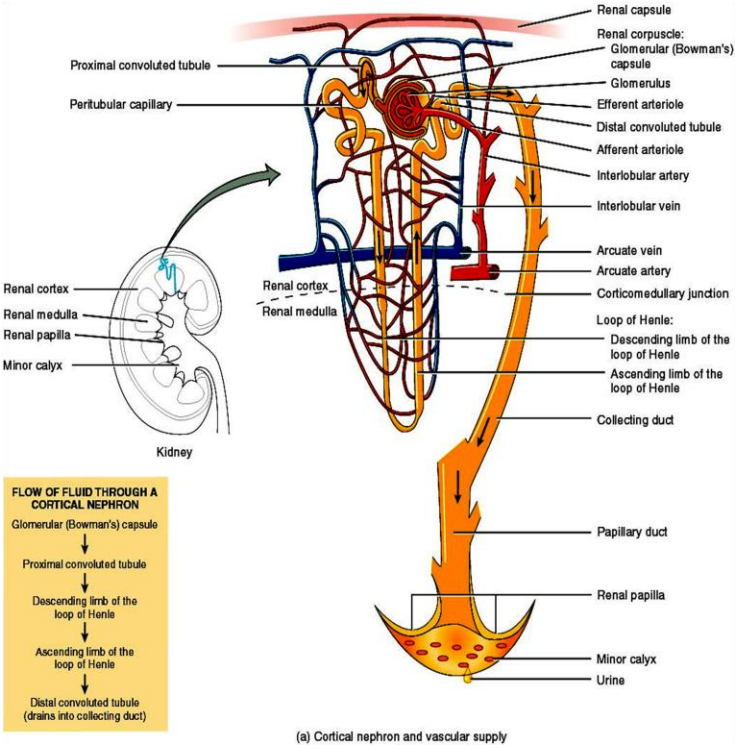
Blood Vessels around the Nephron

- Glomerular capillaries are formed between the afferent & efferent arterioles
- Efferent arterioles give rise to the peritubular capillaries in renal cortex and vasa recta in renal medulla

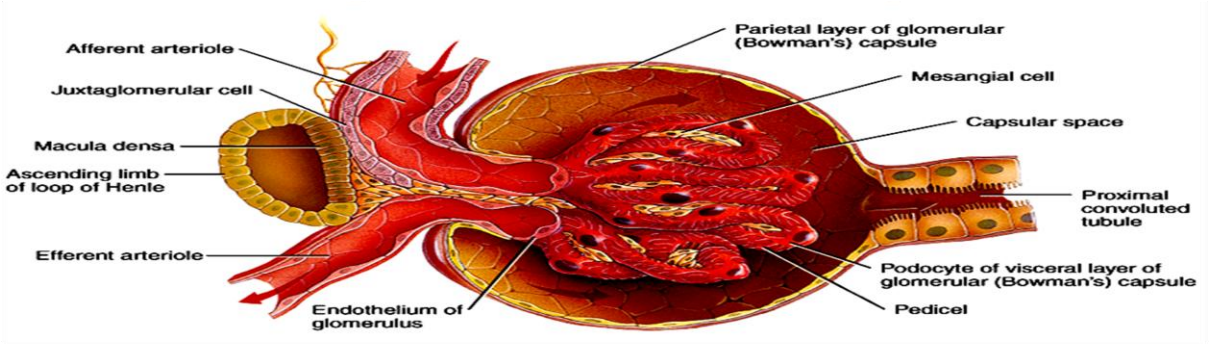


The Nephron

- Kidney has over 1 million nephrons composed of a corpuscle and tubule
- Renal corpuscle
  - site of plasma filtration
- Renal tubule
  - into which filtered fluid (filtrate) passes



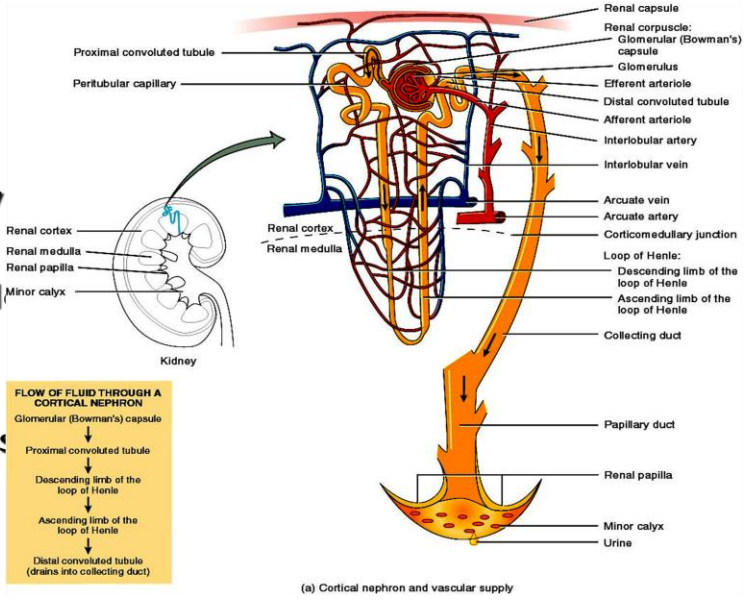
The Nephron-Renal corpuscle



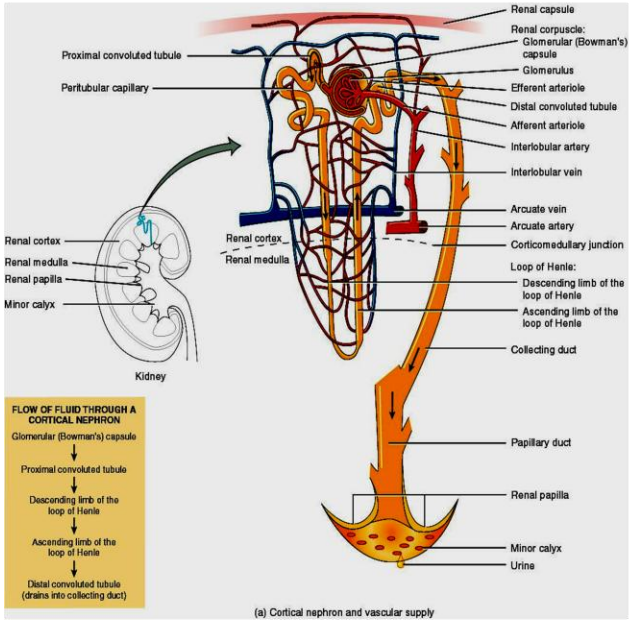
- Kidney has over 1 million nephrons composed of a corpuscle and tubule
- Renal corpuscle = site of plasma filtration
  - glomerulus is capillaries where filtration occurs
  - glomerular (Bowman's) capsule is double-walled epithelial cup that collects filtrate

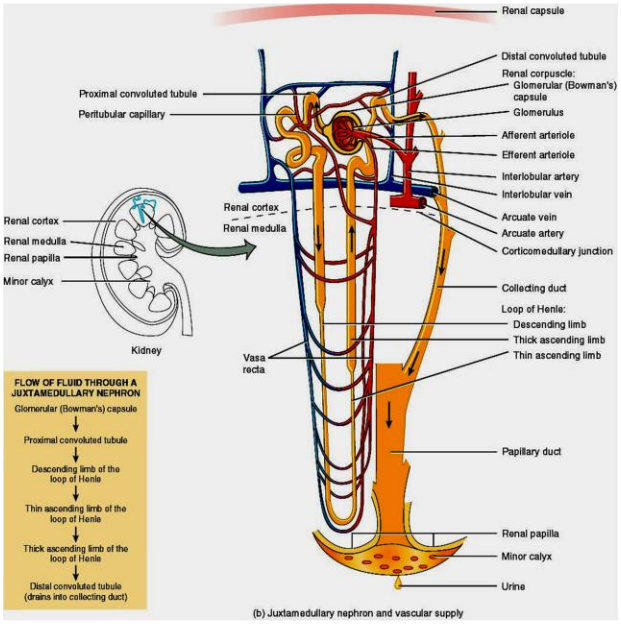
The Nephron-Renal tubule

- Renal tubule
- proximal convoluted tubule
- loop of Henle dips dow into medulla
- distal convoluted tubul
- Collecting ducts and papillary ducts drain urine to the renal pelvis and ureter



Types of nephron





Cortical nephron **Juxtamedullary nephron**

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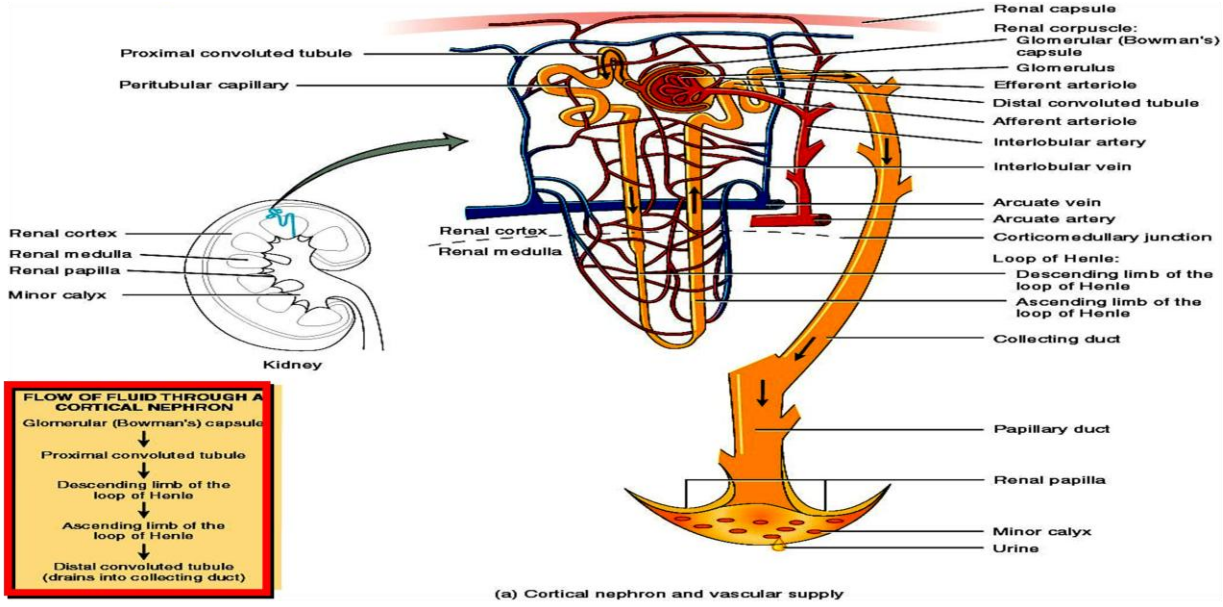
Cortical Nephron



- 80-85% of nephrons are cortical nephrons
- Renal corpuscles are in outer cortex and short loops of Henle lie mainly in cortex

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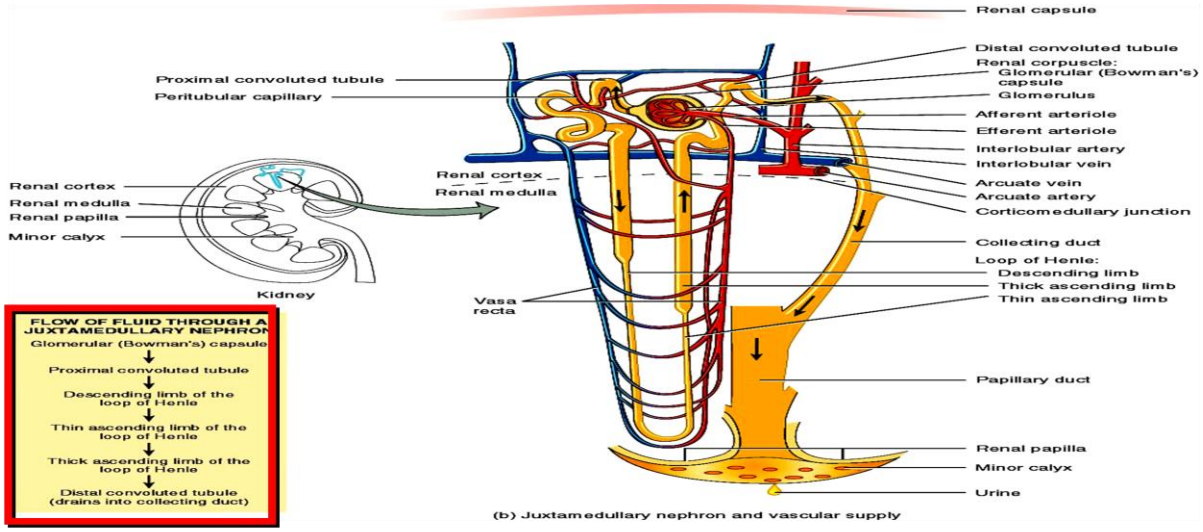
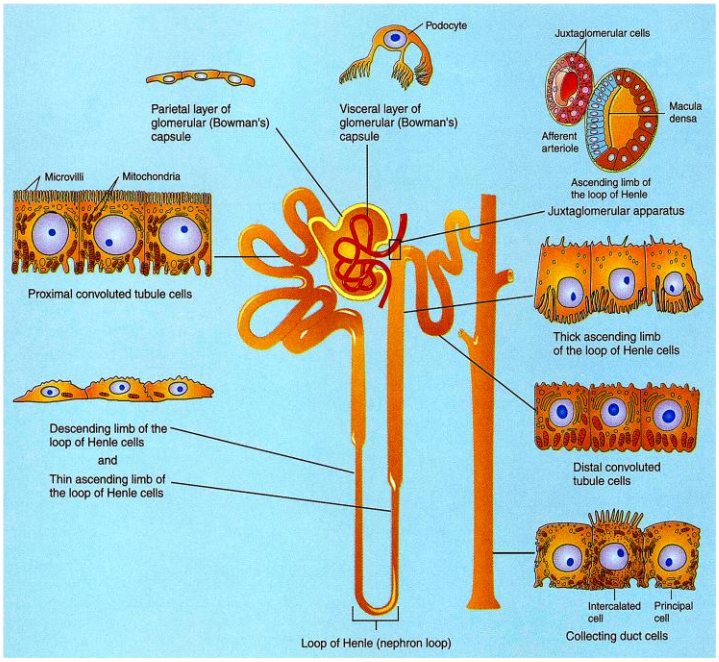
Juxtamedullary Nephron



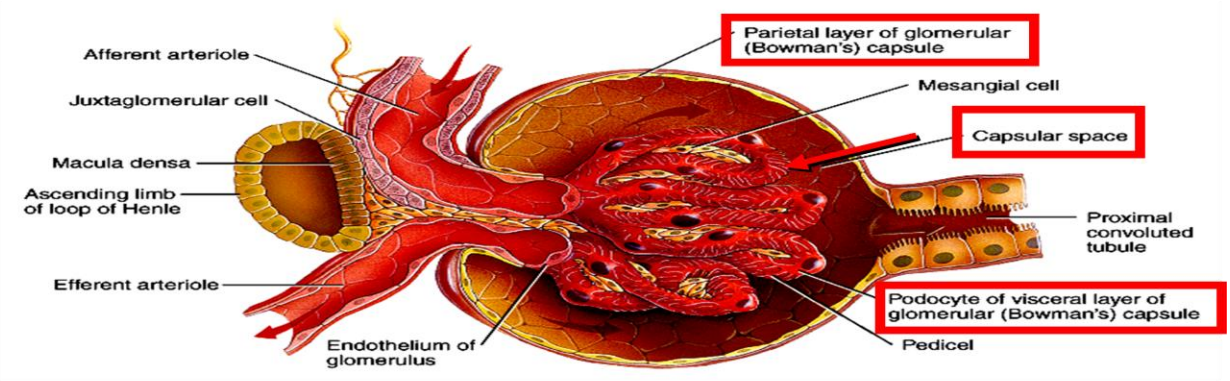
- 15-20% of nephrons are juxtamedullary nephrons
- Renal corpuscles close to medulla and long loops of Henle extend into deepest medulla enabling excretion of dilute or concentrated urine

Histology of the Nephron & Collecting Duct

- Single layer of epithelial cells forms walls of entire tube
- Distinctive features due to function of each region
  - microvilli
  - cuboidal versus simple
  - hormone receptors

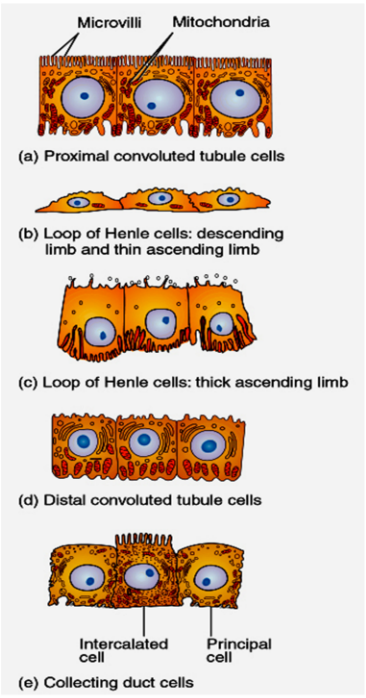


Structure of Renal Corpuscle



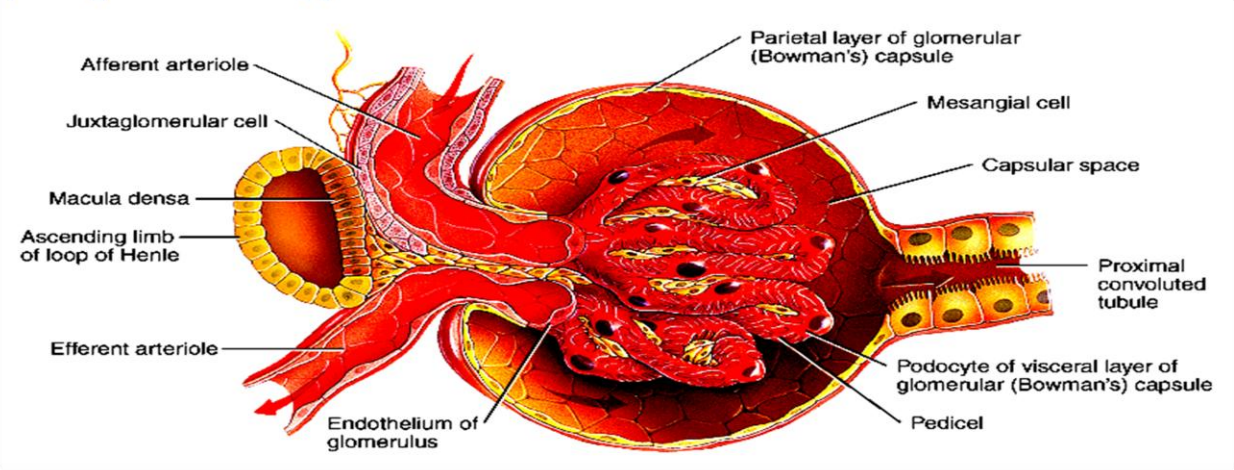
- Bowman's capsule surrounds capsular space
  - podocytes cover capillaries to form visceral layer
  - simple squamous cells form parietal layer of capsule
- Glomerular capillaries arise from afferent arteriole & form a ball before emptying into efferent arteriole

Histology of Renal Tubule & Collecting Duct



- Proximal convoluted tubule
  - simple cuboidal with brush border of microvilli that increase surface area
- Descending limb of loop of Henle
  - simple squamous
- Ascending limb of loop of Henle
  - simple cuboidal to low columnar
  - forms juxtaglomerular apparatus where makes contact with afferent arteriole
    - macula densa is special part of ascending limb
- Distal convoluted & collecting ducts
  - simple cuboidal composed of principal & intercalated cells which have microvilli.

Juxtaglomerular Apparatus



- Structure where afferent arteriole makes contact with ascending limb of loop of Henle
  - macula densa is thickened part of ascending limb
  - juxtaglomerular cells are modified muscle cells in afferent arteriole

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Number of Nephrons

- Remains constant from birth
  - any increase in size of kidney is size increase of individual nephrons
- If injured, no replacement occurs
- Dysfunction is not evident until function declines by 25% of normal (other nephrons handle the extra work)
- Removal of one kidney causes enlargement of the remaining until it can filter at 80% of normal rate of 2 kidneys

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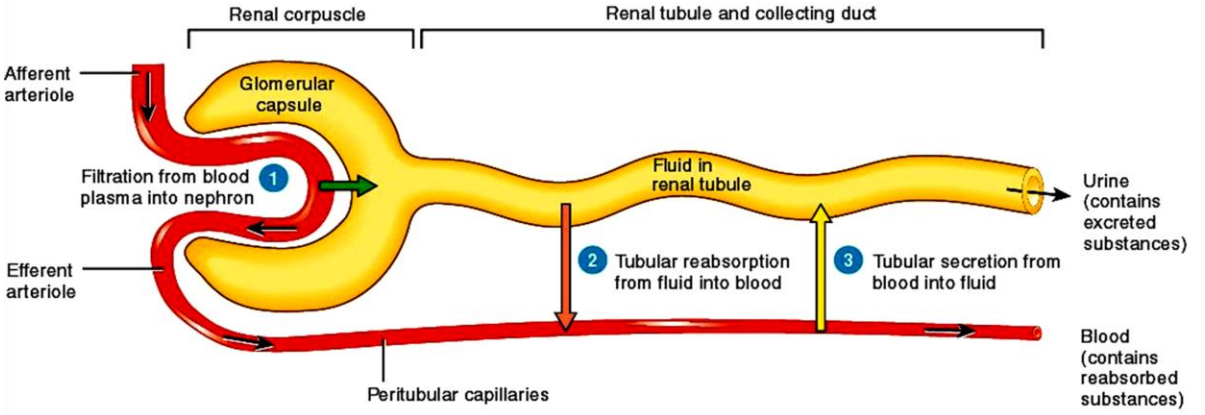
Overview of Renal Physiology

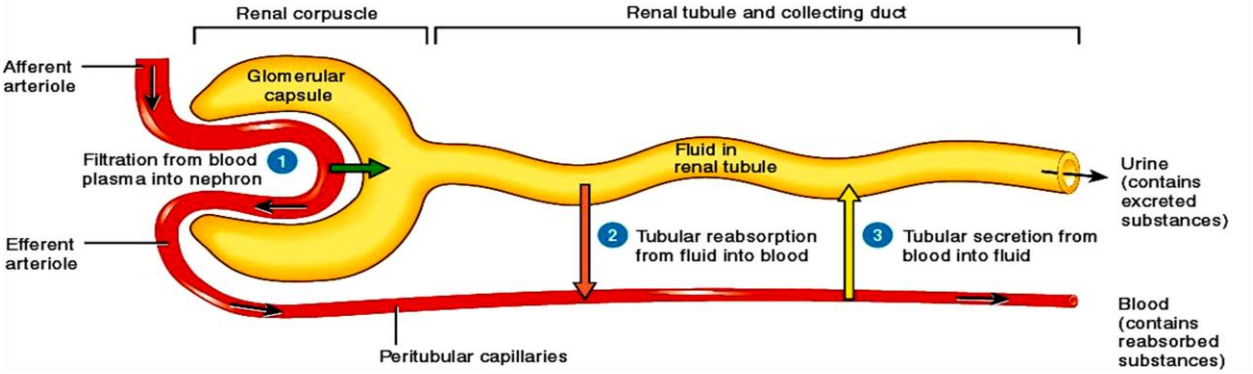
- Nephrons and collecting ducts perform 3 basic processes
  - glomerular filtration
  - tubular reabsorption
  - tubular secretion
- Rate of excretion of any substance is its rate of filtration, plus its rate of secretion, minus its rate of reabsorption

Glomerular filtration



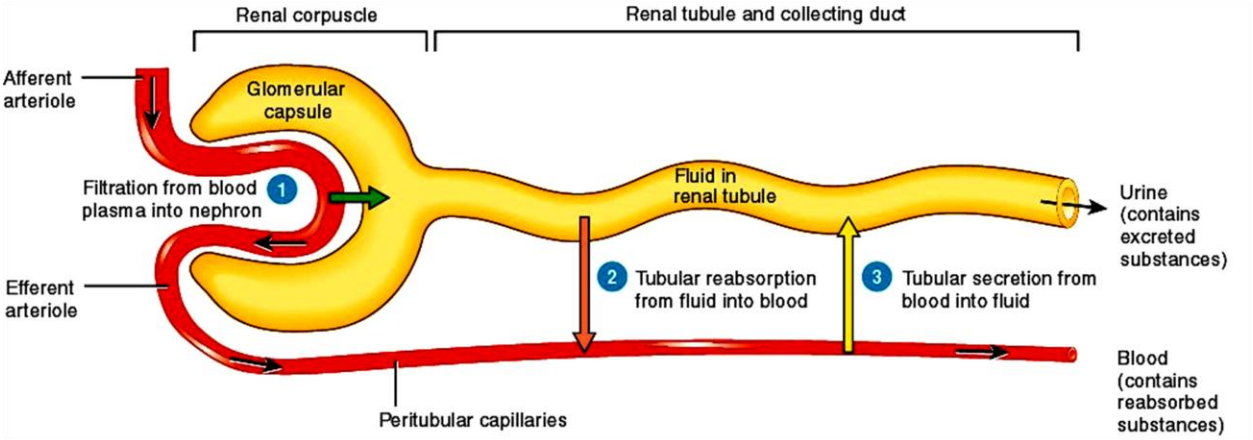
- glomerular filtration
  - a portion of the blood plasma is filtered into the kidney

Tubular reabsorption



- tubular reabsorption
  - water & useful substances are reabsorbed into the blood

Tubular secretion

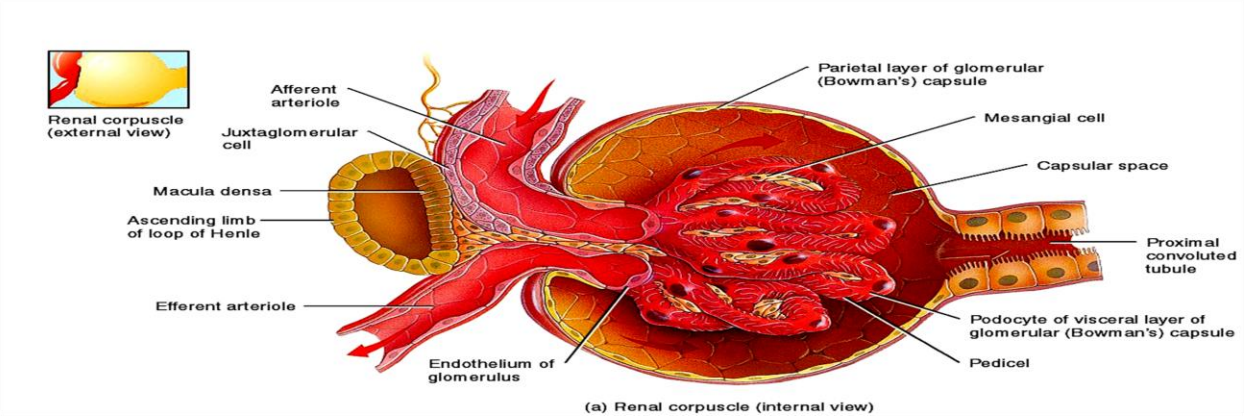


- tubular secretion
  - wastes are removed from the blood & secreted into urine

Glomerular Filtration

- Blood pressure produces glomerular filtrate
- Filtration fraction is 20% of plasma
- 48 Gallons/day
  filtrate reabsorbed
  to 1-2 qt. urine

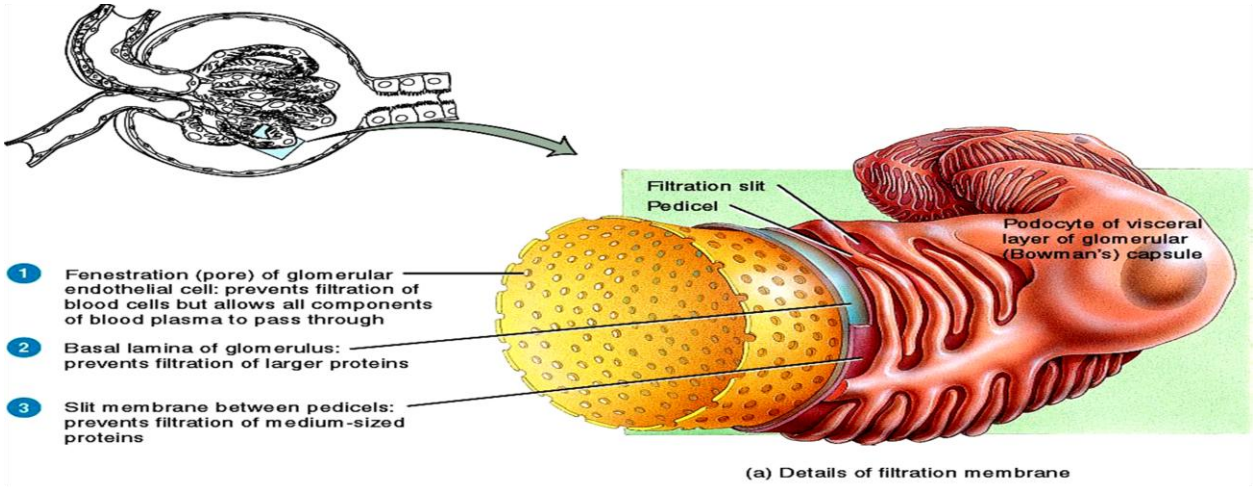
Glomerular Filtration capacity



(a) Renal corpuscle (internal view)

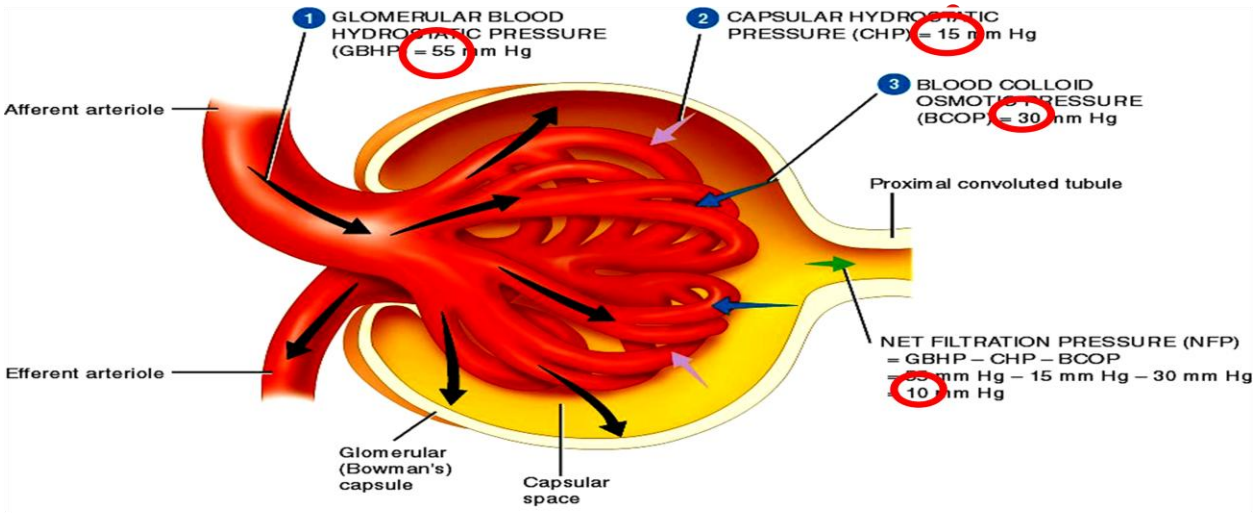
- Filtering capacity enhanced by:
  - large surface area of glomerular capillaries
  - glomerular capillary BP is high due to small size of efferent arteriole
  - Type of capillaries (fenestrated).

Filtration Membrane



- #1 Stops all cells and platelets
- #2 Stops large plasma proteins
- #3 Stops medium-sized proteins, not small ones

Net Filtration Pressure



- NFP = total pressure that promotes filtration
- NFP = GBHP - (CHP + BCOP) = 10mm Hg

Glomerular Filtration Rate

- Amount of filtrate formed in all renal corpuscles of both kidneys / minute
  - average adult male rate is 125 mL/min
- Homeostasis requires GFR that is constant
  - too high & useful substances are lost due to the speed of fluid passage through nephron
  - too low and sufficient waste products may not be removed from the body
- Changes in net filtration pressure affects GFR
  - filtration stops if GBHP drops to 45mm Hg
  - functions normally with mean arterial pressures 80-180

Renal Autoregulation of GFR

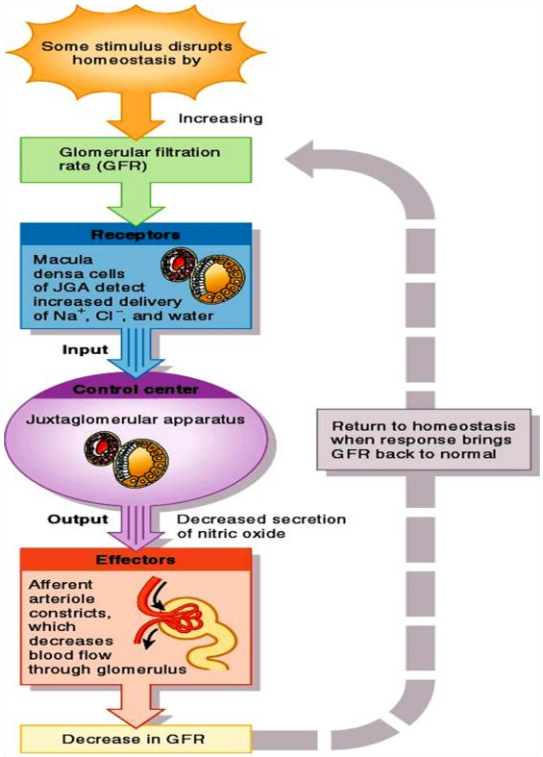
Mechanisms that maintain a constant GFR

despite changes in mean arterial BP:

- ❑ Myogenic mechanism.
- ❑ Tubuloglomerular feedback.
- ❑ Neural regulation.
- ❑ Hormonal regulation.

Tubuloglomerular feedback

- ❑- elevated systemic BP raises the GFR so that fluid flows too rapidly through the renal tubule & Na+, Cl- and water are not reabsorbed
- ❑- macula densa detects that difference & decreases release of NO from the juxtaglomerular apparatus
- ❑- afferent arterioles constrict & reduce GFR



Myogenic mechanism

- ❑systemic increases in BP, stretch the afferent arteriole
- ❑smooth muscle contraction reduces the diameter of the arteriole returning the GFR to its previous level in seconds

Neural Regulation of GFR

- Blood vessels of the kidney are supplied by sympathetic fibers that cause vasoconstriction of afferent arterioles
- At rest, renal BV are maximally dilated because sympathetic activity is minimal
  - renal autoregulation prevails
- With moderate sympathetic stimulation, both afferent & efferent arterioles constrict equally
  - decreasing GFR equally
- With extreme sympathetic stimulation (exercise or hemorrhage), vasoconstriction of afferent arterioles reduces GFR
  - lowers urine output & permits blood flow to other tissues

Hormonal Regulation of GFR

- Atrial natriuretic peptide (ANP) increases GFR
  - stretching of the atria that occurs with an increase in blood volume causes hormonal release
    - relaxes glomerular mesangial cells increasing capillary surface area and increasing GFR
- Angiotensin II reduces GFR
  - potent vasoconstrictor that narrows both afferent & efferent arterioles reducing GFR

Tubular Reabsorption

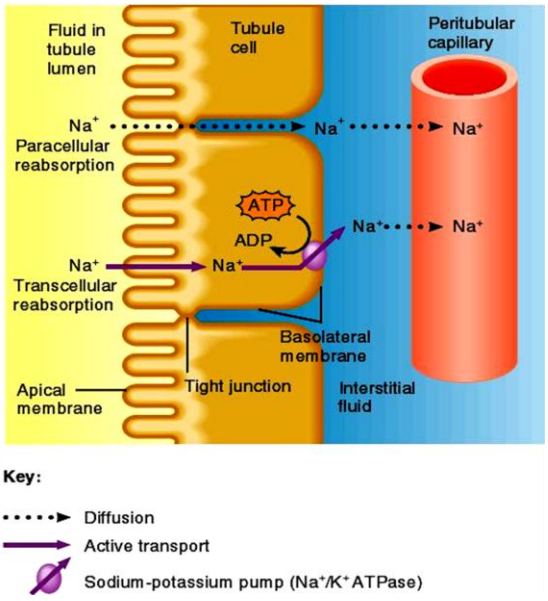
- Normal GFR is so high that volume of filtrate in capsular space in half an hour is greater than the total plasma volume
- Nephron must reabsorb 99% of the filtrate
  - PCT with their microvilli do most of work with rest of nephron doing just the fine-tuning
    - solutes reabsorbed by active & passive processes
    - water follows by osmosis
    - small proteins by pinocytosis

Tubular Secretion

- Important function of nephron is tubular secretion
  - transfer of materials from blood into tubular fluid
    - helps control blood pH because of secretion of H^+
    - helps eliminate certain substances (NH_4^+, creatinine, K^+)

Reabsorption Routes

- Paracellular reabsorption
  - 50% of reabsorbed material moves between cells by diffusion in some parts of tubule
- Transcellular reabsorption
  - material moves through both the apical and basal membranes of the tubule cell by active transport



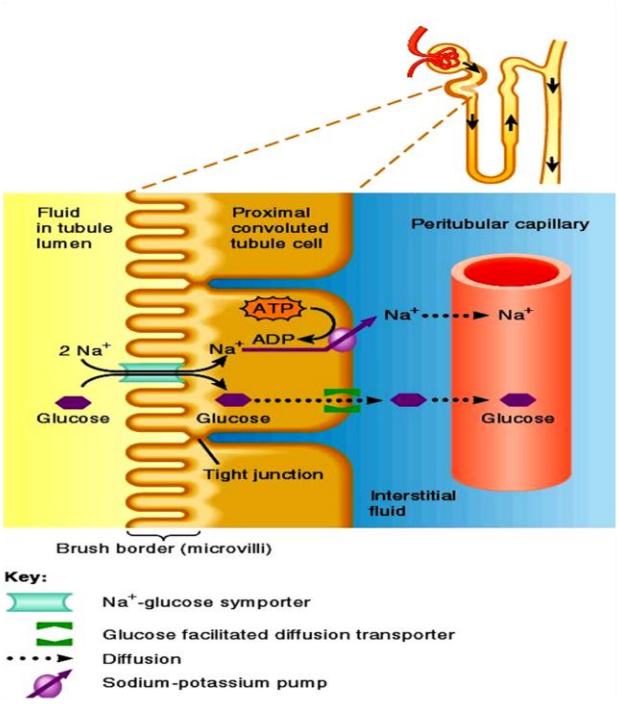
Transport Mechanisms

- Apical and basolateral membranes of tubule cells have different types of transport proteins
- Reabsorption of Na+ is important
  - several transport systems exist to reabsorb Na+
  - Na+/K+ ATPase pumps sodium from tubule cell cytosol through the basolateral membrane only
- Water is only reabsorbed by osmosis
  - obligatory water reabsorption occurs when water is "obliged" to follow the solutes being reabsorbed
  - facultative water reabsorption occurs in collecting duct under the control of antidiuretic hormone

Glucosuria

- Renal symporters <u>can not</u> reabsorb glucose fast enough if blood glucose level is <u>above 200 mg/mL</u>
  - some glucose remains in the urine (glucosuria)
- Common cause is diabetes mellitis because insulin activity is deficient and blood sugar is too high
- Rare genetic disorder produces defect in symporter that reduces its effectiveness

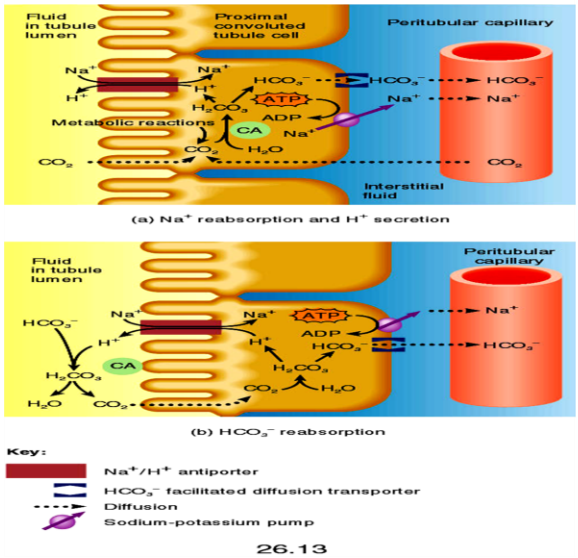
Reabsorption in the PCT



Reabsorption of Nutrients

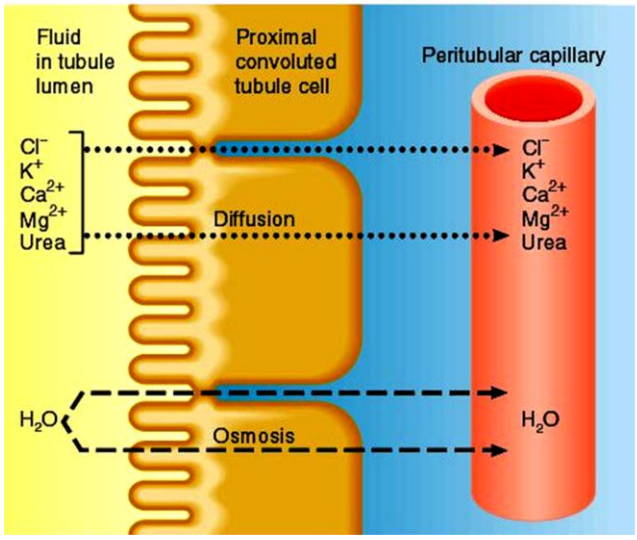
- Na+ symporters help reabsorb materials from the tubular filtrate
- Glucose, amino acids, lactic acid, water-soluble vitamins and other nutrients are completely reabsorbed in the first half of the proximal convoluted tubule
- Intracellular sodium levels are kept low due to Na+/K+ pump

Reabsorption of Bicarbonate, Na+Ions



- Na+ antiporters reabsorb Na+ and secrete H+
  - PCT cells produce the H+ & release bicarbonate ion to the peritubular capillaries
  - important buffering system
- For every H+ secreted into the tubular fluid, one filtered bicarbonate eventually returns to the blood

Passive Reabsorption in the 2nd Half of PCT



- Electrochemical gradients produced by symporters & antiporters causes passive reabsorption of other solutes
- Cl-, K+, Ca+2, Mg+2 and urea passively diffuse into the peritubular capillaries
- Promotes osmosis in PCT (especially permeable due to aquaporin-1 channels

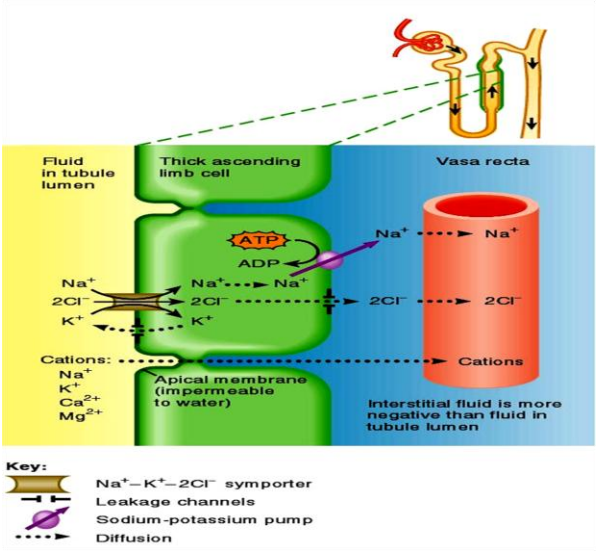
Secretion of NH3 & NH4+ in PCT

- Ammonia (NH3) is a poisonous waste product of protein deamination in the liver
  - most is converted to urea which is less toxic
- Both ammonia & urea are filtered at the glomerus & secreted in the PCT
  - PCT cells deaminate glutamine in a process that generates both NH3 and new bicarbonate ion.
- Bicarbonate diffuses into the bloodstream
  - during acidosis more bicarbonate is generated

Reabsorption in the Loop of Henle

- Tubular fluid
  - PCT reabsorbed 65% of the filtered water so chemical composition of tubular fluid in the loop of Henle is quite different from plasma
  - since many nutrients were reabsorbed as well, osmolarity of tubular fluid is close to that of blood
- Sets the stage for independent regulation of both volume & osmolarity of body fluids

Symporters in the Loop of Henle



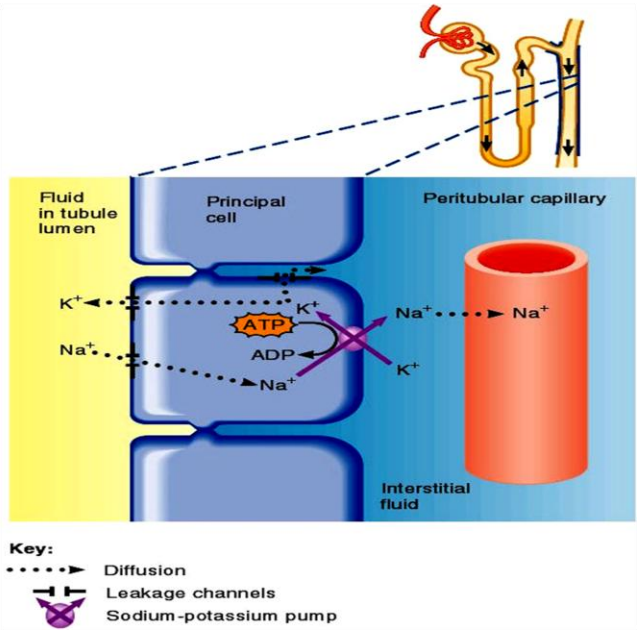
- Thick limb of loop of Henle has Na+ K- Cl- symporters that reabsorb these ions
- K+ leaks through K+ channels back into the tubular fluid leaving the interstitial fluid and blood with a negative charge
- Cations passively move to the vasa recta

Reabsorption in the DCT

- Removal of Na+ and Cl- continues in the DCT by means of Na+ Cl- symporters
- Na+ and Cl- then reabsorbed into peritubular capillaries
- DCT is major site where parathyroid hormone stimulates reabsorption of Ca+2
  - DCT is not very permeable to water so it is not reabsorbed with little accompanying water

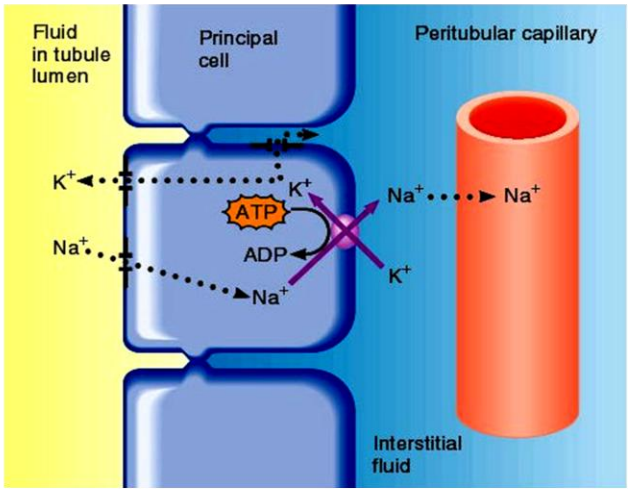
Reabsorption & Secretion in the Collecting Duct

- By end of DCT, 95% of solutes & water. have been reabsorbed and returned to the bloodstream.
- Cells in the collecting duct make the final adjustments.
  - principal cells reabsorb Na+ and secrete K+.
  - intercalated cells reabsorb K+ & bicarbonate ions and secrete H+.



Actions of the Principal Cells

- Na+ enters principal cells through leakage channels
- Na+ pumps keep the concentration of Na+ in the cytosol low
- Cells secrete variable amounts of K+, to adjust for dietary changes in K+ intake
  - down concentration gradient due to Na+/K+ pump
- Aldosterone increases Na+ and water reabsorption & K+ secretion by principal cells by stimulating the synthesis of new pumps and channels.



Hormonal Regulation

- Hormones that affect Na+, Cl- & water reabsorption and K+ secretion in the tubules
  1- Angiotensin II and aldosterone
  - decreases GFR by vasoconstricting afferent arteriole
  - enhances absorption of Na+
  - promotes aldosterone production which causes principal cells to reabsorb more Na+ and Cl- and less water
  - increases blood volume by increasing water reabsorption

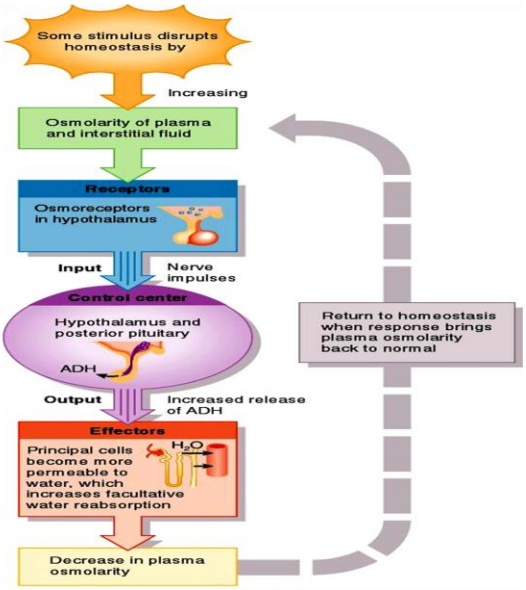
Hormonal Regulation

2- Atrial natriuretic peptide (ANP)

- inhibits reabsorption of Na+ and water in PCT & suppresses secretion of aldosterone & ADH
- increase excretion of Na+ which increases urine output and decreases blood volume

3- Antidiuretic Hormone

- Increases water permeability of principal cells so regulates facultative water reabsorption
- Stimulates the insertion of aquaporin-2 channels into the membrane
  - water molecules move more rapidly
- When osmolarity of plasma & interstitial fluid increases, more ADH is secreted and facultative water reabsorption increases.



Production of Dilute or Concentrated Urine

- Homeostasis of body fluids despite variable fluid intake
- Kidneys regulate water loss in urine
- ADH controls whether dilute or concentrated urine is formed
  - if lacking, urine contains high ratio of water to solutes

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Formation of Concentrated Urine

- Compensation for low water intake or heavy perspiration
- Urine can be up to 4 times greater osmolarity than plasma
- The production of concentrated urine involves:

1- countercurrent mechanism:

  - Long loop juxtamedullary nephrons make that possible
  - Na+/K+/Cl- symporters reabsorb Na+ and Cl- from tubular fluid to create osmotic gradient in the renal medulla

2-Cells in the collecting ducts reabsorb more water & urea when ADH is increased

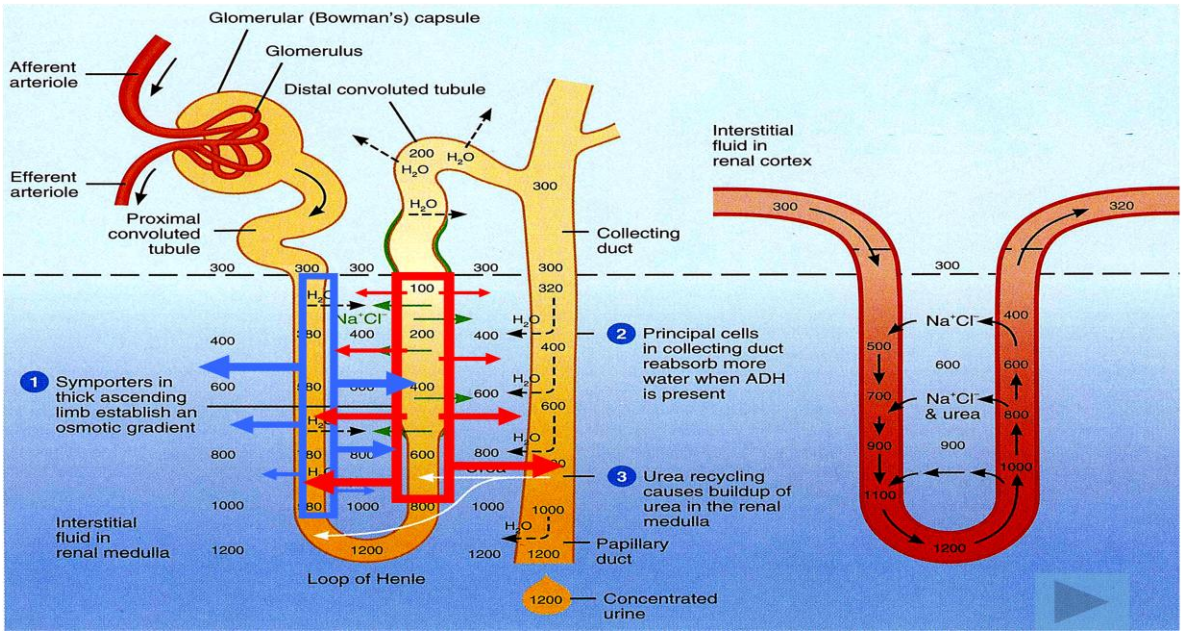
3-Urea recycling causes a buildup of urea in the renal medulla

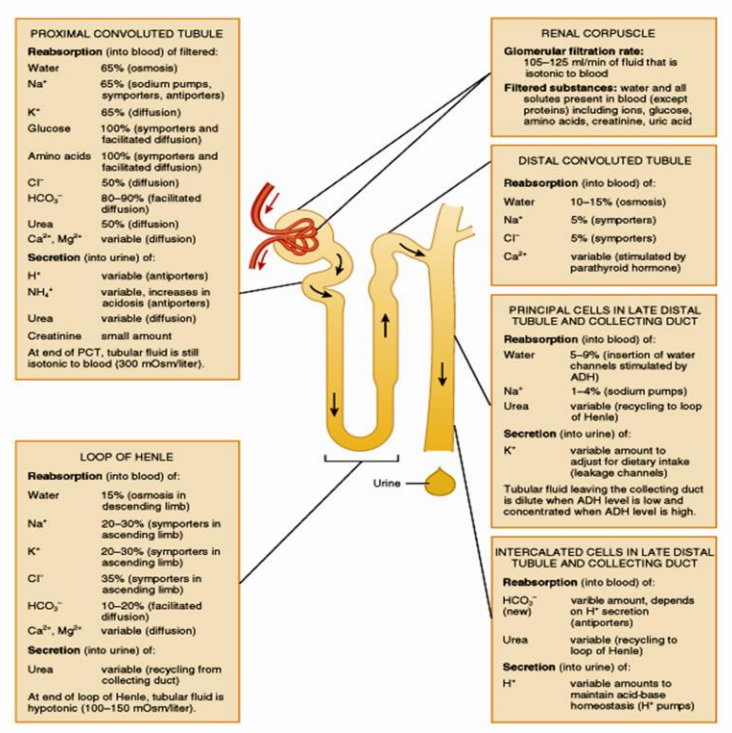
4-Vasa recta minimize excessive loss of solute from interstitium (maintenance of countercurrent gradient).

Countercurrent Mechanism

- Descending limb is very permeable to water
  - higher osmolarity of interstitial fluid outside the descending limb causes water to mover out of the tubule by osmosis
    - at hairpin turn, osmolarity can reach 1200 mOsm/liter
- Ascending limb is impermeable to water, but symporters remove Na+ and Cl- so osmolarity drops to 100 mOsm/liter, but less urine is left
- Vasa recta blood flowing in opposite directions than the loop of Henle -- provides nutrients & O2 without affecting osmolarity of interstitial fluid

Reabsorption within Loop of Henle





Summary

- H2O Reabsorption
  - PCT---65%
  - loop---15%
  - DCT----10-15%
  - collecting duct---5-10% with ADH
- Dilute urine has not had enough water removed, although sufficient ions have been reabsorbed.

Diuretics

- Substances that slow renal reabsorption of water & cause diuresis (increased urine flow rate)
  - caffeine which inhibits Na+ reabsorption
  - alcohol which inhibits secretion of ADH
  - prescription medicines can act on the PCT, loop of Henle or DCT

Evaluation of Kidney Function

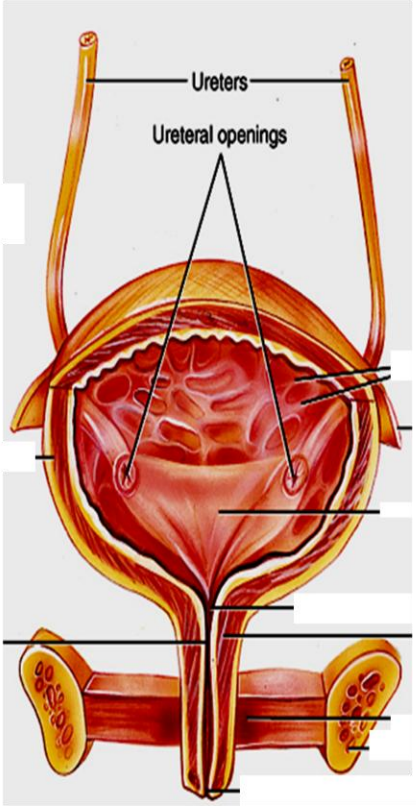
- Urinalysis
  - analysis of the volume and properties of urine
  - normal urine is protein free, but includes filtered & secreted electrolytes
    - urea, creatinine, uric acid, urobilinogen, fatty acids, enzymes & hormones
- Blood tests
  - blood urea nitrogen test (BUN).
    - rises steeply if GFR decreases severely
  - plasma creatinine--from skeletal muscle breakdown
  - renal plasma clearance of substance from the blood in ml/minute (important in drug dosages)

Dialysis Therapy

- Kidney function is so impaired the blood must be cleansed artificially
  - separation of large solutes from smaller ones by a selectively permeable membrane
- Artificial kidney machine performs hemodialysis
  - directly filters blood because blood flows through tubing surrounded by dialysis solution
  - cleansed blood flows back into the body

Anatomy of Ureters

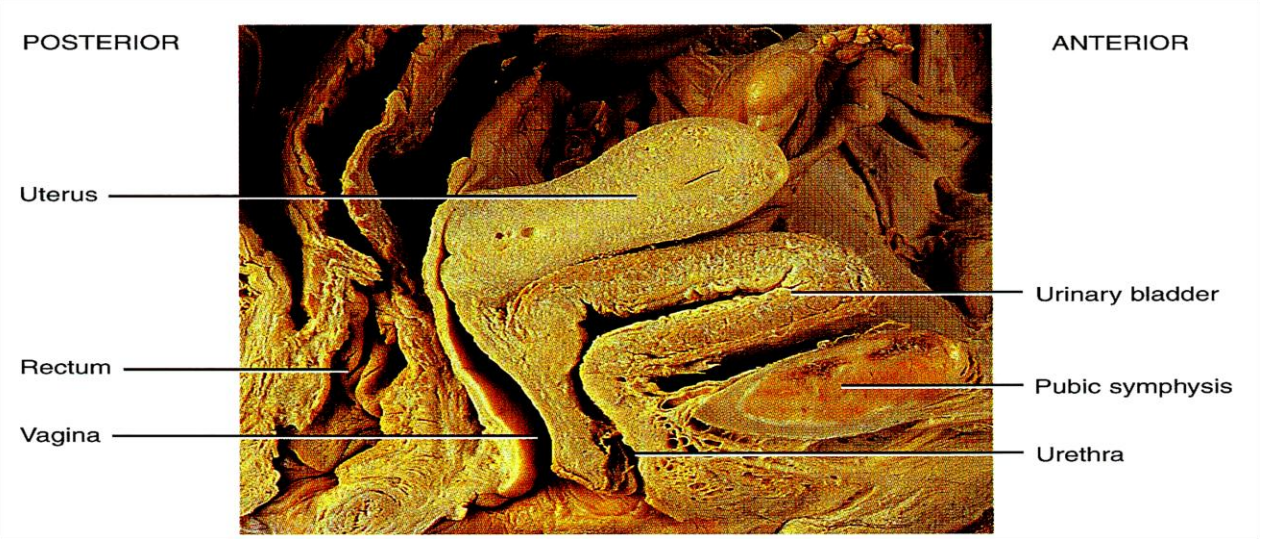
- 10 to 12 in long
- Varies in diameter from 1-10 mm
- Extends from renal pelvis to bladder
- Retroperitoneal
- Enters posterior wall of bladder
- Physiological valve only
  - bladder wall compresses arterial opening as it expands during filling
  - flow results from peristalsis, gravity & hydrostatic pressure



Histology of Ureters

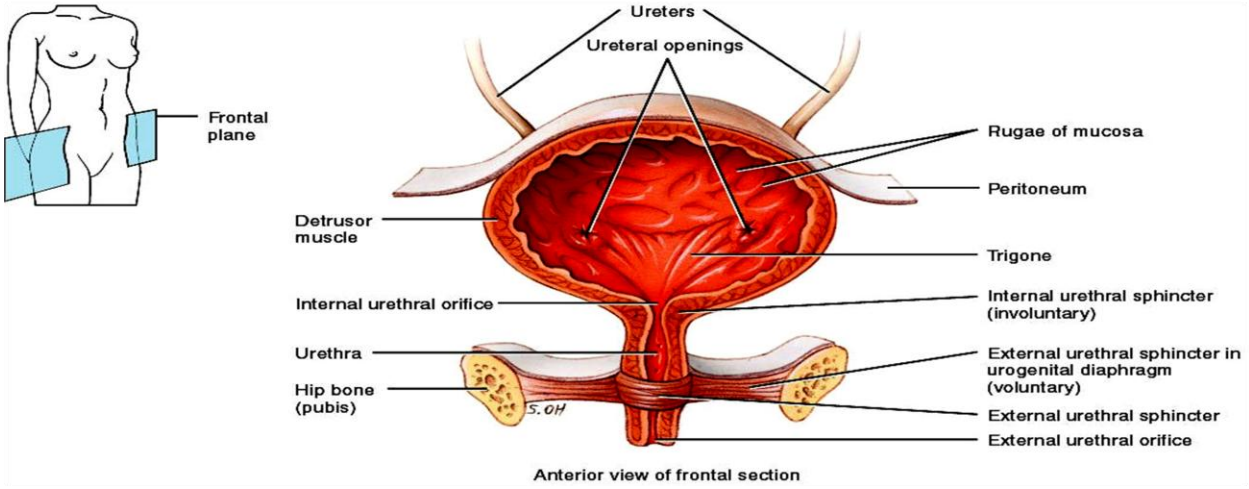
- 3 layers in wall
  - mucosa is transitional epithelium & lamina propria
    - since organ must inflate & deflate
    - mucus prevents the cells from being contacted by urine
  - muscularis
    - inner longitudinal & outer circular smooth muscle layer
      - distal 1/3 has additional longitudinal layer
    - peristalsis contributes to urine flow
  - adventitia layer of loose connective tissue anchors in place
    - contains lymphatics and blood vessels to supply ureter

Location of Urinary Bladder



- Posterior to pubic symphysis
- In females is anterior to vagina & inferior to uterus
- In males lies anterior to rectum

Anatomy of Urinary Bladder



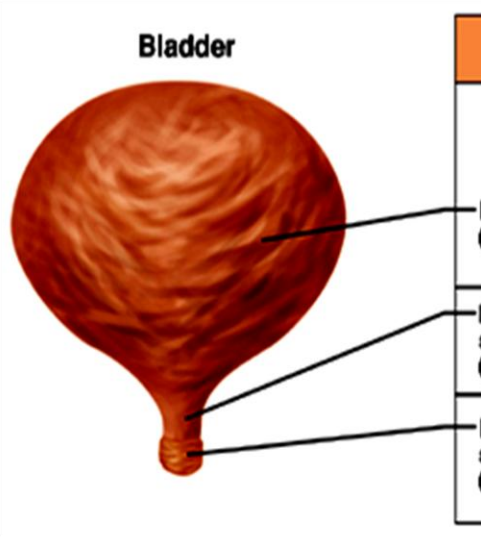
- Hollow, distensible muscular organ with capacity of 700 - 800 mL
- Trigone is smooth flat area bordered by 2 ureteral openings and one urethral opening

Histology of Urinary Bladder

- 3 layers in wall
  - mucosa is transitional epithelium & lamina propria
    - since organ must inflate & deflate
    - mucus prevents the cells from being contacted by urine
  - muscularis (known as detrusor muscle)
    - 3 layers of smooth muscle
      - inner longitudinal, middle circular & outer longitudinal
    - circular smooth muscle fibers form internal urethral sphincter
    - circular skeletal muscle forms external urethral sphincter
  - adventitia layer of loose connective tissue anchors in place
    - superior surface has serosal layer (visceral peritoneum)

Micturition Reflex

- Micturition or urination (voiding)
- Stretch receptors signal spinal cord and brain
  - when volume exceeds 200-400 mL
- Impulses sent to micturition center in sacral spinal cord (S2 and S3) & reflex is triggered
  - parasympathetic fibers cause detrusor muscle to contract, external & internal sphincter muscles to relax
- Filling causes a sensation of fullness that initiates a desire to urinate before the reflex actually occurs
  - conscious control of external sphincter
  - cerebral cortex can initiate micturition or delay its occurrence for a limited period of time



Muscle	Innervation		
	Type	During filling	During micturition
Detrusor (smooth muscle)	Parasympathetic (causes contraction)	Inhibited	Stimulated
Internal urethral sphincter (smooth muscle)	Sympathetic (causes contraction)	Stimulated	Inhibited
External urethral sphincter (skeletal muscle)	Somatic motor (causes contraction)	Stimulated	Inhibited

Release of urine from the bladder, called micturition, is coordinated by a combination of smooth and skeletal muscle relaxation and contraction.

Urinary Incontinence

- Lack of voluntary control over micturition
  - normal in 2 or 3 year olds because neurons to sphincter muscle is not developed
- Stress incontinence in adults
  - caused by increases in abdominal pressure that result in leaking of urine from the bladder
    - coughing, sneezing, laughing, exercising, walking
  - injury to the nerves, loss of bladder flexibility, or damage to the sphincter

Waste Management in Other Body Systems

- Buffers bind excess H+
- Blood transports wastes
- Liver is site for metabolic recycling
  - conversion of amino acids into glucose, glucose into fatty acids or toxic into less toxic substances
- Lungs excrete CO2 and heat
- Sweat glands eliminate heat, water, salt & urea
- GI tract eliminates solid wastes, CO2, water, salt and heat

Aging and the Urinary System

- Anatomical changes
  - kidneys shrink in size from 260 g to 200 g
- Functional changes
  - lowered blood flow & filter less blood (50%)
  - diminished sensation of thirst increases susceptibility to dehydration
- Diseases common with age
  - acute and chronic inflammations & canaliculi
  - infections, nocturia, polyuria, dysuria, retention or incontinence and hematuria
- Cancer of prostate is common in elderly men

Disorders of Urinary System

- Renal calculi
- Urinary tract infections
- Glomerular disease
- Renal failure
- Polycystic kidney disease
- Urinary bladder cancer