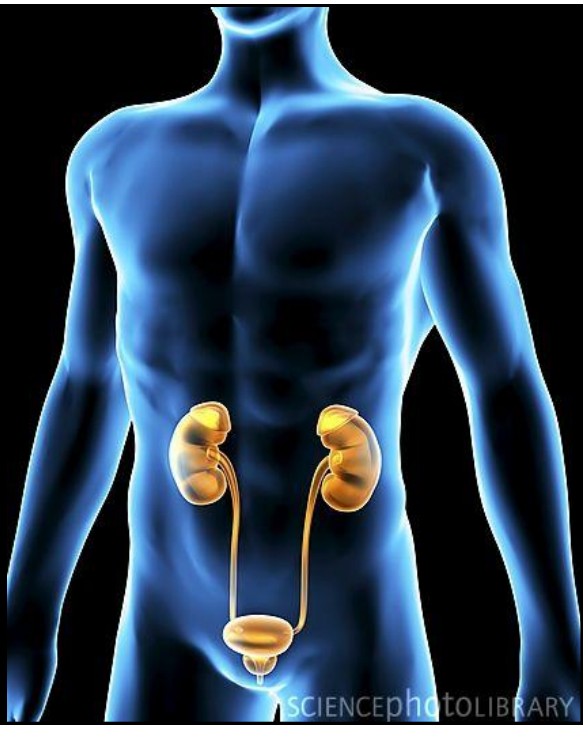
Urinary System



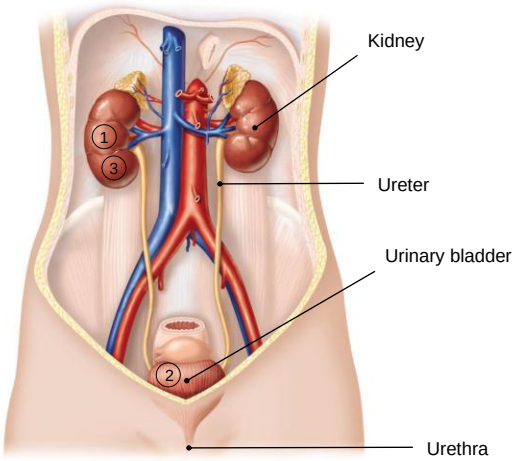
Urinary System - Overview:

Major Functions:

1) Removal of organic waste products from fluids (excretion)
2) Discharge of waste products into the environment (elimination)
3) Regulation of the volume / [solute] / pH of blood plasma

HOWEVER, THE KIDNEY AIN'T JUST FOR PEE'IN…

- Regulation of blood volume / blood pressure (e.g., renin)
- Regulation of red blood cell formation (i.e., erythropoietin)
- Metabolization of vitamin D to active form (Ca^{++} uptake)
- Gluconeogenesis during prolonged fasting



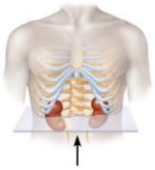
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.1

Urinary System

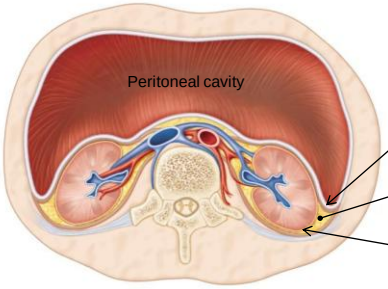
Functional Anatomy - Kidney:

Renal ptosis:
Kidneys drop to lower position due to loss of perirenal fat

Located in the superior lumbar region



"Bar of soap"
12 cm x 6 cm x 3 cm
150 g / kidney



Layers of Supportive Tissue:

Renal fascia:
Outer layer of dense fibrous connective tissue; anchors kidney in place

Perirenal fat capsule:
Fatty mass surrounding kidney; cushions kidney against blows

Fibrous capsule:
Transparent capsule on kidney; prevents infection of kidney from local tissues

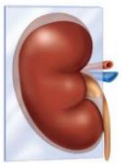
Kidneys are located retroperitoneal

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.2

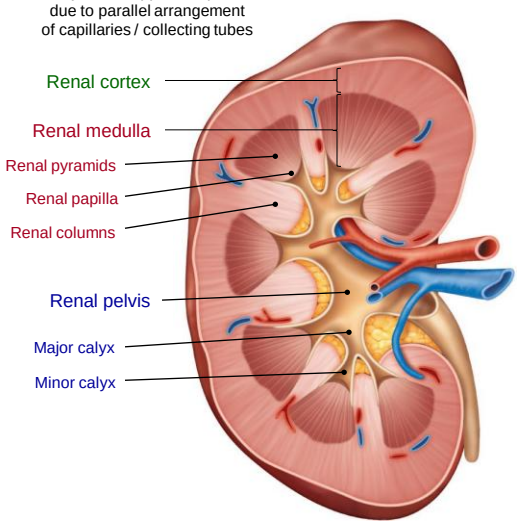
Urinary System

Functional Anatomy - Kidney:

Pyelonephritis:
Inflammation of the kidney

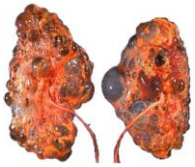


Pyramids appear striped due to parallel arrangement of capillaries / collecting tubes



Renal hilum
- Entrance for blood vessels / nerves

Polycystic kidney disease
(autosomal dominant condition)



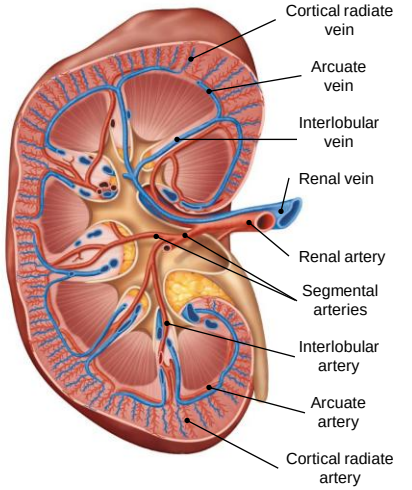
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.3

Functional Anatomy - Kidney:

Nerve supply to the kidney provided via the renal plexus (primarily sympathetic)

Blood Supply to Kidney:

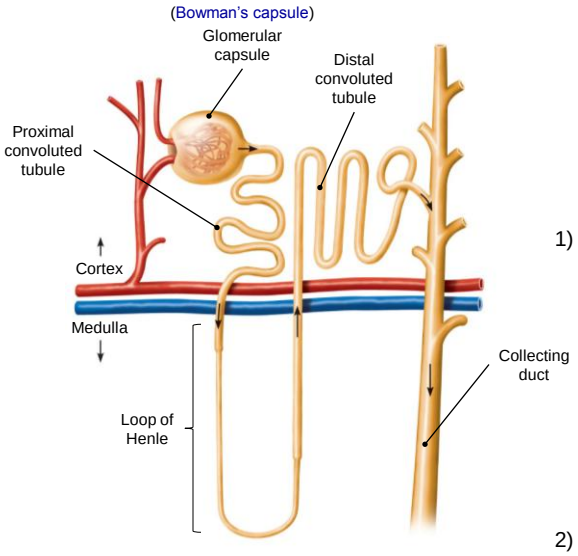
- 1/4 of cardiac output delivered to kidneys
  - 0.25 x 5 L / min = 1.25 L / min



Aorta → Renal artery → Segmental artery → Interlobar artery → Arcuate artery → Cortical radiate artery → Afferent arteriole → Glomerulus (capillary) → Efferent arteriole → Peritubular capillaries → Portal system → Cortical radiate vein → Arcuate vein → Interlobar vein → Renal vein → Inferior vena cava

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figure 25.4

Functional Anatomy - Kidney:



Nephron:

Functional unit of the kidney

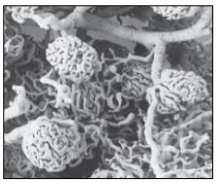
(~ 1 million / kidney; urine formation)

- Filter ~ 180 L of blood plasma / day
- Produce ~ 1 - 1.5 L of urine / day

99% of filtrate returned to blood

Nephron Anatomy:

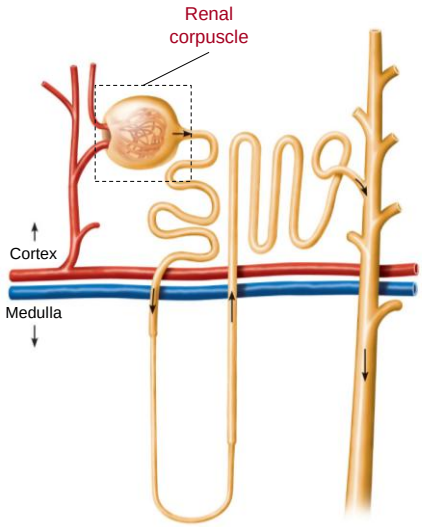
1) Glomerulus
   - Network of capillaries
   - Tightly wound coil (↑ surface area)



2) Renal tubule
   - Location of filtrate (plasma-derived fluid)

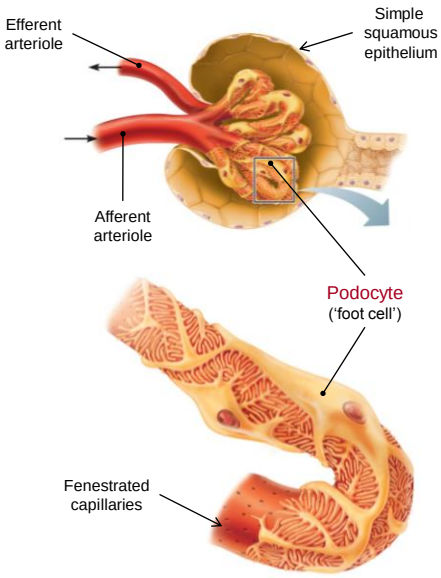
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.7

Functional Anatomy - Kidney:



Renal Corpuscle
(site of filtration)

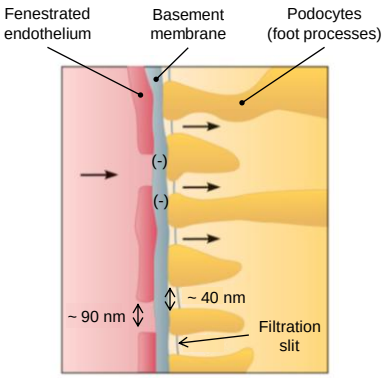
Glomerulus + Glomerular capsule



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.9

Functional Anatomy - Kidney:

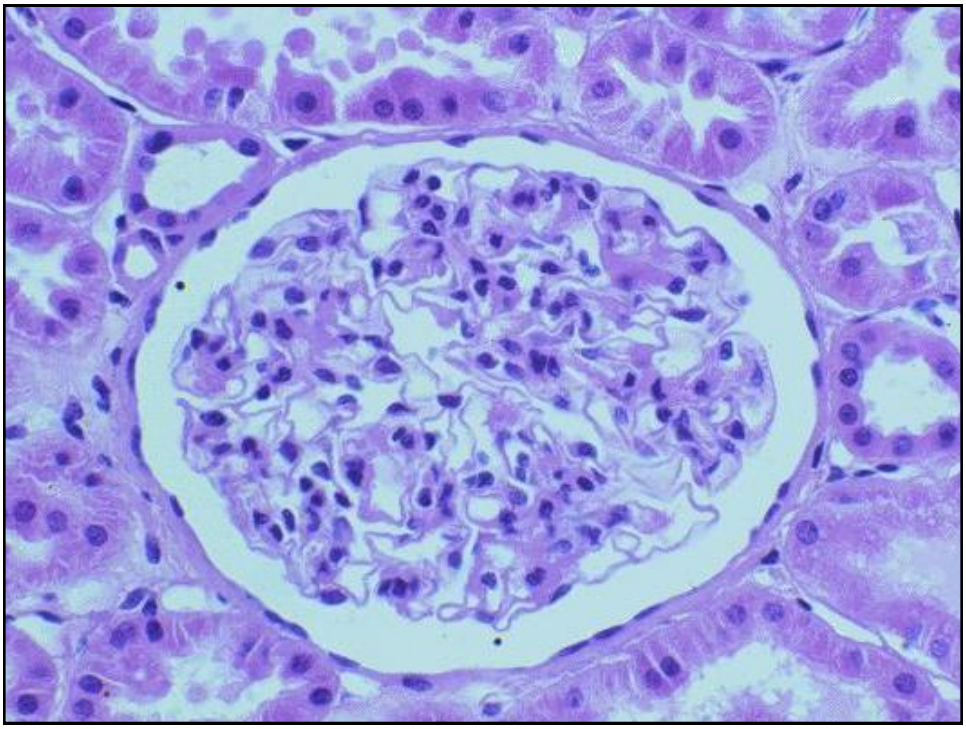
Filtration Membrane:



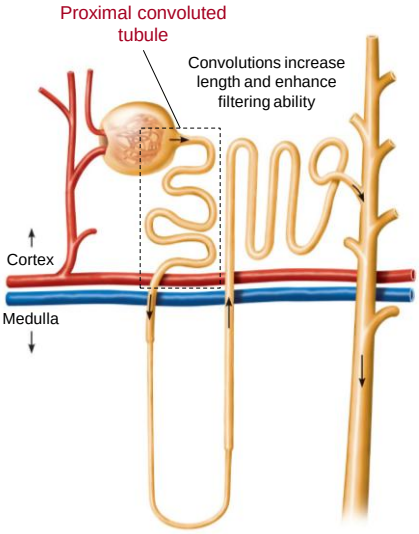
- Size selectivity (fenestrations / slits)
- Charge selectivity (basement membrane)

Glomerular mesangial cells:
Degrade macromolecules "hung up" in filtration membrane

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5 / 25.9



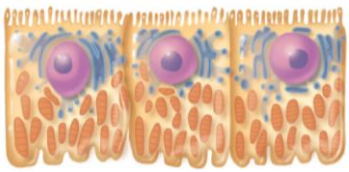
Functional Anatomy - Kidney:



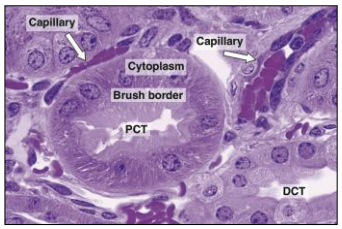
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5

Proximal Convoluted Tubule (PCT)

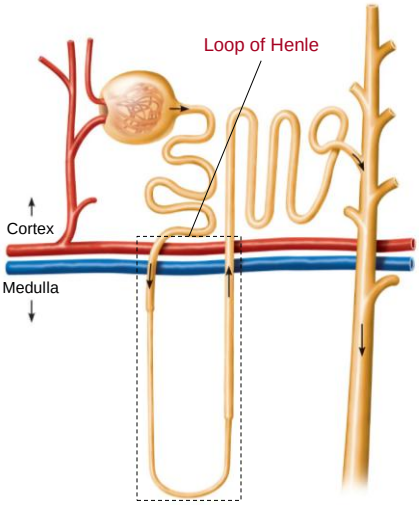
(major site of filtrate reabsorption)



- Simple cuboidal epithelium
  - Dense microvilli (↑ surface area)
- ↑ mitochondria (↑ energy demands)
- Infolded basal membrane (↑ surface area)



Functional Anatomy - Kidney:

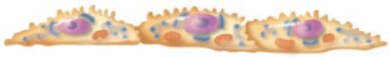


Loop of Henle
(site of filtrate concentration)

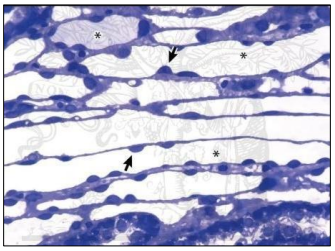
Thick Segment

- Similar in structure to the PCT

Thin Segment

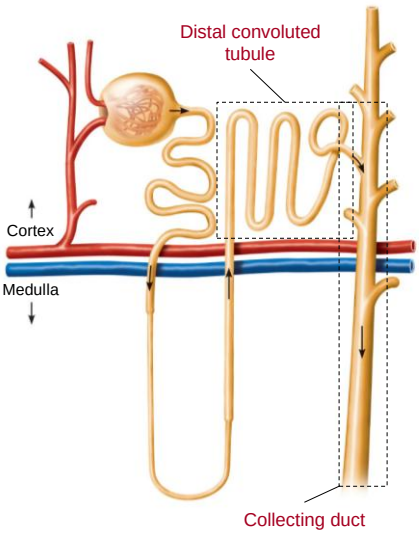


- Simple squamous epithelium
- Freely permeable to water

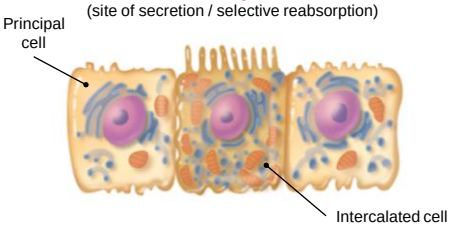


Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5

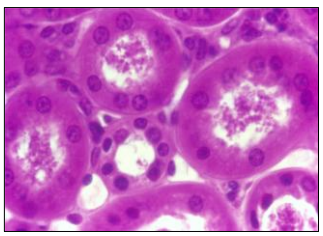
Functional Anatomy - Kidney:



Distal Convoluted Tubule (DCT) & Collecting Ducts
(site of secretion / selective reabsorption)

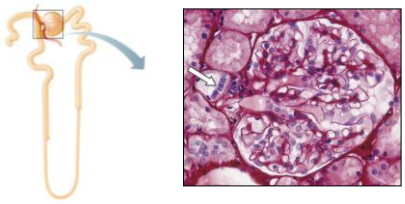


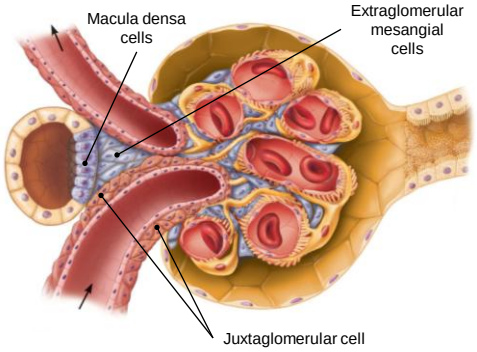
- Simple cuboidal epithelium
  - Intercalated cells (acid-base balance)
  - Principal cells (water / Na^+ balance)
- Smaller lumen; ↑ number of cells (compared to PCT)



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.5

Functional Anatomy - Kidney:





Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.8

Juxtaglomerular Apparatus (JGA)
(Regulator of filtration rate / systemic blood pressure)

- Region where distal end of loop of Henle / DCT lies against afferent arteriole feeding glomerulus

Cell Types:

1) Juxtaglomerular (granular) cells

- Modified smooth muscle cells (afferent arteriole)
  - Prominent secretory granules (renin)
- Mechanoreceptors; measure blood pressure

2) Macula densa cells

- Line loop of Henle / DCT near renal corpuscle
  - Tall cells; nuclei clustered together
- Chemoreceptors; measure [osmotic] of filtrate

3) Extraglomerular mesangial cells

- Cluster between macula densa and JG cells
  - Gap junctions; communication (?)

Functional Anatomy - Kidney:

Types of Nephrons:

1) Cortical Nephrons (85%):

- Located in the upper cortex
- Primarily involved in reabsorption

2) Juxtamedullary Nephrons (15%):

- Bowman's capsule in lower cortex; loop of Henle in medulla
- Primarily involved in filtrate concentration

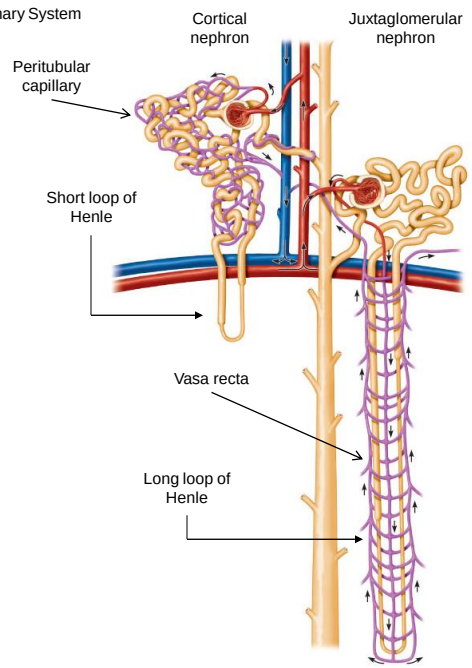
Nephron Capillary Beds:

1) Peritubular Capillaries:

- Arise from efferent arterioles
- Closely associate with PCT / DCT

2) Vasa Recta:

- Arise from efferent arterioles
- Closely associate with loop of Henle



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.7

Renal Physiology - Overview:

(RBF = Renal blood flow)

RPF = RBF (1 – hematocrit)

In a single day, the kidneys filter 60x the normal blood plasma volume present

- Consume 20 - 25% of all oxygen at rest

Major processes occurring in kidney:

1) Glomerular filtration (glomeruli)

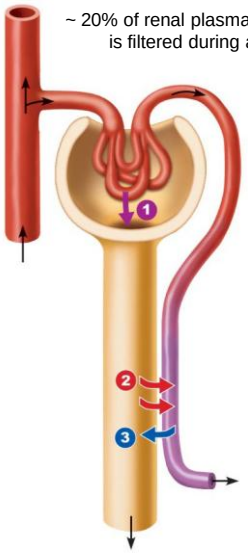
Ultrafiltrate:
All blood borne solutes except proteins that cross into the tubule system

2) Tubular reabsorption (Tubular network)
   - Materials reclaimed from filtrate back into the peritubular capillaries

3) Tubular secretion (Tubular network)
   - Materials moved from peritubular capillaries out into filtrate

Urine:
All metabolic waste and unneeded substances; descend collecting ducts to renal pelvis

~ 20% of renal plasma flow (RPF) is filtered during a pass



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.10

Costanzo (Physiology, 4th ed.) – Figure 6.10

Glomerular Filtration:

Average GFR = 120 – 125 mL / min

As in systemic capillaries, the pressures that drive fluid movement across the glomerular capillary wall are Starling pressures

Starling equation:

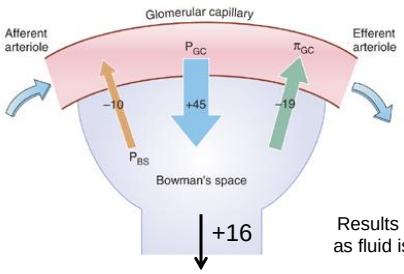
$$GFR = K_f [(P_{GC} - P_{BS}) - \pi_{GC}]$$

Net Filtration Pressure

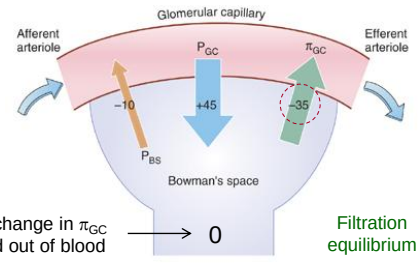
GFR = Glomerular filtration rate (mL / min)
K_f = Hydraulic conductance (mL / min • mm Hg)
P_{GC} = Glomerular capillary hydrostatic pressure (mm Hg)
P_{GS} = Bowman's space hydrostatic pressure (mm Hg)
π_{GC} = Glomerular capillary osmotic pressure (mm Hg)

Since filtration of proteins is negligible, π_{BS} is removed from equation (= 0)

Beginning of glomerular capillary



End of glomerular capillary



Results due to change in π_{GC} as fluid is filtered out of blood → 0

Filtration equilibrium

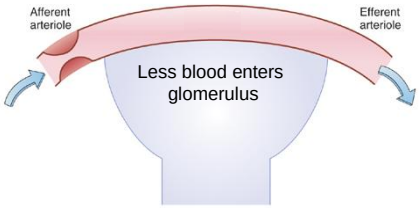
Glomerular Filtration:

Changes in P_{BS} (e.g., kidney stones) and π_{GC} (e.g., nephronic syndrome) are often linked with pathologies

Changes in the GFR can be brought about by changes in any of the Starling pressures

$$GFR = K_f [(P_{GC} - P_{BS}) - \pi_{GC}]$$

- Produced by changes in the resistance of the afferent and efferent arterioles

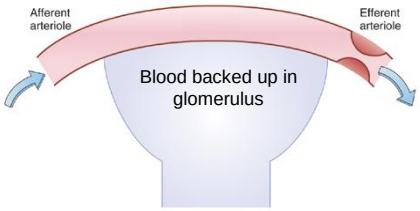


Constriction of afferent arteriole

$\downarrow$ RPF = $\downarrow$ P_{GC} = $\downarrow$ GFR

Constriction of efferent arteriole

$\downarrow$ RPF = $\uparrow$ P_{GC} = $\uparrow$ GFR



Costanzo (Physiology, 4th ed.) – Figure 6.11

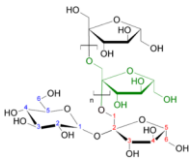
Clinical Application:

For ease of measure, creatinine (endogenous product) also commonly utilized…

Glomerular filtration rate is measured by the clearance of a glomerular marker

What makes a good marker?

1) It must be freely filtered across the glomerular capillaries (no size / charge restrictions)
2) It cannot be reabsorbed or secreted by the renal tubules
3) When infused, it cannot alter the GFR



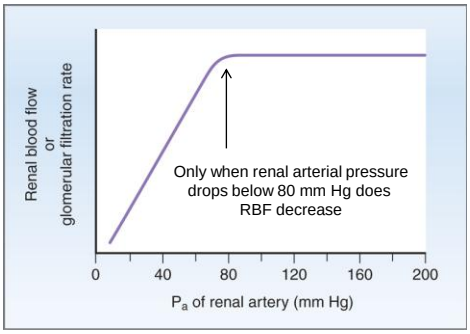
Inulin:
Fructose polymer
(~5000 daltons)

$$GRF = \frac{[U]_{inulin} \times \dot{V}}{[P]_{inulin}}$$

GFR = Glomerular filtration rate (mL / min)
$[U]_{inulin}$ = Urine concentration of inulin (mg / mL)
$[P]_{inulin}$ = Plasma concentration of inulin (mg / mL)
$\dot{V}$ = Urine flow rate (mL / min)

Glomerular Filtration:

Renal blood flow, and thus glomerular filtration rate, is autoregulated over a wide range of mean arterial pressures



Surface area (6 m^2)
Membrane permeability
} Relatively fixed…

$$GFR = K_f [(P_{GC} - P_{BS}) - \pi_{GC}]$$

Recall:

$$Q = \Delta P / R$$

Thus, changes in pressure must be countered with changes in resistance

For renal autoregulation, it is believed that resistance is controlled primarily at the level of the afferent arteriole

Costanzo (Physiology, 4th ed.) – Figure 6.6

$$Q = \Delta P / R$$

Glomerular Filtration:

The major hypotheses explaining renal autoregulation are a myogenic mechanism and tubuloglomerular feedback

Myogenic Hypothesis:
Increased arterial pressure triggers contraction of vascular smooth muscle

↑ renal arterial pressure

↓

Walls of afferent arteriole stretch

↓

Stretch-activated Ca^{2+} gates open

↓

Afferent arteriole constricts; ↑ resistance

Tubuloglomerular Feedback:
Increased [solute] sensed in DCT; triggers contraction of vascular smooth muscle

↑ renal arterial pressure

↓ ↑ GFR

↑ solute / water load in DCT

What is detected? ↓
1) Na^+ / Cl^-
2) Ca^{2+}
3) Total osmolarity

Macula densa cells detect change; send signal

What signal is sent? ↓
1) adenosine
2) prostaglandins
3) kinins

Afferent arteriole constricts; ↑ resistance

To protect against potential renal failure, prostaglandins are produced locally during stressful events and vasodilate both arterioles

Glomerular Filtration:

In addition to autoregulation, extrinsic factors also contribute to renal blood flow regulation

1) Sympathetic Nervous System
(and circulating catecholamines)

- Sympathetic nerve fibers innervate both afferent and efferent arterioles
  - Activate α_1 receptors
  - Trigger vasoconstriction

HOWEVER

- More α_1 receptors on afferent arterioles

THUS

↑ Sympathetic input = ↓ RBF = ↓ GFR

2) Angiotensin II

- Potent vasoconstrictor of both afferent and efferent arterioles

HOWEVER

- Efferent arteriole more susceptible than the afferent arteriole

THUS

Low levels of angiotensin II = ↓ RBF = ↑ GFR

BUT

High levels of angiotensin II = ↓ RBF = ↓ GFR

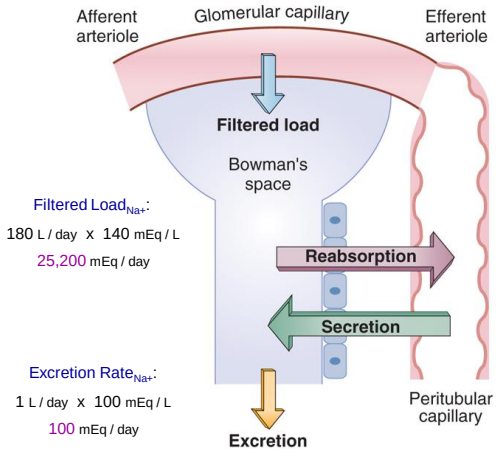
If the ultrafiltrate produced during glomerular filtration in a single day were excreted from the body unmodified, what would be lost in urine?

Ultrafiltrate / day = 180 L

Substance	Amount
Water	180 L (180 kg)
Na^+	25,200 mEq (580 g)
Cl^-	19,800 mEq (701 g)
HCO_3^-	4320 mEq (264 g)
Glucose	14.4 g

Each of the above losses represents more than 10-fold the amount present in the entire extracellular fluid of the body

Tubular Reabsorption:



Filtered Load$_{Na+}$:

180 L / day x 140 mEq / L

25,200 mEq / day

Excretion Rate$_{Na+}$:

1 L / day x 100 mEq / L

100 mEq / day

(99.4% of filtrate load)

Reabsorption Rate$_{Na+}$ = 25,200 - 100 = 25,100 mEq / day

Water and many solutes (e.g., Na^+) are reabsorbed from the filtrate into the peritubular capillaries via membrane transporters

Filtered Load:

Amount of a substance filtered into Bowman's space per unit time

$[P]_X$ = Plasma concentration of X

Filtered load = GFR x $[P]_X$

Excretion Rate:

Amount of a substance excreted in urine per unit time

$[U]_X$ = Urine concentration of X

Excretion rate = $\dot{V}$ x $[U]_X$

Reaborption rate:

Filtered load - Excretion rate

Filtered load must be greater than excretion rate for net reabsorption to occur

Costanzo (Physiology, 4th ed.) – Figure 6.12

Tubular Reabsorption:

A majority of other major nutrients (e.g., amino acids / vitamins) reabsorbed by PCT using similar mechanism

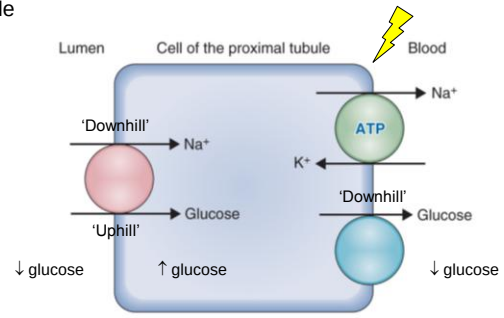
Glucose is a good example for examining the basic underlying mechanisms of tubular reabsorption of nutrients

Glucose:

- Reabsorbed in proximal convoluted tubule

Two-step Process:

1) Na^+-glucose cotransport
   - Occurs at luminal membrane
   - Na^+-glucose cotransporter (SGLT)
   - Secondary active transport
2) Facilitated glucose transport
   - Occurs at peritubular membrane
   - GLUT 1 / GLUT 2 transporters
   - Facilitated diffusion

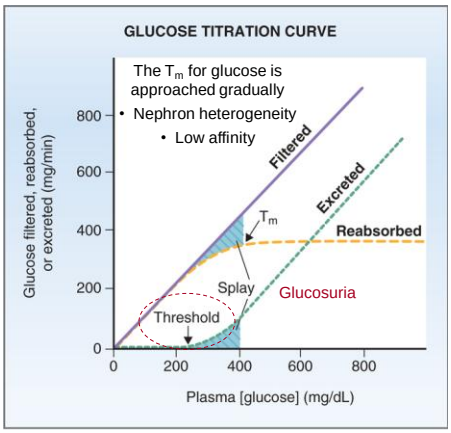


Costanzo (Physiology, 4th ed.) – Figure 6.14

Tubular Reabsorption:

Glucosuria:
Diabetes mellitus?
During pregnancy?

A glucose titration curve depicts the relationship between plasma glucose concentration and glucose reabsorption



Things to Note:

- As the plasma [glucose] increases, the filtered load increases linearly
- All glucose can be reabsorbed up to plasma [glucose] of 200 mg / dL

Transport Maximum (T_m):
Point at which all transport proteins are fully engaged (saturated)

Glucose T_m = 350 mg / dL

- Glucose starts to appear in the urine at plasma [glucose] above 200 mg / dL

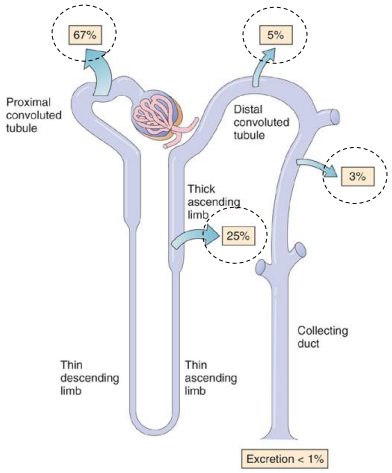
Costanzo (Physiology, 4th ed.) – Figure 6.15

Tubular Reabsorption:

Along with nutrients, the reabsorption of ions is an important component of nephron physiology

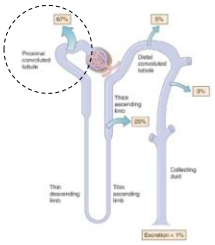
Sodium (Na^+):

- Single most abundant cation in filtrate
- 80% of active transport energy devoted to Na^+ reabsorption
- Net reabsorption of > 99% of filtered load

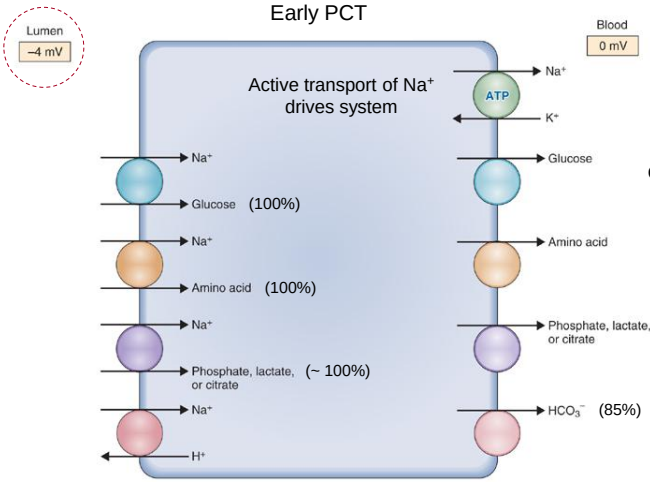


Costanzo (Physiology, 4th ed.) – Figure 6.19

Tubular Reabsorption:



Sodium (Na^+) Reabsorption

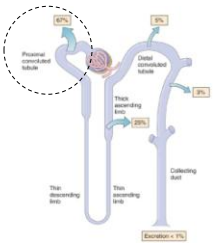


"Highest priority" reabsorptive work

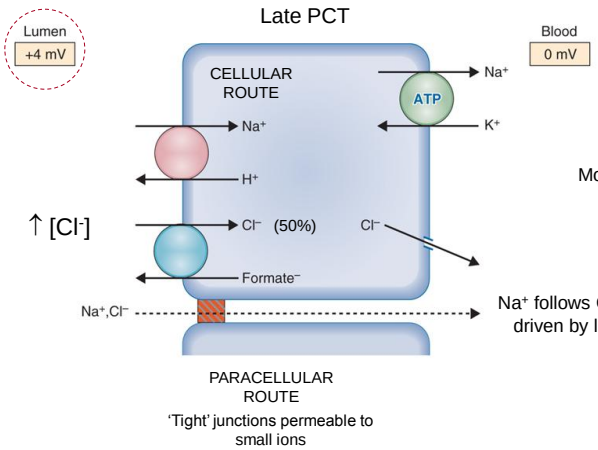
Lumen-negative potential:
Co-transport of Na^+- glucose and Na^+- amino acid bring (+) charge in while leaving (-) in lumen

Costanzo (Physiology, 4th ed.) – Figure 6.20

Tubular Reabsorption:



Sodium (Na^+) Reabsorption



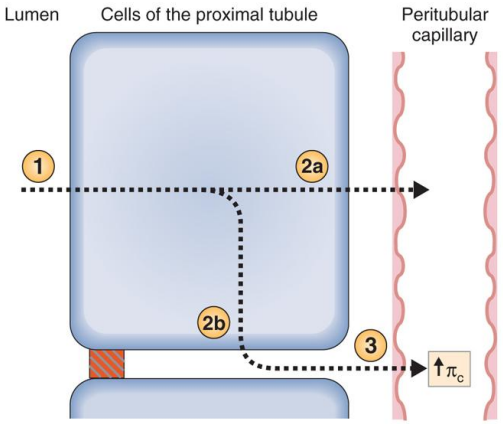
Lumen-positive potential:
Movement of Cl^- down its [gradient] leaves (+) charges in filtrate

Na^+ follows Cl^- through tight junctions driven by lumen-positive potential

Costanzo (Physiology, 4th ed.) – Figure 6.21

Tubular Reabsorption:

Solute and water reabsorption are coupled and are proportional to each other in the PCT – Isosmotic reabsorption



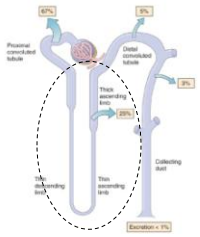
Isosmotic Reabsorption:

1) Na^+ enters cell; water follows passively
2) Na^+ actively pumped out of basolateral membrane; water follows passively
3) Isosmotic fluids collect in lateral intra-cellular space; high osmotic pressure in peritubular capillary drives reabsorption

67% of solute absorbed in PCT
67% of water absorbed in PCT

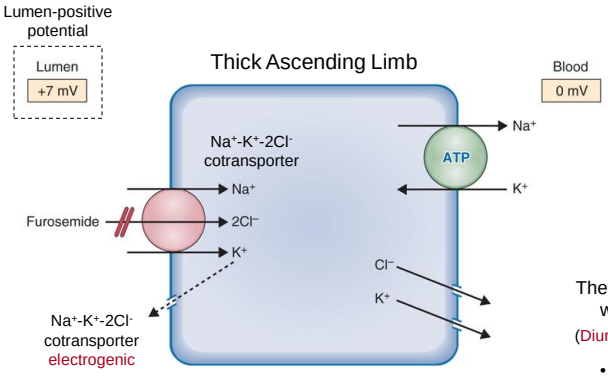
Costanzo (Physiology, 4th ed.) – Figure 6.22

Tubular Reabsorption:



Sodium (Na^+) Reabsorption

Na^+ moves freely into / out of the thin portions of the loop of Henle but there is no net reabsorption



Water is NOT reabsorbed with solutes in this region (diluting segment)

Reabsorption mechanism is load-dependent; the more Na^+ delivered to the region, the more the region reabsorbs

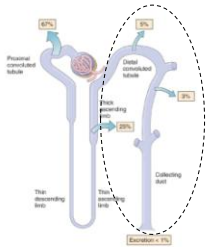
The most potent diuretics, loop diuretics, work at this site (block cotransporters)
(Diuretic = Drug that elevates rate of urination)

- Furosemide
- Bumetanide

} Can block up to 25% of Na^+ reabsorption

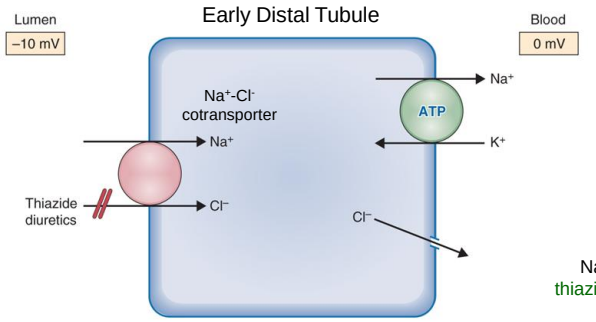
Costanzo (Physiology, 4th ed.) – Figure 6.24

Tubular Reabsorption:



Sodium (Na^+) Reabsorption

Like the loop of Henle, the DCT and collecting duct exhibit load-dependent Na^+ reabsorption

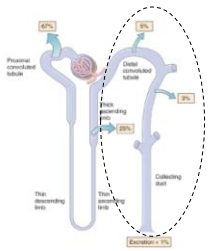


NaCl reabsorption inhibited by thiazide diuretics (block cotransporters)

Water is NOT reabsorbed with solutes in this region (cortical diluting segment)

Costanzo (Physiology, 4th ed.) – Figure 6.25

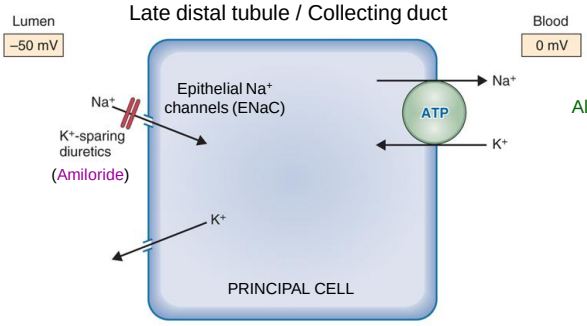
Tubular Reabsorption:



Sodium (Na^+) Reabsorption

Like the loop of Henle, the DCT and collecting duct exhibit load-dependent Na^+ reabsorption

(only 3% Na^+ reabsorbed; fine-tuning)



Aldosterone regulates activity in cell:

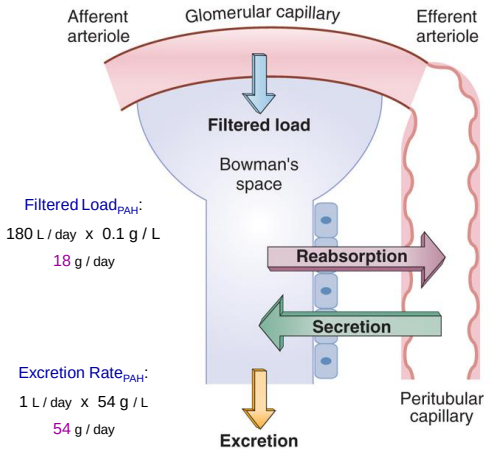
1) ↑ ENaC proteins
2) ↑ Na+-K+ ATPase
3) ↑ enzymes (citric acid cycle)

NaCl reabsorption inhibited by K^+-sparing diuretics (block ENaCs)

Water reabsorption is variable (hormone dependent)

Costanzo (Physiology, 4th ed.) – Figure 6.26

Tubular Secretion:



Filtered Load$_{PAH}$:

180 L / day x 0.1 g / L

18 g / day

Excretion Rate$_{PAH}$:

1 L / day x 54 g / L

54 g / day

Secretion Rate$_{PAH}$ = 54 - 18 = 36 g / day

A few substances (e.g., organic acids / bases) are secreted from peritubular capillary blood into tubular fluid by way of membrane transporters

Filtered Load:

Amount of a substance filtered into Bowman's space per unit time

$[P]_X$ = Plasma concentration of X

Filtered load = GFR x $[P]_X$

Excretion Rate:

Amount of a substance excreted in urine per unit time

$[U]_X$ = Urine concentration of X

Excretion rate = $\dot{V}$ x $[U]_X$

Secretion rate:

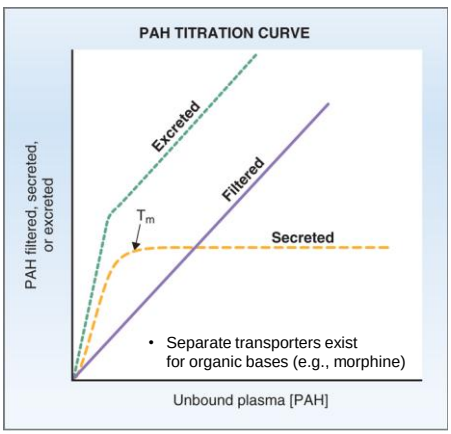
Excretion rate - Filtration load

Excretion rate must be greater than filtration load for net secretion to occur

Costanzo (Physiology, 4th ed.) – Figure 6.12

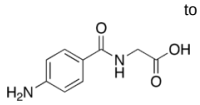
Tubular Reabsorption:

A PAH titration curve depicts the relationship between plasma PAH concentration and PAH secretion



• Transporters for PAH located in peritubular capillaries of PCT

10% bound to blood proteins



Para-aminohippuric acid (PAH)

Things to Note:

- As the plasma [PAH] increases, the filtered load increases linearly
- As with reabsorption, a transport maximum exists for PAH
- At [low] PAH, steep excretion rate; at [high], rate declines as T_m reached

Also transport antibiotics (e.g., penicillin)

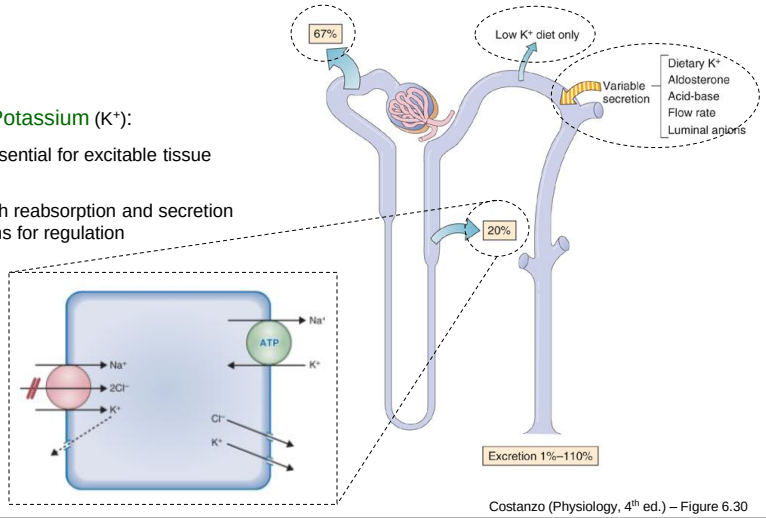
Costanzo (Physiology, 4th ed.) – Figure 6.17

Tubular Reabsorption / Secretion:

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology

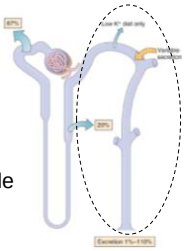
Potassium (K^+):

- Balance essential for excitable tissue function
- Utilizes both reabsorption and secretion mechanisms for regulation



Costanzo (Physiology, 4th ed.) – Figure 6.30

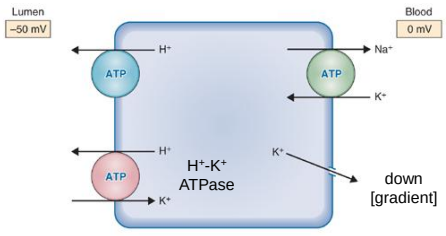
Tubular Reabsorption:



Potassium (K^+) Reabsorption / Secretion

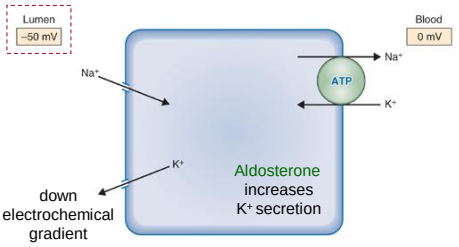
The distal convoluted tubule and collecting ducts are responsible For the fine adjustments to K^+ reabsorption / secretion

K^+ reabsorption is handled by the α-intercalated cells



Relatively uncommon; most often associated with low K^+ diet

K^+ reabsorption is handled by the principal cells



Associated with individuals having normal / high K^+ diet

The magnitude of K^+ secretion is determined by the size of the electrochemical gradient

Costanzo (Physiology, 4th ed.) – Figure 6.31

Tubular Reabsorption / Secretion:

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology

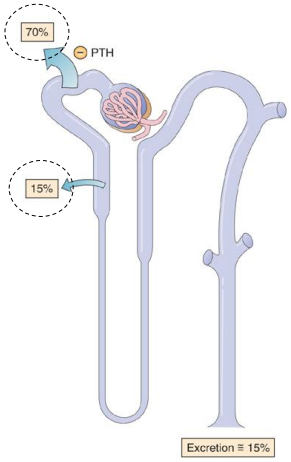
Phosphate (HPO_4^-):

- Important ion for bone and as a urinary buffer for H^+
- Only reabsorbed at PCT

Parathyroid hormone blocks reabsorption

- G-protein coupled system inhibits Na^+-phosphate cotransport leaving phosphate in tubule lumen

Psuedohypoparathyroidism:
Although circulating levels of PTH are high, PTH cannot produce its phosphaturic effects due to renal cells being resistant to PTH action



Costanzo (Physiology, 4th ed.) – Figure 6.32

Urinary System

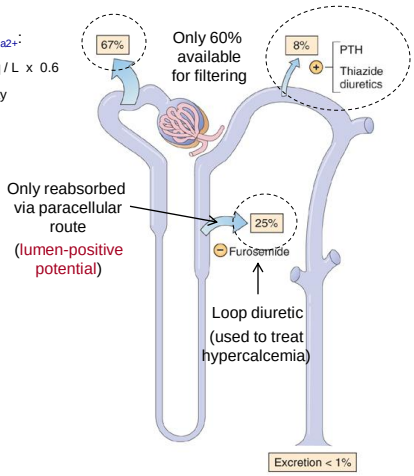
Tubular Reabsorption / Secretion:

Along with nutrients, the reabsorption / secretion of ions is an important component of nephron physiology

Filtered Load$_{Ca2+}$:
180 L / day x 5 mEq / L x 0.6
540 mEq / day

Calcium (Ca^{2+}):

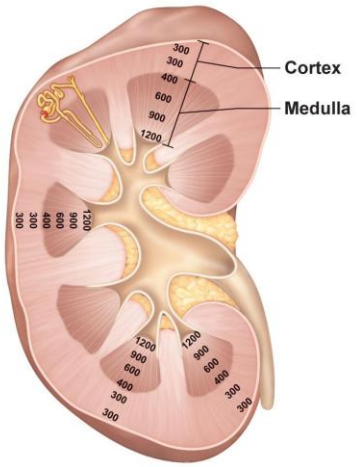
- Important ion for bone and excitable tissue function
- Pattern of reabsorption similar to sodium
- Regulation of Ca^{2+} occurs at DCT



Costanzo (Physiology, 4th ed.) – Figure 6.32

Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant,
at about 300 mOsm



Corticopapillary osmotic gradient:
A gradient of osmolarity in the interstitial fluid of the kidney from the cortex to the papilla rhat allows the kidney to vary urine concentration / volume

What solutes contribute to the osmotic gradient?

What mechanisms deposit these solutes in the interstitial fluid?

1) Countercurrent multiplication
2) Urea recycling

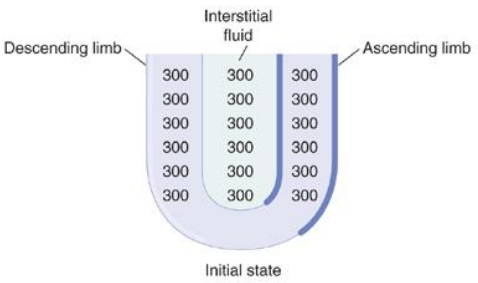
Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.15

Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant,
at about 300 mOsm

1) Countercurrent Multiplication

A function of the loops of Henle, which deposit NaCl in the deeper regions of the medulla



Things to Recall:

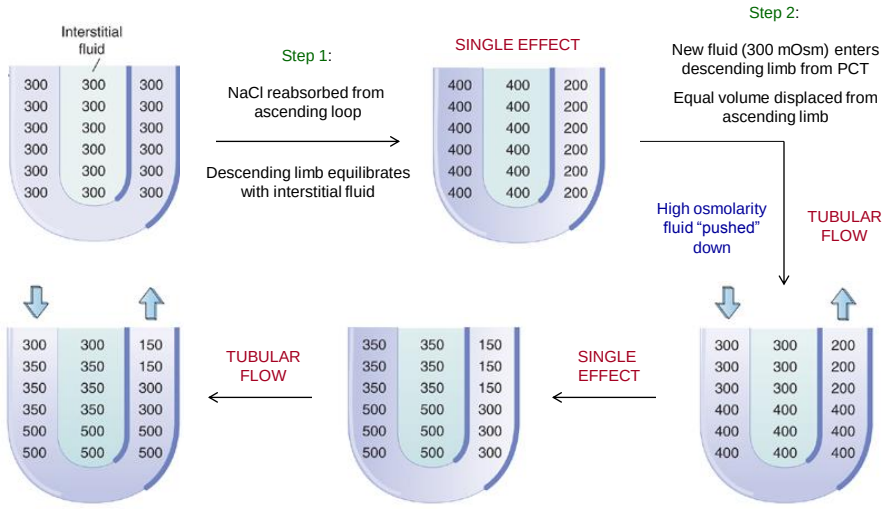
1) The thick, ascending limb of the loop of Henle reabsorbs NaCl
   Na^+-K^+-$2Cl^-$ cotransporter
2) The thick, ascending limb of the loop of Henle is impermeable to water

Costanzo (Physiology, 4th ed.) – Figure 6.37

Regulation of Urine Volume / Concentration:

The size of the corticopapillary gradient depends on the length of the loop of Henle
(Humans = 1200 mOsm)

1) Countercurrent Multiplication



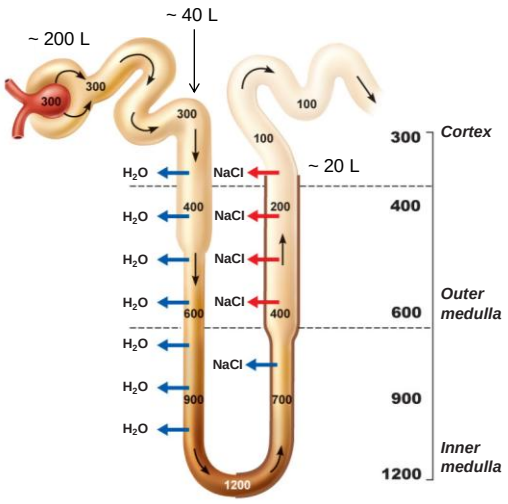
Costanzo (Physiology, 4th ed.) – Figure 6.37

Regulation of Urine Volume / Concentration:

Note:
Constant 200 mOsm difference between two limbs of the loop of Henle

- Limit of NaCl pump power

1) Countercurrent Multiplication



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.16

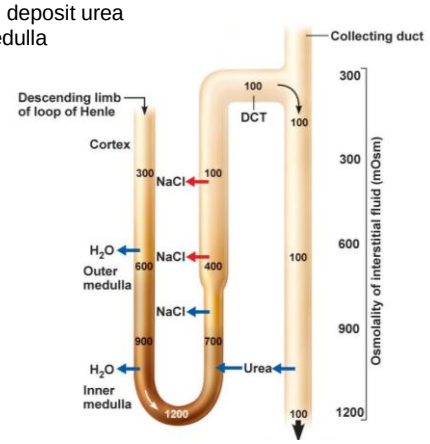
Regulation of Urine Volume / Concentration:

The kidneys keep the solute load of body fluids constant, at about 300 mOsm

2) Urea Recycling

A function of the collecting ducts, which deposit urea in the deeper regions of the medulla

Urea enters the interstitial fluid via diffusion from the inner medullary collecting ducts and moves down gradient into ascending limb of loop of Henle via facilitated diffusion

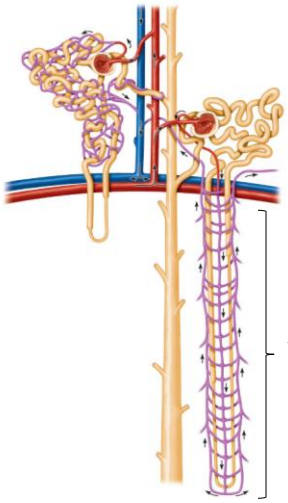


Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.16

Costanzo (Physiology, 4th ed.) – Figure 6.39

Regulation of Urine Volume / Concentration:

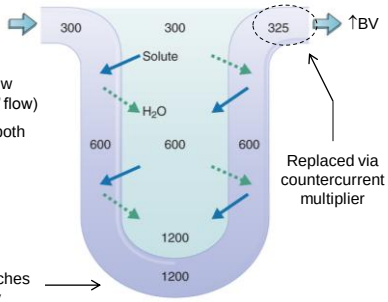
The vasa recta are specialized capillary beds that serve the medulla and papilla of the kidney



Vasa recta participates in countercurrent exchange

- Countercurrent multiplier established gradient (active process)
- Countercurrent exchange maintains gradient (passive process)

- Only 5% of renal blood flow serves medulla ('sluggish' flow)
- Capillaries permeable to both water and solutes



Capillary osmolarity matches interstitial osmolarity

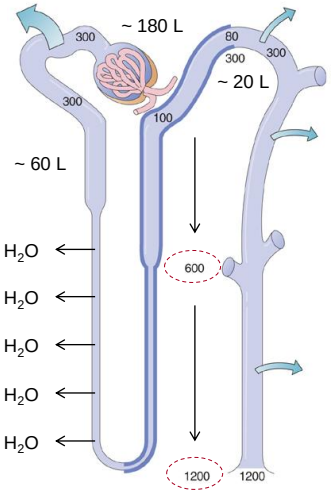
Picks up water additional lost from the loop of Henle

Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.7

Regulation of Urine Volume / Concentration:

Occurs when circulating levels of ADH are high

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)



Formation of Concentrated Urine (~ 1200 mOsml)

- 1 ml fluid / min produced (~ 1.5 L urine / day)

1) The PCT pulls out solutes and water in equal proportions (~ 67%)

   Remember: Isosmotic reabsorption

2) The thick, ascending limb of the loop of Henle actively reabsorbs NaCl (Na^+-K^+-$2Cl^-$ cotransporter); cells impermeable to water

   ADH increases activity of Na^+-K^+-$2Cl^-$ cotransporters leading to enhanced single effect (e.g., steeper gradient)

3) In early DCT, NaCl reabsorbed (Na^+-Cl^- cotransporter); cells impermeable to water

   Filtrate osmolarity reduced to ~ 80 mOsm

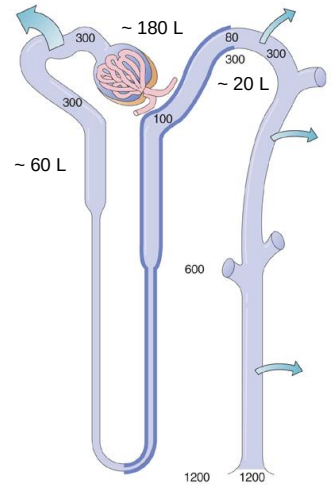
Costanzo (Physiology, 4th ed.) – Figure 6.41

Urinary System

Regulation of Urine Volume / Concentration:

Occurs when circulating levels of ADH are high

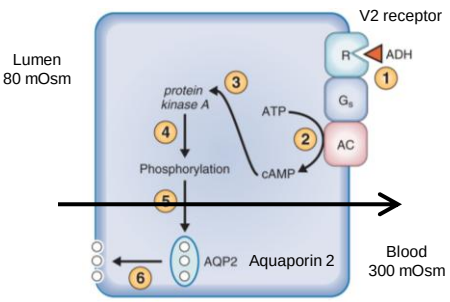
Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)



Formation of Concentrated Urine (~ 1200 mOsml)

- 1 ml fluid / min produced (~ 1.5 L urine / day)

4) In late DCT, the principle cells are permeable to water in the presence of ADH

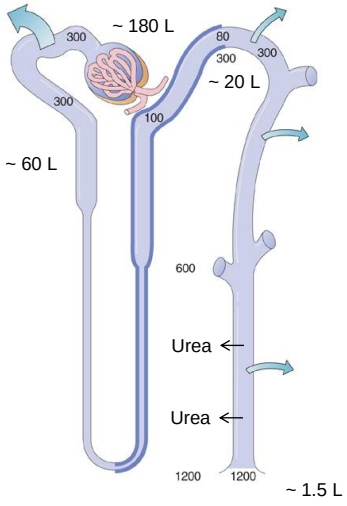


Costanzo (Physiology, 4th ed.) – Figures 6.40 / 6.41

Regulation of Urine Volume / Concentration:

Occurs when circulating levels of ADH are high

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)



Formation of Concentrated Urine (~ 1200 mOsml)

- 1 ml fluid / min produced (~ 1.5 L urine / day)

5) In collecting duct, the principle cells are also permeable to water in the presence of ADH

ADH increases urea recycling in the inner medullary collecting duct via the insertion of urea UT1 transporters

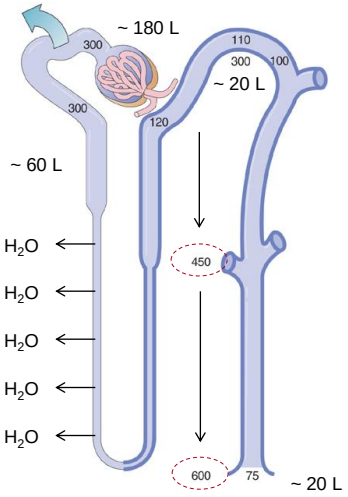
- Urea flows down concentration gradient; enhances corticopapillary osmotic gradient

Costanzo (Physiology, 4th ed.) – Figure 6.41

Regulation of Urine Volume / Concentration:

Occurs when circulating levels of ADH are low

Dilute or concentration urine can be formed depending on the presence / absence of antidiuretic hormone (ADH)



Formation of Dilute Urine (~ 75 mOsml)

- 15 – 19 ml fluid / min produced (~ 22.5 L urine / day)

1) The PCT pulls out solutes and water in equal proportions (isosmotic reabsorption)

2) The thick, ascending limb of the loop of Henle actively reabsorbs NaCl (Na^+-K^+-$2Cl^-$ cotransporter); cells impermeable to water

Corticopapillary osmotic gradient diminished in absence of ADH (↓ transporter activity)

3) In early DCT, NaCl reabsorbed (Na^+-Cl^- cotransporter); cells impermeable to water

4) Late DCT collecting ducts impermeable to water; limited NaCl reabsorbed

Limited urea recycled

Costanzo (Physiology, 4th ed.) – Figure 6.42

Regulation of Urine Volume / Concentration:

Diuretics are chemicals that elevate rates of urination

Pharmacological Drugs:

- Treat hypertension / edema

Furosemide

1) Loop diuretics — Most potent diuretic

- Block Na^+ reabsorption in thick, ascending loop of Henle

Isoren

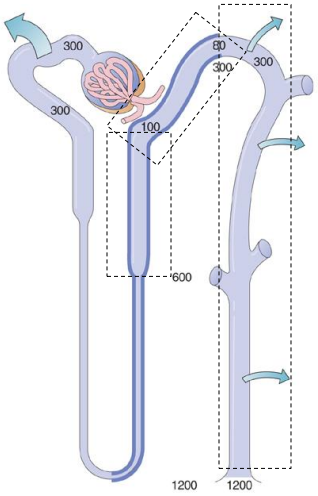
2) Thiazide diuretics

- Block Na^+ reabsorption in early distal convoluted tubule

Amiloride

3) K^+ sparing diuretics

- Block Na^+ reabsorption in late DCT / collecting ducts



Weak diuretic; Targets PCT

Weak diuretic; Blocks ADH release

Costanzo (Physiology, 4th ed.) – Figure 6.41

Pathophysiology:

Conditions which affect ADH release / action can lead to abnormal urine flow rates

Inappropriate Formation of Dilute Urine

Central Diabetes Insipidus:
Circulating levels of ADH abnormally low

Cause: Trauma / tumor

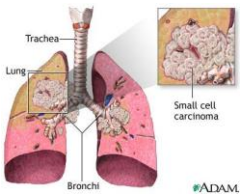
Treatment: Drugs which act as ADH analogues (e.g., dDAVP)

Nephrogenic Diabetes Insipidus:
Circulating levels of ADH normal; principal cells of kidney unresponsive to hormone

Cause: Defect in 2nd messenger system (e.g., genetic)

Treatment: Thiazide diuretics; triggers ↑ water reabsorption in PCT

Inappropriate Formation of Concentrated Urine



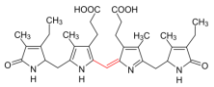
(tumor)

Syndrome of Inappropriate ADH (SIADH):
Circulating levels of ADH abnormally high

Cause: Trauma / tumor

Treatment: Drugs which block ADH activity (e.g., demeclocyline)

Urine:



Urochrome:
Pigment produced by gut flora;
waste product of RBC destruction

Physical Characteristics of Urine:

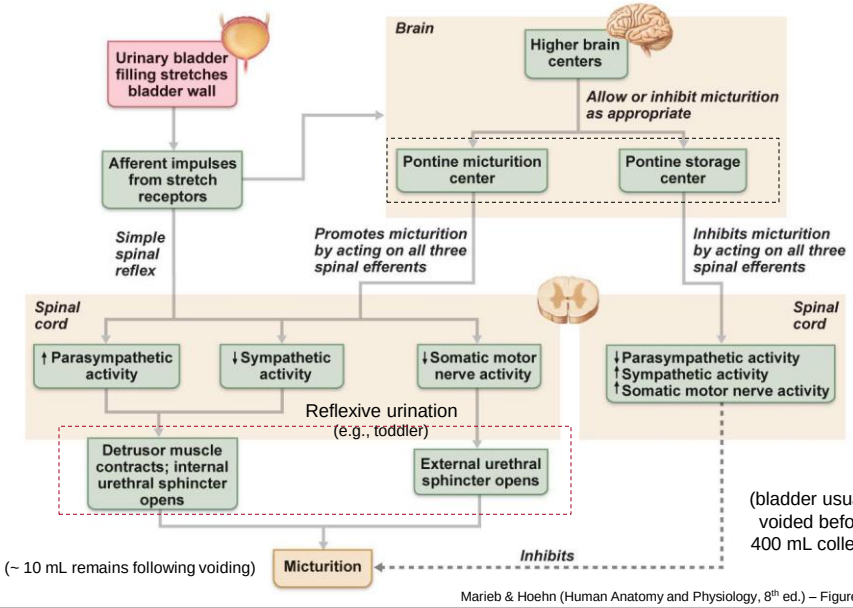
1) Color & Transparency
Dilute = clear / pale yellow
Concentrated = deep yellow

2) Odor
Fresh = slight odor
Old = ammonia-like odor
(bacterial metabolism)

3) pH
Acidic (pH ~ 6)

Micturition:

Incontinence:
The inability to voluntarily control micturition



Marieb & Hoehn (Human Anatomy and Physiology, 8th ed.) – Figures 25.22