RENAL SYSTEM

Osmoregulation
Extracellular vs Intracellular Water
Osmotic Equilibrium & Water Balance
Kidney Anatomy: structure & blood flow
Kidney Physiology:
Filtration & Glomerular Filtration Rate
Reabsorption (convoluted tubules, loop of Henle, col. duct)
Secretion and Excretion (collecting duct)

Reading: Chapters 17 & 18

Osmoregulation

Maintaining osmotic balance

(non-nutritional homeostasis)

Distribution of body fluids

Intracellular Fluid = ICF fluid inside cell

Extracellular Fluid = ECF fluid outside cell

Fluid Distribution in a 67 kg individual

Water = 60% of body weight

(0.6) x 67 kg = 40 liters of water

Water is divided into 2 compartments: ICF = 60%

ECF = 40%

Fluid Distribution in a 67 kg individual

ICF	ECF
60% of body water	40% of body water
25 L (60% of 40L)	15 L (40% of 40L)
Cytoplasm	Plasma (3 L) Interstitial Fluid (12L)
More Proteins	
High in K^+	High in Na^+ and Cl^-
Ions & nutrients	Ions, nutrients, wastes
300 mOsm	300 mOsm

**** Osmotic Equilibrium ****

What is osmosis?

Non-nutritional homeostasis

Involves: -ion concentration of body fluids

-volume of body fluids

-why is this important?

There are many strategies for maintaining osmotic equilibrium

Mammals Balance Water Intake with Water Loss

Water Loss	**Water Intake**
850 ml (skin & lungs)	750 ml (moist foods)
150 ml (feces)	1500 ml (liquids)
1500 ml (urine)	250 ml (metabolism)
2500 ml (total)	**2500 ml (total)**

Sites of Regulation

1. THIRST: -variable sensitivity in humans

2. Osmoregulation in KIDNEYS (urine production)
   - -principle regulation of water loss
   - -wide variety of consumption:
     - *we get 400 to 2500 ml of water/day
     - *we get 10 to 25 000 mg of NaCl/day

   BUT, Osmolality of body fluids changes by <1% !

There is an obligatory water loss of ~400 ml (why?)

Mammalian Kidney

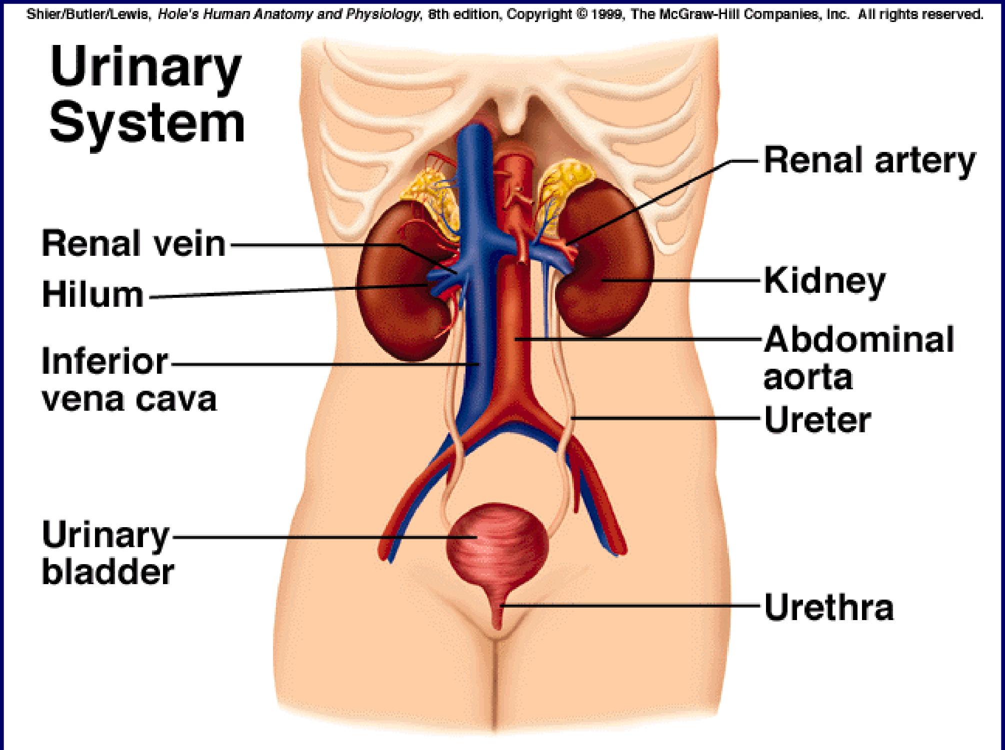
Three Main Functions:

1. Remove wastes
2. Regulate fluid volume
3. Regulate ion concentrations
4. *Are there any other functions?*

Kidney Anatomy

Location -lateral to vertebral column

-by 11th & 12th ribs



Kidney Anatomy

Landmarks: -Hilum = point of exit/entry for blood vessels & ureter

-Capsule = protective fibrous layer

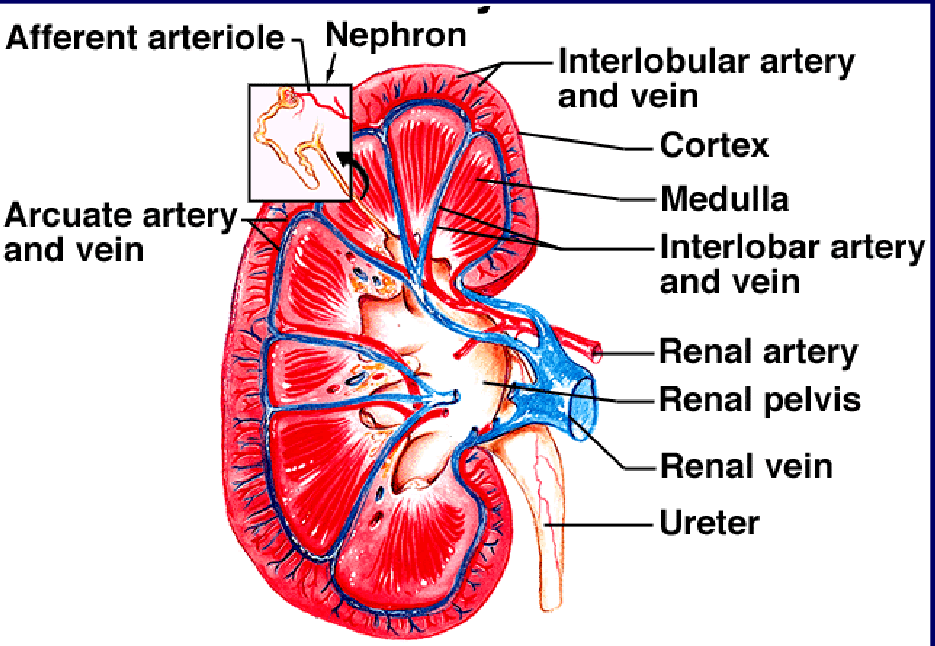
-Outer Layer = Cortex (granular)

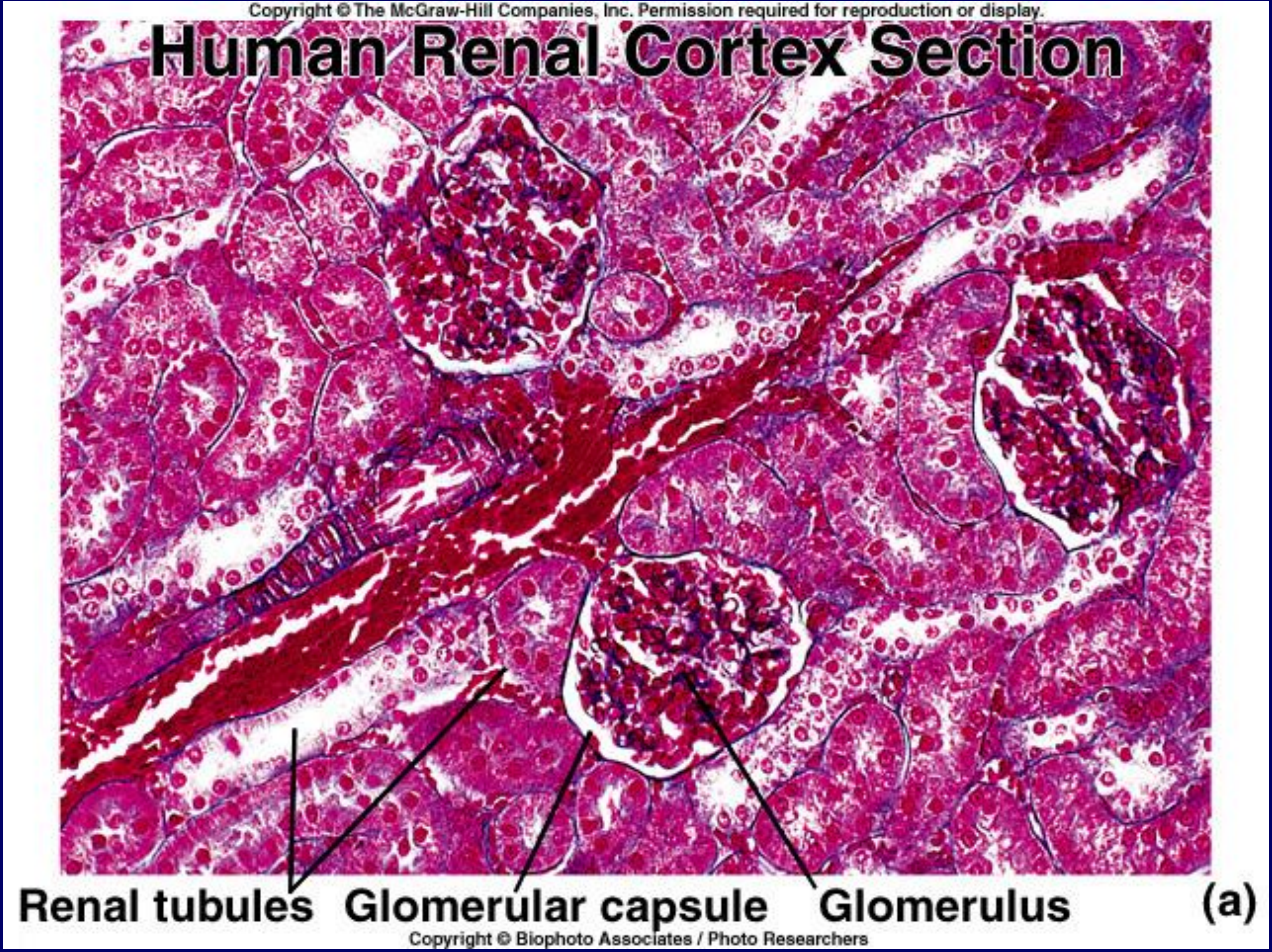
Bowman's Capsules

-Inner Layer = Medulla (striated)

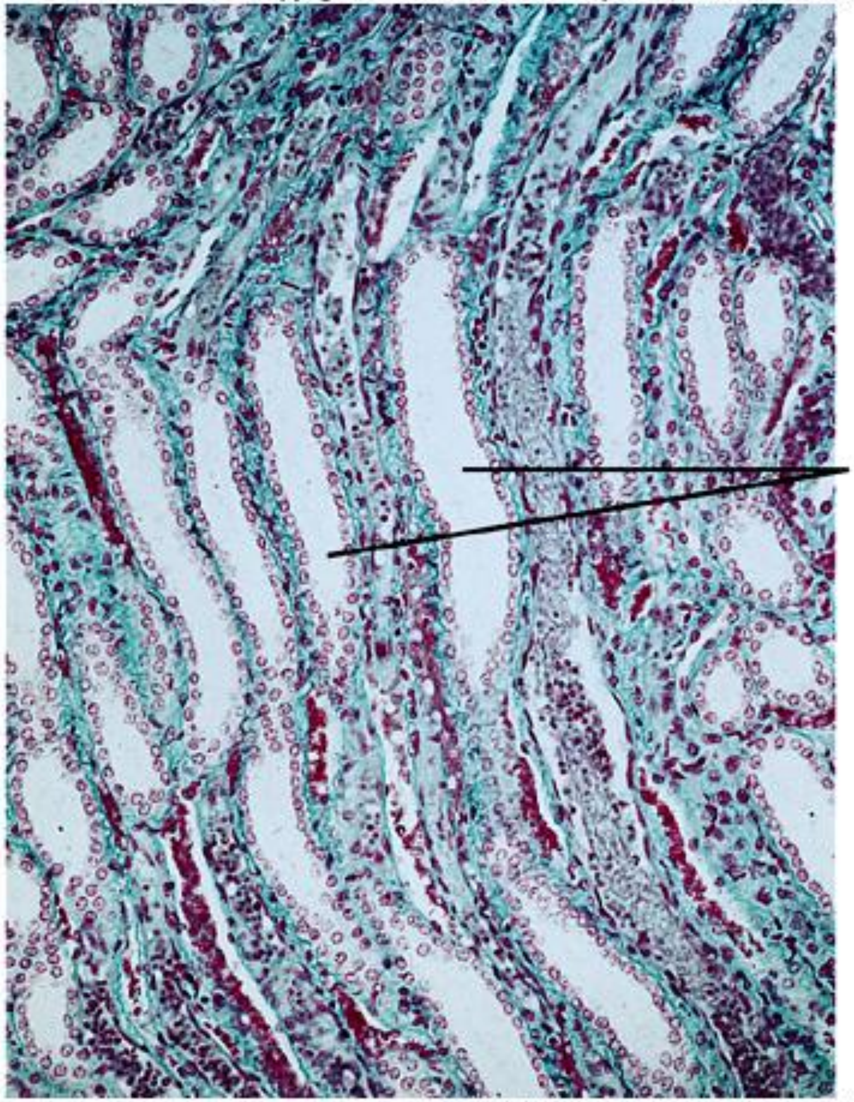
Renal Pyramids

Loops of Henle & Collecting




Human Renal Cortex Section
Renal tubules
Glomerular capsule
Glomerulus
(a)

Renal Medulla



Flow of Filtrate

Collecting Duct

Minor Calyx

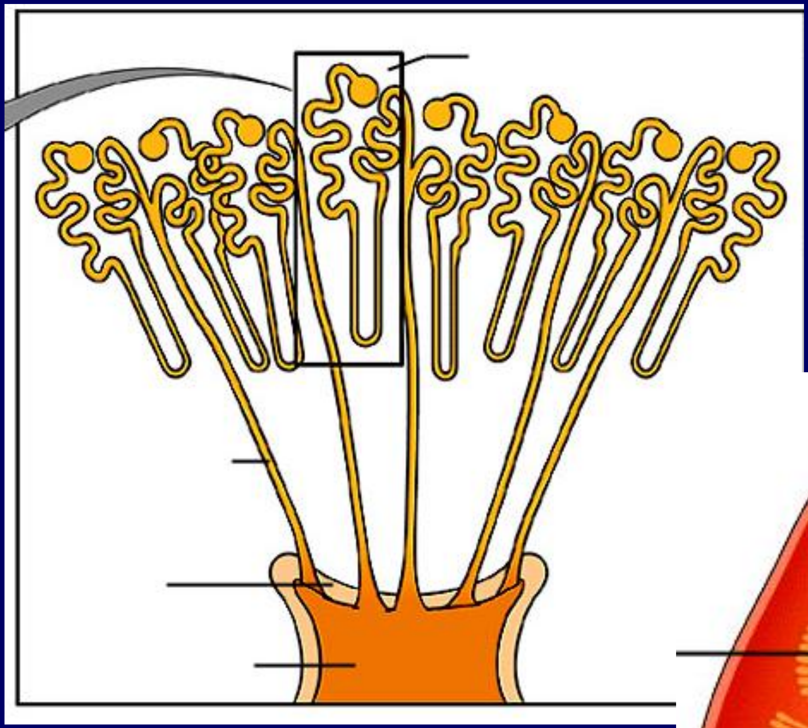
Major Calyx

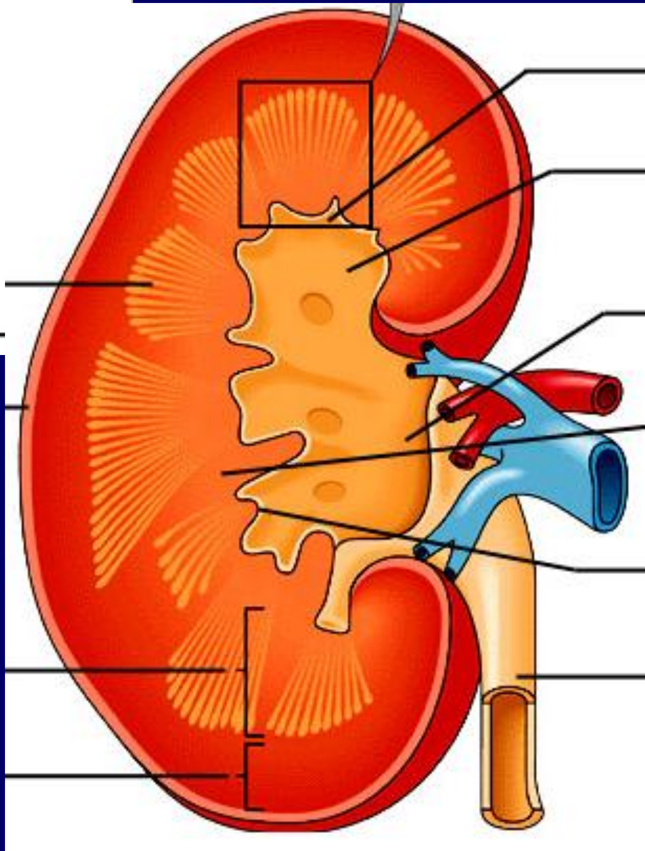
Renal Pelvis

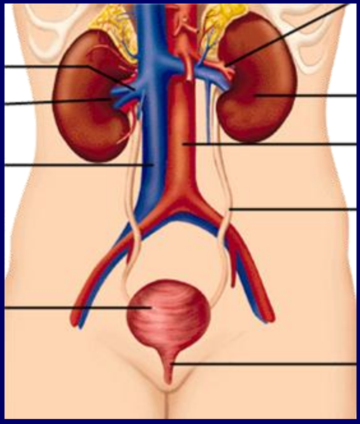
Ureter (peristalsis)

Urinary Bladder

Urethra







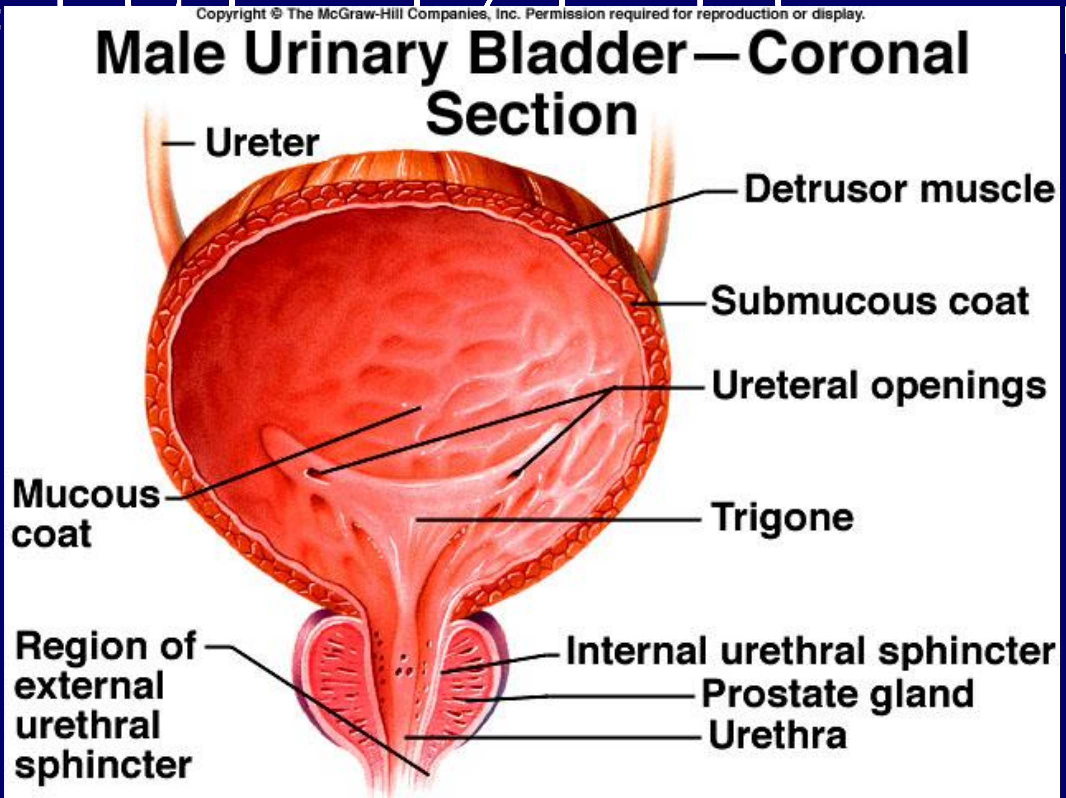
Urinary Bladder

-Stores Urine (200-300 ml = ~ 1 cup)

-Stretch receptors → spinal cord → internal sphincter relaxes (smooth)

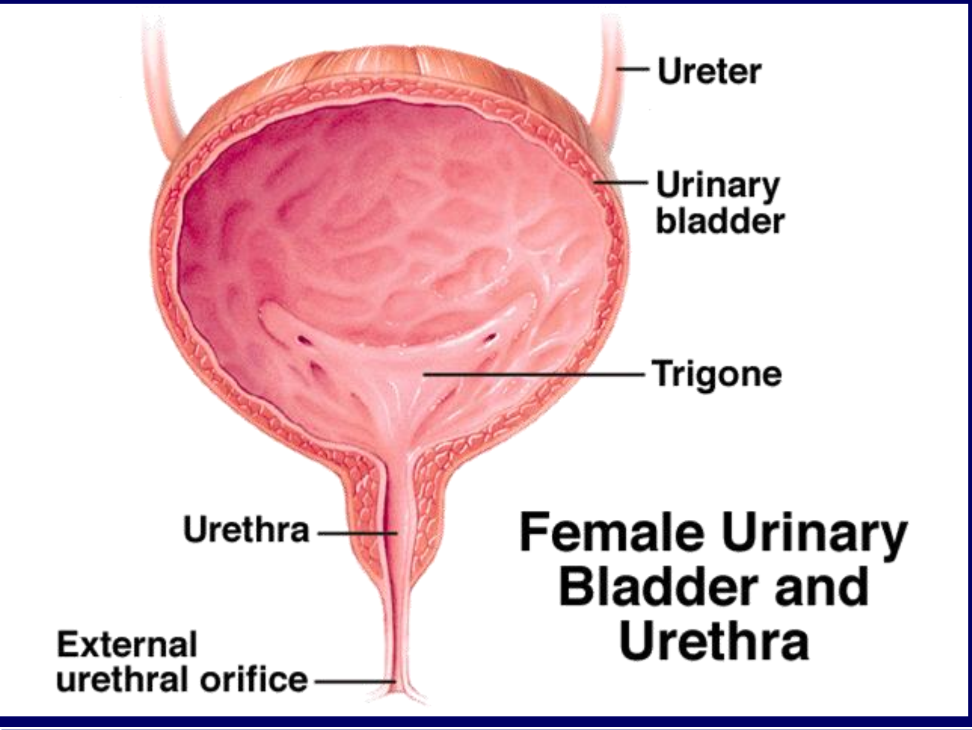
-External sphincter = … priate)

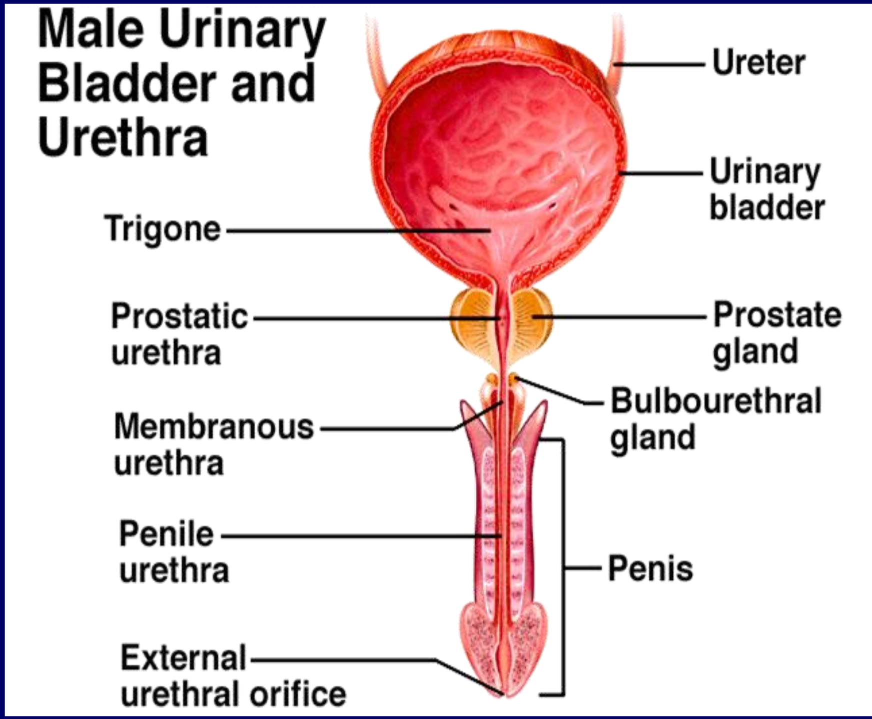
-Epithelial type?



Urethra

-Tube that carries urine out of the body
-1.5” in females, separate from reproductive system
-8” in males, it has both urinary & reproductive functions





Cystitis = inflammation of urethra & bladder
10 x more common in females? Why? Treatment?

Blood Supply

Aorta

↓

Renal Artery

↓

Peripheral Branches (*interlobar, arcuate, interlobular arteries*)

↓

Afferent Arteriole (takes blood to glomerulus)

↓

Glomerulus (ball of capillaries)

↓

Efferent Arteriole (takes blood away)

↓

Peritubular capillaries *(vasa recta)*

↓

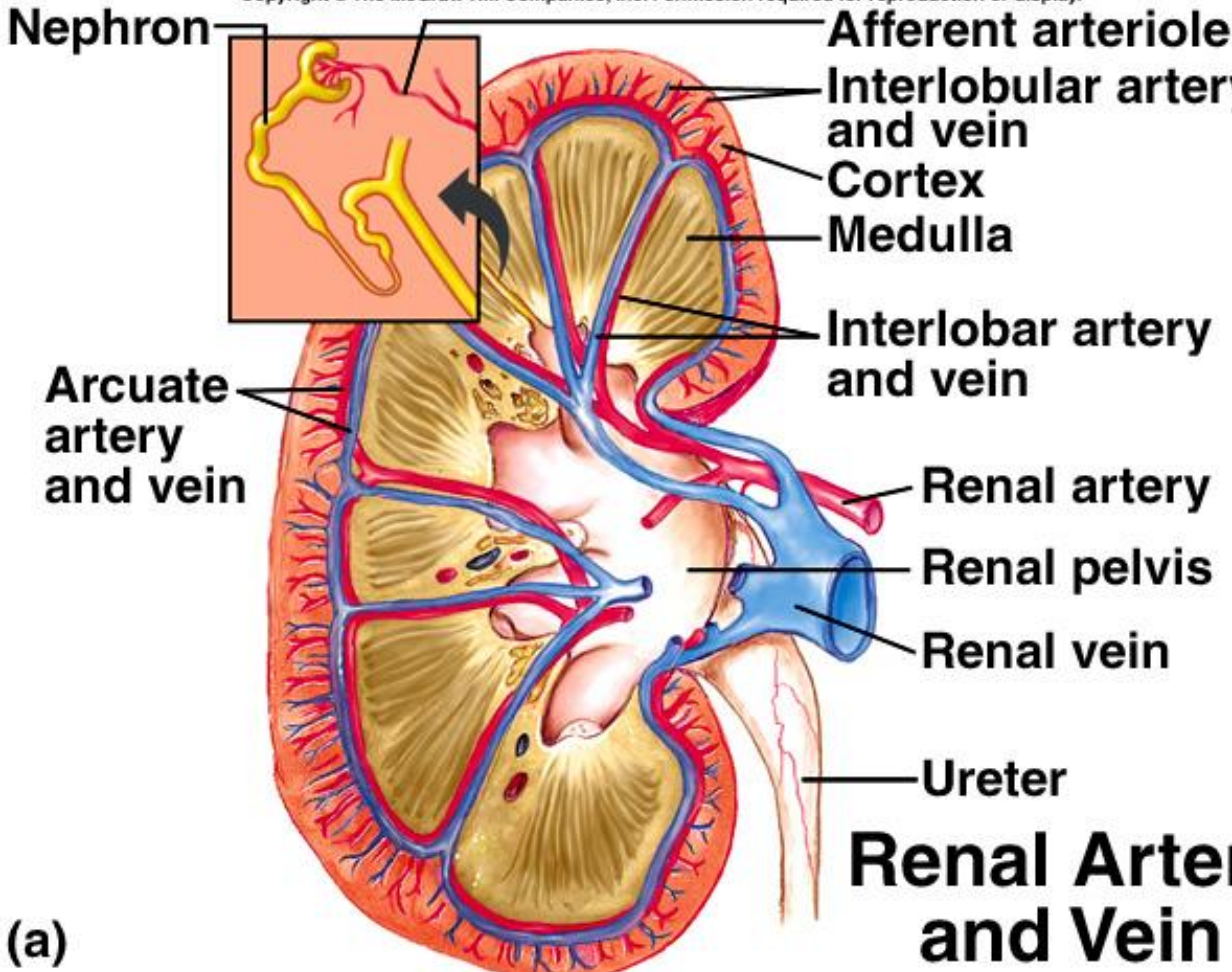
Peripheral Branches (*interlobular, arcuate, interlobar veins*)

↓

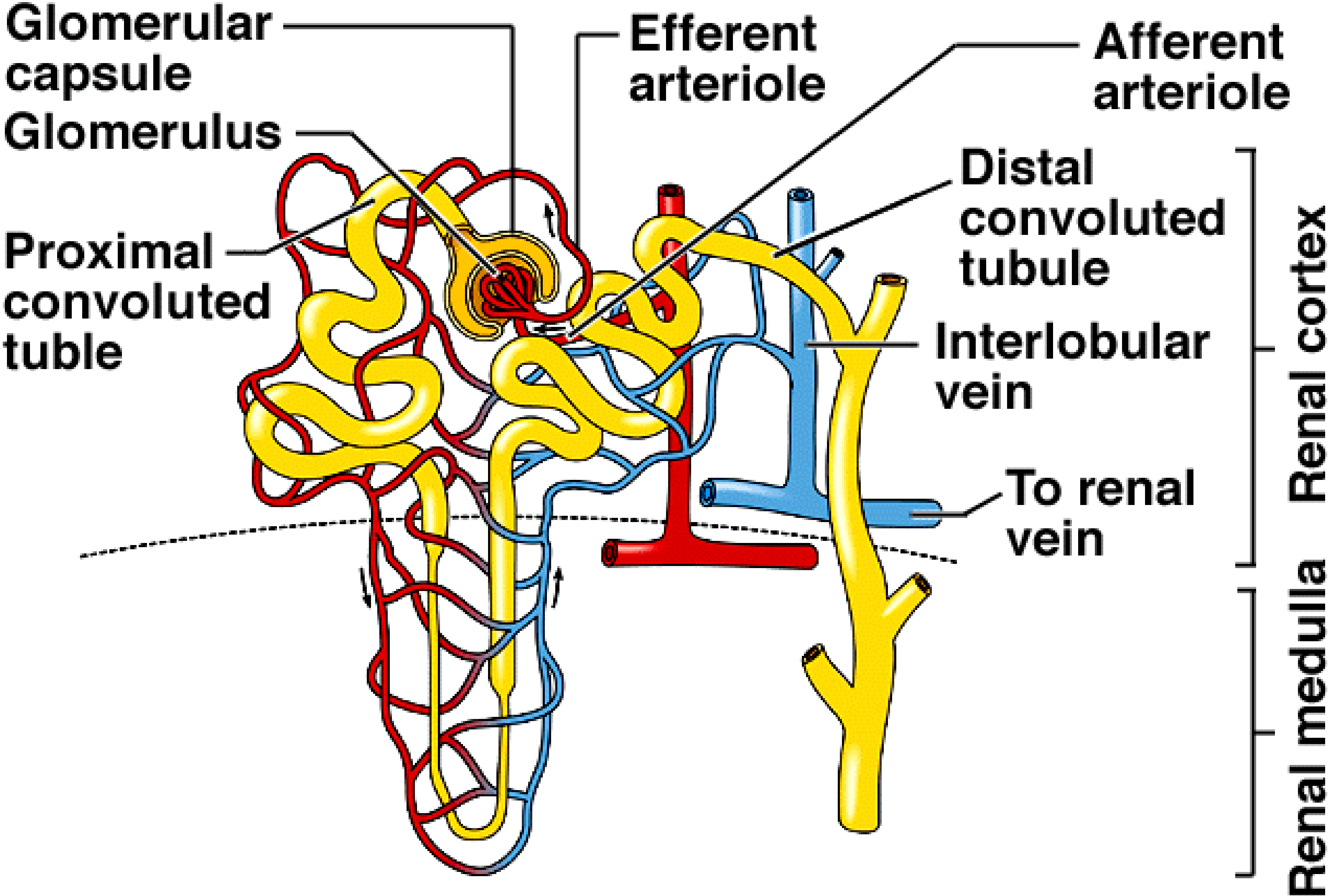
Renal Vein

↓

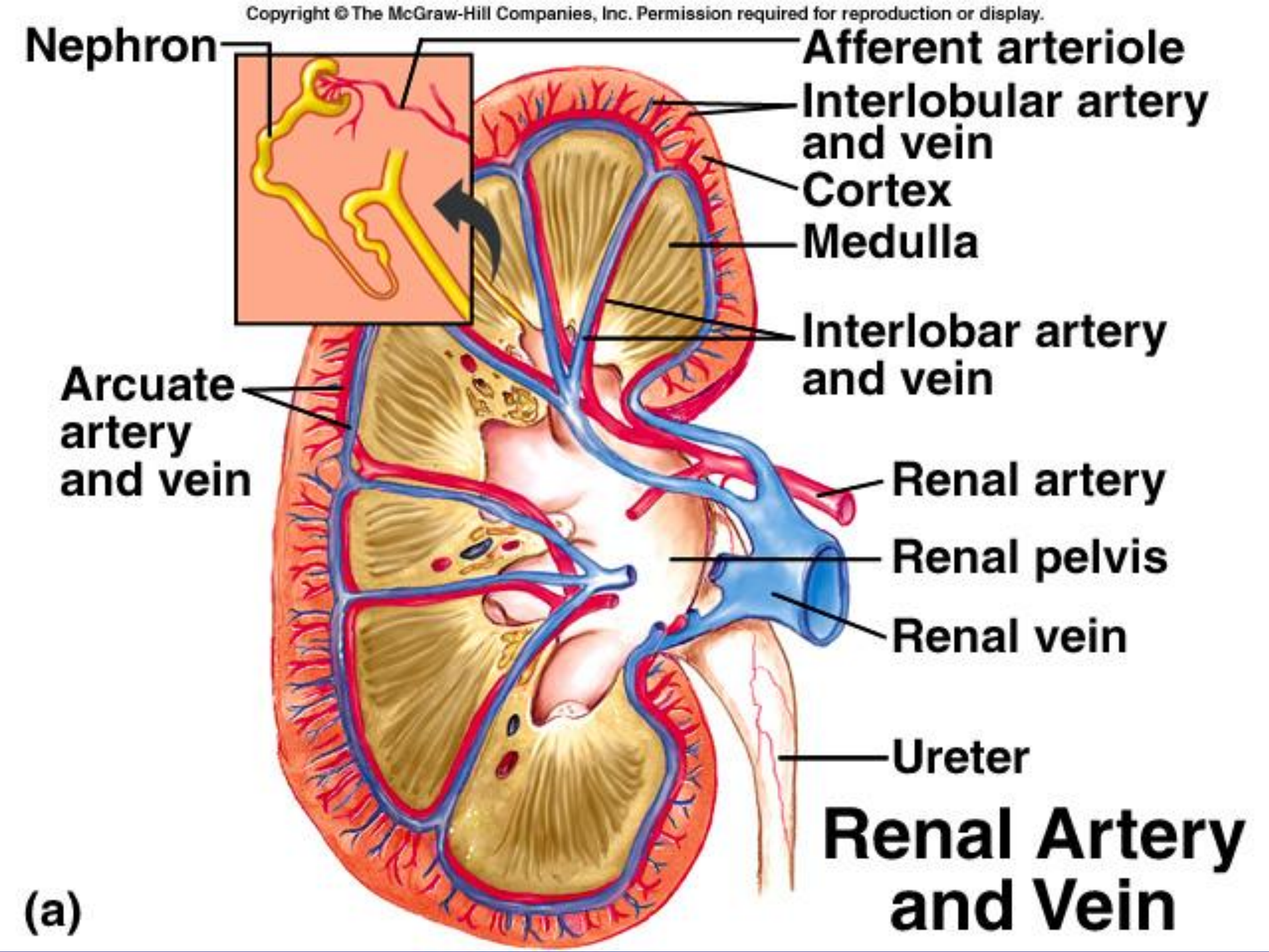
Inferior Vena Cava



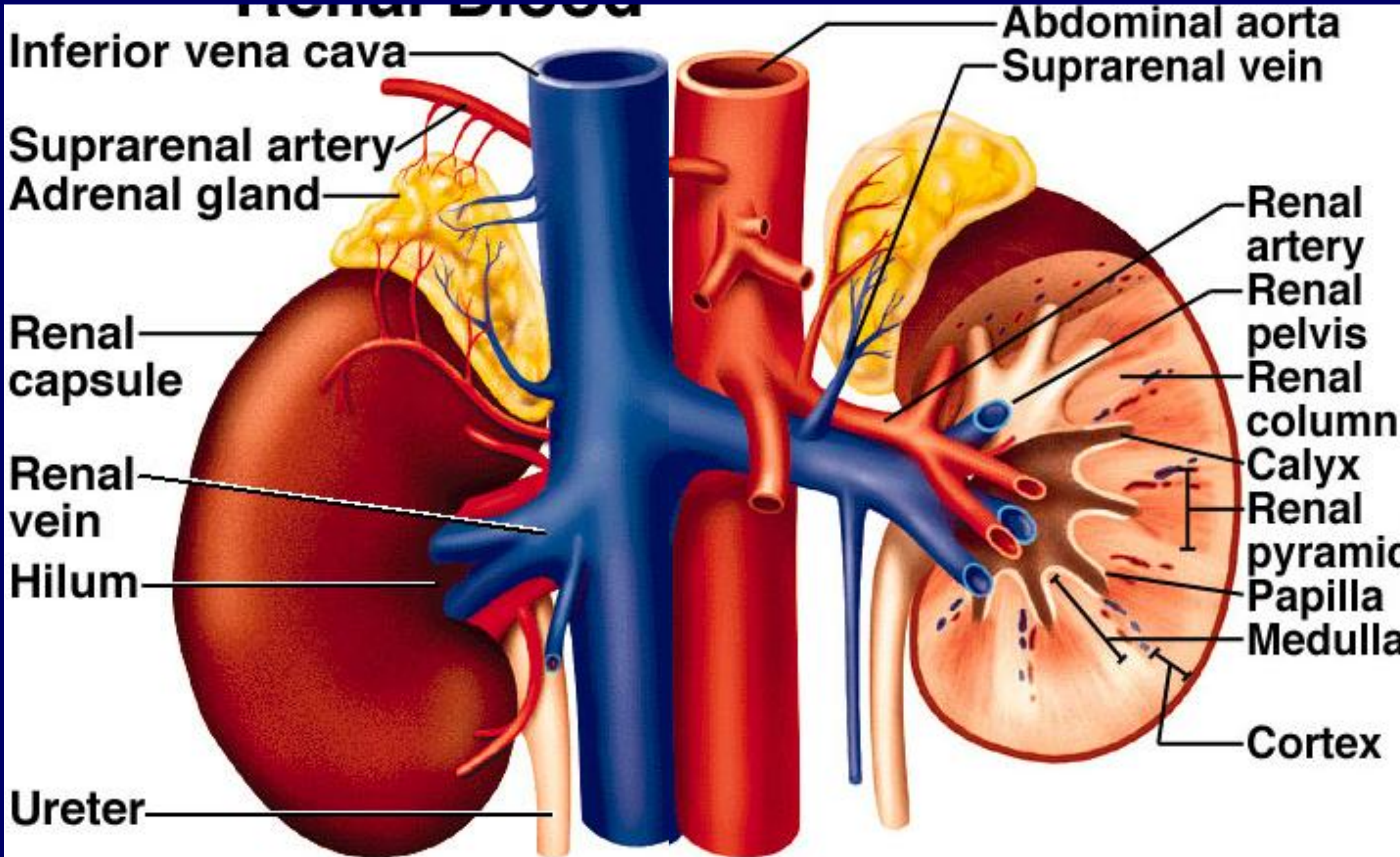
Renal Artery and Vein



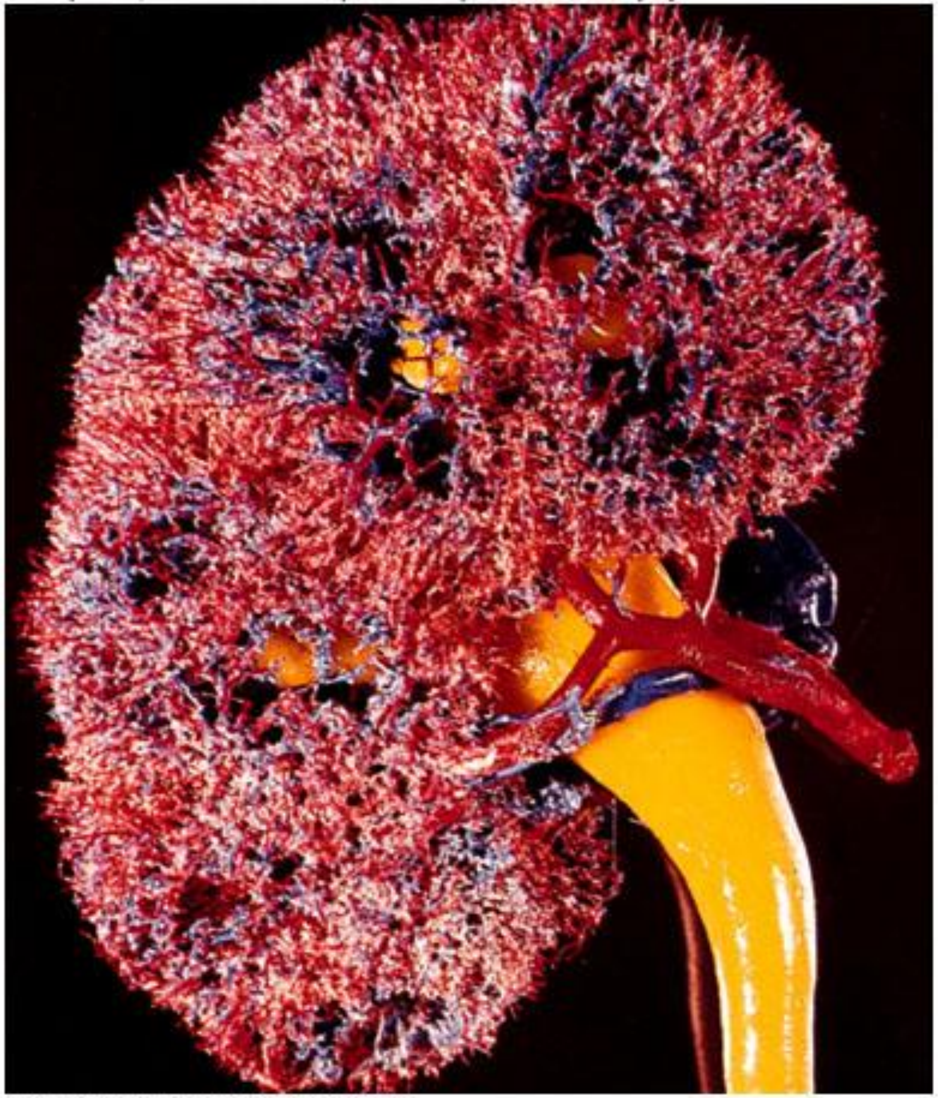
Glomerular capsule
Efferent arteriole
Afferent arteriole
Glomerulus
Distal convoluted tubule
Proximal convoluted tubule
Interlobular vein
To renal vein
Renal cortex
Renal medulla



Renal Artery and Vein


Inferior vena cava
Abdominal aorta
Suprarenal vein
Suprarenal artery
Adrenal gland
Renal artery
Renal pelvis
Renal capsule
Renal column
Calyx
Renal vein
Renal pyramid
Hilum
Papilla
Medulla
Cortex
Ureter

Renal Arterial System — Corrosion Cast



(b)

Glomerulus

-ball of leaky capillaries

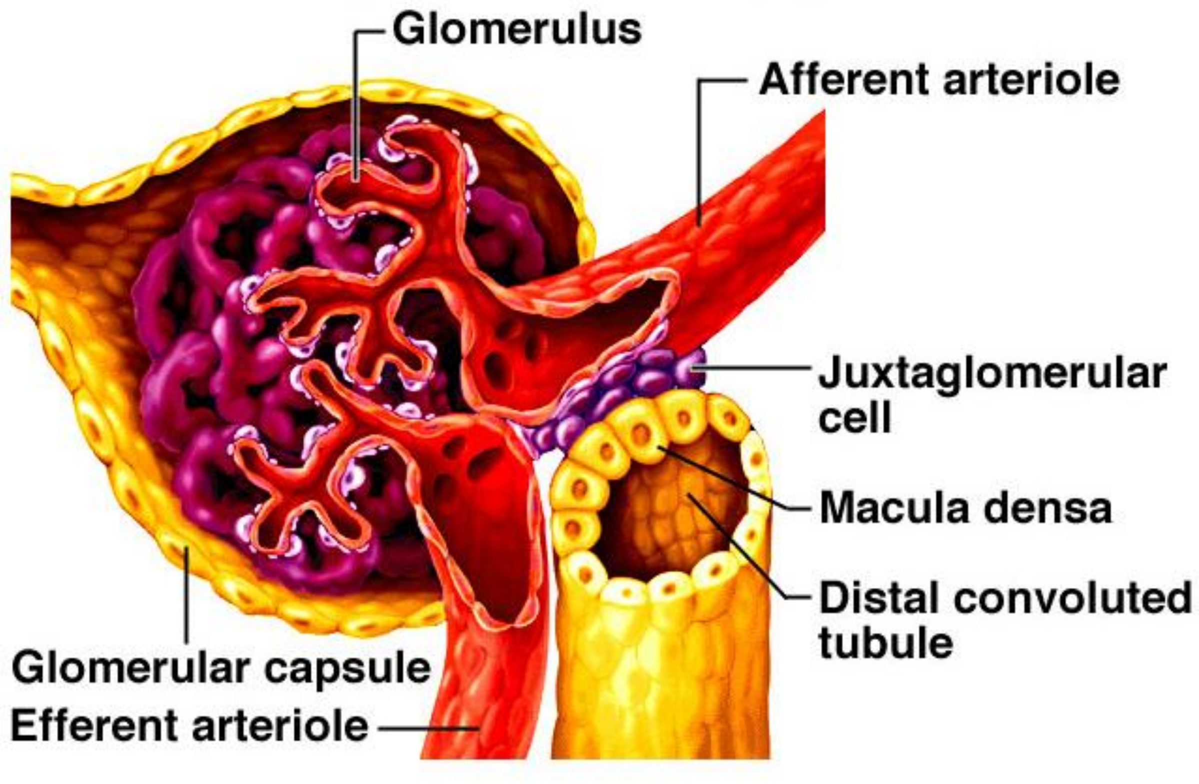
-afferent arteriole = large

-efferent arteriole = small

-high hydrostatic pressure inside the glomerulus

-surrounded by Bowman's capsule (= glomerular capsule)

-1 million per kidney



Nephron

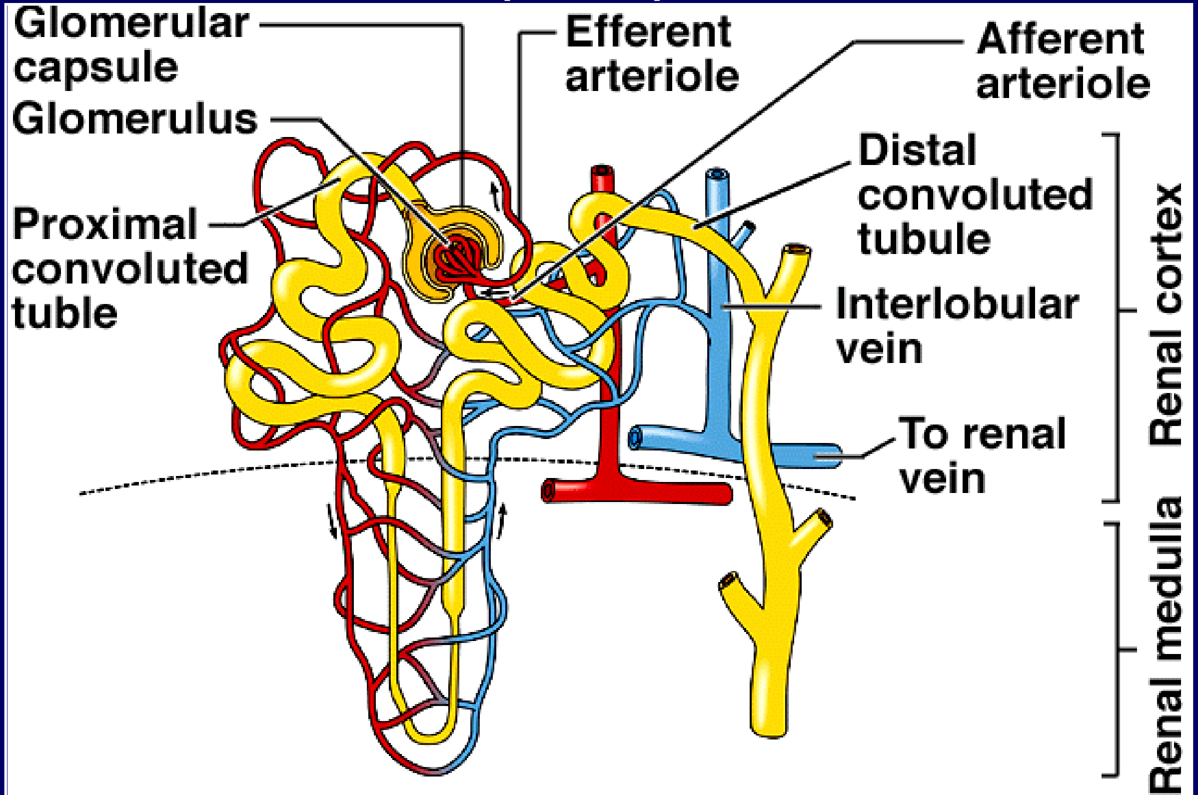
-series of small tubes

-surrounded by peritubular capillaries

-1 million per kidney

-functional unit of kidney

-process blood → into filtrate (urine)



Nephron

-Bowman’s/glomerular capsule (funnel like opening)

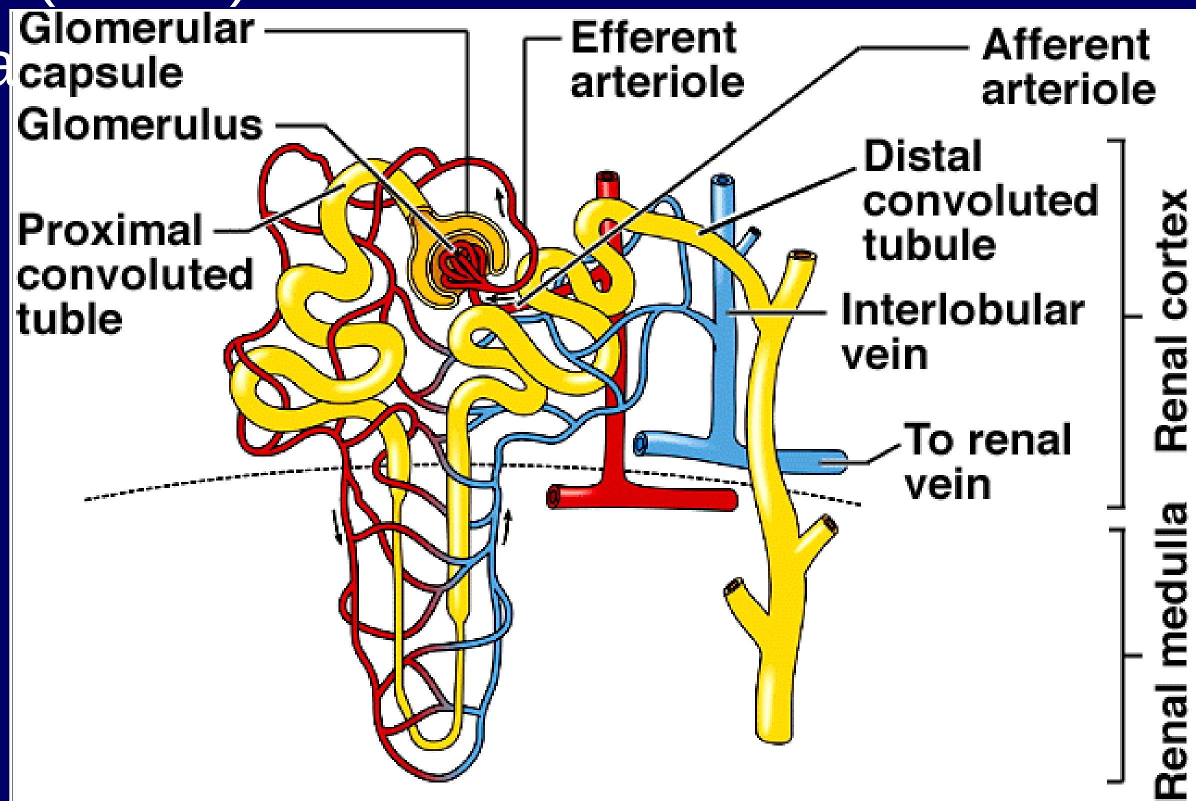
-proximal convoluted tubule (in cortex)

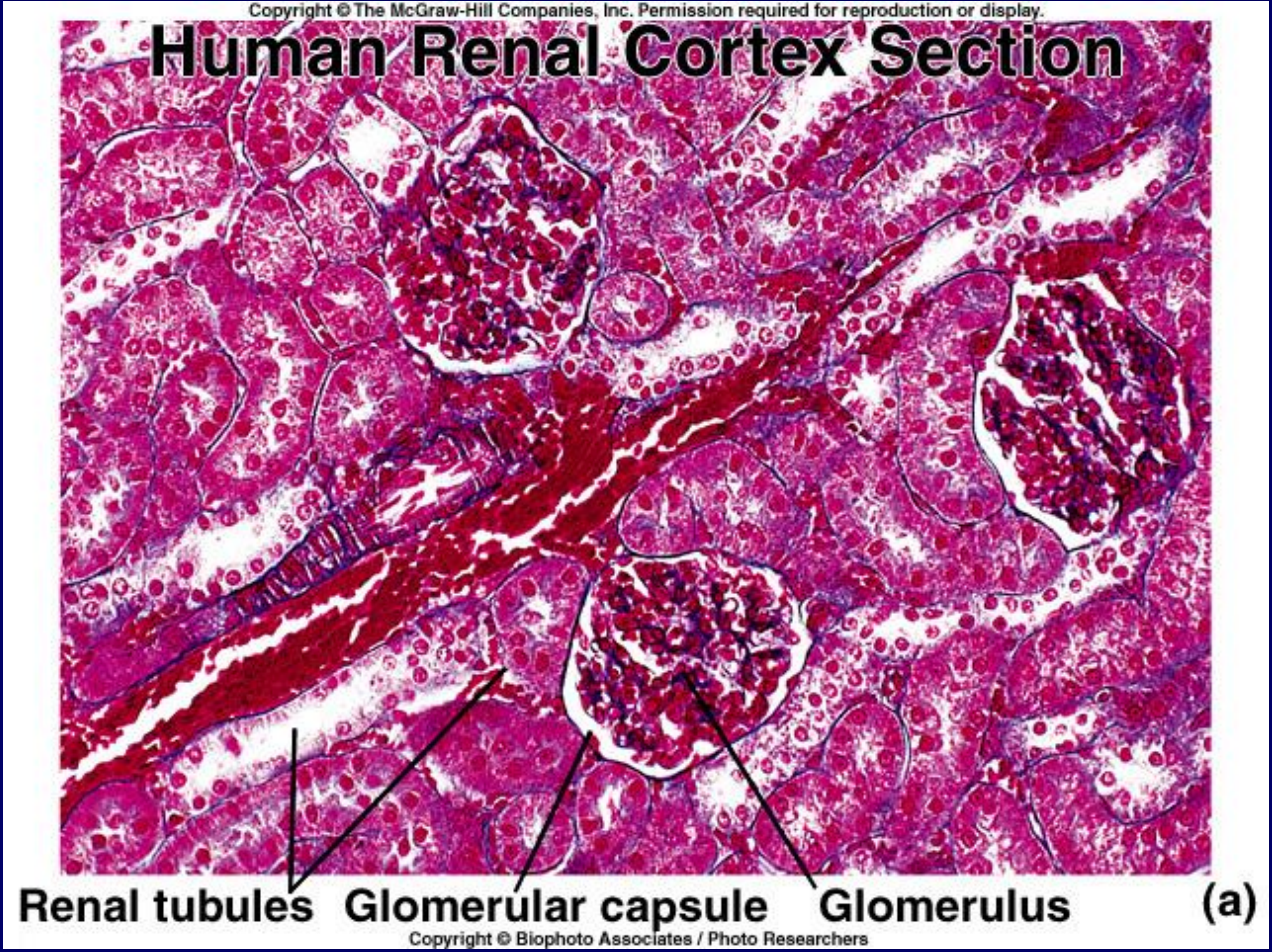
-tubes straighten as they enter medulla

-loop of Henle (descending and ascending limbs)

-distal convoluted tubule (cortex)

-collecting duct (medulla

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Human Renal Cortex Section
Renal tubules
Glomerular capsule
Glomerulus
(a)
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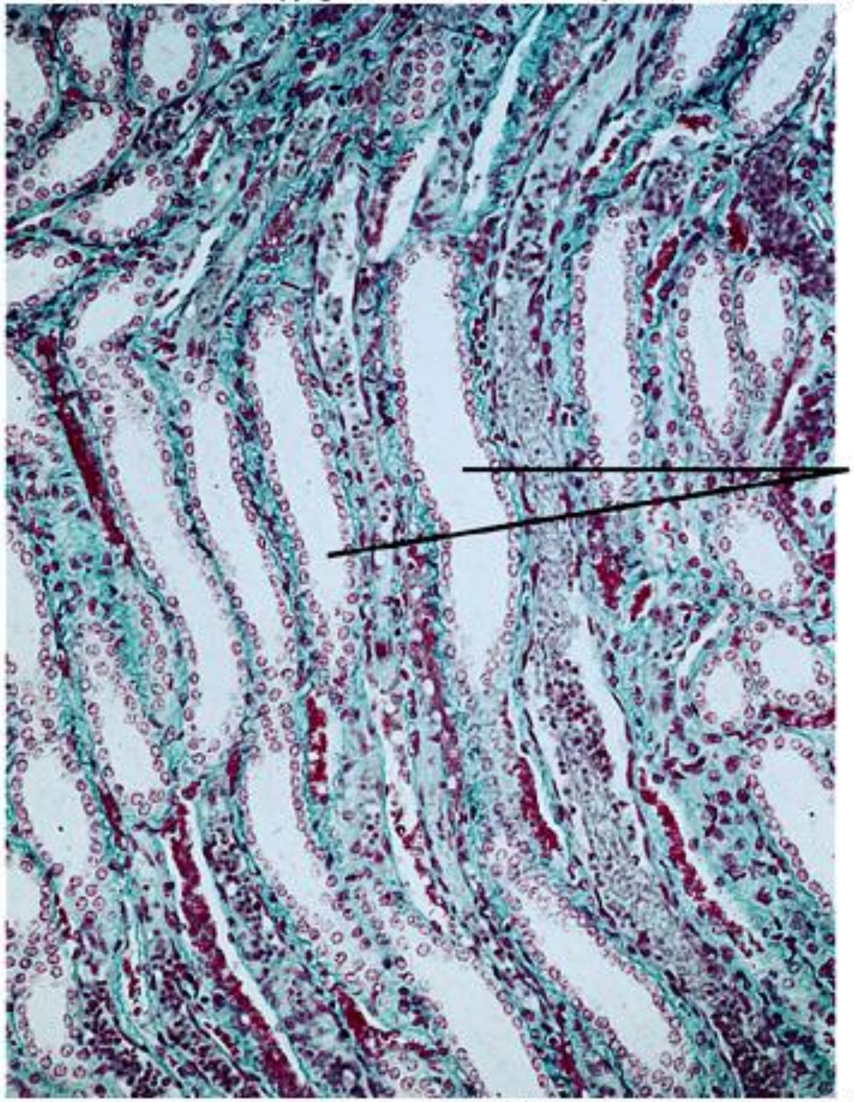
Renal Medulla



Three Primary Functions

1. **Remove Cellular Wastes**
2. **Regulate Body Fluid Volume**
3. **Regulate Ion Concentration**

These 3 tasks are achieved because the kidney is capable of:

Filtration: substance moves from blood to the glomerular filtrate

Reabsorption: substance moves from filtrate back to blood

Secretion: substance moves from blood to the filtrate (urine)

Excretion: elimination of a waste product from body

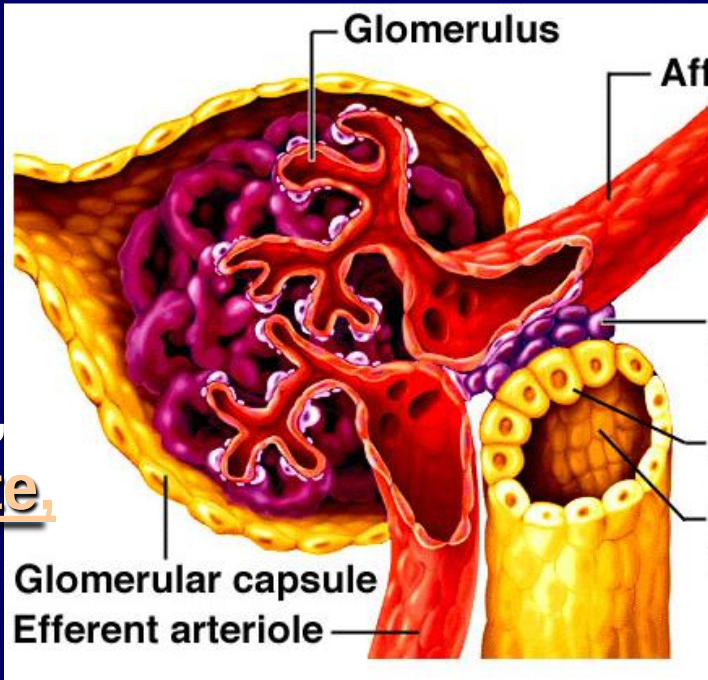
Filtering Plasma

Fluid is pushed OUT of plasma in glomerulus into Bowman's Capsule

-High hydrostatic pressure at glomerulus:

Why? The efferent artery is small, relative to afferent artery

FILTRATE = water, ions, glucose, a.a.'s, hormones, vitamin C, waste, but, NO CELLS!



Glomerular Filtration Rate

-volume of filtrate made by both kidneys = 115 ml/min (women) 125 ml/min (men)

-about 7.5 L of filtrate made every hour or 180 L/day (45 gallons!)

REMEMBER: -180 L of filtrate made every day
-1.5 L of urine lost every day
-most of the filtrate is reabsorbed

Tubular Reabsorption
(PCT + loop of Henle + DCT)

Proximal Convoluted Tubule (PCT)

-located mainly in cortex

-microvilli → *what does this tell you about function?*

-most of the filtrate is reabsorbed here (~87%)

-volume of filtrate is reduced but it's isosmotic w/ plasma (300 mOsm)

-active transport of Na^+ from filtrate back to blood

-water & Cl^- follow passively

-glucose moves to capillaries by facilitated diffusion & active transport

-NO hormonal control here

Tubular Reabsorption
(PCT + loop of Henle + DCT)

<u>Loop of Henle</u> (2 main functions)

1. If excess water is consumed = -lots of dilute urine made
   -helps decrease body fluid volume

2. If there is dehydration = -sml. amount of concentrated urine made
   -help increase body fluid volume

Tubular Reabsorption
(PCT + loop of Henle + DCT)

Descending limb of the loop

-permeable to water

-impermeable to salt (probably)

-interstitial space = very salty (due to activity of ascending limb)

-water moves out

-filtrate gets more concentrated

-bottom of loop = filtrate 1200 mOsm (hypertonic relative to plasma)

Tubular Reabsorption
(PCT + loop of Henle + DCT)

Ascending limb of the loop

-permeable to salt

-impermeable to water

-NaCl diffuses OUT

-Na is actively transported OUT

-Cl follows passively

-filtrates becomes more dilute

-interstitial space get very salty

-top of loop = filtrate 100 mOsm (hypotonic relative to plasma)

Tubular Reabsorption
(PCT + loop of Henle + DCT)

Distal Convoluted Tubule (DCT)

-reabsorption of any remaining nutrients

-sensitive to ALDOSTERONE

-Adrenal Cortex senses Na^+/K^+:

-if low Na^+ → aldosterone → Na^+ reabsorbed

-if high K^+ → aldosterone → K^+ secreted

Regulation of Body Fluid Volume (Collecting Duct along with loop of Henle)

Collecting Duct

-hypotonic filtrate enters collecting duct (CD)

-CD is impermeable to water unless ADH is present

-AHD increases the permeability of the CD to water

Overhydration

Collecting Duct Impermeable (water stays in CD)

↓

Hypotonic Filtrate Excreted

↓

Reduction of Body Fluid Volume

Dehydration

Hypothalamus Senses Reduction in Fluid Volume (osmoreceptors)

↓

ADH released from posterior pituitary

↓

Collecting Duct More Permeable

↓

Water moves OUT of CD passively (gradient formed by loop of Henle)

↓

Hypertonic Filtrate Excreted

Three Primary Functions

1. **Remove Cellular Wastes**

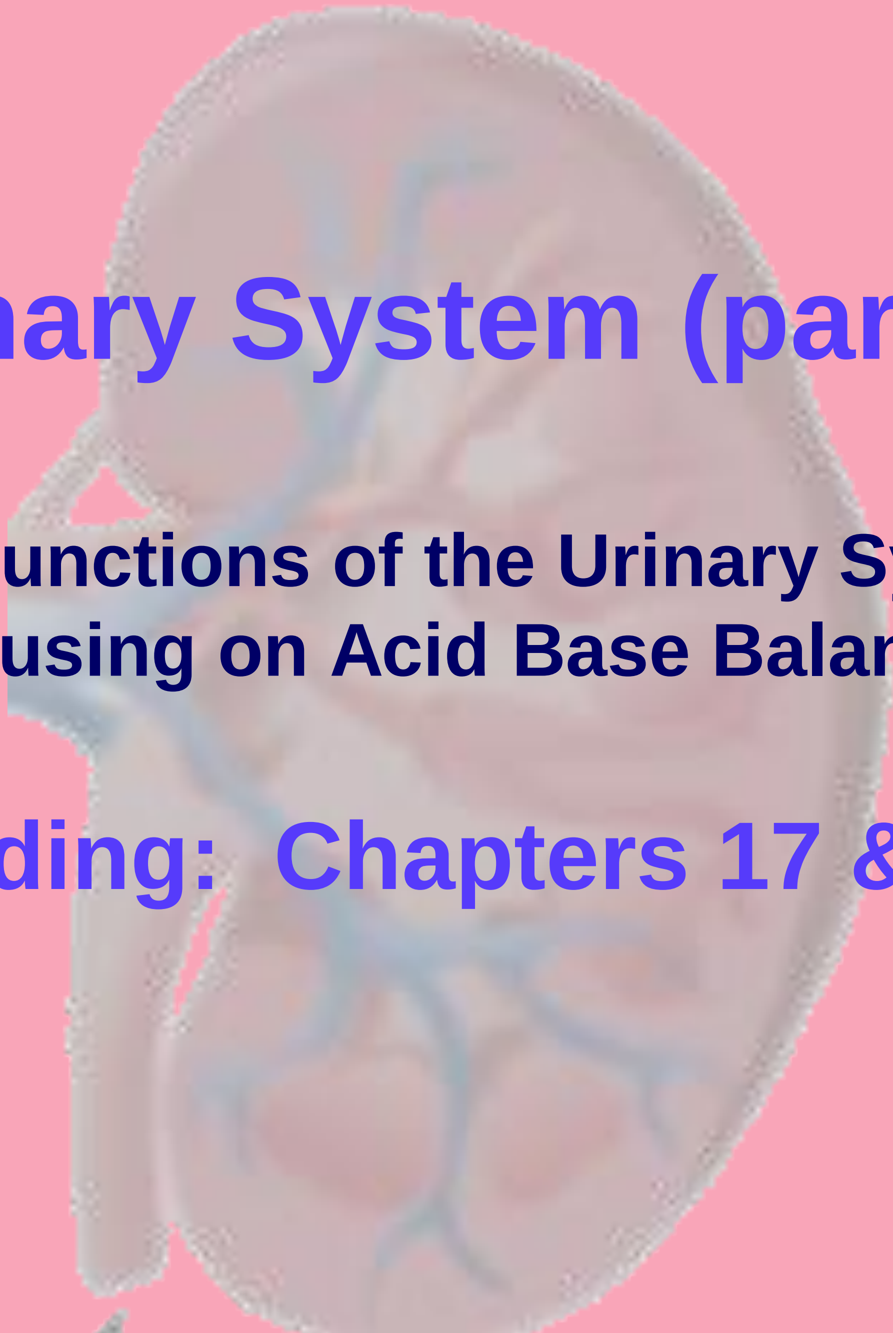
   -by filtration in glomerulus & by excretion in calyx & beyond

2. **Regulate Body Fluid Volume**

   -by reabsorption in loop of henle (NaCl gradient) & CD (ADH)

3. **Regulate Ion Concentration**

   -by secretion and reabsorption in DCT (aldosterone)



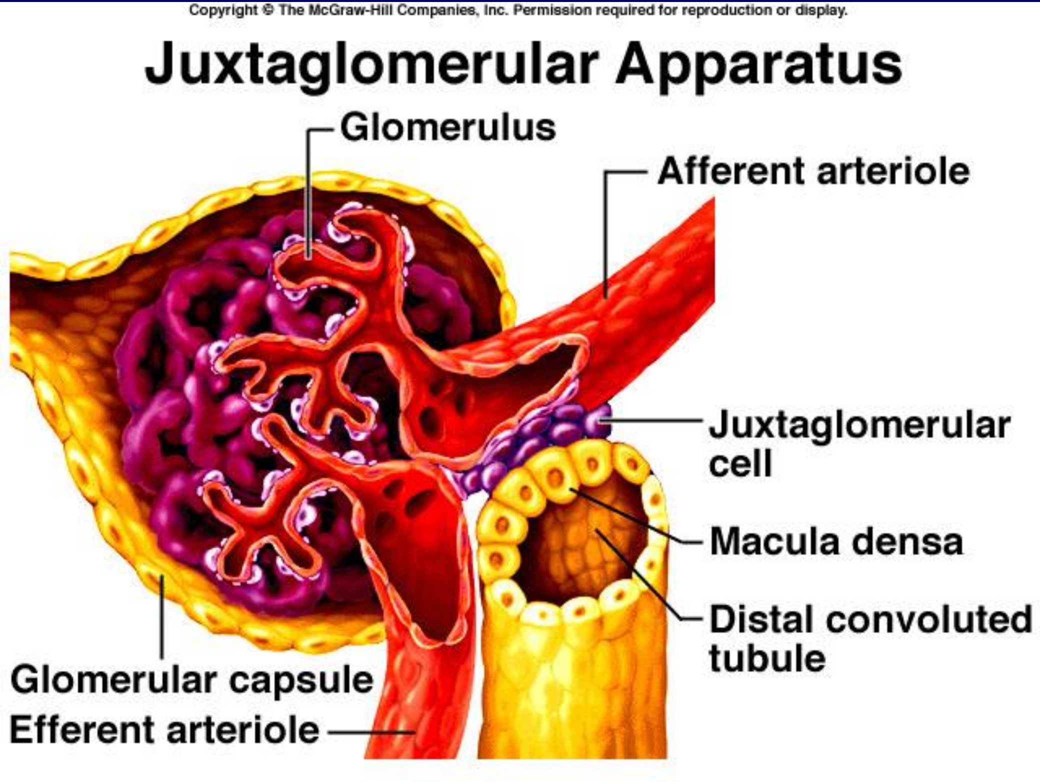
Urinary System (part II)

Other Functions of the Urinary System: Focusing on Acid Base Balance

Reading: Chapters 17 & 18

Renal Control of Blood Pressure

Juxtaglomerular Apparatus = macula densa (cells of DCT) + afferent arteriole



A. Low Blood Pressure

Juxtaglomerular Apparatus

Renin-Angiotensin system

Vasoconstriction (Na^+ reabsorb/ K^+secrete)

B. High Blood Pressure/High blood volume

Inhibits renin secretion

Inhibits ADH production

Systemic vasodilation

Atriopeptin (Atrial Natruiretic Hormone)

-produced by heart in response to stretch

-Excretion of more salt and water-diuretic

-Inhibits aldosterone activity

C. Erythropoietin

*Monitors Oxygen Tension

*Released by kidney as [O_2] in plasma drops

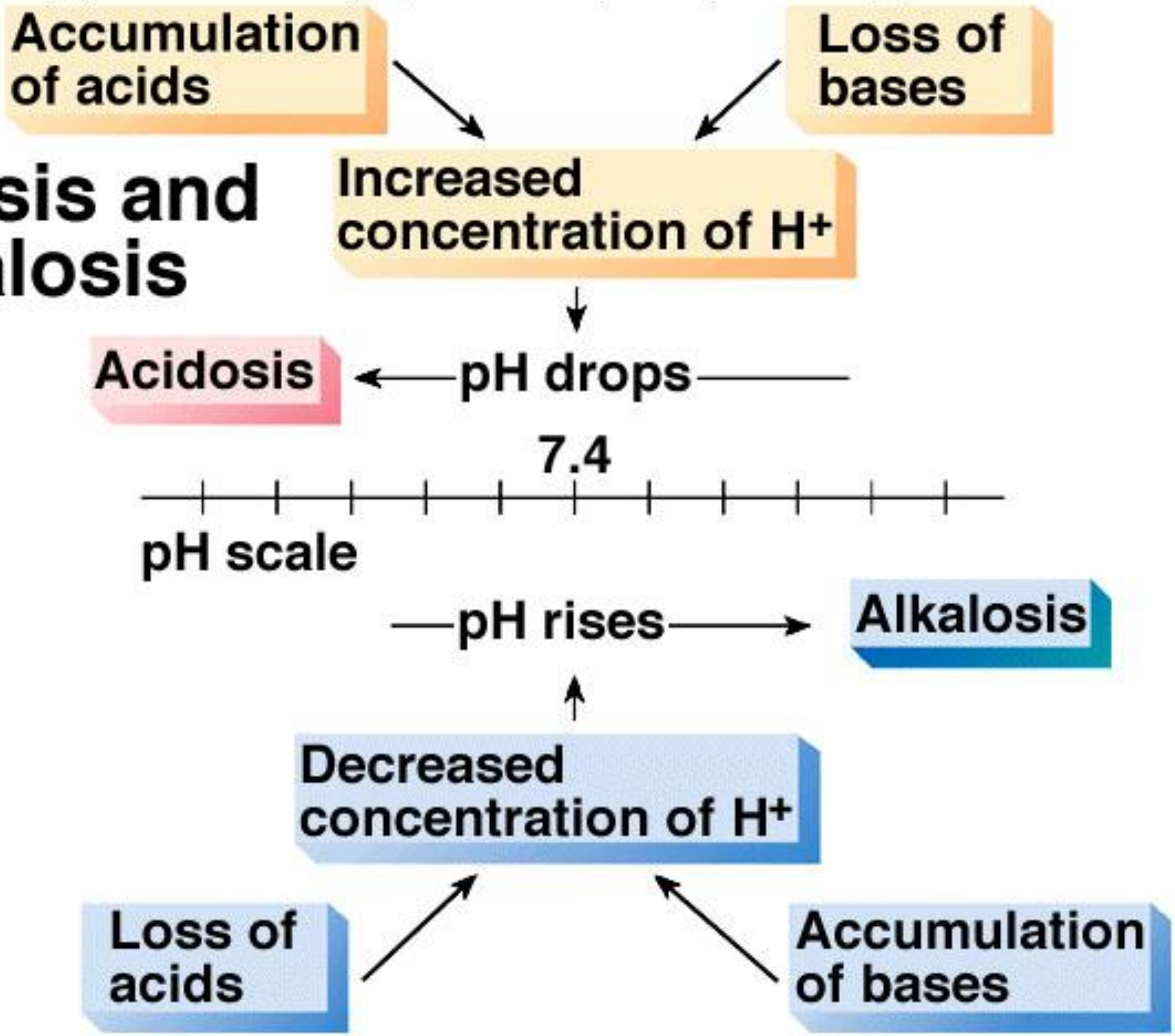
*Acts on ___________________, stimulating ________ production

Regulation of pH

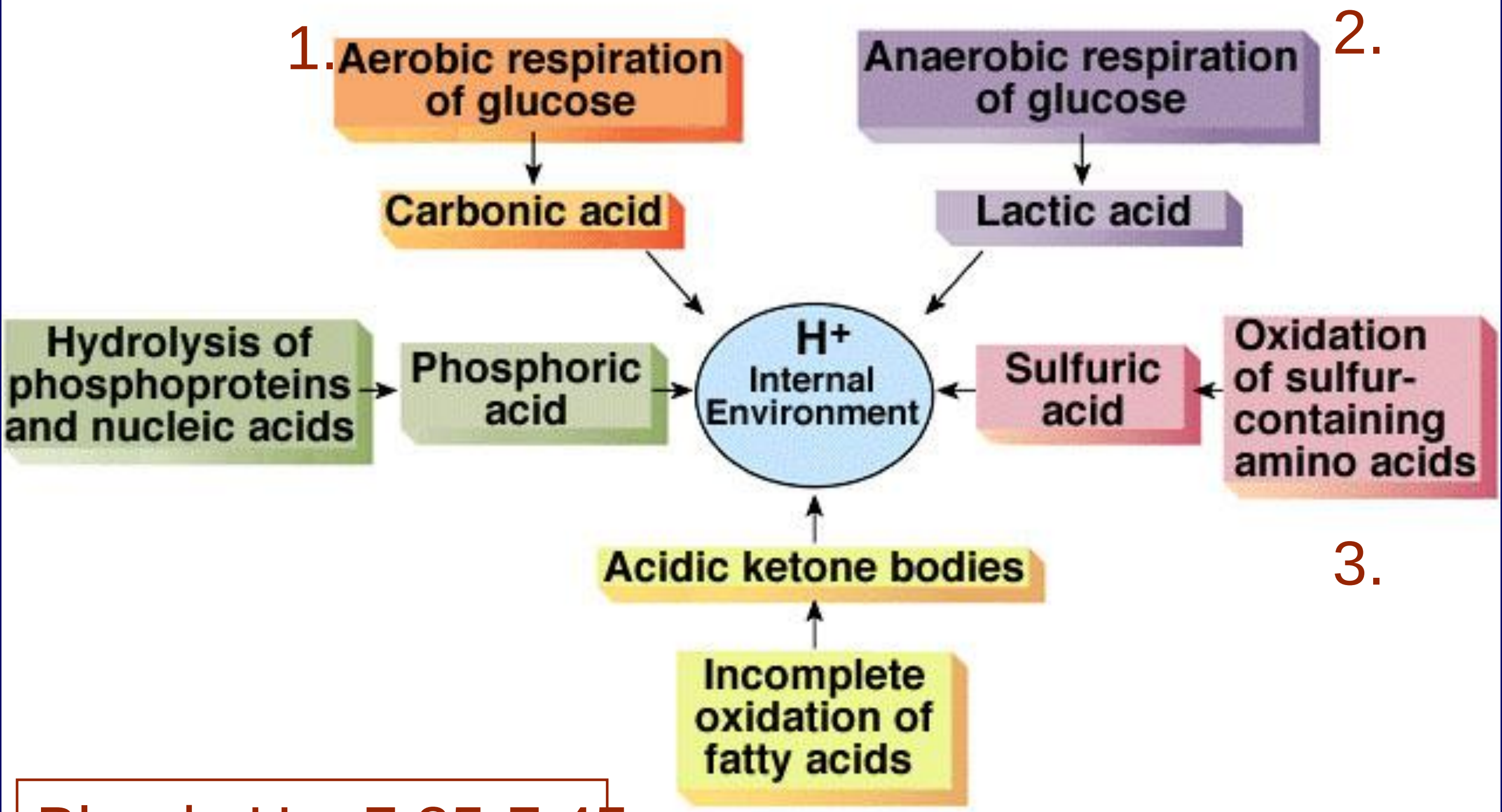
Normal Blood pH = 7.35-7.45

Maintained by chemical buffers AND physiological buffer systems

Acidosis and Alkalosis



Hydrogen Ion Sources



Blood pH = 7.35-7.45

Where does H^+ come from?

1. Aerobic Respiration of Glucose

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{energy}$$

$$\downarrow$$

$$CO_2 + H_2O \text{ --> } H^+ + HCO_3^-$$

Where does H^+ come from?

2. Anaerobic Respiration of Glucose

$C_6H_{12}O_6$ + ~~O_2~~ → energy + lactic acid (**H^+**)

Where does H^+ come from?

3. Oxidation of sulfur containing a.a.

$$H_2SO_4 \rightarrow SO_4^{2-} + \mathbf{2H^+}$$

Despite these 3 sites of acid (H+) production…
blood pH is close to neutral **(7.35-7.45)**

Regulation of blood pH

CHEMICAL BUFFERS = 1st line of defense

ACID: Dissociates to release 1 or more H^+ when in H_2O

BASE: Accepts H^+ when in H_2O

Chemical and Physiological Buffers

First line of defense against pH shift

- **Chemical buffer system**
  - Bicarbonate buffer system
  - Phosphate buffer system
  - Protein buffer system

Secondary line of defense against pH shift

- **Physiological buffers**
  - Respiratory mechanism (CO_2 excretion)
  - Renal mechanism (H^+ excretion)

Three Chemical Buffer Systems

1. Protein Buffer Systems:

${}_{2}HN$ --- aa --- aa --- aa --- $COOH$

${}_{3}HN$ COO^{-}

amino group
acts like base when
pH is too low

carboxyl group
acts like acid when
pH is too high

e.g. Hb (most of the H+ yielded in CO_2 transport is carried by Hb)

Three Chemical Buffer Systems

2. Carbonic Acid Bicarbonate Buffer System:

Bicarbonate (HCO_3^-) can act a weak base (pick up H^+)

Carbonic Acid (H_2CO_3) can act as a weak acid (release H^+)

$$H^+ + HCO_3^- \dashrightarrow H_2CO_3$$

Three Chemical Buffer Systems

3. Phosphate Buffer System:

PO_4^{4-} ions = a major intracellular ion

$H_2PO_4^{-} \rightarrow H^{+} + HPO_4^{2-}$

Dihydrogen P = weak acid, can buffer strong bases

$HPO_4^{2-} + H^{+} \rightarrow H_2PO_4^{-}$

Monohydrogen P = -weak base, can buffer strong acid

-also in urine to buffer acids

Chemical buffers try to keep pH between 7.34 and 7.45…but under extreme conditions the chemical buffers can't keep up!

What happens if pH gets out of range?

ACIDOSIS (<7.35)

-depression of CNS by inhibiting synaptic transmission

-if less than 7.0 → low nerve function → disorientation, coma, *death*

What happens if pH gets out of range?

ALKALOSIS (>7.45)

-over-excitability of CNS & PNS

-nerves send impulses repetitively, even w/out normal stimulus

-nervousness, muscle spasms, convulsions, *death*

1. pH also affects enzyme function

2. We can only live ~ 1 min at pH extremes

So, pH is closely monitored!

Regulation of blood pH

PHYSIOLOGICAL BUFFERS = 2nd line of defense

These buffer systems work when pH changes lead to alkalosis or acidosis

Physiological Buffer Systems

*Metabolic Imbalance → Respiratory Compensation

→ Exhale CO_2

→ Begins within minutes

→ Finished within 2 hours

*Respiratory Imbalance → Metabolic Compensation

→ Mainly in kidney

→ Secretion of H^+

→ Reabsorption of HCO_3^-

→ Begins within minutes

→ Takes days to finish

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

ACIDOSIS & ALKALOSIS (causes & compensations)

Respiratory Acidosis = Increased pCO_2 → LOW pH

Cause = -hypoventilation

-emphysema, COPD, pulmonary edema, trauma to respiratory center, airway obstruction,…

Compensation = metabolic (kidney)

inc. secretion of H^+ (PCT)

inc. reabsorption of HCO_3^- (PCT, DCT, CD)

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

ACIDOSIS & ALKALOSIS (causes & compensations)

Respiratory Alkalosis = Decreased pCO_2, ↑ pH

Cause = hyperventilation
O_2 deficit, altitude, anxiety, pulmonary disease

Compensation = metabolic
reduced secretion of H^+
reduced reabsorption of HCO_3^-
what else could you do as a treatment?

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

ACIDOSIS & ALKALOSIS (causes & compensations)

<u>Metabolic Acidosis</u> = ↓ bicarbonate, ↓ pH

Cause = -Loss of HCO_3^-
-Due to diarrhea with lower GI losses,
-Due to kidney dysfunction

Compensation = Respiratory
Hyperventilation to blow off CO_2

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

ACIDOSIS & ALKALOSIS (causes & compensations)

Metabolic Alkalosis = ↑ bicarbonate, ↑ pH

Cause = Loss of acid (vomiting, gastric suctioning)
Excessive intake of alkaline drugs

Compensation = Respiratory
Hypoventilation, slows CO_2 loss

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

END