Lecture 4: Micturition

How the urine move from kidney to bladder by peristaltic contraction?

1- Electrical peacemaker will sense **the stretch of pelvis by urine**

2- An action potential will make a **peristaltic wave** which **2-6 cm/sec from pelvis to bladder**

3- Increase the pressure in the ureter from **2-5 cm H2O up to 20-80 cm H2O**

4- Propel of urine from pelvis to bladder

What is the role of sympathetic nervous system in peristaltic contraction?

sympathetic nerves innervating the ureter may modify the **rate** or **force** of peristalsis

What happened if there is obstruction in ureter?

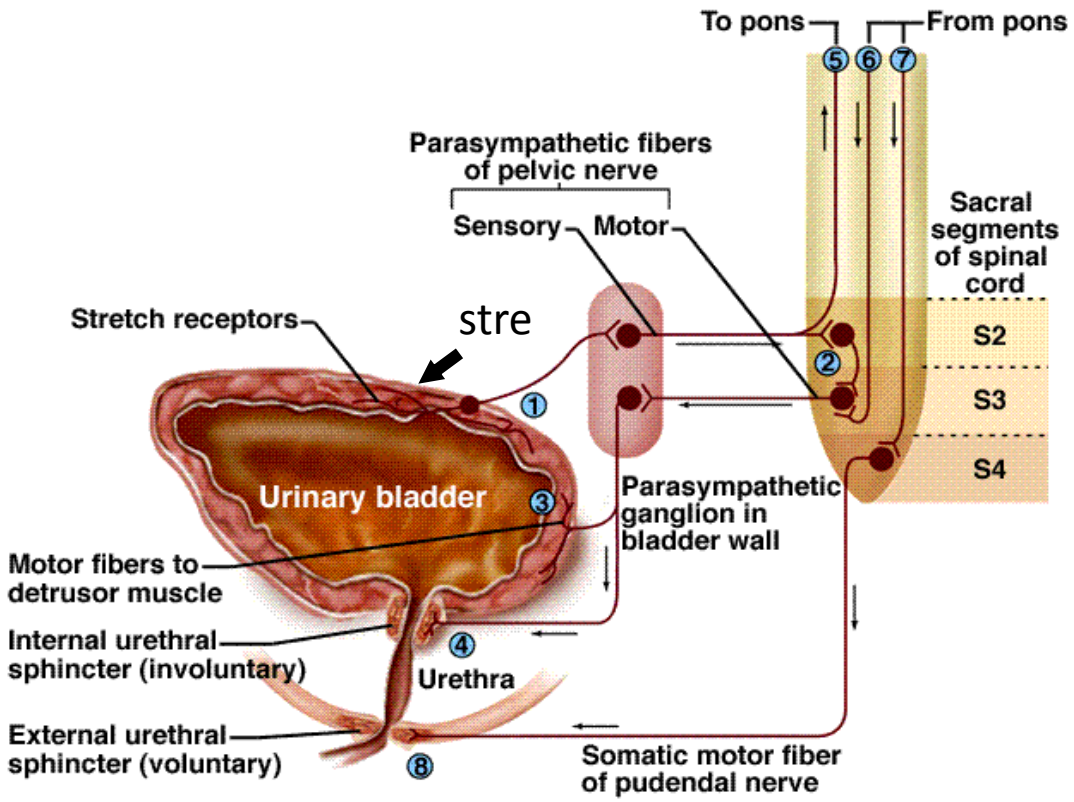
Interruption of the flow of urine by an obstruction (such as a kidney stone) stops flow, increases pressure which can back up through the ureter into the pelvis and lead to **hydronephrosis** and the pain is sensed by **autonomic fibers of ureters**

What is the anatomical component of micturition?

- Detrusor muscles of bladder → Smooth muscles (involuntary)
- Internal urethral sphincter → Smooth muscles (involuntary)
- External urethral sphincter → Skeletal muscle (voluntary)
- Parasympathetic nerves → Control smooth muscles
- Sympathetic nerves → Control smooth muscles
- Pudendal nerves → Control skeletal muscles

What is the mechanism of micturition reflex?

1- Urine will move from kidneys to bladder through ureter by **peristaltic contraction**
2- The bladder will start filling. The **tone** and **pressure** will start changing.
3- **Stretch receptors** in the wall of bladder will sense increase in pressure (**intravesical pressure**)
4- **Parasympathetic fibers** will **Send afferent signals** to **higher control** through **pelvic fibers** when it reaches to threshold level or **conscious level** **(150-200 ml)**
5- **Parasympathetic fibers** will **send efferent signals** which lead to **contract** the wall of the bladder and **relaxation** the **internal urethral sphincter.** **(involuntary)**
6- **Through Pudendal nerves:**
   - **Excitatory impulses** from **pontine region** will send back to external urethral sphincter and close it.
   - OR **Inhibitory impulses** from **midbrain** will send back to external urethral sphincter and relax it. **(voluntary)**



Is micturition a voluntary controlled?

Yes, it is under voluntary control in adults.

What is the role of sympathetic in bladder?

- Relaxation of bladder
- Contraction of internal urethral sphincter
  To prevent semen from entering the bladder during ejaculation

What is the type of micturition reflex

Autonomic spinal reflex (S2 – S3 – S4) which facilitated or inhabited by higher center

What happened for the last amount of urine after urination in males and females?

- In females it empties by **gravity**
- In males it empties by contraction of **bulbocavernous muscle**

Why children are voiding urine without control?

Because their **higher control is not complete yet** and they need training to control it.

What is the diseases and abnormalities that affect the micturition?

- **Spinal shock :** damage of spinal cord and the lose the connection with CNS
  During: bladder overfilled and urintation become **incontinence**
  After: Automatic micturition “lose control of external urethral sphincter’
- **In females :** recurrent pregnancy will lead to weakness of pelvic muscle and that lead to incontinence

What is the cystogram? And how it's done?

Study the relationship between **intravesical volume and pressure.**

1- Insert a catheter in the bladder
2- Empties the bladder from urine
3- Secrete a saline fluid in the bladder
4- Put 50 ml and record the intravesical pressure
5- Repeat the last step for many times
6- You gain a curve and that curve will give you the diagnoses

- ## What is the difference between cystogram and Cystometrogram?

- **Cystogram** is the process
- **Cystometrogram** it is the graph that you obtain from process

- ## What is the phases of voiding?

1- **Initial phase:** start filling of bladder and pressure start increasing at 50 ml
2- **Pleatu phase:** increase in volume without increase in pressure
3- **Voiding phase:** start feeling of desire to void the urine which start from 150 or 200 and pressure will increase rapidly after 300 ml
4- **Urgent voiding:** after 400 ml bladder cannot hold urine.

- ## What is the role of abdominal muscle in urination?

Voluntary contraction of abdominal muscles helps **the expulsion of urine by increasing intra-abdominal pressure,** but voiding can be initiated with straining.

Lectures 5 & 6: Secretion and reabsorbation

How much of the plasma will be filtered in the kidney?

Cardiac output is **5 L/min** → **20%** of it will go to the kidney (**1 L/min**) → only the plasma will be filtered which represent **60%** of blood flow (**600 ml/min**) → **20%** of the plasma will be filtered (**125 ml/min**) which called **GFR** → Out of 125 ml only **1 ml** in pass to pelvis per min.

- That means **99% reabsorbed** and only **1% is excreted in urine**
- Can be calculated by: **Urinary excretion = Filtration + Secretion - Filtration**

What is the normal and abnormal amount of urine?

- Less than **400 ml/day called oliguria**
- More than **3.5 L/day called polyuria**
- The normal average is **1.5 L/day**

How does molecules move from tubules lumen into epithelial cells?

Specialize type of epithelial cells, which have:

1- Transcellular routes (through cell membrane):

- **Luminal side (apical side or brush border)**
- **Basolateral side**

2- Paracellular routes (between cells junction):

- **Tight junction between adjacent cells**

How does molecules move from interstitium to Peritubular capillaries?

Ultrafiltration (bulk flow) a passive process driven by the **hydrostatic and colloid osmotic pressure gradients**

- **Transporters and carrier proteins in each side are different in structure and function**

What are the mechanisms of reabsorbation and secretion?

Mechanisms of cellular transport in the nephron are:

Active transport

"Active transport can move a solute **against an electrochemical gradient** and **requires energy** derived from metabolism"

Primary active transport

Transport that is coupled directly to an energy source such as **ATP**

Sodium-potassium pump

(found in **basolateral membrane** along renal tubules)

Secondary active transport

Transport that is coupled indirectly to an energy source due to **concentration gradient of ion**

- **Na-K-2Cl co-transport**
- **glucose-sodium co-transport (SGLT)**
- **amino acid-sodium co-transport**
- **H+/Na counter-transport**

Passive Transport

Simple diffusion

(without carrier protein)

Cl, HCO3-, urea , creatinine

Facilitated diffusion

(require carrier protein)

Glucose and amino acids at the basalateral border (GLUT)

Osmosis

Water is always reabsorbed by a passive (nonactive) physical mechanism called osmosis ,

which means water diffusion from a region of **low solute concentration (high water concentration)** to

one of **high solute concentration (low water concentration).**

Pinocytosis

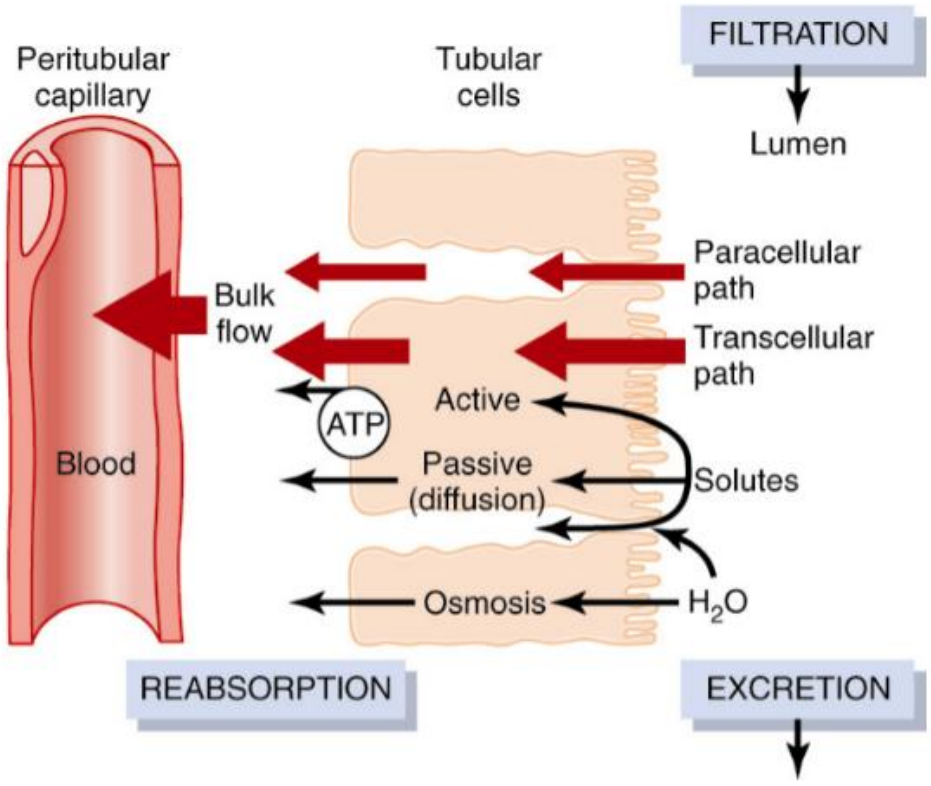
(Additional reading)

The proximal tubule, reabsorb **large molecules such as proteins** by pinocytosis. In this process, the protein attaches to the brush border of the luminal membrane, then invaginates to the interior of the cell until it is completely pinched off and a vesicle is formed containing the protein. Once inside the cell

the protein is digested into its constituent amino acids, which are reabsorbed through the **basolateral membrane** into the interstitial fluid. Because pinocytosis requires energy, it is considered a form of **active transport.**

(1) Co-transport : movement of two molecules in the same direction but they opposite in concentration gradient

(2) Counter-transport: movement of two molecules in opposite direction based on their concentration gradient



What are the transporters and carrier proteins that involve reabsorbation and secretion?

4. Proximal convoluted tubules

- **At luminal side:**

- Sodium/H+ counter transport
- Sodium/Glucose co-transporter (SGLT)
- Sodium/Amino acids co-transporter

- **At basolateral side:**

- Sodium/Potassium pump or ATPase
- HCO3/Cl counter transport
- Glucose channels (GLUT)
- Amino acids channels

1. Distal convoluted tubules

- **At luminal side:**

- Sodium/Cl co-transporter
- Ca Channels

- **At basolateral side:**

- Sodium/Potassium pump or ATPase
- Cl channels
- Ca/Na exchanger

3. Thick ascending limp of henle:

- **At luminal side:**

- Na/K/2Cl co-transport

- **At basolateral side:**

- Sodium/Potassium pump or ATPase

2. Late Distal convoluted tubules and Collecting ducts:

- **At luminal side:**

A. "Principle cells":

- Sodium channels "Reabsorb 3 Sodium"
- Potassium channels "Secrete 2 Potassium"

B. "Intercalated cells":

- Active H+ pump
- Potassium channels **"reabsorbation"**

- **At basolateral side:**

- Sodium/Potassium pump or ATPase

What are the primary active transporters?

1- Sodium/Potassium pump
2- H+ pump in intercalated cells

What are the secondary active transporter?

Any transporter that have **co-transport** (symporters) or **counter-transport** (anti-porters) in its mechanism

How Primary active transport take place?

1- **Sodium/Potassium pump** allow movement of **3Na from cells to interstitium** and **2K from interstitium to cells**.
2- So, cells has a poor sodium and due to that sodium will move from lumen to cells coupled with other molecules by **secondary active transport**.

How Secondary active transport take place?

1- **Co-transport:** movement of two molecules in the same direction but they opposite in concentration gradient

2- **Counter-transport:** movement of two molecules in opposite direction based on their concentration gradient

Why sodium need transporter and cannot diffuse passively to the cell?

Because it is a **polar molecule** due to that, it cannot pass the lipid membrane passively

How bulk flow take place?

1- In **Peritubular capillaries the high plasma oncotic pressure** is due to fluid **filtration in glomerulus**

2- **increase GFR** → increase oncotic pressure & decrease hydrostatic pressure in efferent & Peritubular capillaries → increase bulk flow from lateral space to Peritubular capillaries → **increase reabsorption**

3- **decrease GFR** → decrease oncotic pressure & increase hydrostatic pressure → decrease bulk flow → fluid go back to lumen through tight junction → **decrease reabsorption**

How water reabsorbed?

- **In proximal convoluted tubules:**

a. Water is freely permeable. **(most of water absorbed here)**
b. Many solutes reabsorbed along PCT.
c. **Therefore, movement of these solutes will lead to pull water too through tight junctions.**
d. At the end of PCT the osmolarity of fluid will remain the same **"isotonic".**

- **In Descending loop of henle:**

a. Water is freely permeable.
b. This part is impermeable for many solutes
c. Less solutes reabsorbed along DLH.
d. At the end of DHL the osmolarity of fluid will be more concentrated **"Hyperosmolar"**

- **In Thin , Thick ascending loop of henle and early potion of distal convoluted tubules:**

a. Water is impermeable
b. Solutes reabsorbed along Tubules.
c. At the end of these tubules the osmolarity of fluid will be more diluted **"Hypo-osmolar"**

- **In late potion of distal convoluted tubules and Collecting Ducts:**

a. **Water is impermeable** only if there are ADH it will become permeable.
b. Solutes reabsorbed along Tubules.
c. At the end of these tubules, the osmolarity of fluid will be more diluted **"Hypo-osmolar"** if there is no ADH.

- **Interstitium in cortex is hypo-osmolar while in the medulla it is hyperosmolar**

How HCO3 (bicarbonate) is reabsorbed?

1- HCO3 found normally in the tubule lumen but **cannot pass through luminal membrane directly.**

2- **HCO3 will bind with H+** which come from cell by **Sodium/H+ counter transport** and formed **H3CO2 (carbonic acid)**

3- Breakdown of **H2CO3** into **H2O and CO2** through **luminal carbonic anhydrase**

4- **CO2 will cross membrane passively** because it is **lipid soluble**

5- **CO2 will bind with H2O** inside the cell and form **H2CO3**

6- **H2CO3 will break to H+ and HCO3** through **cystolic carbonic anhydrase**

7- **HCO3** will go to interstitium through **HCO3/Cl counter-transport** then it will go to the blood

How Na/K/2Cl co-transporter in Thick ascending loop work?

1- It will allow movement of Na,K,2Cl from lumen to the cells

2- K will go inside the cell and back to the lumen **(recycling)**

3- This recycling to prevent output of some cations (Ca and Mg) with urine.

How Na/Cl co-transporter and Ca channels in DCT work?

1- It will allow movement of Na and Cl from lumen to the cells

2- Ca channels will work under control of **Parathyroid hormone**

3- Ca enter to the cells and go to the interstitium by **Ca/Na exchanger**

How glucose reabsorbed?

- Glucose enter the tubular cells by secondary active transport "co-transport", It use **SGLT** "a specific transport protein "which needs Na"

- Then it's cross the cell membrane into the interstitial spaces by facilitated transport "passive transport" which use **GLUT's** "do not need Na"

When glucose will start appear in the urine? And what that called?

It will start appear in the urine when the plasma concentration of glucose reach to **180 mg/dl** and that called **renal threshold**

When the tubules will reach their maximum capacity of glucose reabsorbation? And what is it called?

When all nephrons have reached their maximal capacity to reabsorb glucose which called "**Tmg=maximum saturation of transporters**=**375 mg/min** in **men** and **300 mg/min** in **females**"

What are the main component of Glucose titration curve?

- **Ideal curve**: when all Tmg in all tubules are identical and glucose remove from all tubules
- **Actual curve:** which represent **the magnitude** that inversely proportional with **avidity**

What are the regulation mechanism of reabsorbation and secretion?

1.Glomerulotubular balance: prevents overloading of distal parts when GFR increases.

2. Peritubular capillary reabsorption is regulated by hydrostatic and colloidal pressures through the capillaries.

3. Arterial blood pressure: if increased it reduces tubular reabsorption. (increase in blood pressure will reduced GFR in response of myogenic mechanism and the decrease reabsorbation)

4. Nervous Sympathetic:
-Increases Na+ reabsorption.

5-Tubuloglomerular feedback: it will observe concentration of sodium chloride by macula dense in distal tubules and what will lead to:
1- constriction and dilatation of afferent arteriole which affect on GFR
2- release renin which increase reabsorabtion of sodium and play a role in production of angiotensin II

6-Hormonal:
- Angiotensin II : release aldosterone
- ADH : H2O reabsorbation
- ANP : Sodium excretion and diuresis
- Parathyroid hormone: Increases Ca reabsorption & decreases phosphate reabsorption

(1) ADH: Antidiuretic hormone
(2) ANP: atrial nitric peptide
(3) Diuresis: increase urine output

What is the role of aldosterone?

Aldosterone

Function

- 1-increases Sodium and water reabsorption
- 2-stimulates Potassium secretion

When does it secreted?

- (1) Increased extracellular potassium concentration.
- (2) Increased angiotensin II levels, which typically occur in conditions associated with **sodium and volume depletion or low blood pressure (so it will increase blood pressure)**

Site of secretion

- Aldosterone, secreted by the **zona glomerulosa cells** of the **adrenal cortex.**

Mechanism of action

- by stimulating the sodium-potassium ATPase pump on the **basolateral side of principle cells in the cortical collecting tubule membrane.**
- Aldosterone also increases the sodium and potassium channels of the luminal side of the membrane .

Diseases associated with aldosterone

- Absence of aldosterone, as occurs with adrenal destruction or malfunction **(Addison's disease)**
- Excess aldosterone, as occurs in patients with adrenal tumors **(Conn's syndrome)** is associated with:
  1- sodium retention 2- decreased plasma potassium concentration

- **General notes:**

- **Sodium is passively cross membrane in thin ascending limb only in form of NaCl.**

- **Counter-current multiplier is a mechanism that occur in loop of henle to maintain the osmolarity of medulla.**

- **Inner Medullary collecting ducts is highly permeable of urea to maintain the osmolarity.**

- **Small change from 4 to 5.5 mmoles/l in K+= hyperkalemia**

- **K+ reabsorbed in PCT passively. While in cortical collecting ducts, it secreted actively.**

⇑ = Reabsorbtion, ⇓ = Secretion. Review of Substances

Substance	PCT	D. limb	A. limb	DCT	C. Tubules
Na	⇑	–	⇑	⇑	⇑ ⊛
K^+	⇑	–	⇑	⇓	⇓ ⊛
Cl^-	⇑	–	⇑	⇑	–
Glucose	⇑	–	–	–	–
H_2O	⇑	⇑	–	⇑	⇑ ✱
HCO_3	⇑	–	–	–	–
PO_4	⇑	–	–	–	–
Urea	⇑	–	–	⇑ ✱	⇑ ✱
Amino. A	⇑	–	–	–	–
PAH	⇓	–	–	–	–
H^+	⇓	–	–	⇓	⇓ ⊛

✱ In Presence of ADH.
⊛ Under the influence of Aldosterone.

Lecture 7: Regulation of body fluid

What are the body fluid compartment?

1- **Intracellular (inside the cells):** contain most of the fluid
2- **Extracellular (outside the cell):** contain fluid in the:
- Blood (vascular)
- Interstitium (between cells)

What does the fluid contain?

- Water
- Solutes (Electrolytes – glucose – urea – proteins ..etc)

What are the pressure in the fluid?

1- Oncotic pressure created by proteins
2- Osmotic pressure created by electrolytes

What is the most important electrolyte that regulate body fluid and control osmolarity?

Sodium chloride (NaCl)

What is the normal concentration of sodium in the blood?

Between **140-145 mEq/L** and that create an osmolarity of **300 mOsm/L**

What are the mechanism that observe changing in osmolarity and volume?

1-Osmoreceptor –ADH mechanism.

2- Thirst mechanism

Osmoreceptors-ADH mechanism

What happened if a person is in dehydrated condition in such a patient that have excessive diarrhea?

Decrease ECF volume → **increase ECF osmolarity** that surrounding the osmoreceptors in the hypothalamus → movement of water from intracellular **(osmoreceptors cells)** to extracellular → stimulation of osmoreceptors and send signals to **posterior pituitary in hypothalamus** → **release ADH also called (arginine vasopressin)**

What happened if a person is take high amount of water in short time?

Decrease Sodium concentration → **decrease ECF osmolarity** that surrounding the osmoreceptors in the hypothalamus → movement of water from extracellular to intracellular **(osmoreceptors cells)** → stimulation of osmoreceptors and send signals **to posterior pituitary in hypothalamus** → **decrease ADH**

Where and what ADH does?

1- It works on **collecting ducts** when it binds with V1 receptors and allow **water reabsorbation** to maintain osmolarity
2- It works in **blood vessels** when it binds with V2 receptors in **vessels to constrict and increase blood pressure**

Note: It only works on vessels when there is loss of 1 or more L of blood and body fluids

Synthesis in: **Supraoptic nuclei of hypothalamus**

Stored and secreted from: **Posterior pituitary gland "Neural secretion"**

What are the non-osmotic conditions that lead to release ADH does?

Osmotic stimuli	Effect on AVP secretion
Changes in serum osmolality	Increase or decrease depending on changes in osmolality
Nonosmotic stimuli	
Hemodynamic changes associated with low effective arterial blood volume	Increase
Act of drinking especially cooler fluids	Decrease
Nausea	Increase
Hypoglycemia	Increase
Renin angiotensin system (AgII)	Increase
Hypoxia and hypercapnia	Increase

AVP: Arginine vasopressin

What is the name of pores that allow water reabsorbed through collecting ducts by ADH?

Aquaporeins-2

Thirst mechanism

What are the mechanism that effect on thirst center?

A. Increase thirst:

- **Increased** osmolarity ECF.
- **Decreased** ECF volume.
- **Decreased blood pressure.**
- **Angiotensin II.**
- **Dryness of the mouth.**

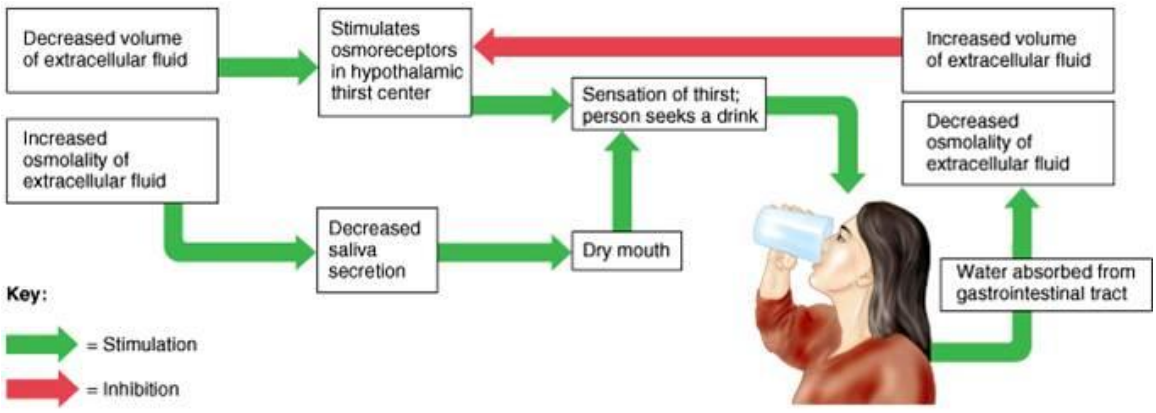
B. Decrease thirst:

- **Decrease** osmolarity ECF.
- **Increase** ECF volume.
-**Gastric distention.**

What is the meaning of Gastric distention decreases thirst?

Like in **obesity people**, the volume of their stomach in increased and that allowed taking more amount of food, which contain water. Thus, that will lead to decrease thirst center.

What are the mechanism?



When the edema happened by ADH?

When there are **inappropriate secretion of ADH** that will lead to hypo-osmolar condition of ECF and sodium concentration will be 120 mEq\L and below.

What is the most dangerous type of edema?

- Brain edema

What is the role of Ag II in osmolarity?

- Has very weak effect on osmolarity by releasing of aldosterone. **The major role of Ag II is maintain Sodium quantity "not osmolarity" in tubules.**

What are the most powerful mechanism that maintain ECF osmolarity? ADH-thirst or AgII-Aldosterone?

ADH-thirst is the most powerful feedback system in the body for controlling extracellular fluid osmolarity and sodium concentration

Lectures 8: Urine concentration

What are the difference between Facultative and obligatory Water reabsorbation?

Obligatory: Reabsorbation of water without hormonal control in PCT and descending limb

Facultative: Reabsorbation of water under control of ADH in DCT and collecting ducts

What is the goal of concentrate and dilute urine?

To maintain the osmolarity of blood which is around **300 mOsm.**

- If blood is become hyperosmolar → urine will become hyperosmolar
- If blood is become hypo-osmolar → urine will become hypo-osmolar

How much the osmolarity of medullary interstitium?

1200-1400 mOsm.

What are the mechanism that concentrate and dilute urine?

1- Hyperosmolar medullary interstitium
2- Role of ADH "discussed in Lecture 7"

How Hyperosmolar medullary interstitium are produced?

1- **Counter current multiplier by loop of henle:** the inflow is parallel to the outflow but opposite in direction.
Note: you have to see these videos:
https://www.youtube.com/watch?v=NIJQjTbhIJU
https://www.youtube.com/watch?v=P5Otmw9CkII

2- **Urea recycling in medulla:** Urea will secreted from inner medullary collecting ducts to interstitium under control of ADH. Then again reabsorbed by tubules.
Note: you have to see that video:
https://www.youtube.com/watch?v=92PFTLHE_H0

How Hyperosmolar medullary interstitium can be maintained?

By **Counter current exchanger** of **Vasa Recta**

How counter current exchanger of vasa recta work?

Vasa recta composed of **Descending** and **Ascending** limbs in form of U shape and the **blood flow is very slow to prevent wash out of solutes.**

1- **Descending limb:** Solutes will reabsorbed and water will secreted due to hyperosmolarity of interstitium
2- **Ascending limb:** Solutes will secreted and water will reabsorbed hypo-osmolarity of interstitium.

Note: you have to see that video:
https://www.youtube.com/watch?v=iZbAKdGHoU8

What are disorders that may affect urine concentration?

	Diabetes insipidus	Nephrogenic diabetes insipidus	Diabetes mellitus
Cause	Inability to produce ADH	Kidney not respond to ADH or problem in counter recurrent multiplier	Insulin not respond to its receptors
Manifestation	-Polyuria -Polydipsia -Dehydration	_____	- Hyperglycemia - Glucouria
Specific gravity	Low (diluted urine)	Low (diluted urine)	High (concentrate urine)
Treatment	Hormone replacement by nasal spray	_____	

Lectures 9 : Basics of Acid-Base balance

What pH represent?

Hydrogen ion concentration in the blood

What is the type of blood sample should be taken to measure pH and Why?

Arterial blood sample **(not venous),** because it represents the actual contents of blood such as Oxygen, nutrients.. Etc.

What is the normal range of pH?

- **in general:** 0-14
- **in the blood:** 7.35-7.45
- **Extracellular fluid (ECF):** 7.4

Can the pH in the body change?

Yes, like exercise body will add some hydrogen to blood through lactic acid and change pH.

How can we calculate the pH?

pH= 1/H+ concentration log OR **pH**= - log [H+]

What acids and what bases?

- Acids are H+ donors
- Bases are H+ acceptors

When we said it is acidosis or alkalosis?

- pH less than 7.35 **(acidosis)**
- pH more than 7.45 **(alkalosis)**

What is the survival range of pH in the blood?

Between **6.8 and 8. More or less** will lead to death

What are the strong and partial acids and bases?

- **Strong acid** = HCL **(complete dissociation)**
- **Weak acid** = Lactic acid,CO2,H2CO3 "Carbonic acid" **(Partial dissociation)**
- **Strong base** = NaOH **(complete dissociation)**
- **Weak base** = NaHCO3,HCO3 **(Partial dissociation)**

Why venous blood is more acidic than arterial?

Because it has higher CO2 concentration than arterial blood

Why acids more than bases in our bodies?

1. Food that contain proteins and lipids are rich in acids
2. The end cellular metabolism in mitochondria produced CO2 which source of H+ from the following reaction:

   $CO_2 + H_20 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$

Why pH is tightly regulated and small changes in pH is a serious condition?

- Most enzymes work only in specific pH **(change in pH → enzymes become inactive)**
- Change in pH cause disturbance in electrolytes which is a serious condition
- Can affect some hormones
- Acidosis can cause depression of synaptic ending and lead to coma such as a patient with **diabetes ketoacidosis**
- Alkalosis can cause **convulsion** and **tetany**

Lectures 10: Buffer systems

What are the systems that regulate pH?

- **Chemical buffer system: (first line)**
  Buffer system (immediately)
- **Physiological buffer system: (second line)**

1. Respiratory system (from minutes to hours)
2. Renal system (from hours to days) **The most effective regulator of pH**

What are the components of chemical buffer system?

1. Bicarbonate buffer (intracellular and **extracellular**)
2. Phosphate buffer (intracellular and **renal tubule fluid**)
3. Protein buffer (**the most important intracellular**)

What is the goal of buffer systems?

Convert **strong acids and bases** to **weak acids and bases** to maintain blood pH

What is the most important feature that buffer must have?

pH that very close to the pH of sites that buffer work in to observe the changes in pH.

Chemical mechanism:

- **Phosphate buffer:**

What are the components of bicarbonate buffer system?

- Hydrophosphate: HPO_4^{2-} which bind to H+ to Increase pH
- Dihydrophosphate: $H_2PO_4^-$ which bind to OH to Decrease pH

Why it has a good role in renal tubules?

Because it has pH that so close to the pH of fluid in the tubules

- **Bicarbonate buffer:**

  What are the components of bicarbonate buffer system?

  - **Sodium bicarbonate**: NaHCO3 regulated by kidney
  - **Carbonic acid:** H2CO3 regulated by lungs through equation:
    CO2 + H2O ⟶ H2CO3

  Why it is the most important extracellular buffer system?

  Because it regulated by **kidney and lungs**

  What is the concentration of HCO3 in the blood and what it is called?

  Its concentration in blood equals = **27mEq/L** and is called **alkali reserve.**

  Which is more in the blood HCO3 or H2CO3?

  HCO3 is more than H2CO3 with ratio of **20:1**

  How bicarbonate buffer work?

  We must have acid and base to react with each other. Then:

  $HCl\ (strong\ acid) + NaHCO_3 \leftrightarrow H_2CO_3\ (week\ acid) + NaCl$

  OR

  $NaOH\ (strong\ base) + H_2CO_3 \leftrightarrow NaHCO_3\ (weak\ base) + H_2O.$

  How can we calculate blood pH through bicarbonate buffer?

  By **Handerson-Hasselbalch equation**: $pH = 6.1 + \log \frac{HCO3^-}{0.03 \times PCO2}$

  Note that 6.1 represent pH of the buffer not the blood

- **Proteins buffer:**

  What are the components of bicarbonate buffer system?

  - Hemoglobin:
    Carboxyl group gives H+ “Decrease pH”
    Amino group accept H+ “Increase pH”
  - Plasma proteins
  - Intracellular proteins

Physiological mechanism:

- **Respiratory mechanism:**

  What are the components of system?

  The only component regulated here is CO2 (carbon dioxide) which is volatile acids.

  It cannot deal with fixed acids such lactic acids that accumulate in skeletal muscles.

  What is the general mechanism?

  pH can be adjusted by changing **RATE** and **DEPTH** of breathing.

  Patient with acidosis → Hyperventilation → wash out CO2 → increase pH

  Patient with alkalosis → Hypoventilation → retain CO2 → Decrease pH

  What happened if a healthy person has FAST hyperventilation?

  He will stop ventilation after 15 seconds because amount of CO2 reduced and chemoreceptors in the brain will observe this reduction. Therefore, it will inhibit ventilation.

  What happened if a healthy person has chronic hyperventilation?

  Patient with **Anorexia** will develop alkalosis due to reduction in CO2.

- **Renal mechanism:**

What is the normal secretion of H+ and reabsorbation of HCO3 per day?

Secretion H+ = 4400 mEq/day

Filtration HCO3 = 4320 mEq/day

So, the 80 that remains must be titers by buffer system as sodium salt

What is the general mechanism?

- Secretion of H+:

- Sodium/H+ counter transport **(PCT, Thick ascending loop and early DCT)**
- H+ pump **(Late DCT and collecting ducts)**
- Secretion of H+ with ammonia

- Reabsorbation of HCO3:

- Reabsorbation of 99% of filtered HCO3 **(PCT, Thick ascending loop and early DCT)**
- Generate a new one HCO3 by intercalated cells **(Late DCT and collecting ducts)**
- Generate new two HCO3 from glutamine

HCO3 that filtered (PCT, Thick ascending loop and early DCT) :

1-HCO3 found normally in the tubule lumen but cannot pass through luminal membrane directly.

2-HCO3 will bind with H+ which come from cell by Sodium/H+ counter transport and formed H3CO2 (carbonic acid)

3-Breakdown of H2CO3 into H2O and CO2 through luminal carbonic anhydrase

4-CO2 will cross membrane passively because it is lipid soluble

5-CO2 will bind with H2O inside the cell and form H2CO3

6-H2CO3 will break to H+ and HCO3 through cystolic carbonic anhydrase

7-HCO3 will go to interstitium through HCO3/Cl counter transport then it will go to the blood

Ammonia buffer:

Acidosis → metabolize of glutamine into Two NH_3 (ammonia) and Two HCO_3 → Two H+ will bind with two NH_3 to form two NH_4 (ammonium) → Secreted of NH_4 to tubules → NH_4 bind with Cl to form ammonium chloride → excreted with urine

In Late DCT and collecting ducts by phosphate buffer:

Acidosis → increase cell metabolism → generate a new one HCO_3 at DCT → Secretion of H+ through ***H+ pump*** → Acidic urine → Phosphate bind to H+ → Excreted with urine

Why there is a buffer system for tubules by ammonia and phosphate?

Because H+ reduced tubular pH 4.5. This is the lower limit that can be achieved in normal kidneys. Further decrease will cause tubular acidosis.

What is the most important buffer of renal tubules? Ammonia or phosphate?

Ammonia because excreted two H+ and formation two HCO_3

What does titer acid means?

For each on H+ excretion, new one HCO_3 will formed

What does Increase NH_4 excretion sign of?

Chronic acidosis

Lectures 11: Acid-base disorders

What are the normal values?

- pH< 7.35 acidosis
- pH > 7.45 alkalosis
- PCO2= 35-45 mmHg
- HCO3- = 22-26 mEq/L

What are the differences between Hypercapnea and Hypocapnea?

PCO2= more than 45 = Hypercapnea

PCO2= less than 35 = Hypocapnea

What are the difference between Complete and partial compensation?

- **Complete compensation:** when values return to normal ranges
- **Partial compensation:** when values remains outside normal ranges

When we can say it is compensated or not?

-Compensated if pH = 7.35-745

-Uncompensated if pH= more than 7.45 and less than 7.35

What are the principle effects of Acidosis and Alkalosis?

Acidosis: depression of the CNS through decrease of synaptic transmission

Alkalosis: over excitability of the central and peripheral nervous systems

What is the most common cause of acid-base imbalance?

Respiratory alkalosis

What are the causes and symptoms?

Disorder	Causes	Symptoms
Respiratory Acidosis	- CNS depression (anesthesia). - Resp. muscle paralysis - diaphragm paralysis, - Rib fractures - Obstructive lung diseases e.g. Emphysema - Pulmonary edema.	**1. General weakness** **2. Disorientation** **3. coma**
Metabolic Acidosis	- Diabetic ketoacidosis. - Severe diarrhea. - Hypoaldosteronism - Acute renal failure	
Respiratory Alkalosis	- Hyperventilation **(primary cause)** - High altitude. - Hysterical - Anorexia nervosa. - Early salicylate intoxication	**1. Numbness** **2. Lightheadedness** **3. Nervousness** **4. muscle spasms or tetany** **5. Convulsions** **6. Loss of consciousne**
Metabolic Alkalosis	- Severe vomiting. - Excess antacids. - Hyperaldosteronism - Severe dehydration	

Summary

Disorder	analysis	compensation	Treatment
Respiratory Acidosis	**pH = less than 7.35** **PCO_2 = more than 45** **HCO3 = Normal**	- Excretion of H+ - Retains HCO3	Restore ventilation IV Lactate solution
Respiratory Alkalosis	**pH = more than 7.35** **PCO_2 = less than 35** **HCO3 = Normal**	- Excretion of HCO3 - Retains H+	Breath in paper bag IV chloride solution
Metabolic Acidosis	**pH = less than 7.35** **PCO_2 = Normal** **HCO3 = less than 22**	- Hyperventilation - Excretion of H+ - Retains HCO3	IV Lactate solution
Metabolic Alkalosis	**pH = more than 7.35** **PCO_2 = Normal** **HCO3 = more than 26**	- Hypoventilation - Excretion of HCO3 - Retains H+	Electrolyte replacement IV chloride solution

Questions

1) PH= 7.12, PaCO2= 60mmHg, $HCO3^{-}$ = 24meq/L.

a) Compensated metabolic acidosis.

b) Uncompensated metabolic acidosis,

c) Compensated respiratory acidosis,

d) Uncompensated respiratory acidosis

2) PH= 7.51, PaCO2= 40mmHg, $HCO3^{-}$ = 31meq/L.

a) Normal,

b) Compensated respiratory acidosis,

c) Uncompensated respiratory alkalosis.

d) Uncompensated metabolic alkalosis

Answers are: 1-D 2-D