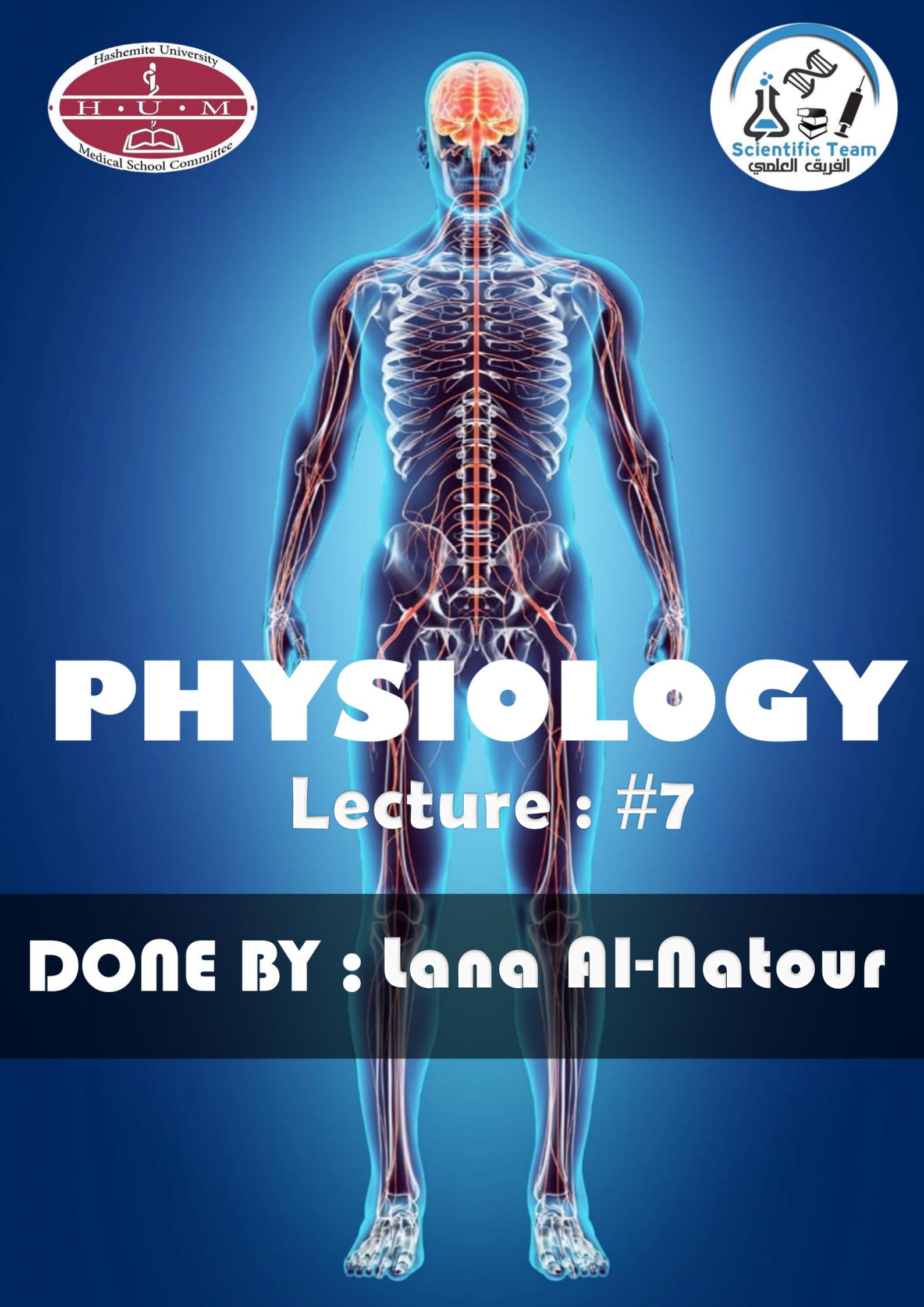


PHYSIOLOGY

Lecture : #7

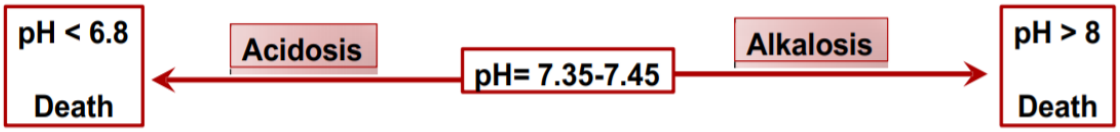
DONE BY : Lana Al-Natour

Acid-Base Regulation-II

so as we said before the buffers are the first line of defence :
if we have too much acid ,a base from buffer system will interact with.
If we have too much base,an acid from the buffer system will interact with.
وهدول buffers رح يحاولوا يضعفوا ويخففوا من مقدار تأثير في pH

Respiratory system is more faster than the renal system

Respiratory regulation of acid-base balance
Alkalosis= excess removal of H+ from the body fluids
هلا حكينا HCO3-بتعمل في حالات acidosis بحيث بترتبط بال hydrogen ions عشان ما تتغير قيم PH وهلا لما ما يكون عنا قيم hydrogen ions عالية بتزيد HCO3- وبصير عنا alkalosis
Acidosis= excess addition of H+



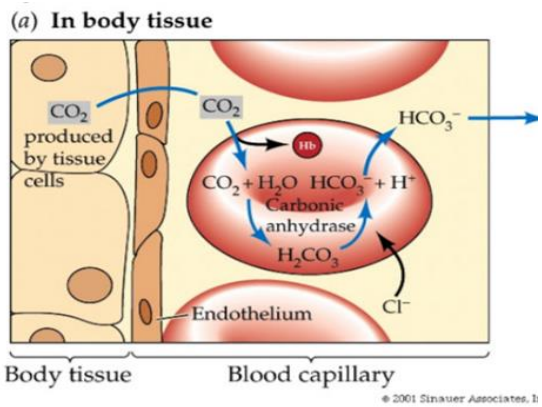
Respiratory Regulation of A/B

2nd line of defence against acid-base disturbances in the body.

- **By modulating CO2 excretion.**
- **Normally, PCO2 = 40 mmHg (35-45 mmHg).**

• ↑CO2 formation → ↑ECF CO2 → ↑ ECF PCO2 & Vice versa.

↑ECF CO2 → ↑H2CO3 → ↑H+



$$pH \propto \frac{HCO3}{PCO2}$$

هلا C02 بيجي من metabolism in the cells وبتطلع على circulation اما ان يكون dissolved وبالتالي اله hydrostatic Pressure او انه بيرتبط مع H2o بوجود CA وبيكون H2CO3((عبارة عن acid ضعيف ورح يصيرله disassociate الى +H و -HCO3))

دائما CO2 بربطه مع HYDROGEN IONS

- Response occurs within 3-12 minutes.
- ↑↑ ventilation (RR) → ↓↓ PCO2 → ↑PH

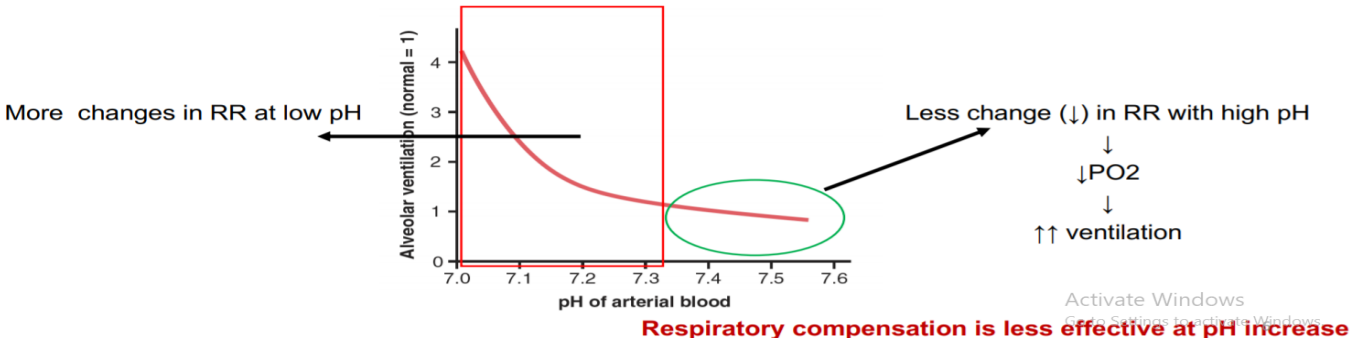
عشان يتخلص من CO2

- ↓↓ ventilation (RR) → accumulation of CO2→↑↑ PCO2→ ↓PH
- ↓↓ [H+] → ↑pH → ↓↓ ventilation (RR) → accumulation of CO2→↑↑ PCO2.

في حالات alkalosis الجسم بده يحتفظ بال hydrogen ions عشان يقلل من pH

- ↑↑ [H+] → ↓pH → ↑↑ ventilation (RR) → ↓↓ PCO2

في حالات acidosis الجسم بالاول بده يعادل hydrogen ions بال HCO3- وبالتالي too much hydrogen ions وبالتالي lung رح تزود ventilation ورح تقلل pressure of CO2 وبتتحمس اكثر في حالات acidosis وعشان ارفع PH



هلا عندي في الوسط على محور السينات normal PH وتحركنا لليسار وكان عندي نزول في pH رح يزيد alveolar ventilation وبتطلع CO2 الزيادة من الجسم واذا زاد pH لما تحركنا لليمين يعني alkalosis وبالتالي lung رح تخفف ventilation عشان تحافظ على hydrogen ions طيب هلا الاكسجين شو نعمل فيه ما دام lung عم تخفف respiration رح يقل شوي الاكسجين عن normal و الاكسجين القليل رح يحفز ventilation وبالتالي في metabolic alkalosis الرئة ما رح تكون effective زي لما تكون في حالات acidosis

So hyperventilation is more dominant than hypoventilation

YouTube video for respiratory regulation of acid base balance :

https://www.youtube.com/watch?v=GKFxuHKVh10

Renal Regulation of Acid-Base Balance

وهون منحكي الشغل النظيف بده وقت عشان هاي regulation بطيئة بس potent ☺

3rd line of defence against acid-base disturbances and the most powerful.

- Kidneys conserve HCO3 - and excrete acidic (↓ acid in ECF) or basic urine(↓base in ECF) depending on body needs

حكينا انه في 2 types of acids يلي هي : volatile زي CO2 وبتطلع عن طريق lungs و non-volatile يلي بتطلع عن طريق kidneys

- Kidneys eliminate non-volatile acids (H2SO4, H3PO4) (~ 80 mmol/day)
- Filtration of HCO3 - (~ 4320 mmol/day)
- Secretion of H+ (~ 4400 mmol/day)
- Reabsorption of HCO3 - (~ 4319 mmol/day)
- Production of new HCO3 - (~ 80 mmol/day)

H+ is not excreted as free H+ but rather in combination with other urinary buffers, especially phosphate and ammonia

production حسب حاجة الجسم بتصير

- Excretion of HCO3 - (1 mmol/day)

Acidosis:

- increased H+ secretion

- increased HCO3- reabsorption

- production of new HCO3 –

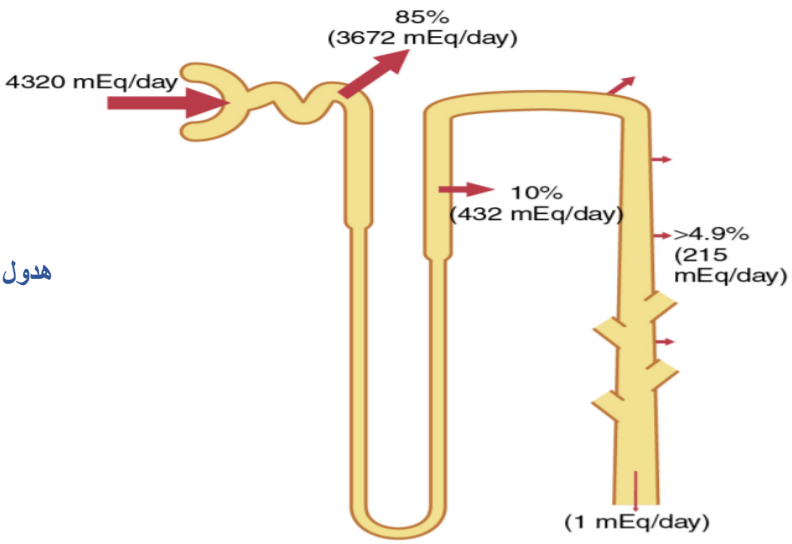
Alkalosis:

- decreased H+ secretion

- decreased HCO3- reabsorption

- loss of HCO3 - in urine

Key point: For each HCO3- reabsorbed, there must be a H+ secreted



هدول مناطق reabsorption لل HCO3-

Mechanisms of HCO3 - reabsorption and Na+-H+ exchange in PT, thick loop of Henle & early DT

((ادرسوا على الرسمة عشان توصل الفكرة اسرع ☺))

Na-K ATPase → Dec. IC Na → [] gradient

هلا sodium potassium pump يلي موجودة على basolateral ((primary transport))رح تساعد على انه تشغل sodium –hydrogen pump ب secondary transport بسبب الاختلاف يلي صار في gradient
طيب هلا hydrogen ions من وين اجت ؟ اجت من dissociation of H2CO3 الى HCO3- و H+

↓

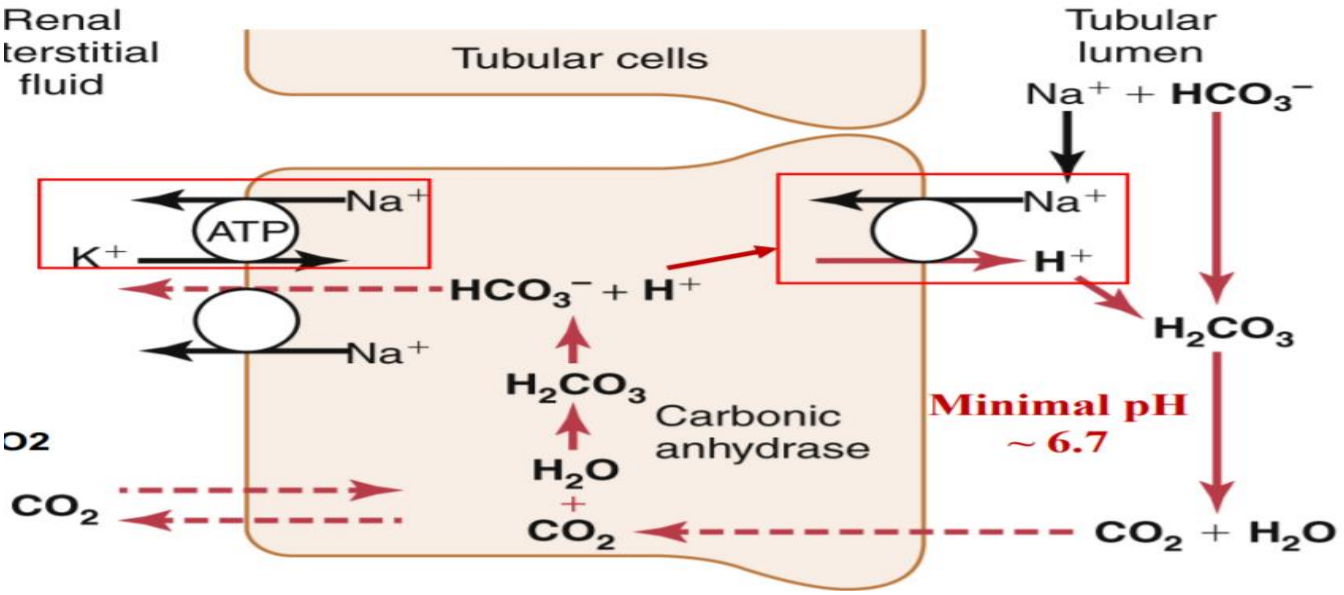
<u>H+ secretion into the tubular fluid by Na-H counter-transport</u>

NO CHANGE IN LUMINAL pH (EXCEPT COLEECTING DUCTS)

HCO3 reabsorption starts with formation of H2CO3 → CO2

Reabsorption → Na-HCO3 co-transport

Replacement of filtered HCO3



هون صار عنا انه CO2 دخل من tubular lumen لداخل cell (diffusion) وبيتحد مع الماء وبتطلع H2CO3 وبعدين بيتفكك وبصير H+ و HCO3- وهلا رح يروح HCO3- على interstuimعن طريق HCO3- sodiumcotransporter وبعدها H+ رح يطلع على lumen عن طريق exchanger وبيرتبط مع HCO3- buffer يلي جاي من filtrate

هلا هون عملية تكوين CO2 ما بتأثر على pH وبالتالي رح تكون minimal pH=6.7 وهي اقل حد ممكن يوصله PCT

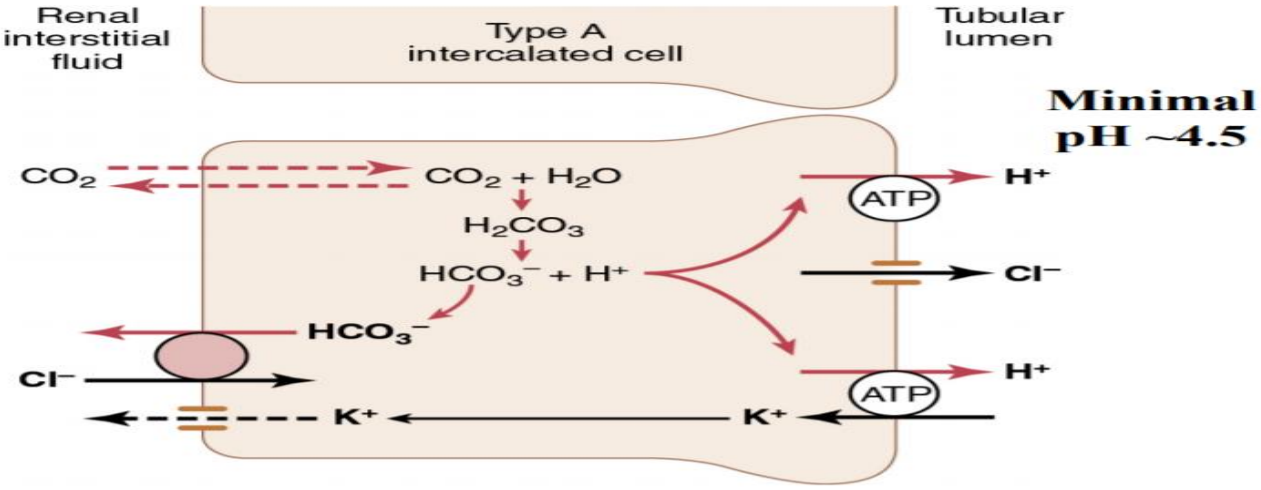
عملية دخول HCO3- للinterstuim عشان تعوض filtered bicarbonate وبنفس الكمية وما صار عندي اي خسارة لل HCO3-

HCO3 - reabsorption and H+ secretion in intercalated cells of late distal and collecting tubules

Primary Active secretion of H+ by H+–ATPase & and H+- K+-ATPase

CHANGE IN LUMINAL → pH acidification of U

one HCO3 is absorbed for each H+ secreted → HCO3-Cl counter transport (PT, LH,CD)
one Cl is passively secreted H+.



بينما هون CO2 بيجي من interstuim وبعدين بيمسك بالماء وبصير عنا H2CO3 وبعدها HCO3- و H+ وهلا بطرح H+
على lumen لازم اطرح بداله HCO3- على interstuim وعنا 2 types لل hydrogen secretion يلي هي
H+/k+ cotransporter و primary transport (atpase)
وطيب HCO3- كيف ادخله؟عن طريق CL-/HCO3- cotransporter
و pH هون ممكن ينزل اكثر مش زي بال PCT عشان عنا 2 mechanisms لل H+secretion وبيوصل لل

YouTube video for renal regulation of acid base balance :

https://www.youtube.com/watch?v=hZPeP_oIdXk

Only a limited number of H+ can be excreted in its free form in urine.

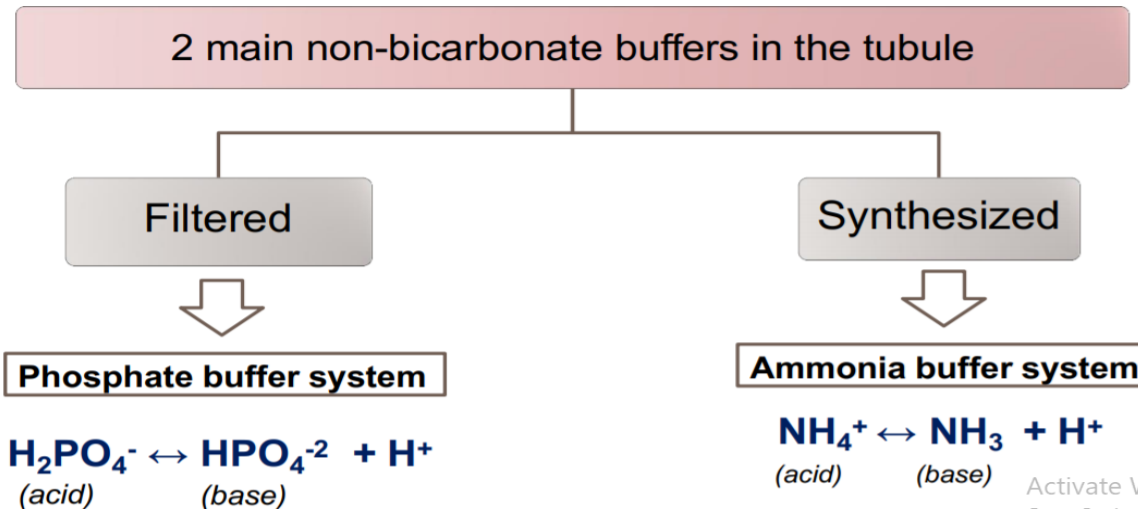
يعني ما منلاقي في urine اي freely hydrogen ions

• Lowest possible urine pH=4.5 → ≈ 0.04 mmol/L of free H+.

• How does the kidney excrete the extra H+?

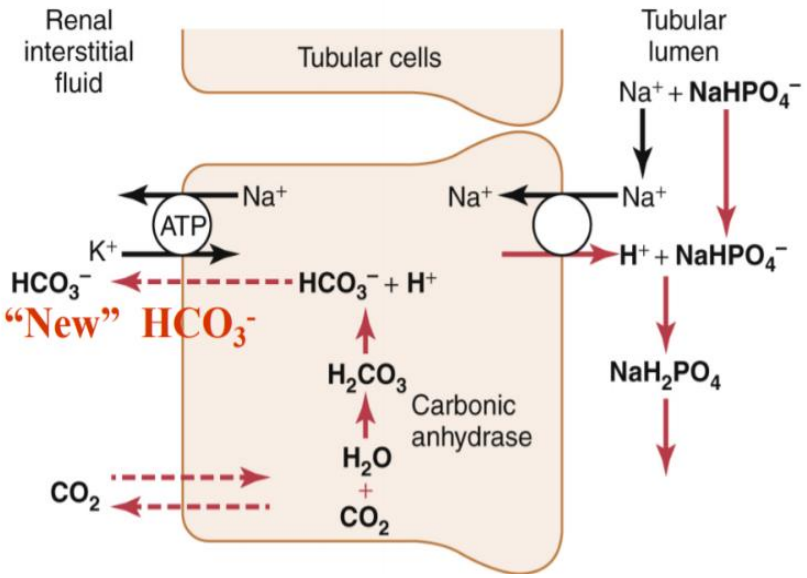
The extra H+ secreted will need to be buffered in the tubular lumen Non-Bicarbonate Buffers in the Tubular Lumen

هلا في حالات الطبيعية bicarbonate بكون buffer ولكن في حالات abnormality بلش non
bicarbonate buffer يشتغل في kidney بمعنى اخر لما يكون عنا كثير +H في urine رح تصير هدول buffers



هلا هدول buffers اما انه موجودة في filtrate او انه بتتصنع في tubules

Buffering of secreted H+ by filtered phosphate (NaHPO4 -) and generation of "new" HCO3



هلا بيجي CO2 من interstuim
وبصير H2CO3 وبعدها H2O و
HCO3- وبصير reabsorption لل
HCO3- وبيطلع H+ لل lumen
وحكينا قاعدة كل ما يطلع H+ رح
يصير Reabsorption for HCO3-
بس هون new مش من filtered

وهلا H+ بيمسك بال phosphate
buffer وبيتكون phosphoric acid

وبينطرح في urine

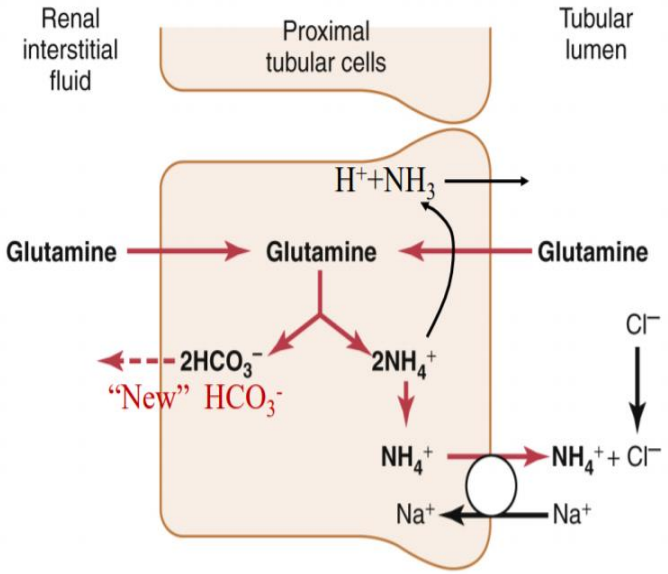
Production and secretion of NH4 + and HCO3 - <u>by proximal, thick loop of Henle and distal tubules</u>

Ammonia buffers are formed in most of the tubules

- **Quantitatively, NH4+ system is more important than the phosphate buffer system for H+ excretion in urine.**
- **It is the most important system in case of acidosis.**
- **Ammoniagenesis(formation of new ammonia) from glutamine**

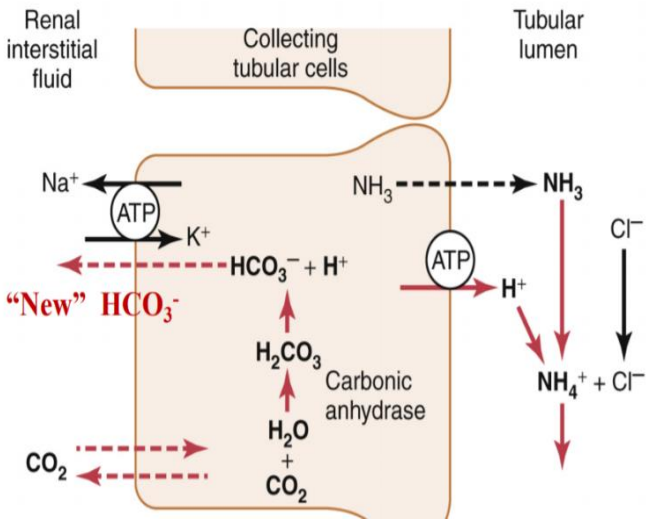
بيجي عنا من circulation نوع من انواع amino acids ويلي هو عبارة عن glutamine ويلي بيجي من metabolisms in the liver وبالتالي بيتفكك الى 2NH4+,2HCO3- والامونيا بصيرلها excretion to the lumen by sodium-NH4+contransporter وبصيرلها الامونيا مع chloride binding وممكن كمان شغلة انه الامونيا يتفكك الى H+, NH3 وبروح على tubular lumen

اهم buffer system بيشتغل في acidosis وهو most efficient than phosphate buffer system



Buffering of H+ by NH3 in <u>collecting tubules</u>

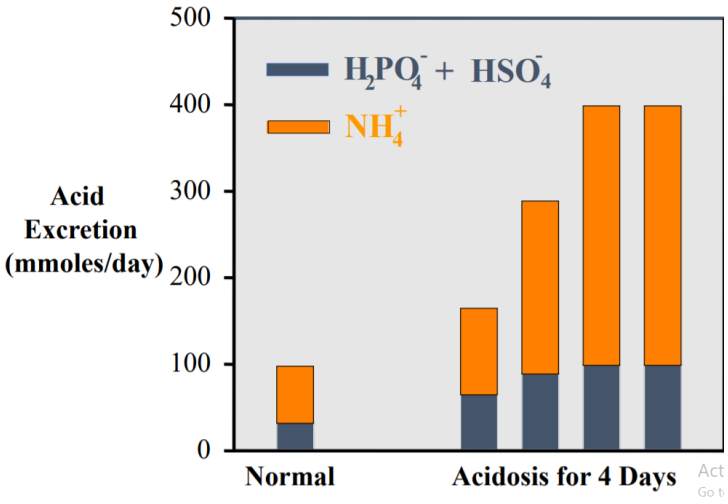
هلا عنا نفس المبدأ زي في proximal tubular cells بس NH3 يلي بتيجي من عند NH4+ رح يصيرلها Diffused to the lumen ورح ترتبط مع H+ و Cl- ويصير عنا ammonium chloride



Phosphate and Ammonium Buffering In Chronic Acidosis

هون منلاقي انه ammonium buffer كثيير efficient في حالات acidosis

وهون منشوف كلما زادت acidosis منشوف كيف ammonium buffer زاد تصنيعه عشان يسوي excretion for hydrogen ions



Quantifying Renal Acid-Base Excretion

طيب هلا كيف بدنا نعرف اديش في acid او base انضافت او انقامت

HCO3 excretion=urine flow rate X [HCO3U]((concentration of HCO3-in the urine)).

HCO3 excretion= adding an H+ to the blood

amount of new HCO3 added to blood:

بتصنع HCO3- جديد لما يكون عنا non-bicarbonate buffers فاحنا منقدر نحسب اديش تصنع bicarbonate جديد من خلال انه نعرف non-bicarbonate buffers excretions

=H+ excretion with *non-HCO3 buffers*

= NH4+ excretion_+phosphate excretion

= V(urinary flow rate) x[NH4u]+ urinary titrable acid

Note :phosphate excretion can be measured by urinary titrable acid

طيب كيف يعني ؟؟عن طريق انه نحط قاعدة قوية على urine وبالتالي عشان نعادل pH ويصير زي pH الموجود في filtration عشان ارجع urine زي ما كان ومجرد ما وصل plasma زي urine وبالتالي بحسب اديش حطينا قاعدة قوية وهي بتكون نفس القيمة لل phosphate excretion to neutralize hydrogen ions

Urinary titrable acid process:NaOH, to a pH of 7.4 number of milliequivalents of NaOH= number of milliequivalents of secreted H to combine with phosphate

Net acid excretion= NH4 excretion+ Urinary titratable acid- HCO3 excretion ((adding an H+ to the blood))

net acid excretion must equal the nonvolatile acid production in the body

acid excretion non volatile acid production ممكن تجيب سؤال على هاي القاعدة وتطلب اديش فاحنا منحسب

Net acid excretion= NH4 excretion+ Urinary titratable acid- HCO3 excretion

In acidosis → acid excretion?? NH4 excretion ↑ ↑ ↑

↓

Net acid excretion ↑

Net acid excretion=HCO3 added to blood

في حالة acidosis رح يتحمس الامونيا buffer عشان يرتبط مع +H وبالتالي حكينا كل ما يطلع non-volatile acids معناها رح ينزاد للدم -HCOO3 وكمية acid excretion رح تساوي كمية -HCO3 يلي رح تنضاف على circulation

In alkalosis → acid excretion??

NH4 excretion=0

HCO3 excretion ↑ ↑ ↑

↓

Net acid excretion is negative =HCO3 is lost & NO new HCO3 formation

في حالة alkalosis ما رح يكون في ammonia buffer وبصير-excretion for HCO3 عشان اقلل من pH وبالتالي acid excretion رح يكون (-)

Table 31-2 Plasma or Extracellular Fluid Factors That Increase or Decrease H^+ Secretion and HCO_3^- Reabsorption by the Renal Tubules

Increase H^+ Secretion and HCO_3^- Reabsorption	Decrease H^+ Secretion and HCO_3^- Reabsorption
↑ P_{CO_2}	↓ P_{CO_2}
↑ H^+, ↓ HCO_3^-	↓ H^+, ↑ HCO_3^-
↓ Extracellular fluid volume	↑ Extracellular fluid volume
↑ Angiotensin II	↓ Angiotensin II
↑ Aldosterone	↓ Aldosterone
Hypokalemia	Hyperkalemia

****قبل ما نبلش بال abnormalities and compensation لازم نعرف انه buffers بيشتغلوا بالاول بعدين renal وبعدها respiratory**

Renal correction of acidosis(low pH)

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

	Acidosis pH< 7.35	
Type	Respiratory	Metabolic
Change	↑PCO2	↓ HCO3
Causes	Hypoventilation- respiratory centers damage Airways obstruction Impaired exchange of gases Neuromuscular dis	excessive acid →Metabolic dis (e.g DM, shock)/Ingestion of Acids→aspirin/Impaired acid secretion HCO3 loss→ diarrhea & RF
Compensation ↑ pH	Renal→↑HCO3 reabsorption	↑HCO3 reabsorption Respiratory→ hyperventilation
Diagnosis	pH ↓ ↑PCO2 ↑HCO3	pH ↓ ↓PCO2 ↓ HCO3

Respiratory related to CO2 while the metabolic related to HCO3-

The tables are important ☺

عند ارتفاع CO2 لازم نعوضهم طريق kidneys بأنه نزود HCO3- reabsorption عشان تتعدل pH

$$pH \propto \frac{HCO3}{PCO2}$$

وعند انخفاض HCO3- لازم نعوضهم ونخفض CO2 عشان pH

In DM: metabolism of fat will occur ,ketoacids will be formed

In shock: no oxygen so anaerobic metabolism will occur leading to lactic acid accumulation

Renal correction of alkalosis(high pH)

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

	Alkalosis pH> 7.45	
Type	Respiratory	Metabolic
Change	↓PCO2	↑HCO3
Causes	Hyperventilation-fever, psychoneurosis, meningitis, early exercise, ascending to high altitude	-Acid loss→persistent vomiting -↑HCO3 →thiazides/loop diuretics-Hypovolemia-Ingestion of alkaline drugs (NaHCO3) ↑aldosterone & cortisol
Compensation ↓ pH	Renal→↓HCO3 reabsorption	Renal→↓HCO3 reabsorption Respiratory→ hypoventilation
Diagnosis	pH ↑ ↓PCO2 ↓ HCO3	pH ↑ ↑PCO2 ↑HCO3

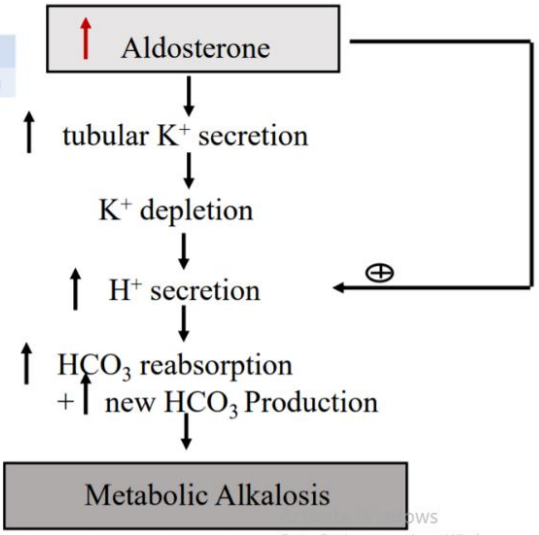
Compensation منتذكر فيها هاي العلاقة :

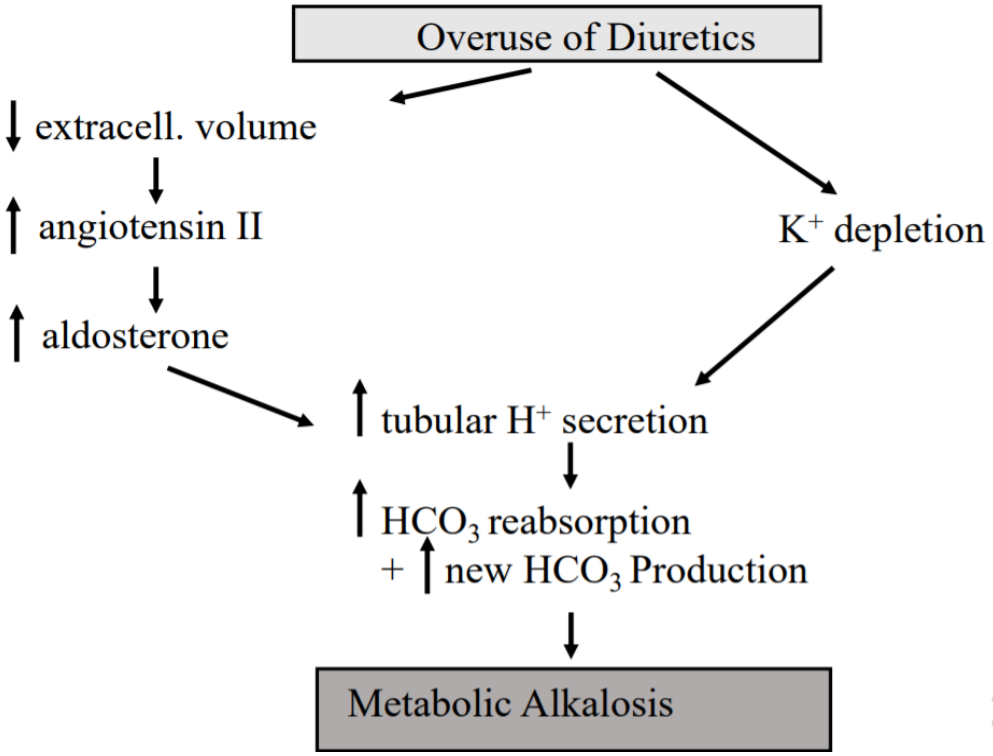
$$pH \propto \frac{HCO3}{PCO2}$$

Note :when aldosterone is increased ,the sodium will be reabsorbed and HCO3- also

Hyperaldosteronism (aldosteronism) and acid base disturbances

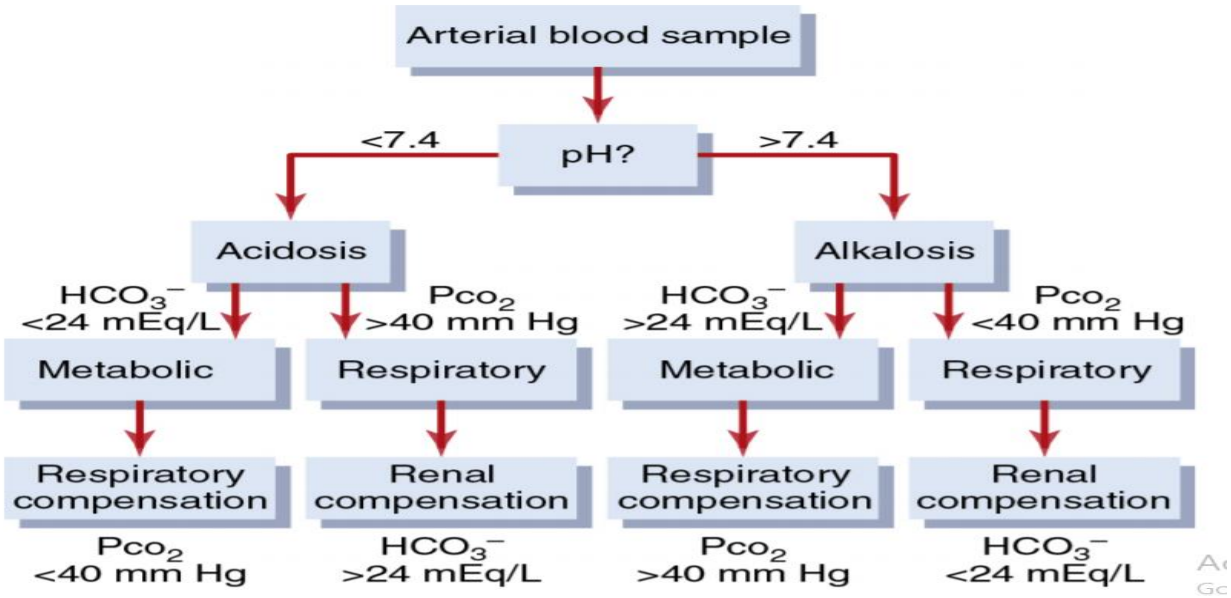
Hormone	Effects
Aldosterone	↑ NaCl, H_2O reabsorption, ↑ K^+ secretion, ↑ H^+ secretion

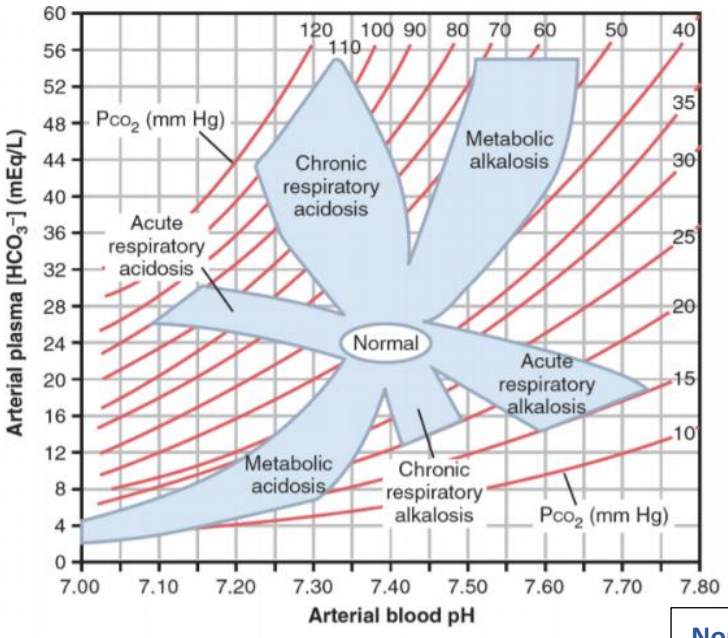




Acid base disturbances caused by overuse diuretics

Classification of Acid-Base Disorders from plasma pH, pCO2, and HCO3-





Mixed disorders

Nomogram

عشان يحكيلنا ممكن انه يكون شخص معاه مثلا acidosis (respiratoy and metabolic) مع بعض عشان compensation يكون عكس بعض

حكت الدكتورة هاي معلومة زيادة بس المهم انه نعرف هل هاد primary انه بس مثلا respiratory acidosis لحاله او mixed وبتصير الفكرة اوضح في الاسئلة يلي جاي

Anion Gap as a Diagnostic Tool

In body fluids: total cations = total anions

Na+ = Cl- + HCO3 - + unmeasured anions

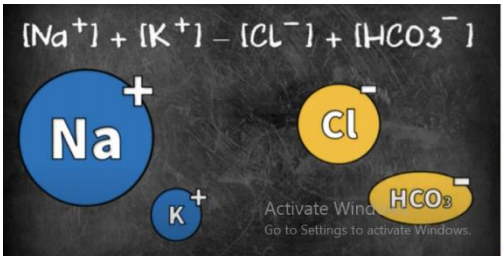
unmeasured anions = Na+ - Cl- - HCO3 - = anion gap

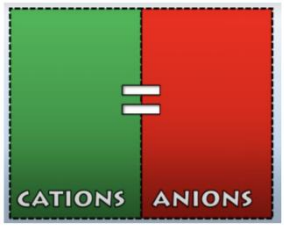
= 142 - 108 - 24 = 10 mEq/L

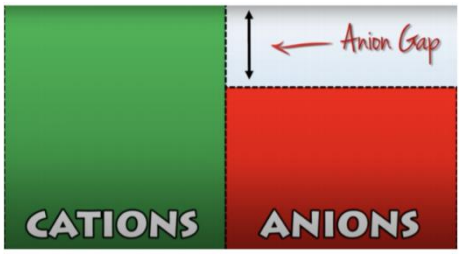
Normal anion gap = 8 - 16 mEq / L

Unmeasured anions for example like protiens,buffers,….

رح نعبر عن cations عن طريق الصوديوم و anions عن طريق الكلوريد و hco3- و unmeasured anions عشان تعبر عن anion gap







2types of anion gap :high or normal

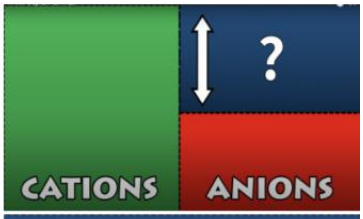
Anion Gap in Metabolic Acidosis when anion gap is increased

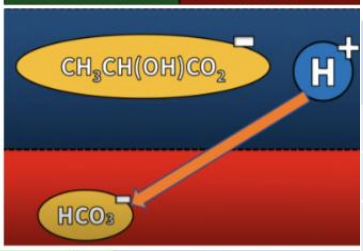
- **↑ anion gap → ↑unmeasured anions (organic acids)**

anion gap = Na+- Cl- - ↓ HCO3-

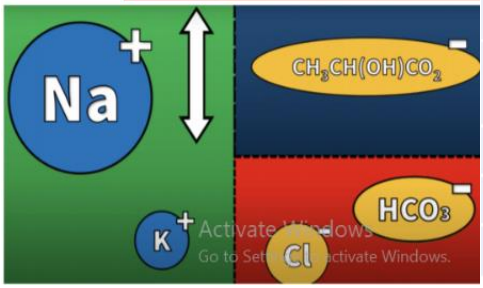
normochloremic metabolic acidosis

هدول الحالات لازم نحفظهم عشان دائما عندهم زيادة في acids





Increased Anion Gap (Normochloremia)
Diabetes mellitus (ketoacidosis)
Lactic acidosis
Chronic renal failure



Aspirin (acetylsalicylic acid) poisoning
Methanol poisoning
Ethylene glycol poisoning
Starvation

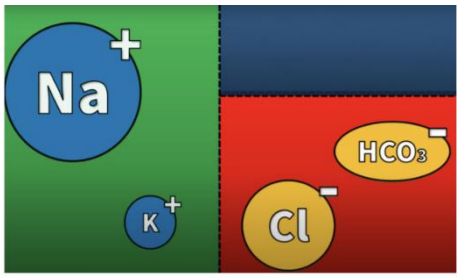
Anion Gap in Metabolic Acidosis (normal anion gap)

- loss of HCO3 - = normal anion gap anion gap

= Na+ - Cl- - HCO3 –

hyperchloremic metabolic acidosis

بهاي الحالة compensation ما بكون من buffers
عشان anion gap is normal وبالتالي بتكون
chloride ions عن طريق compensation



Normal Anion Gap (Hyperchloremia)
Diarrhea
Renal tubular acidosis
Carbonic anhydrase inhibitors
Addison's disease

Questions :

1-A patient presents in the emergency room and the following data are obtained from the clinical labs: plasma pH= 7.15, HCO3 - = 8 mmol/L, pCO2= 24 mmHg

This patient is in a state of:

1. metabolic alkalosis with partial respiratory compensation

2. respiratory alkalosis with partial renal compensation

3. metabolic acidosis with partial respiratory compensation

4. respiratory acidosis with partial renal compensation

Answer:3

pH قليل معناها HCO3-//acidosis قليل معناها metabolic//و co2 اقل من normal

2-Laboratory values for an uncontrolled diabetic patient include the following:

arterial pH = 7.25

Plasma HCO3- = 12

Plasma PCO2 = 28

Plasma Cl- = 102

Plasma Na+ = 142

What type of acid-base disorder does this patient have?

metabolic acidosis with respiratory compensation

What is his anion gap?

Anion gap = 142 - 102 - 12 = 28

Which of the following are the most likely causes of his acid-base disorder?

a. diarrhea

b. diabetes mellitus

c. Renal tubular acidosis

d. primary aldosteronism

answer : DM because it is high anion gap

	pH	H^+	P_{CO_2}	HCO_3^-
Normal	7.4	40 mEq/L	40 mm Hg	24 mEq/L
	7.35-7.45		35-45	22-26

3-Laboratory values for a patient include the following:

arterial pH = 7.34

Plasma HCO3- = 15

Plasma PCO2 = 29

Plasma Cl- = 118

Plasma Na+ = 142

What type of acid-base disorder does this patient have?

Metabolic Acidosis with Respiratory Compensation

What is his anion gap?

Anion gap = 142 - 118 - 15 = 9 (normal)

Which of the following are the most likely

causes of his acid-base disorder?

a. diarrhea

b. diabetes mellitus

c. aspirin poisoning

d. Chronic renal failure

answer :a because it is a normal anion gap

4- Two or more underlying causes of acid-base disorder.

pH= 7.60

pCO2 = 30 mmHg

plasma HCO3- = 29 mmol/L

What is the diagnosis?

Mixed Alkalosis because :

• Metabolic alkalosis : increased HCO3-

• Respiratory alkalosis : decreased pCO2

عشان ما فيه اي compensation ولو كان عنا مثلا metabolic alkalosis لحاله المفروض يزيد CO2 مش يقل

5-A plasma sample revealed the following values in a patient:

pH = 7.12

PCO2 = 50

HCO3- = 18

diagnose this patient's acid-base status:

acidotic or alkalotic? Acidotic

respiratory, metabolic, or both?? Both

Mixed acidosis: metabolic and respiratory acidosis

Good luck hope ☺