PHYSIOLOGY

- SHEET NO. 10+11 – Acid-Base Balance
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In the last lecture, we talked about **Renal Regulation of Potassium**, brief revision:

- Increase Na^+ intake will decrease Na^+ reabsorption in the proximal tubule, water expansion, and increase pressure thus, **increase GFR**.
- Increasing the amount of filtered fluid will increase the distal tubule flow rate, which will increase the washing or flushing of the potassium, thus increasing potassium secretion and excretion.
- This will cause **negative feedback** on the aldosterone, so inhibition of the aldosterone release, thus K^+ excretion back normal.

Acidosis and Alkalosis:

- Intercalated cell $\rightarrow$ reabsorption of K^+
- Principal cells $\rightarrow$ secretion of K^+
- In **acute acidosis**, increasing H^+ in the body will **inhibit Na^+/K^+ ATPase** in the Principal cells, thus, decreasing intracellular K^+ level and K^+ secretion (**hyperkalemia**).
- In **chronic acidosis**, a compensatory mechanism by regulating the buffers will prevent hyperkalemia.
- Thus, **chronic** acidosis leads to a loss of potassium, whereas **acute** acidosis leads to decreased potassium excretion.
- In **acute alkalosis**, decreasing H^+ in the body will **activate Na^+/K^+ ATPase** in the Principal cells, thus, increasing intracellular K^+ level and K^+ secretion (**hypokalemia**).

Causes of Hyperkalemia:

- Renal failure.
- Decreased distal nephron flow (heart failure, severe volume depletion, NSAID, etc).
- Decreased aldosterone or decreased effect of aldosterone (adrenal insufficiency, K^+ sparing diuretics (spironolactone, eplerenone)).
- Metabolic acidosis (hyperkalemia is mild).
- Diabetes (kidney disease, acidosis, insulin).

Causes of Hypokalemia:

- Extremely low intake of K^+.
- Metabolic alkalosis.
- Excess insulin.
- GI loss of K^+ (diarrhea).
- Increased distal tubular flow (salt-wasting nephropathies, osmotic diuretics, loop diuretics).
- Excess aldosterone or other mineralocorticoids.

Renal Regulation of Calcium

- No secretion for calcium, only filtration, and reabsorption.
- The main regulator for calcium level is the **parathyroid hormone** by adjusting the reabsorption.

Now let's start our topic for today. Try to enjoy :)

Acid-Base Balance

The **renal system** works with the **respiratory system** in a harmony to maintain acid-base balance in our bodies, in addition to the **buffer system** too.

The pH in our bodies must be maintained in a narrow range (**7.2-7.4**) to preserve the normal function of the enzymes which perform their function within that narrow pH.

pH value represents the acidity which mainly mirrors the H^+ level in the body. H^+ is precisely regulated at 3-5 x 10 -8 moles/L (pH range 7.2 -7.4).

Metabolic activity in our bodies produces acids, which are classified according to the way the body gets rid of them into **volatile** and **non-volatile acids**.
Volatile acids are eliminated by CO_2 expiration. **Nonvolatile** acids are organic acids produced in larger quantities than volatile acids and cannot be eliminated simply by CO_2 expiration, however, they get titrated before excretion.
Extra: **Volatility** is the tendency of a substance to vaporize, the key difference between volatile and nonvolatile acids is that the volatile acids easily vaporize whereas the nonvolatile acids do not easily vaporize.

What is the reason behind maintaining a pH within a narrow range despite the continuous production of acids from the body?

1. **Body fluid chemical buffers**; first-line, rapid but temporary.
   (Ex. Bicarbonate, ammonia and ammonium, proteins, and phosphate)
2. **Lungs**; second line, rapid, eliminate volatile acids by CO_2 expiration.
3. **Kidneys**; the most powerful but the slower; so it is in the third line, eliminate non-volatile acids.

Buffer Systems in the Body

Buffer: a chemical compound resists the significant drop or increase in the pH; by accepting H^+, releasing H^+, or accepting OH^-.

Main body fluid compartment: ICF, ECF (plasma and interstitial), and urine.
For each one of these compartments, we have an **important buffer** (Bicarbonate, ammonia and ammonium, proteins, and phosphate).

The **effectiveness** of the buffer system depends on:

- the concentration of reactants (buffer substances) in the compartment.
- pK of system and pH of body fluids, and their proximity to each other; buffers work most effectively in a pH **close** to their pk. pk is the constant dissociation of the buffer.

1. **Bicarbonate**: most important **ECF** buffer.

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

- H_2CO_3 is a weak acid, so it does not disassociate easily. It disassociates into H^+ and HCO_3^-.
- The direction of the reaction goes in both ways depending on the body's needs.
- To calculate the pH by **Henderson-Hasselbalch Equation**, we need:
  - ✓ **pk** of the Bicarbonate.
  - ✓ the **concentration of Bicarbonate**.
  - ✓ the **concentration of CO_2**. But because the concentration of CO_2 is hard to obtain, so we calculate the **partial pressure of CO_2** and multiply it by a **constant (α).**
  - ✓ The Henderson-Hasselbalch Equation:

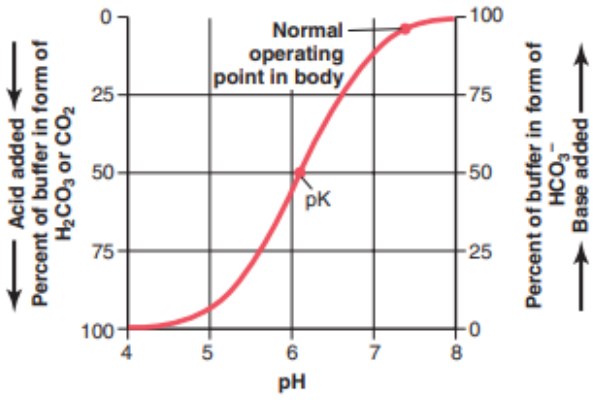
$$pH = pK + \log\frac{HCO3-}{\alpha\ pCO2}$$

pk of bicarbonate = 6.1
α constant = 0.03

  - ✓ If HCO_3^- concentration equals CO_2 concentration, pH will equal pk.

Titration curve for bicarbonate buffer system:

- **The normal operating point in the body** differs for each buffer. for bicarbonate, it's when pH equals 7.4. The effectiveness here is **NOT** at its best, (The effectiveness at best when pk=pH), but their concentration is very high, and the components of the system (CO_2, HCO_3^-) are closely regulated by the lungs and the kidneys, so it's considered the **best buffer**.



- When there is 50% from both reactants (acid and base) in the compartment, pH will equal pK and equal 6.

2. **Phosphate**: it is an important **renal tubular** buffer; why?

- high concentration of phosphate in the tubular fluid (phosphate is a major electrolyte in the **intracellular** compartment and **tubular** fluid but **not** in the **extracellular** compartment)
- pK for phosphate is 6.8 which is close to the pH of urine.

$HPO_4^{--} + H^+ \leftrightarrow H_2PO_4^-$

3. **Ammonia**: important **renal tubular** buffer.

$NH_3 + H^+ \leftrightarrow NH_4^+$

4. **Proteins**: important **intracellular** buffer. By looking at the amount of the protein in our bodies, it must be the most effective candidate for the buffering capacity, however, because the protein is mostly intracellular, it's hard for acids to enter the cell to get titrated by protein so it's very slow and needs hours and days.
   Ex. Hemoglobin in the RBCs
   $H^+ + Hb \rightarrow HHb$
   (60-70% of buffering is in the cells)

Importance of Buffer Systems

- Normal H^+ concentration = 0.00004 mmol/L ($4 * 10^{-5}$ mmol/L)
- Amount of **non-volatile** acid produced ~ 60-80 mmol/day. 80 mmol /42 L = 1.9 mmol/L = 47,500 times > normal H+ concentration.
- We need a high buffering capacity to titrate the non-volatile acid that is produced, to maintain the pH within the normal narrow range.
- The minimum and maximum pH of the body with which a person **can live for only a few hours** is 6.8-8.

Respiratory Regulation of Acid-Base Balance

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

The respiratory system eliminates **volatile** acids by CO_2 expiration, thus increasing H^+ loss.

Acidosis → activation of respiratory centers → adjusting the rate of ventilation → rapid compensation by elimination of volatile acids in the form of CO2.
Alkalosis → reducing the rate of ventilation → keeps H^+ in the body to titrate the Alkalinity.

Feedback Gain = 1.0 to 3.0 (corrects 50 to 75 %) but we still need the kidney.

Renal Regulation of Acid-Base Balance

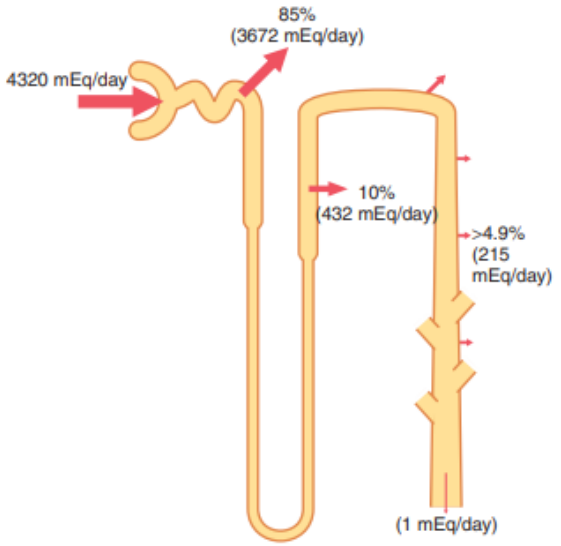
The kidney eliminates **non-volatile** acids by:

- Secretes H^+ mainly by intercalated cells.
- Adjust the reabsorption of HCO_3^-.
- Generates new HCO_3^-.

The kidney conserves HCO_3^- and excretes acidic or basic urine depending on the body's needs.

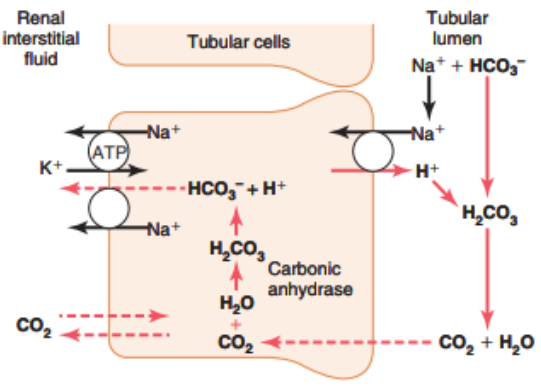
Reabsorption of bicarbonate (and H^+ secretion) in different segments of the renal tubule.

- Key point: For each HCO_3^- reabsorbed, there must be an H^+ secreted (1:1).
- Filtration of HCO_3^- (~ 4320 mmol/day).
- In PCT, 70-80% of the filtered bicarbonate will be reabsorbed.
- In Thin Henle, no change in bicarbonate concentration.
- In Thick Henle, 10% of the filtered bicarbonate will be reabsorbed.
- Late Distal and Collecting tubules; a variable range of reabsorbing; fine-tuning to the bicarbonate level in the blood according to the body's needs. More acidosis leads to more reabsorption of bicarbonate, more alkalosis leads to more excretion of bicarbonate.
- Finally, (1mEq/day) of bicarbonate will execrate, and this could differ according to the acid-base balance in the body.



Mechanisms for HCO_3^- reabsorption, and Na+ - H^+ exchange in the proximal tubule and thick loop of Henle.

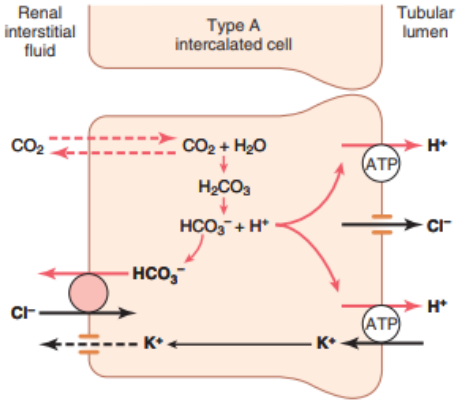
- In the basal surface of tubular cells, we have Na^+/K^+ ATPase and HCO_3^- / Na^+ co-transporter, which is a secondary active transporter that depends on the Na^+/K^+ ATPase's gradient.
- On the proximal surface of tubular cells, we have Na^+/H^+ exchangers.
- HCO_3^- and H^+ will generate in the tubular cells by dissociation of carbonic acid.



- HCO_3^- reabsorption via HCO_3^- / Na^+ co-transporters. H^+ secretion via Na^+/H^+ exchangers.
- In the tubular fluid, secreted H^+ will bind with filtered HCO_3^- to produce carbonic acid which will disassociate into water and CO_2.
- CO_2 diffuses into the cell and binds with the water to produce carbonic acid which will generate HCO_3^- and H^+.
- H^+ secreted, HCO_3^- reabsorbed, and this will repeat over and over, (a continuous process).
- For each HCO_3^- reabsorbed, there must be an H^+ secreted (1:1).
- Minimal pH results from these mechanisms ~ 6.7.

HCO_3^- reabsorption and H^+ secretion in intercalated cells of late distal and collecting tubules.

- Two types of intercalated cells; A and B.
- Type A intercalated cells; in the proximal surface of tubular cells, we have H^+ ATPase pumps and H^+/K^+ antiporters which are both primary active transporters that work against gradient by consuming ATP.
- In the basal surface of tubular cells, we have HCO_3^-/Cl^- exchangers (facilitated diffusion).
- HCO_3^- and H^+ will generate in the tubular cells by dissociation of carbonic acid.
- H^+ secretion via H^+ ATPase pumps and H^+/K^+ antiporters.
- HCO_3^- reabsorption via HCO_3^-/Cl^- exchangers.
- For each HCO_3^- reabsorbed, there must be an H^+ secreted (1:1).
- Minimal pH results from these mechanisms ~4.5, so it's more efficient in increasing urine acidity. (More acidifying the urine).

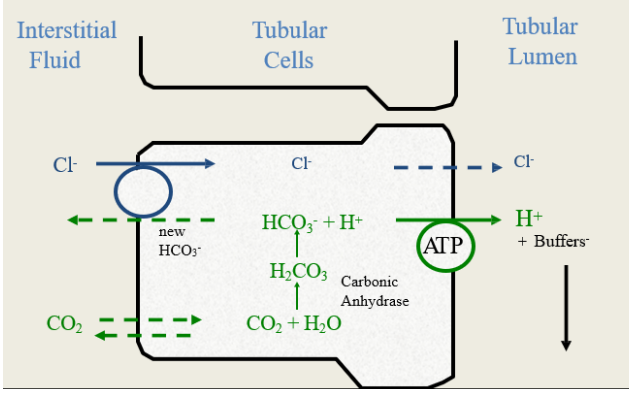


Regulation of H^+ secretion by the kidney

- Increased **plasma CO_2** increases H^+ secretion. i.e., **respiratory acidosis**, Increased plasma CO_2 means that the lung doesn't eliminate CO_2 efficiently.
- Increased **extracellular H^+** increases H^+ secretion. i.e., **metabolic, or respiratory acidosis.**
- Increased **tubular fluid buffers** increase H^+ secretion. i.e., **metabolic, or respiratory acidosis.**

Generates New Bicarbonate

- In acidosis (more H^+), the body will compensate by secrete H^+ and reabsorb HCO_3^- (1:1).
- But we have a huge amount of H^+ thus, we will reach a point where all the filtered bicarbonate is reabsorbed and **not** all the excess hydrogen is excreted. (Still there H^+ not titrated by HCO_3^-).
- Excess H^+ in the tubular lumen will be buffered by a **different buffer other than bicarbonate.**
- For each H^+ secreted **without bicarbonate** reabsorption, this considers **a new bicarbonate generation** to the system.
- This mechanism increases the efficiency of the kidney by buffering all the excess H^+ even without bicarbonate with the generation of new ones.



Importance of Renal Tubular Buffers

Minimum urine pH = 4.5 = $10^{-4.5}$ = 3 x 10^{-5} moles/L
i.e., the maximal [H^+] of urine is 0.03 mmol/L Yet, the kidneys must excrete, under normal conditions, at least **60 mmol of non-volatile acids** each day. To excrete this as free H^+ would require:

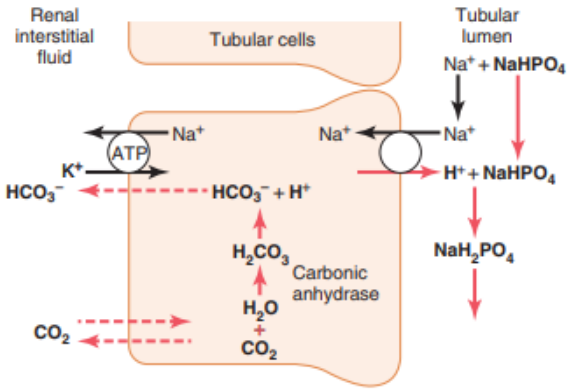
$$\frac{60\ \text{mmol}}{03\text{mmol/L}} = 2000\ \text{L per day !!!}$$

So, tubular fluid volume must be **2000 L** to excrete **60 mmol of non-volatile acids,** which is illogical, however, there must be other buffers than bicarbonate. (Titrating secreted H^+ with HCO_3^- and any excess H^+ with a **different buffer** other than HCO_3^-):
Important **renal tubular** buffers mentioned earlier : **phosphate and ammonia.**

1. phosphate

- Once the phosphate is filtered into the tubular lumen, it is united with H^+ that has been secreted (excess hydrogen that has not been buffered by bicarbonate).
- H^+ binds $NaHPO_4^-$ in the tubular lumen forming NaH_2PO_4.

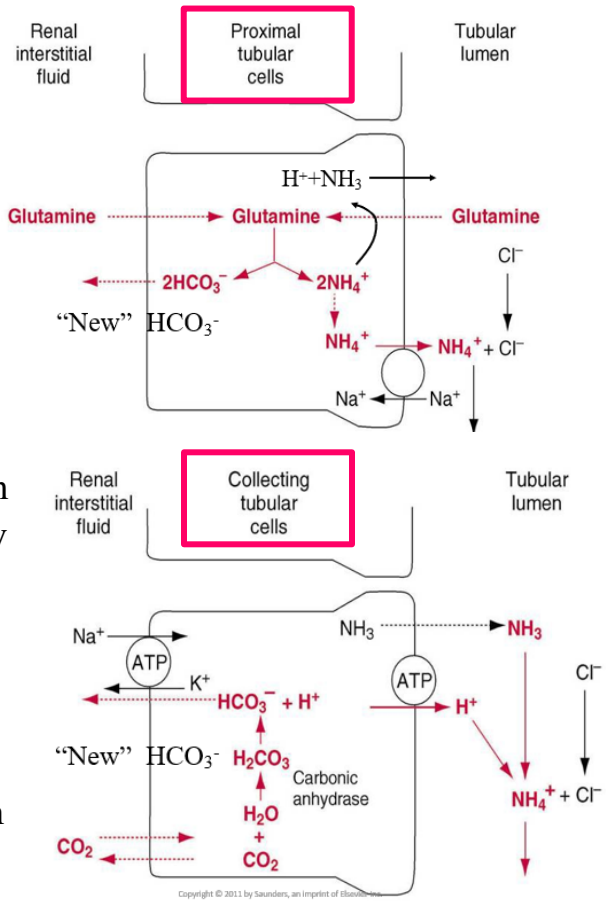
$$NaHPO_4^- + H^+ \rightarrow NaH_2PO_4$$



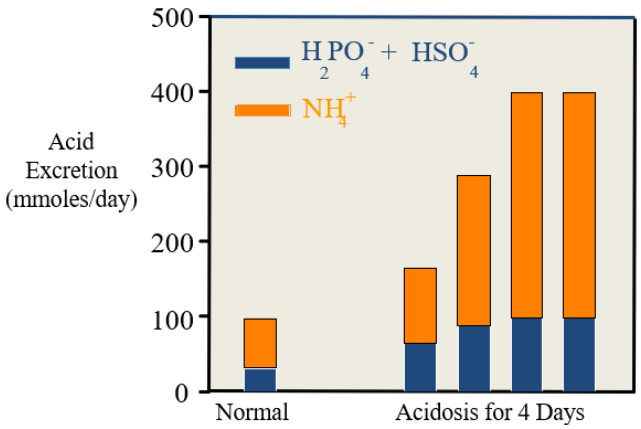
- For each H^+ titrated by phosphate, we consider **the generation of new bicarbonate** (buffering the hydrogen with other buffers than bicarbonate).
- Phosphate normally buffers about 30 mmol/day of H^+ (about 100 mmol/day phosphate is filtered but 70 % is reabsorbed).
- In **chronic acidosis**, phosphate is **not** the major tubular buffer; Phosphate buffering capacity does not change much with acid-base disturbances (the body doesn't physiologically regulate the phosphate production in chronic acidosis).

2. Ammonia and Ammonium

- In the tubular cell of the proximal tubules, thick Henle, and distal tubules, **Glutamine** is broken down into **bicarbonate and ammonium**.
- **Ammonium NH_4^+** is secreted in exchange for Na^+ and bicarbonate will be reabsorbed, so we have a generation of new bicarbonate.
- In the tubular cell of the collecting ducts, ammonium could be broken down into H^+ and ammonia NH_3.
- **Ammonia** secretes into the tubular lumen and binds with the secreted H^+ that is not buffered by bicarbonate or any other buffer to form **ammonium**.
- titration without consuming bicarbonate considers the generation of new bicarbonate.
- The source of ammonia in the tubular lumen is either absorbed from the blood into the tubular cell and then secreted into the lumen or is present in the tubular lumen in high concentration.



Ammonia is more important than phosphate in **chronic acidosis**; the level of phosphate production in the tubular fluid doesn't change in response to chronic acidosis whereas the level of ammonium **increases**. this is because of the physiological regulation on the production of ammonium.
This graph illustrates a comparison between phosphate and ammonium buffers in chronic acidosis.



Quantification of Normal Renal Acid-Base Regulation

- Kidneys eliminate non-volatile acids (H_2SO_4, H_3PO_4) (~ 80 mmol/day)
- Filtration of HCO_3^- (~ 4320 mmol/day)
- Secretion of H^+ (~ 4400 mmol/day)
- Reabsorption of HCO_3^- (~ 4319 mmol/day)
- Production of new HCO_3^- (~ 80 mmol/day)
- Excretion of HCO_3^- (~1 mmol/day)
- Titratable acid $NaHPO_4^-$ (~30 mmol/day)
- NH_4^+ excretion (~30 mmol/day)

Total H+ Secretion = H^+ secreted in exchange for the bicarbonate + H^+ of non-volatile acids produced in the body
4380 mEq/day = 4320 mEq/day + 60 mEq/day

To quantify this equation practically:

- H^+ secreted in exchange for the bicarbonate = bicarbonate reabsorption.
- H^+ of non-volatile acids = H^+ secreted in exchange for buffers other than bicarbonate = titratable acid $NaHPO_4^-$ + NH_4^+ excretion
- NH_4^+ excretion = urinary excretion of NH_4^+ * urinary flow rate
- titratable acid $NaHPO_4^-$; calculated by adding a strong base to the urine, which will cause reversal to the acidification of urine to pH 7.3, then we measure the amount of acid by calculating how much base is needed to titrate the acid.
  this will measure only the titrated acid by phosphate but not ammonia because we measure at pH 7.3 which's perfect for phosphate but not for ammonia.

Thus,
Total H^+ secretion = bicarbonate reabsorption + titratable acid $NaHPO_4^-$ + NH_4^+ excretion
Total H^+ secretion = 4320 mmol/d + 30 mmol/d + 30 mmol/d = 4380 mmol/day

Net H^+ Excretion= H^+ excreted by buffers other than bicarbonate – new H^+ added to blood

- H^+ excreted (titrated) by buffers other than bicarbonate = newly generated bicarbonate = titratable acid $NaHPO_4^-$ + NH_4^+ excretion
- New H^+ added to blood = bicarbonate excreted

Net H^+ excretion= titratable acid $NaHPO_4^-$ + NH_4^+ excretion - HCO_3^- excretion
Net H^+ excretion = 30 mmol/d + 30 mmol/d - 1 mmol/d = 59 mmol/day

Net addition of HCO_3^- to body (i.e., net loss of H^+)

Titratable acid = 30 mmol/day
NH_4^+ excretion = 30 mmol/day
HCO_3^- excretion = 1 mmol/day
Net H^+ excretion = 59 mmol/day
Positive value → loss of acids from the body.

Increased addition of HCO_3^- to the body by kidneys (i.e., increased H^+ loss by kidneys)

Titratable acid = 35 mmol/day (small increase)
NH_4^+ excretion = 165 mmol/day (increased)
HCO_3^- excretion = 0 mmol/day (decreased)
Net H^+ excretion = 200 mmol/day (indicate the ability of the body to secrete H^+ in response to acidosis)
This can increase to as high as 500 mmol/day by increasing the **ammonium buffer**.
Remember: in chronic acidosis, the body regulates the production of ammonium but not phosphate.

Net loss of HCO_3^- from the body (i.e., decreased H^+ loss by kidneys)

Titratable acid = 0 mmol/day (decreased)
NH_4^+ excretion = 0 mmol/day (decreased)
HCO_3^- excretion = 80 mmol/day (increased)
Net H^+excretion = 80 mmol/day (negative)
negative value→ Net bicarbonate excretion, which means H^+ add to the blood.
HCO_3^- excretion can increase markedly in alkalosis.

Classification of Acid-Base Disorders from plasma pH, pCO2, and HCO_3^-

Acidosis: when the plasma pH is less than 7.4, either because of **reduced HCO_3^-** (Metabolic acidosis) or **increased pCO_2** (Respiratory acidosis). the kidney will compensate by:

- increased H^+ secretion and HCO_3^- reabsorption 1:1 (linked together).
- production of new HCO_3^- which also will be reabsorbed but separately from H+ titrated by bicarbonate in TF,but rather with other buffers in TF.

Alkalosis: when the plasma pH is more than 7.4 either because of **increased HCO_3^-** (Metabolic Alkalosis) or **reduced pCO2** (respiratory Alkalosis). the kidney will compensate by:

- decreased H^+ secretion and HCO_3^- reabsorption 1:1 (linked together).
- loss of HCO_3^-in urine.

Renal Compensations for Acid-Base Disorders

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

Respiratory acidosis;

- Increase in the partial pressure of CO_2 will decrease the pH. (An increase in CO_2 in the left arm of the equation will drive the equation to the right, so more carbonic acid is produced thus more hydrogen).
- The kidney compensates by increasing H^+ secretion to achieve the balance, thus all the bicarbonate should be reabsorbed, and excess tubular H^+ should be titrated by other buffers such as ($NaHPO_4^-$, NH_4^+).
- These buffers will secrete the excess H^+ and at the same time, they will generate new bicarbonate which in turn will raise the pH (dual compensatory effect).

Metabolic acidosis;

- Decrease in the bicarbonate concentration in the blood will decrease the pH.
- Reduced the amount of filtered bicarbonate, and complete bicarbonate reabsorption with **too much** excess tubular H^+ which will titrate by other buffers ($NaHPO_4^-$, NH_4^+).
- These buffers will secrete the excess H^+ and at the same time, they will generate new bicarbonate which in turn will raise the pH (dual compensatory effect).

Respiratory Alkalosis;

- Decrease in the partial pressure of CO_2 will decrease the H^+ in the blood, thus, H^+ secretion and bicarbonate reabsorption also decreased.
- This leads to excess bicarbonate in the tubular fluid.
- kidney compensates by increasing bicarbonate excretion and decreasing hydrogen excretion so more hydrogen will be added to the system. which in turn will correct the pH.

Metabolic Alkalosis;

- Increasing the blood level of bicarbonate will increase the bicarbonate filtration thus, more tubular bicarbonate.
- The kidney will compensate by decreasing the reabsorption of bicarbonate and this will result in more excretion of bicarbonate thus, reduce the hydrogen excretion.
- This will help in reducing the pH to the normal level.

Acidosis: pH < 7.4
- metabolic: ⇓ HCO_3^-
- respiratory: ⇑ pCO_2

Alkalosis: pH > 7.4
- metabolic: ⇑ HCO_3^-
- respiratory: ⇓ pCO_2

Classification of Acid-Base Disturbances

Disturbance	*pH*	*HCO_3^-*	*pCO_2*	*HCO_3^-/pCO_2 in plasma*	*Compensation*
metabolic acidosis	⇓	⇓	⇓	⇓	⇑ventilation ⇑renal HCO_3^- production
respiratory acidosis	⇓	⇑	⇑	⇓	⇑renal HCO_3^- production
metabolic alkalosis	⇑	⇑	⇑	⇑	⇓ventilation ⇑renal HCO_3^- excretion
respiratory alkalosis	⇑	⇓	⇓	⇑	⇑renal HCO_3^- excretion

About the table:

- **Metabolic acidosis;** is when the pH is lower than normal, due to the <u>decrease in bicarbonate level.</u> however, pCO_2 would decrease too due to the respiratory compensation by increasing ventilation. We have also renal compensation by increasing HCO_3^- production to titrate more H^+ to correct the pH.
- **Respiratory acidosis**; is when pH is lower than normal, due to the <u>increase in pCO_2</u>. However, bicarbonate would increase too due to the renal compensation by increasing HCO_3^- production to titrate more H^+.
- **Metabolic alkalosis;** is when pH is higher than normal due to the <u>increase in bicarbonate level,</u> However, pCO_2 would increase too due to the respiratory compensation by decreasing ventilation rate. We have also renal compensation by increasing HCO_3^- excretion.
- **Respiratory alkalosis;** is when pH is higher than normal, due to the <u>decrease in pCO_2</u>.However, bicarbonate would decrease too due to the renal compensation by increasing HCO_3^- excretion.

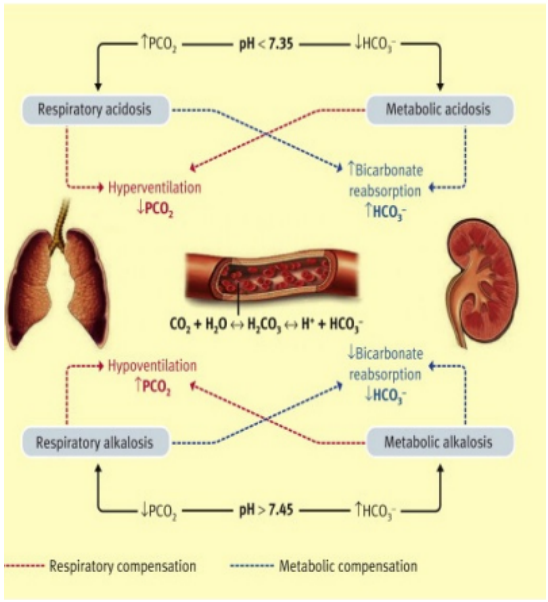
Test	Normal	Decrease Value	Increase Value
pH	7.35-7.45	Acidosis	Alkalosis
PaCO2	35-45	Alkalosis	Acidosis
HCO3	22-26	Acidosis	Alkalosis
PaO2	80-100	Hypoxemia	O2 therapy
SaO2	95-100%	Hypoxemia	----------

Normal values of pH, pCO_2 and HCO_3^-

FOR MEMORIZATION!!

	pH	HCO_3^-	CO_2
Metabolic acidosis	↓	↓	Normal
Metabolic alkalosis	↑	↑	Normal
Metabolic acidosis with respiratory compensation	↓	↓	↓
Metabolic alkalosis with respiratory compensation	↑	↑	↑

This algorithm demonstrates the acid-base balance and how the renal and respiratory systems can compensate.



Clinical case 1

The following data were taken from a patient:
urine volume = 1.0 liter/day
urine HCO_3^- concentration = 2 mmol/liter
urine NH_4^+ concentration = 15 mmol/liter
urine titratable acid = 10 mmol/liter

1. What is the daily net acid excretion in this patient?
2. What is the daily net rate of HCO_3^- addition to the extracellular fluids?

Answer

1. Net acid excretion = Titr. Acid + NH_4^+ excret - HCO_3^-
   = (10 x 1) + (15 x 1) - (1 x 2) = 23 mmol/day
2. Net rate of HCO_3^- addition to body = Net acid excretion = 23 mmol/day

Clinical case 2

A plasma sample revealed the following values in a patient:
Normal pCO_2 (35-45), HCO_3^- (22-26).
pH = 7.12
pCO_2 = 50
HCO_3^- = 18
Diagnose this patient's acid-base status: acidotic or alkalotic? respiratory, metabolic, or both?

Answer

pH is lower than the normal so acidosis
pCO_2 is higher but HCO_3^- is lower so it's **Mixed acidosis**: metabolic and respiratory acidosis

Mixed Acid-Base Disturbances: Two or more underlying causes of the acid-base disorder.

Clinical case 3

A plasma sample revealed the following values in a patient:
pH= 7.60
pCO_2 = 30 mmHg
plasma HCO_3^- = 29 mmol/L
What is the diagnosis?

Answer

Mixed Alkalosis
• Metabolic alkalosis: increased HCO_3^-
• Respiratory alkalosis: decreased pCO_2

Clinical case 4

A patient presents in the emergency room and the following data are obtained from the clinical labs:
plasma pH=7.15,
HCO_3^- = 8 mmol/L,
pCO_2= 24 mmHg
This patient is in a state of:

a. metabolic alkalosis with partial respiratory compensation
b. respiratory alkalosis with partial renal compensation
c. metabolic acidosis with partial respiratory compensation
d. respiratory acidosis with partial renal compensation

Answer

pH is lower than normal so acidosis, HCO_3^-very low but pCO_2 normal, the respiratory system tried to compensate but pH doesn't back normal so **partial compensation**. the answer is **c**

Conditions that accompanied by Metabolic acidosis

- aspirin poisoning (increase H^+ intake)
- diabetes mellitus (increased H^+ production)
- diarrhea (HCO_3^- loss)
- renal tubular acidosis (decrease H^+ secretion and HCO_3^- reabsorption)
- carbonic anhydrase inhibitors (decrease H^+ secretion)

Conditions that accompanied by Respiratory Acidosis

- brain damage
- pneumonia
- emphysema
- other lung disorders

Conditions that accompanied by Respiratory Alkalosis

- high altitude (hyperventilation)
- psychic (fear, pain, etc)

Conditions that accompanied by Metabolic Alkalosis

- increased base intake (e.g. $NaHCO_3$)
- vomiting gastric acid
- mineralocorticoid excess (aldosterone)
- overuse of diuretics (except carbonic anhydrase inhibitors)

How will aldosterone cause metabolic alkalosis?

Increased aldosterone will increase K^+ secretion as well as H^+ secretion. by default, H^+ secretion will increase HCO_3^- reabsorption as well as new bicarbonate production, thus metabolic alkalosis.

How will overuse diuretics cause metabolic alkalosis?

Overuse of diuretics will cause K^+ depletion which will increase tubular H^+ secretion and HCO_3^- reabsorption as well as new bicarbonate production, thus metabolic alkalosis.
overuse of diuretics will also decrease ECF volume, to compensate, angiotensin II will increase thus, aldosterone will increase too which will increase tubular H^+ secretion and you can guess?

Anion Gap

- The anion gap is the difference between serum sodium cations and chloride plus bicarbonate anion, used as a diagnostic tool in acid-base disturbances to make a differential diagnosis, especially in metabolic disorders.

- In our body, total cations equal total anions.
- The **major** cation in the ECF is Na^+ (osmolarity 142 mEq/L).
- The **major** anions in ECF are Cl^- (osmolarity 108mEq/L) and HCO_3^-.
- Na^+, Cl^-, and HCO_3^- are measurable and there are a lot of unmeasured cations and anions (K^+, Ca^{++}, Mg^{++}, Proteins, Phosphate, Sulfate, lactate, etc)
- Unmeasured anions are called **Anion Gap.**
- The osmolarity of all anions = osmolarity of all cations and equals 153 mEq/L.

We can estimate that:
Na^+ concentration = Cl^- concentration + HCO_3^- concentrations + unmeasured anions
Thus,
unmeasured anions = anion gap = $Na^+ - Cl^- - HCO_3^- = 142 - 108 - 24 = 10$ mEq/L
(**Normal anion gap = 8 - 16 mEq / L)**

Anion Gap in Metabolic Acidosis

$$\text{anion gap} = Na^+ - Cl^- - HCO_3^-$$

Metabolic Acidosis is due to a decrease in bicarbonate level. we have two types grouped by their influence on the anion gap:

1. **Normal anion gap metabolic acidosis (hyperchloremic metabolic acidosis)**
   from the equation, if we have low bicarbonate but normal anion gap this means the chloride is high, so in this case, it is called **hyperchloremic metabolic acidosis**. There are different disturbances associated with hyperchloremic metabolic acidosis:
   - diarrhea
   - renal tubular acidosis
   - Addison' disease
   - carbonic anhydrase inhibitors

2. **High anion gap metabolic acidosis (normochloremic metabolic acidosis)**
   If we have low bicarbonate with a high anion gap, that means the chloride is normal so it is called **normochloremic metabolic acidosis.** There are different disturbances associated with normochloremic metabolic acidosis:
   - diabetes mellitus (ketoacidosis)
   - lactic acidosis
   - aspirin (acetylsalicylic acid) poisoning
   - methanol poisoning
   - starvation

Clinical case

Laboratory values for an uncontrolled diabetic patient include the following:
arterial pH = 7.25
Plasma HCO_3^- = 12
Plasma pCO_2 = 28
Plasma Cl^- = 102
Plasma Na^+ = 142

1. What type of acid-base disorder does this patient have?
2. What is his anion gap?
3. 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

1. Metabolic Acidosis with Respiratory Compensation
2. Anion gap = 142 - 102 -12 = 28
3. b

Clinical case

Laboratory values for a patient include the following:
arterial pH = 7.34
Plasma HCO3 - = 15
Plasma PCO2 = 29
Plasma Cl- = 118
Plasma Na+ = 142

1. What type of acid-base disorder does this patient have?
2. What is his anion gap?
3. Which of the following are the most likely causes of his acid-base disorder?
    a. diarrhea
    b. diabetes mellitus
    c. aspirin poisoning
    d. primary aldosteronism

Answer

pH within the normal range, HCO_3^- very low, pCO_2 also low

Very low bicarbonate indicates acidosis. Low pCO_2 is due to respiratory compensation which leads to normal pH.

1. So, Metabolic Acidosis with Respiratory Compensation
2. Anion gap = 142 - 118 - 15 = 9 (normal)
3. a

More examples:

pH	HCO_3^-	PCO_2	Acid-Base Disorder ?
7.34	15	29	Metabolic acidosis
7.49	35	48	Metabolic alkalosis
7.34	31	60	Respiratory acidosis
7.62	20	20	Respiratory alkalosis
7.09	15	50	Acidosis: respiratory + metabolic

Sorry for errors, if there was

Good luck ♥