Physiology Sheets

Number: 9

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Correction:

❖ Renal Control of Acid-Base Balance

•The kidneys play three major roles in the maintenance of normal acid-base balance:

①excretion of H+ (fixed _non volatile H+)

②Reabsorption of filtrated bicarbonate

③Synthesis new 80 mmol of bicarbonate (Gain bicarbonate)

•Keep in mind that for each H+ excreted, one new HCO3- is synthesized, so in order to synthesize new 80 mmol of HCO3-, we need to secrete 80 mmol of H+ to the tubules, but we can't do this; because the minimal PH of the urine is 4.5, and we can't go below this level. And by simple calculation we can conclude that by making the PH of the urine 4.5 (which is the minimal value), we found that the max conc. of H+ we can secrete is 0.03 mmol/L out of 80 mmol !! So, what to do with the 79.7 mmol of fixed H+?

•Actually, if we have 80 mmol of buffers in the tubular fluids, we can get rid of the 80 mmol of H+, but do I have this 80 mmol of buffers? Let's see….

•There are many buffers in the kidney, but the main one is the phosphate buffer.

•The conc. of phosphate in the plasma is 1-1.5 mmol/L, so the phosphate filtration load equals 180L/day* (l-1.5) mmol/L = 200-250 mmol, 90% of them is reabsorbed and the remaining 10% is excreted and works as buffers. By this 10% (of excreted phosphate) the kidney will excrete (20-25) mmol H+ out of 80 mmol, and we can add 5mmol from other buffers to have 30 mmol H+ exerted.

•But how we knew the amount of $H_2PO_4^-$ in urine?
-The normal urine PH range from (4.5-8), and to calculate the conc. of the excreted acids by buffers, we titrate the urine with a strong base (NaOH) to a pH of 7.4; the amount of NaOH added to the urine is proportional to the amount of excreted acid by buffers. SO, if we add 30 mmol of NaOH, this means we have 30 mmol of acid excreted by buffers, and we call these acids **titratable acid.**

•Until now, the kidney excretes 30 mmol by phosphate and other buffers, but we still have 50 mmol of acids that must be excreted!! But how?
-Simply by the ammonia buffer system.

-Ammonia buffer system is composed of ammonia (NH_3) and the ammonium ion (NH_4^+) and is quantitatively more important than the phosphate buffer system.

-Inside the cells we have the amino acid glutamine. The glutamine is broken down by the enzyme glutaminase to form two NH_4^+ and two HCO_3^-. The $2NH_4^+$ are secreted into the lumen by a counter-transport mechanism in exchange for Na^+. The $2HCO_3^-$ are considered new and are transported across the basolateral membrane.
*One of the metabolites of glutamine is glutamate which is metabolized to α-ketoglutarate, which is ultimately metabolized to CO_2 and H_2O and then to HCO_3^-

-Also, we can have ammonia inside the cells, which secreted into the lumen, and then it will combine with the H^+ found in the lumen forming NH_4^+. NH_4^+ is charged, so it can't cross the membrane again, and trapped inside the lumen. We call this process **ammonia trapping**; and by this mechanism the body excretes 50 mmol of acids

-For each NH_4^+ generated (and ultimately excreted), one new HCO_3^- is reabsorbed.

•SO in order to know how much HCO_3^- is gained, we calculate how much H^+ is excreted. As mentioned above, every H^+ excreted in urine has a new HCO_3^- that was gained, and this H^+ was buffered as titratable acid/NH_4^+. So:

Net HCO_3^- gain= NH_4^+ excretion + Urinary titratable acid – HCO_3^- excretion

•Pts with diabetic ketoacidosis (as a result of DM type1) make a lot of ketone bodies, so they might make more than 80 mmol of acids. But the kidney can make up to 500 mmol of NH4CL, so 500 mmol of HCO_3^-, so your body shouldn't develop acidosis regardless what you eat or drink; because the kidney has a high capacity to get rid of acids.
*Maximal capacity is 500 mmol, above that we will have acidosis

*The kidney function is slow; it takes 3-5 days to give its full response.

*The respiratory system has an intermediate speed; it works by hours.

*The buffer system is the fastest.

❖ Acid-Base Disorders

➡If we have acid-base balance disturbances, we should follow three steps:

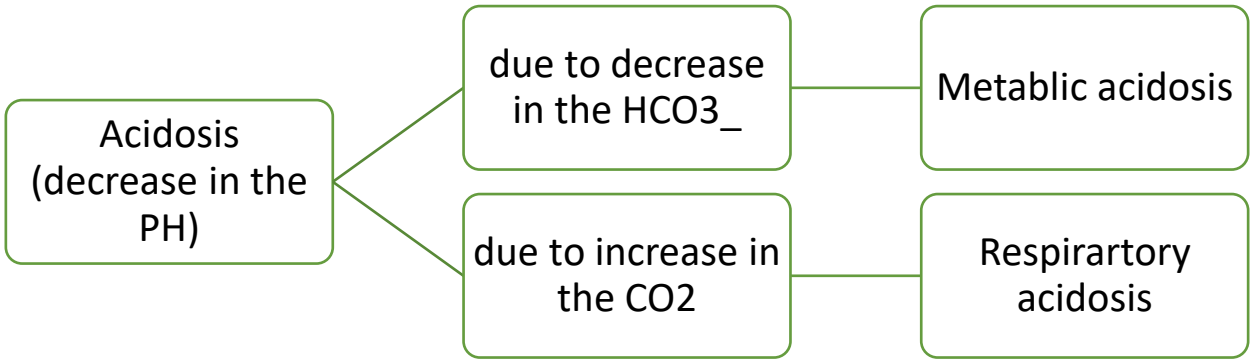
①**Determine if we have alkalosis or acidosis**

-If the PH is less than 7.35; then we have acidosis, but if the PH is more than 7.45; then we have alkalosis. And in order to calculate the PH we need to measure ABGs (Arterial Blood Gases).

-By measuring the ABGs we can know HCO3- conc. and PCO2. Then by the **Henderson-Hasselbalch equation,** we can calculate the PH.

-In normal conditions➡ PH= 6.1+ log (24)/40*.03 = 7.4

②What cases the shift in the PH

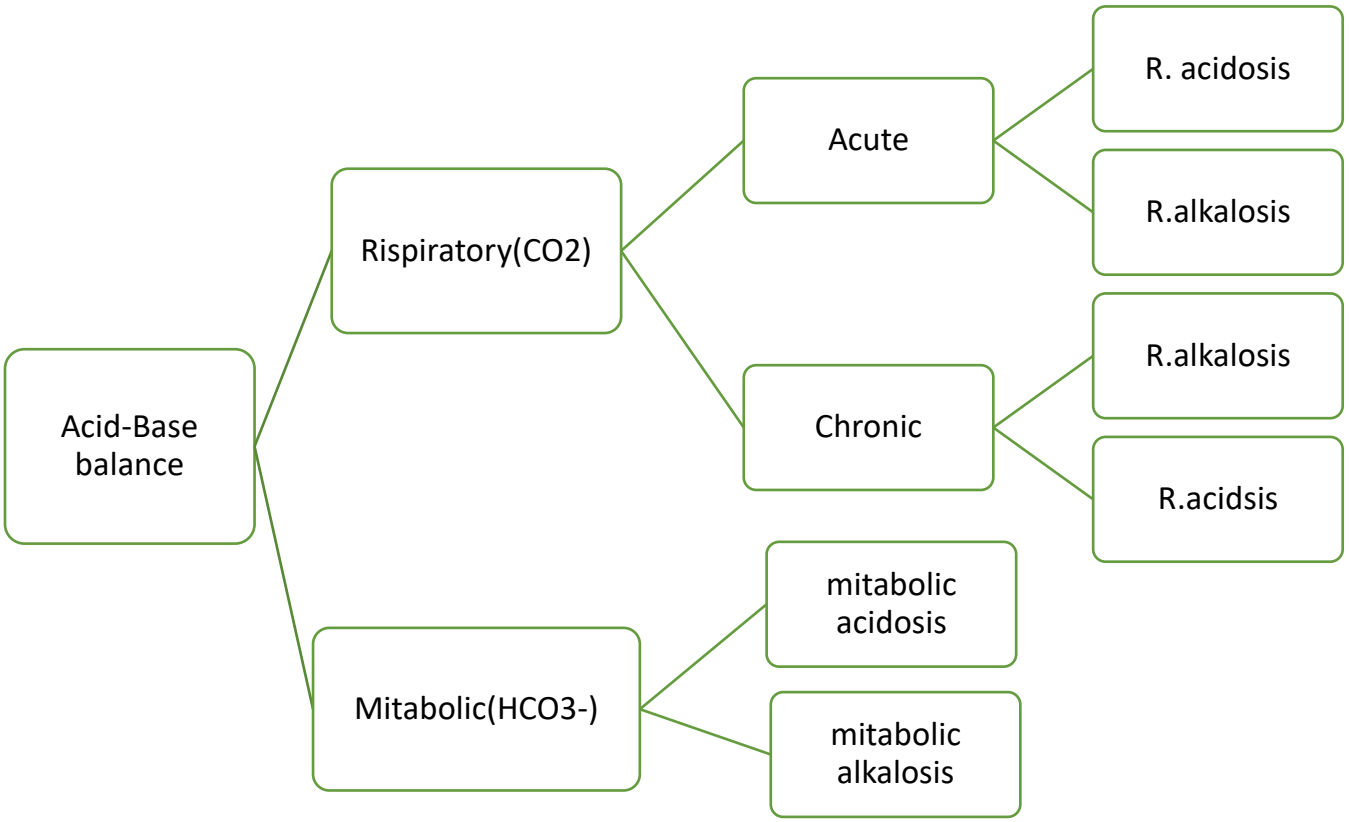


③I look for the other elements if there is compensation

-The compensation could be partial or complete. For example, if we have metabolic acidosis (↓HCO3-), the pCO2 will decrease to bring the PH to its normal range.

•If we have metabolic problem, the respiratory system will respond in a very fast manner; thus we will not have (acute or chronic) metabolic disorders. But if we have respiratory problem (such as pneumonia), the kidney will take time to compensate; thus we will have (acute or chronic) respiratory disorders.

•So, we can divide the acid-base disorders into sex categories:



•The HCO3- and the Pco2 always follows the same direction, for example if one increases, the other will increase to maintain a constant value of PH.

- For each increase/decrease in CO2, there's a compensatory increase/decrease in HCO3-. This is accomplished by renal compensation.

- For each increase/decrease in HCO3-, there's a compensatory increase/decrease in CO2. This is accomplished by respiratory compensation.

•For example, if we have metabolic acidosis (↓HCO3-), the lungs will compensate by Hyperventilation (making the inside air = outside air), so we will have decrease in the Pco2 and increase in the PO2 (maximally

to 150mmhg). But what is the effect of the increase in the PO2 on the body?

-Simply, nothing; because our body is designed to response only to the decrease in the PO2 (below 60 mmhg). So, the increase of PO2 to 150,200,300…..means nothing for the body; because the Hemoglobin is already saturated, and the increase in the PO2 will not affect the saturated, but this is not applied to CO2.

• On the other hand, when there is metabolic alkalosis, there will be hypoventilation, we increase Pco2 and decrease Po2. The body cannot tolerate decrease in Po2 a lot (the minimum tolerable value of Po2 is 60 mmHg), so CO2 retention (in case of hypoventilation) will not be as large as CO2 washout (in case of hyperventilation). And this can explain why for each 1 mEq/L decrease in HCO3-, there's 1.3 mmHg (1 for the sake of the exam) decrease in Pco2, whereas for each 1 mEq/L increase in HCO3-, there's 0.7 mmHg increase in Pco2. So, respiratory compensation of metabolic alkalosis is less efficient than that of metabolic acidosis.

•If we have respiratory acidosis (↑Pco2), the kidney tries to compensate by excreting the excess acid as titratable acid and as NH4+, both of which are associated with HCO3- gain. But it's noteworthy to mention that renal compensation is slow. So, if there's an acute respiratory disturbance, renal compensation will be minimal (for each 10 mmHg increase in CO2, there's only **(1 mEq/L)** increase in HCO3-). On the other hand, if there's a chronic respiratory disturbance, renal compensation will be considerable and will normalize the pH (for each 10 mmHg increase in CO2, there's **(3.5 mEq/L)** increase in HCO3-).

•If we have respiratory alkalosis (↓Pco2), that can be the result of ascending to high altitudes "hyperventilation", there will be decrease in

the HCO_3^- . And because the excretion of HCO_3^- is easier than the synthesis of new HCO_3^- (in the case of respiratory acidosis), for each 10 mmHg decrease in CO_2, there's (**2 mEq/L)** decrease in HCO_3^-. On the other hand, if there's a chronic respiratory disturbance, renal compensation will be considerable and will normalize the pH (for each 10 mmHg decrease in CO_2, there's (**5 mEq/L)** decrease in HCO_3^-.

*** Don't memorize the numbers*

➡Acid-Base disorders from clinical view

• If you have a patient with acid-base disorder, the first think you do is to determine if he/she has alkalosis or acidosis (by looking at the pH), then you looking for the cause of shifting in pH, and finally you see if there is compensation or not.

•Its very important to note that acid-base disorder is not a disease, but part of a disease, for example if a patient has acidosis as a result of diarrhea, then you should treat the diarrhea to relief the acidosis.
But if you have a patient with pH below 7.35 or above 7.45, then this is an emergency (life-threatening) case, you should do everything to restore the normal pH.

➡Types of acid-base disorders:

①Metabolic acidosis

•It caused by overproduction or ingestion of fixed acid or decrease in arterial [HCO3-]. And this is the most common type among the others.

•The decrease in the HCO3- can be caused by diarrhea (the most common cause) and deep vomiting (we meant by **deep**, that the patient will vomit the pancreatic secretion rather than gastric acids)

•The overproduction of fixed acid can be caused by the following:

◊ Diabetic ketoacidosis

◊ Aspirin poisoning

◊ Renal tubular acidosis;

-The accumulation of acids in the body, due to failure of the kidney to either reabsorb filtered HCO3- **(Proximal: type II RTA)** or to secrete H+ **(Distal: type I RTA)**.

-**Type I RTA** is more severe because it's more distal. In proximal RTA, there's still a chance to correct the disturbance in distal segments of the nephron.

②Metabolic alkalosis

•Loss of fixed H+ or increase in arterial [HCO3-]; most of the diuretics increase the wash out of H+; thus alkalosis

③Respiratory acidosis

•Is caused by decreased alveolar ventilation and retention of CO2; such as in patients with COPD, pneumonia and diffusion problems.

④ **Respiratory alkalosis**

•Is caused by increased alveolar ventilation and loss of CO2; as a result of ascending to high altitudes or panic attacks.

➡Summery of the compensatory mechanism:

***M. Acidosis**

✓For every ↓ 1 mEq HCO_3^- → 1.2 mm Hg PCO2 ↓ too.

****M. Alkalosis**

✓**For** every 1 mEq↑ in HCO_3^- → 0.7 mmHg ↑ in O2

*****R. Acidosis**

✓**Acute:** For every 10 mmHg ↑ in PCO2 → 1 mEq ↑ in HCO_3^-

✓**Chronic**: For every 10 mmHg ↑ in PCO2 →3.5 mEq↑ in HCO_3^-

******R. Alkalosis**

✓**Acute**: For every 10 mmHg ↓ PCO2 → 2 mEq ↓ HCO_3^-

✓**Chronic:** For every 10 mmHg ↓ PCO2 → 5 mEq ↓ HCO_3^-

*** Don't memorize the numbers*

**After the compensation, the pH could be restored to its normal value 7.35-7.45 (but not more than that)

➡ These examples are mentioned in the slides:

1- Maha is a 45-year-old female admitted to the E.R with a severe asthma attack. She has been experiencing increasing shortness of breath since admission three hours ago. Her arterial blood gas result is as follows:

pH = 7.22, PaCO2 = 55, HCO3- = 25

- pH is below 7.35 >Acidosis
- PaCO2 is high> Respiratory Acidosis
- HCO3- is normal> Slight renal compensation (because it's an acute respiratory disturbance).

2- Maher is a 55-year-old male admitted to E.R with a recurring bowel obstruction. He has been experiencing intractable vomiting for the last several hours despite the use of antiemetics. Here is his arterial blood gas result:

pH = 7.50, PaCO2 = 42, HCO3- = 33

- pH is above 7.45 >Alkalosis
- PaCO2 is normal.
- HCO3- is high > Metabolic alkalosis

*These two patients are uncompensated. Patient in example 1 has respiratory acidosis with minimal renal compensation. Patient in example 2 has metabolic alkalosis with no respiratory compensation.

➡Some questions from the slides:

Q1: 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

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

Q2: Indicate the Acid -Base Disorders in Each of the Following Patients

	pH	HCO_3^-	PCO_2	Acid-Base Disorder ?
Case 1:	7.34	15	29	
Case 2:	7.49	35	48	
Case 3:	7.34	31	60	
Case 4:	7.62	20	20	

➡**Answers:**

Q1>>net acid excretion = Titr. Acid + NH_4^+ excret - HCO_3^-

= (10 x 1) + (15 x 1) - (1 x 2)

= 23 mmol/day

net rate of HCO_3^- addition to body = 23 mmol /day

Q2:

Case1: Metabolic acidosis

Case2: Metabolic alkalosis

Case3: Respiratory acidosis

Case4: Respiratory alkalosis

"الحياه دائماً تقدم لك فرصة ثانية تسمى غداً"