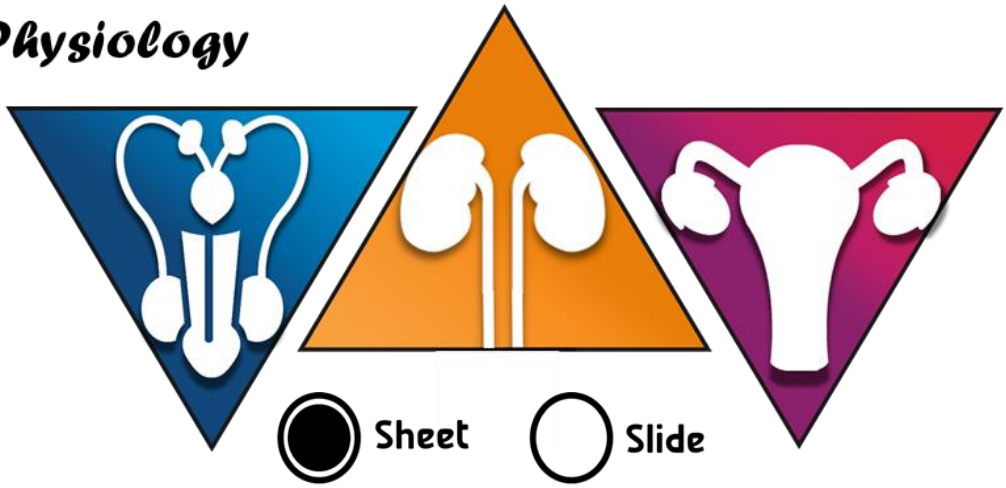
Urogenital system

Physiology



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Sorry if there was any mistake, kindly contact me if you found any. There are 86 slides for this sheet, I've tried to add some important ones, you can refer to them if you have enough time + you can skip the extras, the last two pages include questions and examples from the slide.

Extra summary of the previous lecture:

- The major threat to pH is the fixed 80 mmol of acids that are produced daily in the extracellular fluid. Which (if not handled) is not compatible with life (pH should not ever drop below 6.8 (or rise above 8).
- The H+ that can be excreted in urine is only 0.1 mmol, because the capacity of the H+ pumps, which locate in the collecting duct cells, is limited, so urine pH cannot drop below 4.5 which is not a significant mechanism of H+ clearance.
- HCO3- in the blood is limited, it doesn't exceed 24 mmol, but getting rid of H+ by combining with HCO3- to form CO2 that is removed by ventilation, helps only for a couple of days (4 days approximately).
- Because HCO3- is precious, this is why in addition to being almost completely resorbed from kidney by the mechanisms that are mentioned in the previous sheet, the kidney produces additional 80 mmol of it. (a net gain of bicarbonate to neutralize the fixed acids).
  I said almost because it's sometimes normal to find 1 mmol in urine because this is what the doctor said at (36:10) in UGS-Physiology-Lecture-8 video.
- In the proximal tubules, H+ is secreted by Na+/H+ counter-transporter, which is capable of only 5 folds difference in gradient, when this transporter stops, there will be no more HCO3- production, this is why excess H+ should be buffered, there are only about 25mmol of buffers, the remaining 55mmol are produced by 55mmol NH4+ production.
- Net HCO3- gain= NH4+ excretion + Urinary titratable acid – $HCO3^-$ excretion

Extra BASIC CHEMISTRY INFORMATION

1- Ammonia= NH3, Ammonium= NH4+
2- Isohydric solutions: have same pH, because H+ is constant, thus values remain constant.
3- Base or alkaline: a substance that accepts H+ or reacts with H+. (e.g. HCO_3^{-1}, it can react with H+ to give H_2CO_3 which is an acid)

4- Acid: a substance that releases H+, (because it's already bound to H+ e.g: HCl, HCO3 …)
5- Increasing the concentration of a substance in the left side of a reaction this would shift the reaction in the forward direction, but increasing the concentration of a substance in the right side of a reaction, would shift the reaction in the reverse direction)
6- pH= -log (H+)
in **acidic** conditions, H+ concentration increases, and according to the previous formula, **pH decreases**. BUT, In **basic** (alkaline) conditions, H+ concentration decreases, **pH increases.**
7- When a strong alkali reacts with weak acid, the result will be strong acid and weak base, and vice versa.
8- Strong acids and alkali dissociate completely in the solution, such as HCl and NaOH, meaning that you will find neither **H**Cl nor Na*OH* in any solution, because they immediately dissociate into **H+**&Cl- and Na+&*OH-*,respectively (irreversible reaction). On the other hand, weak bases and acids don't dissociate completely, this is why you can find them in the solution undissociated, for example, you can find HCO3-, H2CO3, H+, in the same solution (NaHCO3- + **H+** ⇌ Na^+ + H2CO3)
9- Don't forget that negative and positive attracts. This is why NaHCO3 (Na+HCO3-) and HCO3- are used interchangeably.

Acid-Base Balance

There are three main (defending) mechanisms against changes in pH, by regulating H+ concentration in the body to prevent alkalosis and acidosis:

1) The First Line of Défense**: <u>Buffer Systems</u>**

- This system is **rapid** or momentarily (instantaneous), it works immediately in response to changes in H+ concentration.
- <u>Definition of Buffers</u>: substances that reversibly bind H+, they combine with H+ to maintain a constant pH. In other words, buffers' role is not to <u>add</u> or <u>remove</u> hydrogen from our body, but they actually **trap** hydrogen until other more effective systems (lungs/ kidneys) take action.
- <u>General Buffering Reaction</u>: $H^+ + A^- \rightleftharpoons HA$
<u>How this system works then?</u> If we added HCl (H+) to this solution, we expect the pH to drop to 2, but what actually happens is that, there will be a slight decrease in the pH, because buffer system maintains pH and resists extreme

changes (extreme decrease here) {similarly, if we added NaOH (less H+) to this solution, pH will not become 10, there will be only a slight increase in the pH too.}

- Examples on Buffers:
  - Bicarbonate Buffer System (HCO_3^- -H_2CO_3): $\mathbf{H^+ + HCO_3^-} \rightleftharpoons \mathbf{H_2CO_3}$
  - Phosphate Buffer System (HPO_4^{--} -$H_2PO_4^-$): $\mathbf{H^+ + HPO_4^{--}} \rightleftharpoons \mathbf{H_2PO_4^-}$
  - Proteins, although they constitute 60-70% of total chemical buffering of body fluids **intracellularly**, they are not effective because they don't work in acute conditions since H+ cannot rapidly cross the cellular membranes, they are more notable in chronic conditions. (buffering is a side function of proteins, they have other more important functions). {Acute conditions mainly occur extracellularly where the effect of proteins is insignificant}
  - Others

- There are 3 characteristics that determine the **buffering power/strength**: (will be discussed in detail)
  1- pKa (the pH should be near the pKa of the system)
  2- absolute concentrations of the components of the buffering system (more concentrations mean more control on the pH)
  3- The capacity to renew (replenishment) the buffer after it is Consumed, this one is the most important factor.

2) The Second Line of Defence: **Respiratory System,**

- This system has **intermediate response**, they don't immediately work when pH changes, but it acts within minutes, but gives a full response within few hours. In other words, it needs few hours to give its maximum response, this is obvious because our lungs already work (non-stop).
- It is **two times** more effective than buffer systems, it is approximately 75% effective, 75% close to normal, this corresponds to have a feedback **gain** of 1 to **3.**
- What is gain, and how could be calculated?
  If pH suddenly decreased and it dropped from 7.4 to 7, respiratory system can return the pH to **7.3,** the error will be

about 0.1 (why? Because correction from 7 to 7.3 is 0.3, the value is supposedly 7.4, so error is 0.1, then we calculate gain according to this equation, gain = correction/ error = 3)

3) The Third Line of Défense: **Renal System**,

- The kidney has a relatively **slow response**, it needs about 5 days for full response, but it can start to work within hours though. Despite its slow response, it is the most powerful regulator of acid-base systems, it is 100% effective in normal people, because it can produce up to 500 mmol of NH4+ in extreme conditions (normally 55 are needed as mentioned in the first page and previous lecture)
  (don't forget that 500 mmol of NH4+ in turn can contribute 500 mmol of new HCO3- that is added to blood, this usually helps in chronic ketoacidosis, but if it was acute, the patient might die before kidney starts working, here comes clinicians' role).

BUFFERS

Henderson-Hasselbalch Equation (very important, you should memorize it)

$$pH = pK_a + \log \frac{[\text{conjugate base}]}{[\text{acid}]}$$

- For the following system; $H^+ + A^- \rightleftharpoons HA$
  Conjugate base = A-
  Acid = HA
- pKa is the pH of the buffer when [HA] = [A-], to prove this; when they are equal, [HA]/[A-]= 1, and log (1)= 0. As a result, pH=pKa according to the aforementioned equation.
  In other words, pKa is the pH when both [HA] and [A-] are equal and each one constitutes 50% of the buffer system, see the curve below.

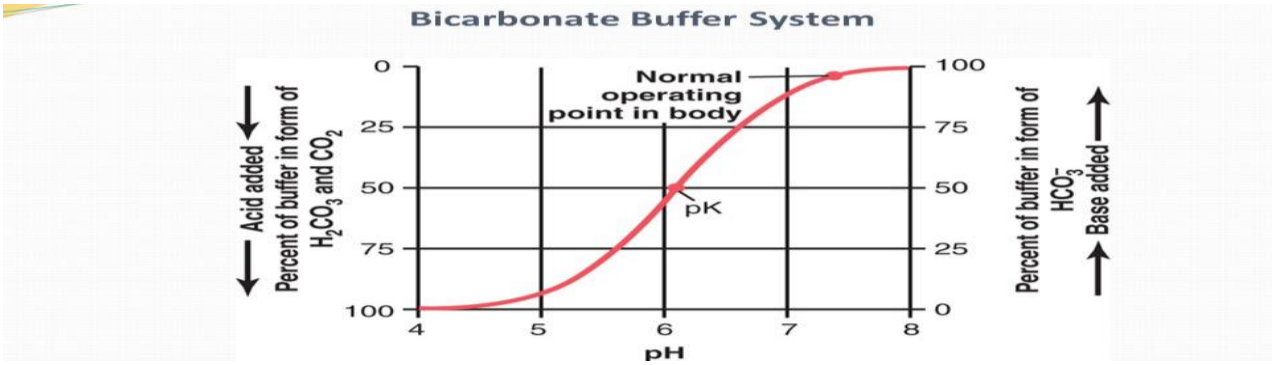
Bicarbonate Buffer System

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

But don't forget that H2CO3 is not stable, and it easily dissociates into water and carbon dioxide.

$$H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO2 + H2O$$

- Applying the Henderson-Hasselbalch Equation for Bicarbonate. Calculate the pH of the solution, the following numbers will not be given in exam, b3een Allah, ehfazoha.
  pKa of bicarbonate = 6.1
  A^- = HCO3- = 24 mmol/L
  HA= CO2= 40 mmHg (0.03 is the coefficient that we use in order to convert it into the same unit (mmol)) so;
  CO2= **40*0.03= 1.2 mmol**
  Answer: pH= 7.4 because
  pH = 6.1 + log (24/1.2) **=6.1+log(20)=7.4**



What should we learn from this curve: (the extra note 3 in the first page can help you)

- The curve is sigmoid in shape, steep portion in the middle around pKa (where buffer works most effectively), and somehow two plateaus at its sides.
- At the pKa, the [HCO3-]=[CO2] making the [HCO3-]/[CO2]=1 and the log([HCO3-]/[CO2])=0 (so, according to the equation pH=pKa)
- If more HCO3- is added to the solution with pH=pKa:
  - [HCO3-]/[CO2] >1
  - Log([HCO3-]/[CO2]) > 0
  - This will lead to an increase in pH (the higher the pH {more alkaline}) to become more than the pKa, this makes sense, because we're adding a base.
- If more CO2 is added
  - [HCO3-]/[CO2] < 1
  - Log([HCO3-]/[CO2]) < 0
  - This will lead to a decrease in pH (the less the pH {more acidic}) to become less than the pKa, and this makes sense too, because we're adding an acid.

- The buffer system will be effective for 1 pH unit on either side of pKa, where the curve is steep, meaning that the buffering capacity for bicarbonate extends from 5.1 to 7.1, or 6.1-1= 5.1 to 6.1+1=7.1 (because pKa is 6.1). Beyond these limits, the buffering capacity will rapidly diminish (plateau), meaning that any addition of HCl at this point (below 5.1) will lead to a huge shift in the acidity.
  (extra: any addition of NaOH at the point (above 7.1) will lead to a huge shift in the pH making it more basic)
  (extra: where would you expect the buffer system to be most effective? Around the central part of the curve where pH=pKa)

- We expect that pH should be near the pKa of the system to be more effective, because it was one of the characteristics that determine the power of the buffering system.
  BUT pKa of bicarbonate is actually 6.1, pH of blood (extracellularly) is about 7.4, this is not close enough! But **bicarbonate** is the most powerful **extracellular** buffer.
  (important extra: don't forget that there are 2 other characteristics that make the bicarbonate powerful as an extracellular buffer, its <u>concentration</u> is 24 mmol and its <u>renewal capacity</u> (addition) or even its removal are controlled by the kidney)

<u>Phosphate Buffer System</u>

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

- pKa of phosphate = 6.8, don't forget that you can calculate pH using Henderson-Hasselbalch Equation.
- Phosphate pKa (6.8) is closer to 7.4 when compared with the pKa of bicarbonate (which is 6.1), but bicarbonate's concentration is more than phosphate extracellularly (phosphate's concentration= 1.2 mmol). Thus, the HCO3- in the bicarbonate system is about 20X more than the CO2, while the $HPO4^{-2}$ in the phosphate system is about 4X more than $H2PO4^-$ (you can calculate the ratio by using the HH equation, as you know the pH and the pKa), in addition to that, phosphate has lower renewal capacity (it doesn't make sense to take phosphate from bones for buffering) and thus has less power than bicarbonate buffering system. This is why **phosphate buffer system** plays a minimal role extracellularly, but a major role in

renal tubular fluid and **intracellular fluid** where it works at its maximum buffering strength.

- What makes phosphate a good buffering system in the tubular fluid of kidney?
  Water is normally reabsorbed to a greater extent than phosphate by renal tubules, reabsorption of water = 99% while reabsorption of phosphate= 90%, this is why phosphate becomes greatly concentrated in the tubule (approximately 10X)
  pH of tubules (which is 7) is closer to pKa of phosphate than pH of blood (extracellularly, which is 7.4), {7 is closer to 6.8 than 7.4}.

	pka	**concentration**	**Renewal (most important esp. extracellularly)**	**Effective location**
Protein	7	70% of total	No renewal	Intracellular (chronically)
Phosphate	6.8	1.2	No renewal	Renal-tubular (+intracellular)
bicarbonate	6.1	24	Renal bicarbonate gain	extracellular

Ammonia buffer system

- it is composed of ammonia (NH3) and the ammonium ion (NH4+)
- pka of this system is 9.2
- Ammonia (NH3) doesn't actually work as an extracellular buffer why? because its concentration is too little, NH4+ is 100X more than NH3 so, the ratio is 1/100, and as you can see its pKa is not close to pH.
- The pKa is not even close enough to the pH of the tubules (which is 7), despite that, it's actually even more important quantitively than phosphate in the **tubules (**more detail later in this sheet).

Note from the doctor: the buffers can give substances in acidic and basic forms as we saw above, in **isohydric solutions** where H+ value is fixed (pH is also fixed by definition), we can easily predict the pH by knowing the ratio(base/acid) for any buffer within the system, because we already know the pKa of these buffers.

RESPIRATORY SYSTEM

Excessive intake of Salicylic **acid** (aspirin) can cause acidosis, when the acids increase, ventilation will increase, as a result.

As a result, ketoacidosis causes hyperventilation (to wash out the accumulated CO2) When does Hyperventilation occur? when CO2

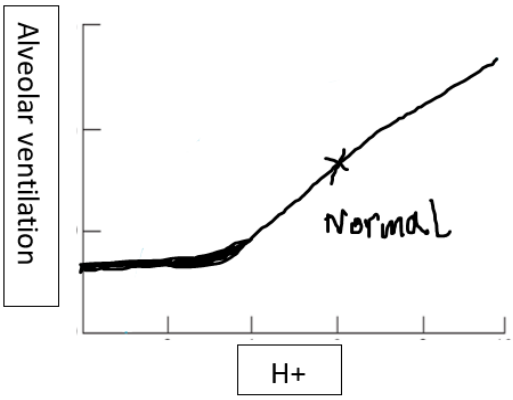
production is more than its removal, hyperventilation comes to make alveolar air closer to atmospheric air (arterial O2 should become high, CO2 become less).

$$H^+ + HCO_3^- \rightleftharpoons CO2 + H2O$$

#CHECK: When acids increase (more H+), this will make the reaction moves in the forward direction, as a result, CO2 concentration will increase, it will be eliminated by ventilation.

What happens in response to metabolic acidosis (less bicarbonate)? When the peripheral chemoreceptors detect an increase in arterial [H+], they reflexly stimulate the respiratory center to cause hyperventilation, causing more acid-forming CO2 to be exhaled and increasing the [O2] in the blood. Extra note, the hyperventilation action isn't limited as the hypoventilation because you can rise the O2 concentration to the maximum without response in contrast to hypoventilation as discussed below.

What happens in response to metabolic alkalosis(more bicarbonate)? When the peripheral chemoreceptors detect a decrease in arterial [H+], they reflexly inhibit the respiratory center to cause hypoventilation. In turn, hypoventilation produces an increased PCO2 and decreased PO2, which is the respiratory compensation for metabolic alkalosis. But you can see that PO2 is decreasing via this process, and when hypoventilation is severe and maintained, PO2 may become 60 mmHg or lower, and this is very dangerous, so, this compensatory reaction has a certain limits, meaning that, no more hypoventilation is predicted when PO2 goes below 60 mmHg.



As a result, 1 unit decrease in pH (acidosis) has more effect on respiration than 1 unit increase in pH (alkalosis), this is because the body has no problems with hyperventilation (which occurs to compensate for acidosis), but it raises a red flag for hypoventilation (which occurs to compensate for alkalosis) which may end with hypoxemia (this will be explained in detail, later in this sheet), notice the plateau when the hypoventilation exceeds its limits.

RENAL SYSTEM (mentioned in section 3)

- pKa of the NH3-NH4+ system is 9.2 which is not even close enough to the pH of the tubules (which is 7), despite that, it's actually even more important quantitively than phosphate in the **tubules** (as we said, it can reach 500 mmol/day), it specifically works on the collecting duct of the kidney. BUT that doesn't change the fact that the main (extra:initial) tubular buffer is phosphate.
- The mechanism of excretion is different between the PCTs and the collecting ducts.
  1- MECHANISM 1(In the proximal tubule): ammonia inside the cells, diffuses into the lumen, then it will combine with H+ which is also secreted in the lumen of the tubule forming NH4+. NH4+ is charged, it cannot cross the membrane again, and trapped inside the lumen. this process is known as ammonia trapping; but we said before that concentration of NH3 is little, we need another mechanism.
  Inside the cells we have the amino acid glutamine. The glutamine is broken down by the enzyme glutaminase to form two NH4 + and two HCO3 −. The 2NH4 + are secreted into the lumen by a counter-transport mechanism in exchange for Na+. The 2HCO3- 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 CO2 and H2O (by Krebs cycle) and then to HCO3-.
  NOTE: each time we secrete H+, we gain/ reabsorb HCO3, so secretion of H+ helps to replenish the HCO3- (do you remember when we said that bicarbonate has a great renewal capacity? And this what makes a powerful extracellular buffering system)
  2- MECHANISM 2; (In the collecting duct), H+ is secreted by H+-K+ ATPase in intercalated cells, and NH3 diffuses from the medullary interstitum (around the thick ascending limb) into the lumen. There, it combines with H+ forming NH4+ that's charged and is thus not reabsorbed back.
  So, H+ (that comes from the pump) combines with NH3 (that diffuses from the medullary interstitium into the lumen) forming charged, non-reabsorbable NH4+. And, because the diffusible NH3 which becomes trapped in the lumen, this is called Diffusion Trapping of Ammonia.(the second mechanism wasn't mentioned by the doctor).

Acid- Base Disorders

We solve such problems by the following 3 steps:

① Determine if we have alkalosis or acidosis How?– by measuring ABGs (Arterial Blood Gases) and determine if it's acidosis or alkalosis.

How to calculate pH?

1- By measuring the ABGs we can know HCO3- concentration, pO2, pCO2 and H+/pH. Then by the Henderson-Hasselbalch equation, we can calculate the PH. (In normal conditions: PH= 6.1+ log (24)/(40*.03) = 7.4)
2- If pH of blood = 7.4, but pH actually ranges from 7.35-7.45, if it dropped below 7.35, there would be acidosis, but if it was above 7.45, there would be alkalosis.
3- Why bicarbonate and CO2 concentrations are important? because they can tell us the type of the disorder (whether metabolic or respiratory).

- **Types of acidosis:**
  - **Metabolic acidosis** (due to bicarbonate decrease, leading to excess of H+ over HCO3- → Log([HCO3-]/[CO2]) < log(20)→pH<7.4)
    e.g.: HCO3- from 24 to 12, pH< 7.4
    pH= 6.1 + log (12/1.2) = 7.1
  - **Respiratory acidosis** (increased CO2, leading to excess H+)
- **Types of alkalosis**
  - **Metabolic alkalosis** (increased bicarbonate in blood)
  - **Respiratory alkalosis** (caused by hyperventilation)
- **Complex or Mixed**
  - **Mixed/ complex Acidosis**= Metabolic and Respiratory Acidosis
  - **Mixed/ complex Alkalosis**= Metabolic and Respiratory Alkalosis

    Examples:

    a- COPD and diarrhea (COPD leads to an increase in CO2(respiaratory acidosis), because it is not effectively removed, WHILE diarrhea leads to loss of bicarbonate(metabolic acidosis))

b- Aspirin (salicylic acid) is contraindicated with COPD patients because it increases the acidity, leading to more depletion of bicarbonate (metabolic acidosis).

c- Patients, who have COPD and diabetes myelitis type-1, would have the effect as COPD patients who consume aspirin, this will cause a huge shift in pH because DM-type 1 patients usually have diabetic ketoacidosis and make a lot of ketone bodies which consume the bicarbonate (metabolic acidosis).

② What causes the shift in pH?

If it was bicarbonate, it'd be metabolic. If it was CO2, it'd be respiratory.

Respiratory acidosis (CO2 is high)

- Could be as a result of drug overdose, that suppresses respiration, then *hypoventilation* (which leads to accumulation of CO2).
- Some diseases in respiratory system such as COPD which is chronic and obstructs airways (extra: pneumonia)

Metabolic acidosis (HCO3- is low)

- Diarrhea like in cholera (extra: no enough time to resorb it)
- Vomiting of intestinal contents (intestinal secretions such as pancreatic juices contain bicarbonates, this can lead to its depletion)
- Body production of H+, such as Diabetes Myelitis Ketoacidosis. Ingestion of Acids such as aspirin poisoning
- Kidney problems such as renal tubular acidosis
    - If there was no reabsorption of HCO3- (normally 90%, most of which in the proximal tubule)
    - If there was no secretion of H+ (usually by intercalated cells distally)

Type-1 (Distal Renal Tubular Acidosis) is more serious than **Type-2 (**Proximal Renal Tubular Acidosis), because it is too late to be corrected in type 1, while type 2 is in the proximal tubule, things can be corrected later at the distal part. To sum it up, The accumulation of acids in the body, due to failure of the kidney to either reabsorb filtered HCO3- (Proximal: type 2 RTA) or to secrete H+ (Distal: type 1 RTA).

NOTE: (acidosis is more common than alkalosis in clinical practice, especially metabolic acidosis, more specifically the one which is caused by diarrhea)

Metabolic alkalosis (HCO3- is high)

- Ingestion of bicarbonate.
- Pyloric stenosis, because we are losing H+, (extra: usually by vomiting gastric contents alone, we lose HCl)
- Extra: loop diuretics and hyperaldosteronism cause alkalosis

Respiratory alkalosis (CO2 is low)

Caused by hyperventilation, and it is more common than the metabolic.
(EXTRA: hypoxemia due to high altitudes or panic attacks)

③ Is there a compensation?

pH= 6.1+ log (kidney/lung)

Compensation means that HCO3- (kidney) and Co2 (lung) always follow the same direction, if one increases, the other will increase to maintain a constant value of PH.

#Partial compensation, both follow each other, but with a **value less than expected** (there are numbers that help us determine whether the compensation is complete or partial but we will not memorize them).

- Respiratory compensation is **faster** than renal compensation

	pH	HCO3-	CO2	response
Metabolic acidosis	↓	↓ primary	↓ compensatory	Hyperventilation (immediate)
Metabolic alkalosis	↑	↑ primary	↑ compensatory	Hypoventilation (immediate)
Respiratory acidosis	↓	Acute↑,Chronic↑↑ compensatory	↑ primary	Increase renal HCO3- resorption (delayed)
Respiratory alkalosis	↑	Acute↓,Chronic↓↓ compensatory	↓ primary	decrease renal HCO3- resorption (delayed)

- Notice in metabolic disorders, pH follows HCO3- and CO2.

- Already mentioned Extra: By normal fully compensated state, I think it means that the value is not exactly 7.4, but it can be within the normal range from 7.35- 7.45.
- If we have metabolic acidosis, there will be respiratory compensation which is fast. The CO2 will decrease in attempt to bring the PH to its normal range. It doesn't actually bring the pH into normal but makes its value approximately 75% of the normal pH, because as we previously said respiratory, is unlike the kidney, cannot fix it 100%.

  Metabolic acidosis: $pH\downarrow\downarrow = 6.1 + \log(HCO_3^- \downarrow\downarrow / CO_2)$

  Compensation (hyperventilation): $pH\downarrow = 6.1 + \log(HCO_3^- \downarrow\downarrow / CO_2\downarrow)$

  What clinicians can do in this case? Give the patient more bicarbonate.

- For each increase in **HCO3-**, there's a compensatory increase in CO2, AND For each decrease in **HCO3-**, there's a compensatory decrease in CO2. This is why metabolic acidosis and alkalosis are accomplished by **respiratory compensation**.
  However **metabolic alkalosis** receives **less help** from respiratory system in comparison with metabolic acidosis, what does that mean?

  If we have **metabolic acidosis** (less HCO3), the lungs will **compensate by Hyperventilation** (trying to make the composition of the alveolar air closer to the atmospheric air), by decreasing CO2 and increasing O2 and our body is designed to respond to hypoxemia or the decrease in O2 (below 60 mmHg) but, it is not responsive to hyperoxia. Even if O2 increases to 150(pO2 in atmosphere is 160 mmHg and 10 mmHg of those lubricate the inspired air, so the maximum pO2 that can be achieved is 150 mmHg) and CO2 becomes 0, the body will have no problem; because Haemoglobin is already saturated, and **any increase in O2** will **not affect** the saturation, but this is not applied to CO2.
  On the other hand, when there is **metabolic alkalosis**, there will be hypoventilation, we increase CO2 and decrease O2. The body **cannot** tolerate any **decrease** of **O2** below 60 mmHg, because Haemoglobin might not be saturated,

- For each increase in **CO2**, there's a compensatory increase in $HCO3^-$, and for each decrease in CO2, there is a compensatory decrease in

HCO3-. This is accomplished by **renal compensation**. As you can see above, this happens in respiratory alkalosis and respiratory acidosis.

Respiratory acidosis: $pH\downarrow\downarrow = 6.1 + \log(HCO_3^- / CO_2\uparrow\uparrow)$

No Compensation: if bicarbonate concentration hasn't changed
Partial compensation: if bicarbonate partially increased, $HCO_3^-\uparrow$
Complete compensation: if bicarbonate completely increased $HCO_3^-\uparrow\uparrow$

Here are the numbers, that can help us determine if there is a complete or partial compensation, bs el good news is that these *numbers are not for memorization except the first one), they will be given in the exam*

1- **Metabolic Acidosis** ✓For every 1mEq decrease in HCO3-, there will be **1.2mmHg** decrease in CO2 too.
2- **Metabolic Alkalosis** ✓For every 1 mEq increase in HCO3-, there will be 0.7 mmHg increase in CO2 (we explained earlier, why the respiratory compensation for metabolic alkalosis is limited, explained later in more details)
3- **Respiratory Acidosis** ✓Acute: For every 10 mmHg increase in CO2, there will be 1 mEq increase in HCO3- ✓Chronic: For every 10 mmHg increase in CO2, there will be 3.5 mEq increase in HCO3-
4- **Respiratory Alkalosis** ✓Acute: For every 10 mmHg decrease in CO2, there will be 2 mEq decrease in HCO3- ✓Chronic: For every 10 mmHg decrease in CO2, there will be 5 mEq decrease in HCO3-

#Extra: If we have metabolic problem, the respiratory system will respond in a relatively fast manner; thus, we will not have (acute or chronic) metabolic disorders. But if we have respiratory problem, the kidney will take time to compensate; thus, we will have (acute or chronic) respiratory disorders.

EXAMPLE: If CO2 acutely dropped from 40 to 30 (respiratory alkalosis), we expect HCO3- to decrease to 22 (24-2) as a complete acute compensation.

If HCO3- decreased by less than 2 mEq (more than 22), there might be partial compensation.

If it decreased by more than 2 mEq (less than 22), we expect a mixed disorder(meaning that in addition to respiratory alkalosis, we have superimposed metabolic acidosis too) but it is impossible for the compensation to exceed its predicted values.

Critical Thinking: If a patient came with 7.4 pH, would it be enough to rule out acid-base disorders? No, let's have an example,

A COPD patient, his CO2 was 80mmHg or 2.4 mmol instead of 40mmHg or 1.2mmol, there is 80-40=40 mmHg increase in CO2 (respiratory acidosis),

Our Expectations

The patient will have a compensatory increase in HCO3- that equals to 3.5*4= 14 (For every 10 mmHg increase in CO2, there will be 3.5 mEq increase in HCO3-)

Then HCO3- equals 14+24= 38 (COPD causes **chronic** respiratory acidosis)

pH = 6.1 + log(38/2.4), we expect pH to be 7.3

Our Findings

bicarbonate was 48 instead of 38,

we calculated the pH, it was 7.4

pH = 6.1 + log(48/2.4)= 7.4

you shouldn't say it's normal because his CO2 is high, the person actually has mixed disorder (respiratory acidosis and metabolic alkalosis)

explanation: bicarbonate has increased more than expected (more than 3.5/10 mmHg CO2)

If there was no compensation, pH = 6.1 + log(24/2.4)= 7.1

(this might be seen in this patient especially if he was hospitalized and we performed the test before his renal compensation started, because kidney is slow.)

FURTHER EXPLANATION at 43:00-44:22 (I took them FROM 2015)

- CO2 retention (in case of hypoventilation) will not be as large as CO2 washout (in case of hyperventilation). This can explain why for each 1mEq/L decrease in HCO3-, there's 1.2 mmHg decrease in CO2, whereas for each 1mEq/L increase in HCO3, there's 0.7 mmHg increase in CO2. This is why respiratory

compensation of metabolic alkalosis is less efficient than that of metabolic acidosis.

- If we have respiratory acidosis, the kidney tries to compensate by excreting the excess acid as titratable acid and NH4+ as well, both of which are associated with HCO3- gain. But 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 (1mEq/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 (3.5mEq/L) increase in HCO3-).
- If we have respiratory alkalosis, there must be a compensation to decrease HCO3-. in **acute respiratory disorders**, for each 10 mmHg decrease in CO2, there's (2mEq/L) decrease 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 decrease in CO2, there's (5mEq/L) decrease in HCO3-.

Examples from 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

Answer: 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

Answer: 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? And What is the daily net rate of HCO_3^- addition to the extracellular fluids ?

ANSWER:

net acid excretion=Titr.Acid + NH_4^+ excret - HCO_3^- =(10x1) +(15x1)-(1 x 2)= 23mmol/day

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

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

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

ANSWER

Case1: Metabolic acidosis
Case2: Metabolic alkalosis
Case3: Respiratory acidosis
Case4: Respiratory alkalosis

ومع آخر شيت لدكتور ينال، أنا سعيدة إني قدرت أقدّم اشي للدفعة بفضل ربنا، بتمنالكم جميعًا كل الخير في السنوات السريريّة ولأي حد لن تسمح له ظروفه يكمّل هذه السنة، فأهم شيء لا تيـأس، فكلنا زملاء في هذا المشوار وبالنهاية كلنا رح نتخرج والأهم من عدد السنوات والعلامات هو مين حيقدر فينا يضل فعلًا "إنسان"، شكرا لكل حد كان سبب بأي شكل من الأشكال حتى ولو بكلمة طيبة، وطبعًا شكر خاص لنادية صويص اللي كانت الداعم الأول بموضوع الشيتات وشكر تاني لعيون آية دعّاس وجود أيمن:م