Physiology sheet lec #34 :

Requirments of diluted urine : there should be no ADH or very little ADH , no interstitial hyper osmolarity , and we can use diuretics these are the cases where urine can be diluted .in case of concentrated urine there should be ADH without ADH there is no concentration even if there is medullary interstitium hyper osmolarity because ADH opens the water channels , hyper osmolarity from the medulla, urea because it is responsible for 50% of concentration , active vesa recta because it reserve this concentrated urine .

How we can know that the urine is concentrated or diluted ? by measuring free water clearance ( water without any solutes) we calculate it by substracting osmolar clearance from volume , if the free water clearance is positive it means that the urine is diluted , if it was negative that means that the urine is concentrated in other words if the urinary osmolarity/plasma osmolarity is less than 1 the clearance will be positive if it is more than 1 the clearance will be negative.

Disorders of Urine Concentrating Ability : if there is no ability to concentrate ADH that means that there is no urine. the reasons of ADH deficiency may be diabetes insipidus "relative or absolute deficiency of ADH" , or because of the absence or the abnormalities in the receptors " for the action of the hormone you have to had the hormone and the receptor in the case that they are not active this is called nephrogenic diabetes insipidus " so it is a failure to respond to ADH because of the receptors is impaired for Nacl reabsorption , drugs induced renal damage , malnutrition " decreased urea concentration " remember that urea is responsible for 50% of the urine concentration , kidney disease: pyelonephritis, hydronephrosis , chronic renal failure.

Ability to concentrate urine "the graph ": normally the maximum urine concentration is 1200 mOsm/L , but if the number of nephrons become less the concentration ability will become less and this is an indication of renal decease so the diluted will become minimum 50 and them it goes to 300 which is the maximum.

Total renal excretion ( the table ) " the dr said that the numbers is not very important he just read the slides "

Concentration of extracellular osmolarity :

 the mechanism of secretion of ADH: it is secreted in response to changing in osmolarity "hyperomolarity and hypernatremia " so ADH stimulates thirst with the help of other hormone which is angiotensin 2.

 Osmoreceptor antidiuretic hormone (ADH) feedback mechanism :

There is water deficit ,ADH increases the osmolarity of the extracellular fluid and that activates the osmoreceptors in the hypothalamus , ADH secretion high in the posterior pituitary , plasma ADH high , water reabsorption so it will increase water excretion so this will make a negative feedback on the water deficit.

Hypothalamus is the source of ADH , it is secreted in the hypothalamus receptors then released to posterior pituitary and acts on the distal tubules and collecting ducts of the kidney.

The stimuli for ADH secretion : increase osmolarity , decreased blood volume " cardiopulmonary reflexes ", regulation of blood pressure :when there is a decrease in the blood volume the receptors in the right atrium is stimulated and it will stimulate the receptors in the hypothalamus so it will release ADH that will reabsorp water so it will increase the extra cellular fluid volume and that will increase the blood pressure , other stimuli the most important one is the nicotine : people who smoke do not have much urination because when there is an increase in the sympathetic stimulation the ability to urinate will be more because GFR will decrease so reabsorption will decrease.

Slide 31 : if the plasma osmolarity increases ADH increase and the curve is curvy linear not linear .

Factors that decreases the ADH secretion is the opposite of that who stimulate it .Other factors: clonidine (antihypertensive drugs) , haloperidol (antipsychotic, Tourette’s), alcohol.

Slide 33 and 34 the dr read the slides .

Slide 35 : for the normal curve whatever the sodium intake is regulation for sodium in the plasma to be almost constant by the way of losing water or conserving water , ADH causes reabsorption and if it is blocked then this will change relatively at least the sodium concentration so there will be a variation in the sodium concentration so the curve will change , so if we the intake of sodium is high it's concentration will be high and vice versa that means that there is no regulation for sodium concentration , but in the normal situation whatever is the intake of sodium the concentration will be constant, so the relation will be linear and that is the normal negative feedback which decrease the variation . an example of the negative feedback receptors is the baroreceptors that regulate the blood pressure if they are absent the blood pressure will too high then too low " high variation ".

if we block aldosterone receptors there will be no change in the sodium concentration if ADH is present because ADH that controls the water ,so aldosterone will go parallel it will decrease the sodium concentration but not too much " there is no variation" so the variation will happened when we are changing in water not sodium and in this case the water regulation is still normal , angiotensin 2 has a direct effect on sodium concentration but not like aldosterone , aldosterone is more important in regulating sodium floride .

The next lecture is regulation acid base balance (PH):

We talked in previous lectures about the renal and urinary systems that the main function for them is to regulating acid base balance by buffers.

How is acid base balance regulated? By two major systems : respiratory system and renal system , respiratory throw CO2 and O2 conservation , normal PH is between 7.35 to 7.45 decrease in the PH is called acidosis and increase in PH is called alkalosis , in the case of acidosis the decrease of PH means more hydrogen ions because PH=log 1/{H+} or –log {H+}.

There are two types of acidosis and alkalosis : first type is due to up normality in the renal system that is called metabolic acidosis or metabolic acido-alkalosis so the cause of metabolic is usually the kidney , the next type is respiratory and the cause is the lung for example if someone has a respiratory failure he is not taking a good respiration that means that he is collecting more CO2 in his blood , CO2 will bind to water and in the presence of carbonic anhydrase this will form carbonic acid and in the presence of carbonic anhydrase 2 carbonic acid will dissociate to hydrogen and bicarbonate so this will increase hydrogen concentration so in conclusion respiratory failure causes acidosis . now in case of acidosis in the metabolic the kidney will make effect by bicarbs excretion and reabsorption , if we have less bicarbs in our body there will be acidosis . so if we want to differentiate between metabolic or respiratory we look to CO2 and bicarbs , if the CO2 is high it will be respiratory , if the bicarbonate is low it will be metabolic and vice versa applied to alkalosis. If we are talking about respiratory alkalosis it means CO2 is very high " hyper ventilation" and this might occur in physicotic people and this will stimulate the nerves in the neuromuscular junction and that causes spasm and if it is dangerous that will make him eat his tongue لسانه" بلع " and the treatment for this cases is by butting a bag and make them breath in it .

So in order to prevent acidosis and alkalosis from happening we have to regulate hydrogen concentration to stay almost normal . normally our body from metabolism and the food we eat that is rich with phosphorous and phosphate makes phosphoric acid and also here is sulfate that makes sulfuric acid these acid have to be excreted they are called "non-volatile acids " so each day we are consuming 80 mmol of non-volatile acids .

What is the volatile acids ? CO2 is one of them and they can be regulated by respiration .

Slide 2 : hydrogen is precisely regulated at PH range (7.2-7.45) below 7.2 is acidosis and above 7.45 is alkalosis .

1. Body fluids chemical buffers (rapid but temporary) : proteins is an important intracellular buffer ( it's concentration intracellular is more than extracellular) and the best example for a protein that is extracellular is the hemoglobin in the RBC's
2. Lungs (rapid, eliminates CO2) : when hydrogen increase that will increase ventilation and CO2 loss and this what we might face in the case of diabetes mellitus in this case there will be acidosis because of the retention of ketone bodies ( if there is no insulin carbohydrate will be converted to ketone bodies that are acids and those people will have hyperventilation then it will stop and begin again and continue like that in a cycle
3. Kidneys (slow, powerful); eliminates non-volatile acids :

There is something in the regulation that is called gain it is equal

(how much is being corrected/ how much is still in error) if the gain is high the system will be more powerful as a regulator and controller system , so the gain in the kidney is very high but unfortionatilly it's very slow , in contrast, the gain in the respiratory is low but they are quick an example in the control of blood pressure there are two systems the first is the short term system which is the baroreceptor they regulate the blood pressure in ml seconds but there gain is low it means that they don't correct the blood pressure 100% there will still be some error . the kidney eliminates the non-volatile throw secretion of hydrogen , reabsorption of bicarbonate and the most important one is the generation of new HCO3- because the food generates acids so the body need to compensate for this by geberating new bicarbonate and the source for this generation is the CO2 . what buffers generate bicarbonate ? ammonia and phosphate these buffers have a function of generate new bicarbonate but the others reabsorb bicarbonate.

Slide 3 : buffers system of the body :

1. Bicarbonate : most important extracellular buffer because it's very rapid
2. Phosphate
3. Ammonia
4. Protein : is an important intracellular buffer

(60-70% of buffering is in the cells)

Slide 4 : importance of buffer system :

Normal hydrogen concentration (the number is not very important ), Amount of non-volatile acid produced ~ 60-80 mmol/day from food and this 80 mmol most be excreted then we will divide it by 42 which is percentage of extracellular fluid in our body if the body weight is 70 then 70\*60=42

So the result will be 47,500 times > normal H+ concentration so it is much less than the normal PH so it must be excreted .

Slide 5 :same as the slide

Slide 6 : the curve

From the curve we can notice that in the middle there is a significant changing in the PH but in the peripheries there is a little change , if Pka is more closer to PH the effectiveness of the buffering system is more .

Slide 7 : in the bicarbonate buffer the Pka is 6.1 which is not very close to normal extracellular PH (7.4) but it is okay because it's very rapid and also it’s regulated by two systems : lungs and the kidney.

Slide 8 : if the concentration of hydrogen is more that will increase the alveolar ventilation and that decrease Pco2 which make a negative feedback on PH , so the respiratory centers don't respond to Pco2 but for [H+] because hydrogen stimulates the respiratory centers .

The dr talked about some points from dr yanal lectures which is the central and peripheral chemoreceptors : the central chemoreceptors they adapt after a while so the peripheral chemoreceptors will remains effective only , in case of chronic respiratory disease because of chronic change of PH the central chemoreceptors adapt so they are no more responses to hydrogen concentration or PH but the peripheral are sensitive to changing in PO2 because of that we must be very careful with chronic respiratory disease patient not to give them 100% oxygen or he will die because the oxygen will inhibit the chemoreceptors farther that it was previously so in there will be no more chemoreceptors .

Feedback Gain = 1.0 to 3.0 is not that much high but it is high in the renal although they are slow and we said previously that the gain is what is corrected / error for example if the blood pressure is 100 then it increased to 120 the baroreceptors will modify it to 105 the correction is 15 and the error is 5 so the gain is 3 which is very low but body fluid renal system it will increase the blood pressure to 100.001 the correction is almost 20 and the error is almost zero so the gain is 20/0 which equals infinity so the gain is infinite (very high).

Slide 9 : Kidneys eliminate non-volatile acids (H2SO4, H3PO4) (~ 80 mmol/day) then filtration will occur to bicarbonate and the filtered will be reabsorb and around 1 mmol will be excreted and the new 80 mmol of H+ will be titrated by generating a new bicarbonate 80 mmol by the use of ammonia and phosphate

Kidneys conserve HCO3- and excrete acidic or basic urine depending on body need.

Slide 10 : bicarbonate in the proximal tubule will not remain like sodium it will decrease because there are more reabsorption for bicarbonate but not like glucose and amino acids 100% and the excretion will be 1 mEq/day and the reabsorption in more in the proximal tubule not because of the carbonate but because of hydrogen.

Slide 12 : in the proximal tubules the bicarbonate that is filtered is reabsorbed , hydrogen is secreted in exchange with sodium , hydrogen will bind to bicarbonate then it will transform to carbonic acid and then it will dissociate by the help of carbonic anhydrase to HCO3- and water and CO2 is a gas and it's lipid soluble, it will get out of the cell and bind to water forming carbonic acid and then it will dissociate to bicarbonate and hydrogen , the bicarbonate will be reabsorbed . the buffer is bicarbonate and the Pka is 6.8 and the tubular PH the lowest is 6.8 not more or less because tight junctions is not so tight in the proximal tubule but in the distal tubule they are tight so the distal can maintain higher gradient for PH ( it might reach 4.5) and it’s the least PH can be maintained so there is no urine with PH less than 4.5 , in the distal tubule there is a hydrogen pump and the buffer is carbonate buffers so the highest PH is 6.7 due to looseness of the tight junctions in the proximal tubule and the minimal is 4.5 due to strong tight junctions in the distal tubules.

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