Sereen Draghmeh

Renal Physiology L3

We are still finishing the slides from the previous lecture

Regulation of Glomerular Filtration

- Remember the GFR is the volume of plasma/fluid that has been filtered through ALL the nephrons in one minute
- The body needs to control the filtration rate to maintain homeostasis
    - if the GFR was higher than normal
        - this means we are filtering more plasma/fluid than normal
        - you may think that is a good thing, since we will be able to remove the toxins faster but its not, there will be substances that the kidney wont be able to absorb efficiently.
    - If the GFR was lower than normal
        - This means we are filtering less plasma/fluid than normal
        - the body wont be able to remove waste products, and so they will accumulate and stay longer in our body
        - plus the reabsorption will be higher than normal, in which even the substances our body doesn't want to reabsorb will get reabsorbed
- Homeostasis of body fluids requires constant GFR by kidneys.
- If the GFR is too high, needed substances cannot be reabsorbed quickly enough and are lost in the urine.
- If the GFR is too low -everything is reabsorbed, including wastes that are normally disposed of.

Determinants of Glomerular Filtration Rate

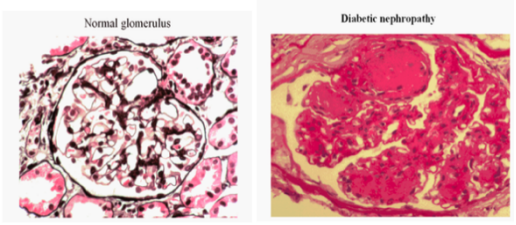
Normal Values:

- GFR = 125 ml/min
- Net Filt. Press = 10 mmHg
    - We said that this is needed in order to have normal GFR, in which there is a direct relationship between the net filtration pressure and the GFR
    - This direct relationship gives us a coefficient (cause remember whenever there is a direct relationship there is always a coefficient, y= k (coefficient) x)
        - The coefficient in this relationship is called the filtration coefficient which is denoted as Kf
- Kf = 12.5 ml/min per mmHg, or 4.2 ml/min per mmHg/ 100gm (400 x greater than in many tissues)
    - As we said there is a direct relationship between GFR and net filtration pressure so
        - GFR = Net filtration x Kf
            - Kf = GFR/Net filtration
                - Kf= 125/10
                - Kf = 12.5 ml/min

- And if we want to compare it between the weight of the kidneys and the weight of the muscles with any other capillary bed we need to calculate it per 100 gm and it will be 4.2 ml/min per mmHg /100gm
- Coefficient here in kidney (per 100gm of which) is 400 times greater than other tissues coefficient, which is 0.04 (100gm) which makes sense since kidneys need to have a better filtration because this is its function

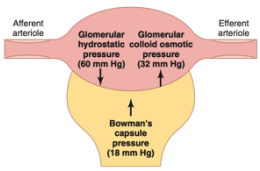
Glomerular Capillary Filtration Coefficient (Kf)

- Kf = hydraulic conductivity x surface area
  - Hypothetically speaking this is another way we can obtain the Kf but its impossible to do that experimentally so usually what we do is we measure GFR and the net filtration pressure and we divide them to obtain it
- Kf = GFR/net filt pressure
  - This coefficient is NOT variable, its not changeable from day to day and it's not very different between different healthy people
  - Since we said the coefficient is NOT variable that means the body CANT use it to control and maintain the GFR, BUTT it can change in pathological diseases, for example a decline in the blood vessels in the kidneys (like the loss of the glomeruli) so the surface area would decrease so that would result in a change of GFR , so there are factors that can change Kf but they are PATHOLOGICAL
    - SO ITS NOT A PHYSIOLOGICAL REGUALTORRR
  - And remember a decrease in Kf would cause a decrease in GFR
- Disease that can reduce Kf and GFR
  - Damage of capillaries
  - Basement Membrane thickens
  - chronic hypertension
  - obesity / diabetes mellitus
  - glomerulonephritis



Bowman's Capsule hydrostatic Pressure (P_B)

- factors that affect the GFR are factors related to the net filtration pressure for example bowman's capsule hydrostatic pressure (pressure of fluid that got filtrated in bowman's capsule)
- Lets quickly just refresh our memories and make a few things clearer so we don't get mixed up

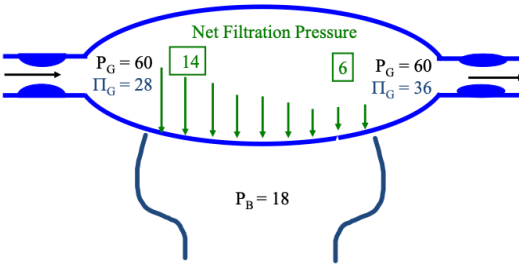


  - So we know that GFR is the plasma/fluid that is being filtered and we know that what surrounds the glomeruli is the bowman's capsule, so as the glomeruli is getting filtered all the unwanted substances and toxins will drop down to the bowman's capsule, and this will create a hydrostatic pressure in the bowman's capsule which will OPPOSE filtration

- this pressure is a result of filtration so it depends on GFR, so if GFR is high the pressure will also build up causing a high bowman's capsule hydrostatic pressure, and if GFR was low, the fluid that entered the bowman's capsule would be low so the hydrostatic pressure of bowman's capsule is low
- so you can say that this pressure (BP) is a function of GFR, so it cant be regulator/determinant of GFR
- Normally changes as a function of GFR, not a physiological regulator of GFR
- In pathological conditions the Pb can change for example obstruction in the roots or the urine passage ways, like the ureters or the urinary bladder or a tumor or kidneys stones – anything that cause obstruction, this will cause a blockage of filtered fluid so it will accumulate in the bowman's capsule resulting in an increase of the hydrostatic pressure of bowman's capsule, so that would affect the net filtration pressure by decreasing it since it OPPOSES the net filtration pressure, so in this case the GFR would decrease since we said they're directly proportional
- Increases with Tubular Obstruction kidney stones tubular necrosis Reducing GFR
- Urinary tract obstruction
- Prostate hypertrophy/cancer

Factors Influencing Glomerular Capillary Oncotic Pressure (πG)

- Factors that affect the capillary oncotic pressure
  - The capillaries carry blood form the arterial blood which contains proteins so the first factor is the arterial plasma oncotic pressure
    - Arterial Plasma Oncotic Pressure (πA)
      - Increase π A → increase π G
    - As you can see from the picture, as we move from the afferent end of the glomeruli (left side) to the efferent end of the glomeruli (right end) the fluid is decreasing (due to filtration) , the oncotic pressure would increase, because the fluid is decreasing as you move along the glomeruli, so there would be more solutes left in the glomeruli so there is an increase in oncotic pressure (as you can see it increased from 28 to 36)
    - So the glomeruli oncotic pressure depends on the protein content that reaches the glomeruli which is the exact same as the arterial afferent oncotic pressure
    - This glomeruli oncotic pressure also affects the net filtration pressure in which it will affect GFR
      - Lets break this down
        - An increase in the oncotic pressure (more protein build up) would cause a decrease in the net filtration pressure since as we said it's a force that opposes filtration (and remember forces that oppose filtration decrease the net filtration pressure)
        - This decrease in net filtration pressure would as we know decrease the GFR since they have a direct relationship (so a decrease in one would cause a decrease in the other)



- So you can say the consequence of increasing the oncotic pressure is that the GFR would decrease
- But if you look at the hydrostatic pressure it stayed the same

- The second factor is the FF which is the percentage of filtered fluid out of the renal plasma flow
  - Filtration Fraction (FF)
    - Increase FF→increase π G
      - FF = GFR / Renal plasma flow = 125 / 650 ~ 0.2 (or 20%)
  - We talked about this in the last lecture in which we said the FF is a ratio with a value of 20% and in most cases its constant
  - Remember the FF = GFR/Renal plasma flow
  - If we change the FF and lets say we said it increased, there could be 2 reasons for this
    - GFR increased
    - Renal plasma flow decrease
  - So the FF can affect the oncotic pressure
    - so if the FF increased which means the amount of fluid that was filtered out increased, the oncotic pressure would increase, since as we said, this would cause more solutes and proteins to build up
    - if the FF decrease, this means the amount of fluid that was filtered out decrease, so the oncotic pressure would decrease, causing less build up of proteins and solutes.
    - If there is an initial increase in GFR, the FF would increase so the oncotic pressure would increase causing a decrease in GFR in the end (think sequentially)
      - So if the GFR increases in the beginning the FF would increase which makes sense, and this as we said would increase the oncotic pressure, so more protein build up and this would cause a decrease in net filtration pressure, so in the end it would cause a decrease in the GFR
    - If the renal blood flow decreased, the FF increased, the oncotic pressure increases so the GFR decreases

- If you look at the graph you can see the afferent and efferent end and we are calculating the glomeruli colloid osmotic pressure.
  - Red line - Normal
    - You can see that the normal is the red line in which the filtration factor here is 20%, you can see that as you go from the afferent to the efferent end the glomeruli colloid osmotic pressure increases because along the way we have more fluid being filtered out so more protein build up so greater oncotic pressure
  - Blue Line – Higher FF
    - If we look at the blue line where the filtration factor increased more than 20%, you can see that the whole curve, shifted upwards, cause that means there is more fluid being filtered so more protein build up so a greater oncotic pressure
  - Green Line – Lower FF
    - If we look at the green line, the filtration factor decreased to less than 20%, which means less fluid is being filtered so less protein build up so less oncotic pressure, so the whole curve shifted downwards
  - And as you can see for all of the lines the oncotic pressure increased as we went from the afferent end to the efferent end so the net filtration pressure decreased along the way.

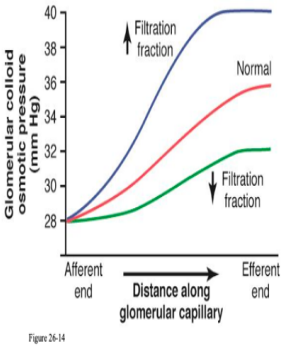
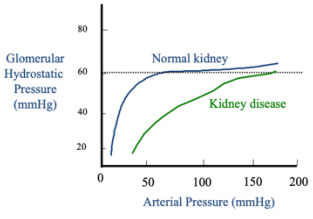


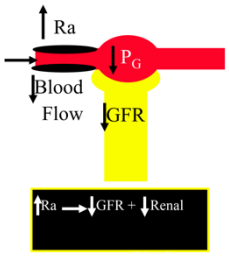
Figure 26-14

Glomerular Hydrostatic Pressure (P_G)

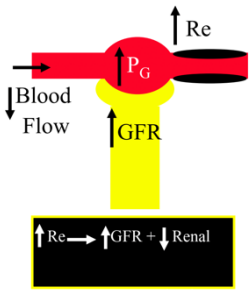
- Very important role in regulating the GFR
- Is the determinant of GFR most subject to physiological control
  - It's a physiological regulator since the body has tools to regulate it
- Factors that influence PG
  - arterial pressure (effect is buffered by autoregulation)
    - logically thinking a person with hypertension would have a high arterial pressure so logically it should affect the glomeruli hydrostatic pressure by increasing it, BUTTTT that is not the case, the systemic arterial blood pressure doesn't really affect the glomeruli hydrostatic pressure, this is due to kidney regulating their glomeruli hydrostatic pressure so that no fluctuations can occur , its like its buffering the systemic pressure that is entering the kidney so that it doesn't affect it a lot, since this glomeruli hydrostatic pressure is very important to maintain
    - in which they performed an experiment on animals and saw that when they changed the mean arterial pressure from 60 mmHg(very low) to 180 mmHg, they noticed that the glomeruli hydrostatic pressure stayed nearly constant
    - the systemic arterial pressure can affect the glomeruli hydrostatic pressure, but only in the extremes of pressure but like from 60-180 mmHg pressure, this pressure is buffered by a process called renal autoregulation that we will understand later



- afferent arteriolar resistance



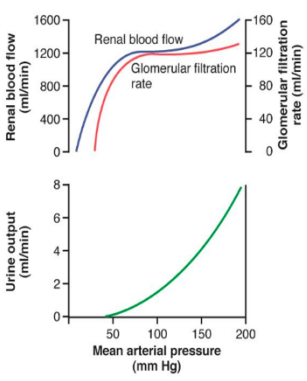
  - if I increased the resistance by causing constriction, the blood that will enter the glomeruli would decrease (due to reduced blood flow) so we expect the glomeruli hydrostatic pressure to decrease (since it wont get filled properly) and this would cause a decrease in renal flow
    - so a decrease in glomeruli hydrostatic pressure and a decrease in renal flow means less GFR
  - if I decreased the resistance by causing vasodilation, we will expect more blood to enter the glomeruli, thus causing an increase in the hydrostatic pressure of the glomeruli
    - so an increase in the hydrostatic pressure would cause an increase in GFR
- efferent arteriolar resistance



  - if I increased the resistance by causing constriction, that would cause less blood to leave the glomeruli, so it would increase the glomeruli hydrostatic pressure and this would cause a decrease in renal flow
    - so an increase in the glomeruli hydrostatic pressure would cause an increase in GFR
  - while if I decreased the resistance by causing vasodilation, that would cause an increase in the blood that leaves the glomeruli so it would decrease the hydrostatic pressure
    - so a decrease in hydrostatic pressure would decrease the GFR

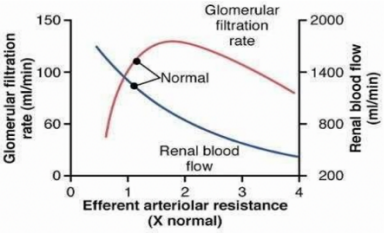
Autoregulation of renal blood flow and GFR but not urine flow

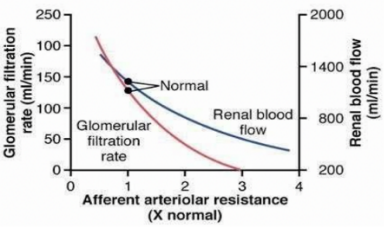
- we are going to see the effect of the mean arterial pressure on the urinary output (amount of urine that is excreted in a minute in ml), the renal blood flow and on the glomeruli filtration rate
- we have two graphs
  - the first graph (the one on top) represents the effect of the mean arterial pressure on the renal blood flow and glomeruli filtration rate
    - you can see that even as the mean arterial pressure increased, the renal blood flow and the glomeruli filtration rate stayed constant since both are being autoregulated by the kidney
  - the second graph (the bottom one) represent the effect of the mean arterial pressure with the urine output
    - you can see that as the mean arterial pressure increase the urinary output increased, this is because there is no autoregulation that occurs
      - we don't see autoregulation here, because the kidney plays with the reabsorption of it, in which an increase in pressure causes an increase in filtration but decreased reabsorption, as a result, excess fluid is excreted in the urine to maintain pressure equilibrium

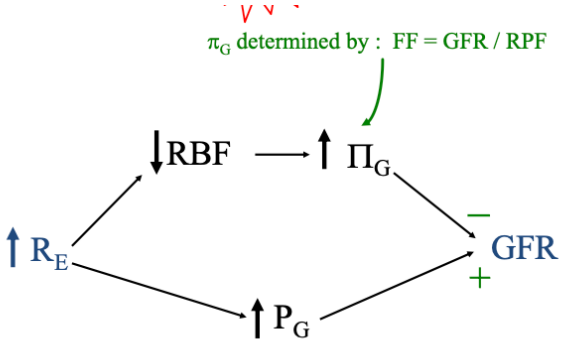


Effect of changes In afferent arteriolar or efferent arteriolar resistance

- Here we are trying to see the effect of the resistance on the renal blood and glomerular filtration rate
  - If we look at the afferent graph (the one at the bottom)
    - As the resistant increases, you can see that the glomerular filtration rate would decrease (red line), which makes sense, cause this is the entrance of the blood, if I blocked the entrance there would be less blood and fluid in the glomeruli so less being filtered
    - As the resistance increase, you can see the same thing in which the renal blood flow (blue line) would also decrease
  - If we look at the efferent graph (the one at the top)
    - As the resistance increases , you can see that the renal blood flow (blue line) decreases, which makes sense, since I'm blocking the blood from leaving the glomeruli so the renal blood flow would be slower
    - If you look at the GFR (red line), you can see that at 1x resistance the GFR was normal, then when I increased it to 2x, the GFR increased and when I also increased in to 3x the GFR was still higher than the normal, BUTTT when I increased to 4x, the GFR started declining
      - This is called a biphasic relationship
      - This is due to the fact that as we said before, an increase in efferent resistance would cause an increase in hydrostatic pressure which would increase GFR to a certain extent, in which after 3x resistance, an increase in resistance would cause a high decrease in renal flow so that would cause an increase in FF , increasing oncotic pressure thus decreasing the GFR







Summary of Determinants of GFR

↑GFR If → ↑ K_f
↑GFR If → ↓ P_B
↑GFR If → ↓ Π_G
↑Π_G If → ↑Π_A → ↓GFR
↑Π_G If → ↑FF
↑GFR If → ↑ P_G
↑P_G If → ↓R_A → ↑ GFR
↑P_G If → ↑R_E → ↑ GFR
(as long as ↑R_E < 3-4 x normal)

?