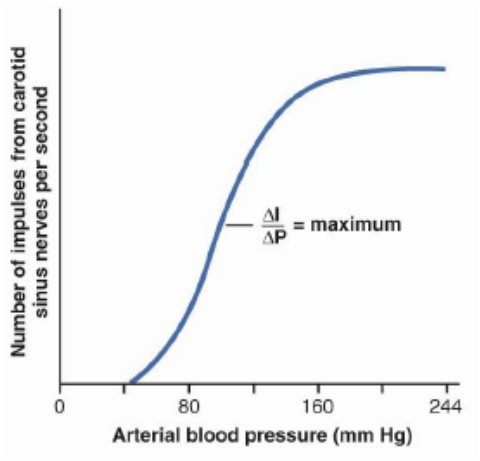
CVS Physiology Lecture 18
Blood Pressure Regulation -1

Please study the previous sheet before studying this one, even if the first part in this sheet is revision.

- In the previous lecture we were talking about the Baroreceptor Reflex; the High Pressure Baroreptors which are the *aortic and carotid baroreptors*. They respond to the changes in the arterial blood pressure and send impulses to the vasomotor center or the cardiac center and accordingly they regulate the blood pressure. And there must be other Low Pressure Baroreceptors found in low pressure places (will be discussed in this sheet).
  They are very fast (neural); important for Short Term Regulation.
  Reflex is initiated by stretch receptors called baroreceptors or pressoreceptors located in the walls of the large systemic arteries.
  A rise in pressure stretches baroreceptors and causes increase in the impulse rate → suppress VMC and cardiac accelerator center -→ decrease pressure back to normal to normal.

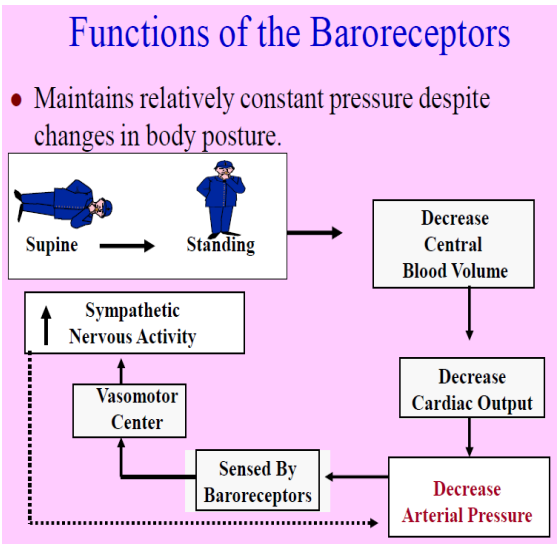
- As pressure increases the number of impulses from carotid sinus increases which results in:
  1) inhibition of the vasoconstrictor
  2) activation of the vagal center in the heart



- The curve shows the relation between the number of impulses to the arterial blood pressure, you can notice that Baroreceptor reflex responds to pressures between 60 and 180 mmHg and functions most effectively/ it is most sensitive around the normal MAP *100mmHg.* So it is called "***pressure buffer system***"; any small change in the pressure around 100mmHg causes very big change in the impulses rate, and they are less sensitive when the pressure in very high.

- These receptors, like any neural system, <u>they reset and adapt to the change</u>, so if the pressure increases for long time (eg. Become 120 mmHg) the baroreptors deals with it as if it is the normal value. They are <u>unimportant in long term control</u> of arterial pressure and we need other regulators for intermediate and long term regulation.

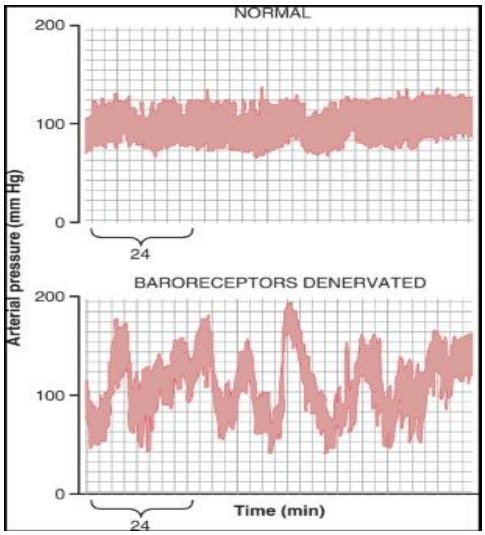
- Baroreceptor reflex maintains relatively constant pressure despite changes in body posture. So when you change your position from supine to standing position, the MAP is decreased, and through the short term regulation within seconds the MAP is increased toward its normal value. Same thing happens if you change it from standing to supine, the blood pressure is increased

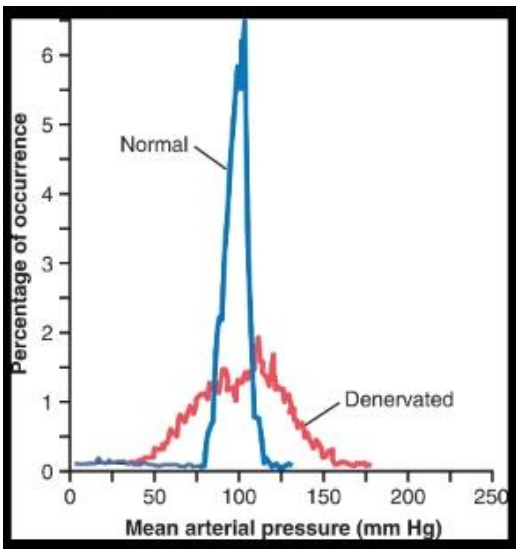


due to the gravity but through the Short term regulation it is decreased toward its normal value. (mechanism discussed in the previous lecture)

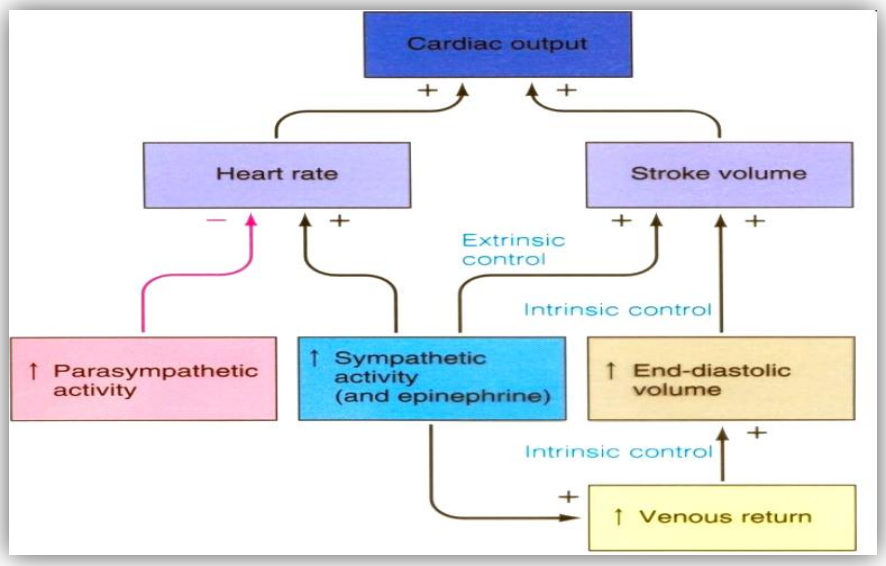
- In older people, due to atherosclerotic changes, the arteries become rigid and the baroreceptors are less responsive to stretch, so when they get up from sleep the blood pressure drops, baroreceptors are not as effective as in younger people, so they feel dizzy and might fall down, that is why we advice them to get up slowly.

- In order to prove the importance of the buffer function of the baroreptors (work around the MAP), a study recorded the arterial pressure changes in an animal with normal baroreptors animal and another one from an animal with denervated baroreptors (nerves are removed) . As you can see from the figures below, in the normal most of the time the pressure is most of the time around 100mmHg and the variation is very small, while in the denervated one the pressure is around 100mmHg but with a huge variation.
  Baroreceptores oppose either increases or decreases in arterial pressure thereby <u>reducing daily variations in arterial pressure.</u>

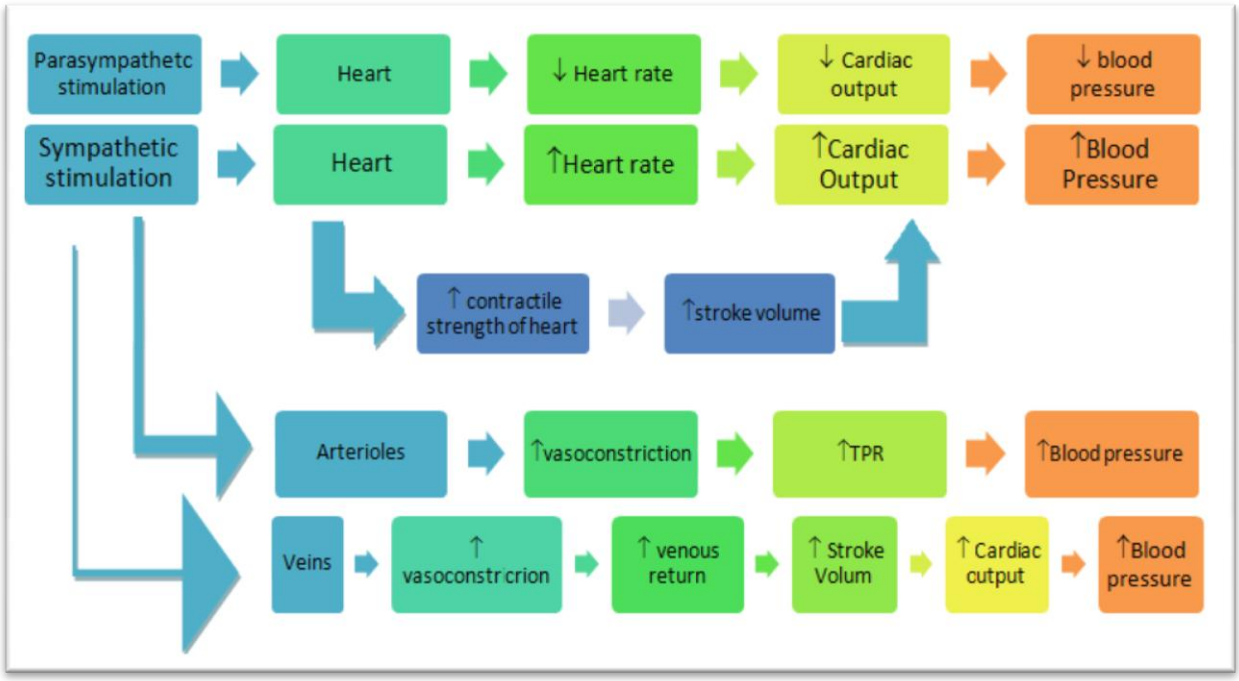




- Any factor increases the venous return will increase the C.O.
  When extracellular blood volume is increased → plasma volume is increased → MSFP (mean systemic filling pressure) is increased → increase the pressure gradient between the veins and the Rt. Atrium → increase venous return → increase EDV → increase SV → increase C.O



— In the following figure the Effects of sympathetic and parasympathetic nervous systems on factors that influence the MAP. Remember that the parasympathetic only works on the heart while sympathetic works in both vessels and heart as well.



❖ **Low Pressure Baroreceptors:**

— Located in low pressure places; Rt. Atrium and Rt. Ventricle.

— They are sensitive to <u>changes in volume</u> (accordingly changes in pressure)

— It works through ***"atrial- hypothalamic reflex";*** by stimulating the ADH –Vasopressin, very important vasoconstrictor- secretion in case of low blood pressure, or inhibiting ADH in case of high blood pressure.

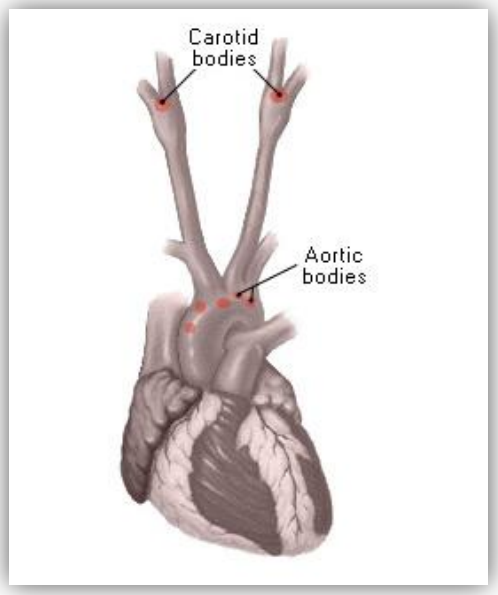
– An increase in volume in Rt atrium or Rt ventricle → more stretch → send impulses to the Hypothalamus → hypothalamus decreases secretion of ADH – Vasopressin- → decrease the reabsorption of water from the kidney tubules → increase urine output → decrease extracellular blood volume → decrease MSFP → decrease venous return → decrease EDV → decrease SV → decrease the C.O → decrease the pressure back to its normal value**.**
*Also ADH works as a potent vasoconstrictor; if ADH secretion decreased less than the basal rate → decrease TPR → decrease the pressure back to its normal value**.**
And vice versa.

— Also works through **"Atrio- renal reflex" (between kidney and right atrium)**:

– increase in Rt. Atrial pressure due to increase in volume → afferent arteriolar vasodilation in the nephrone → increase blood flow to the kidney → increase in GFR (Glumerular Filtration Rate) → increase urine formation → decrease extracellular blood volume → decrease MSFP → decrease venous return → decrease SV → decrease the pressure.

– decrease in Rt. Atrial pressure due to increase in volume → afferent arteriolar vasoconstriction in the nephrone → decrease blood flow to the kidney → decrease in GFR (Glumerular Filtration Rate) → decrease urine formation (conserving fluid) → increase extracellular blood volume → increase MSFP → increase venous return → increase SV → increase the pressure**.**

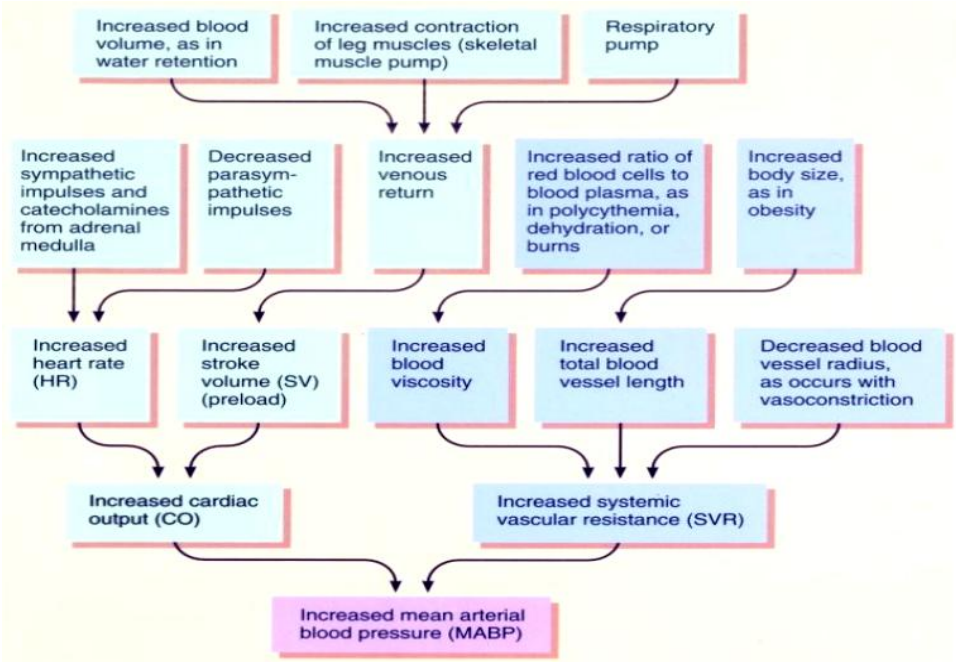
❖ **Chemoreceptors:**



- The other short term regulators of blood pressure are the chemoreceptors.
- Located at the same areas of baroreceptors (they are not the same), *"carotid bodies"* near the carotid bifurcation and *"aortic bodies"* on the arch of the aorta.
- They have very high blood flow to the extent that the venous and arterial blood oxygen difference is very minimal and the interstitial blood O2 and CO2 is almost the same as arterial due to the fast blood flow.
- Called Peripheral chemoreceptors in contrast with Central chemoreceptors that are found in the medulla oblongata.
- They respond to **pO_2, pCO_2 and pH** changes (remember that increase in H+ means decrease in pH).
- Stimulated when the pO_2 is low, pCO_2 is high and H+ is high, and more sensitive to the pO_2**.**
  - If blood pressure decreases → the blood flow to these chemoreceptors decreases → there will be a decrease in decrease pO_2, increase pCO_2 and increase in H+ →stimulation of chemoreceptors → send impulses to the cardiovascular center → stimulate the cardiac acceleratory area → send more sympathetic and less parasympathetic to the heart → increase in the contractility and heart rate → increase in the SV and CO
    And stimulate the vasoconstrictor area→ send more sympathetic to the vessels → vasoconstriction → increase TPR
    By increasing the CO and TPR the MAP is increased towards its normal value.
  - If blood pressure increases → the blood flow to these chemoreceptors increase → there will be an increase in decrease pO_2, decrease pCO_2 and decrease in H+ →inhibition of chemoreceptors → send impulses to the cardiovascular center →inhibits the cardioaccelatorty and stimulates the cardioinhibitory → send less sympathetic and more parasympathetic to the heart → decrease in the contractility and heart rate → decrease in the SV and CO
    And suppress the vasoconstrictor area → send less sympathetic to the vessels → vasodilation → decrease TPR
    By decreasing the CO and TPR the MAP is decreased towards its normal value**.**
- These receptors are not stimulated until the pressure falls below 80 mmHg (responds to less pressure value that baroreceptors do) , so they are the second line after the baroreceptors.

Blood Pressure Regulation – 2

- **Factors affecting total peripheral resistance:**
  1. Arteriolar radius (4^{th} power) :
     Affected by vasoconstrictor and vasodilator substances.
  2. Blood viscosity:
     affected by number of RBCs and concentration of plasma proteins.
- **Factors affecting the MAP**:
  - The least factor that might change is the total blood vessel length which may be increased in case of obesity for example.

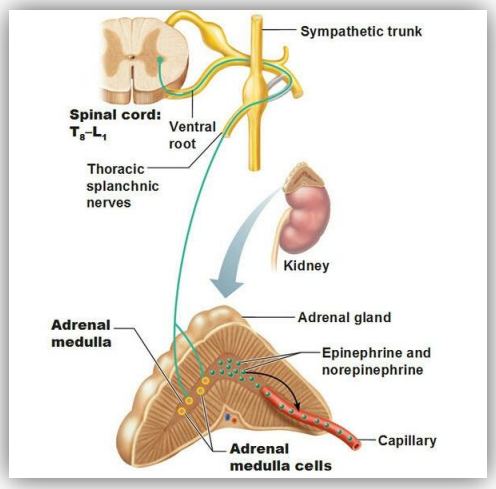


- **Intermediate and Long Term Regulation:**
  - We said before that we need those regulators because short term regulators adapt the change.
  - Hormones and chemicals (epinephrine, norepinephrine, ADH, Angiotension, rennin, ANP) go through the blood to the whole body so their effect is wider.

- Suggest that there is a patient who is bleeding due to a car accident, in this case the blood volume is decreased → MAP is decreased → the baroreceptors are activated within minutes trying to increase the pressure.

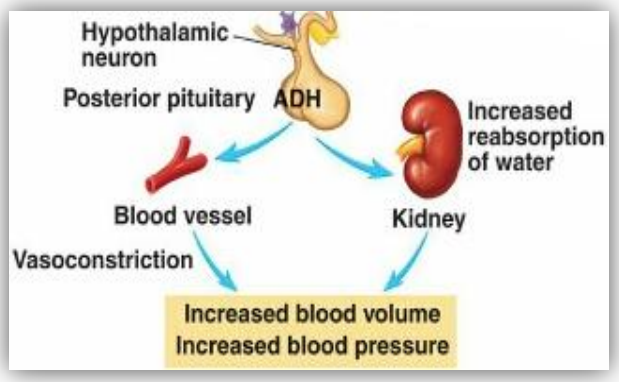
If he still bleeding within 10 minutes other systems are activated:

<u>The Epinephrine – Adrenal medulla system</u>, when BP goes down → sympathetic nervous system is stimulated → stimulation of the sympathetic goes to the adrenal medulla → increases the secretion of adrenal medulla (*epinephrine* 80% and *norepinephrine* 20% and both are derived from Tyrosine), so within 10 min his epinephrine and NE are up →

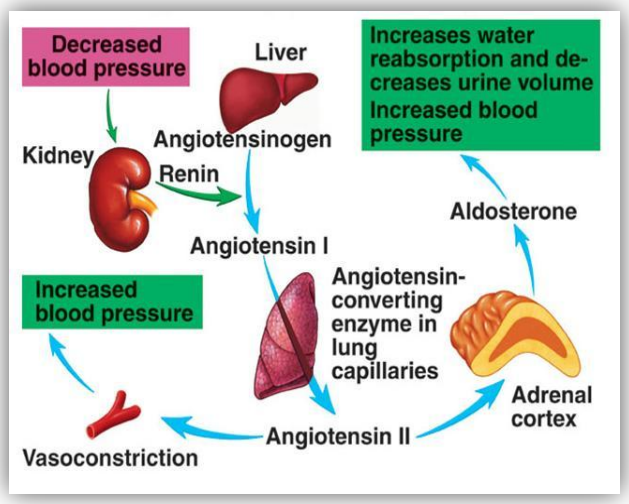


vasoconstricts the blood vessels and increase the heart rate and contractility trying to maintain the blood pressure.

Unfortunately, after half an hour he is still bleeding and the blood pressure is dropping, now other system is activated which is **ADH (vasopressin) system,** ADH secretion is increased causes vasoconstriction anywhere in the body and conserve water trying to maintain the BP . this system needs 30 minutes to work..



After one hour, still there is no medical emergency service, a third system is activated which is the **Renin-Angiotensin-Aldosterone system**; when the MAP is decreased the pressure in the afferent arteriole goes down → the macula densa increase the secretion of *Renin*. Renin works on *Angeotensinogen* (14 amino acids peptide, α 2 globulin, synthesized in the liver and found in the plasma), it will be broken into *Angeotensin I* (10 amino acids peptide) by Renin → Angeotensin I circulates in the body, and primarily in the lungs it is broken down into *Angeotensin II* (an octapeptide – 8 amino acids) and it is the most potent vasoconstrictor in the body so it will constrict all the vessels, also it is a +ve inotropic agent; increases heart contractility trying to increase the pressure up.



Angeotensin II goes to the adrenal cortex and adrenal medulla, in the cortex there are 3 layers (Zona glomerulosa(outer), zona fasiculata and zona reticularis), primarily zona glumerulosa is stimulated to secrete aldosterone (steroid) → stimulate Na+ and water reabsorption → increase extracellular fluid volume → increase plasma and blood volume → increase MSFP → increase venous return → increase EDV and SV trying to increase the BP.

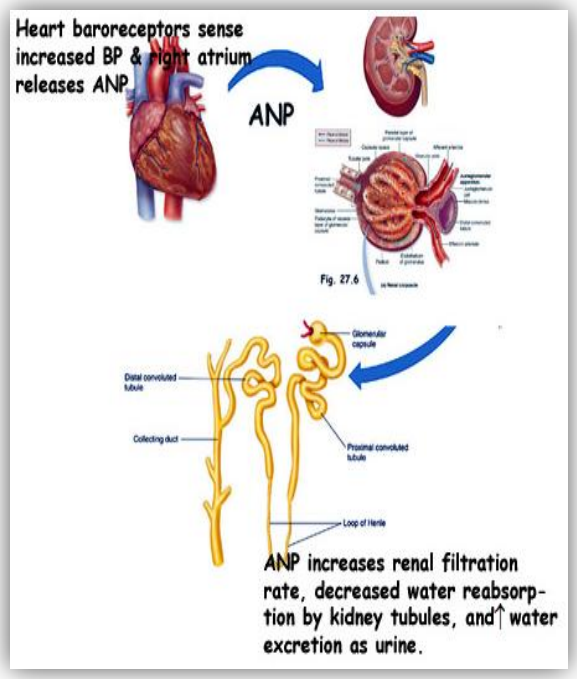
If the BP was not increased he might go into hypovolemic/hypotensive shock, in the first stage (10-30 min or one hour depending on how much blood he loss) it might be reversible, the 2nd stage is pregressive and the 3rd stage is irreversible and cause tissue death.

The hormones mentioned above all work one side, while the fourth hormone **ANP – Atrail Natriuretic peptide-** works on the other side. In case of decrease in the BP and decrease in the Rt atrial pressure → decreade in ANP secretion → decrease GFR and decrease in urine output and vise versa.

If the BP goes below 60 mmHg, his brain is going to suffer from ischemia. Now the last chance for this person is the **CNS Ischemic response**, it sends extensive sympathetic stimulation everywhere trying to increase the BP. If it works he is safe, if it doesn't he will die.

To sum up the story above, the **Intermediate and Long Term Regulation is done by:**

1. **Epinephrine – Adrenal medulla system:**
   - works as intermediate term needs ~ 10 min. to work causes vasoconstriction
2. **ADH (vasopressin) system**:
   - needs ~ 30 min to work causes vasoconstriction
3. **Renin-Angiotensin-Aldosterone system:**
   - needs ~ 1hour to be effective.
   - Renin is synthesized and stored in modified smooth muscle cells in afferent arterioles of the kidney and released in response to a fall in pressure.
   - Angiotensinogen converted into Angiotensin I by Renin, the angiotensin I is converted into angiotensin II by Angiotensin converting enzyme mainly in the lungs. Angiotensin II (A II) is very potent vasoconstrictor. AII also stimulates aldosterone synthesis and secretion from the adrenal coretx (Zona glomerulosa), from the renal nephrone and so water.AII is also a positive inotropic agent.



4. **Atrail Natriuretic peptide (ANP):**
   - 28 a.a peptide released mainly from the Rt. Atrium in response to stretch. It causes increase in GFR so increase Na+ and water. Its concentration decreases when BP is low and its concentration increases if BP is high, mainly due volume overload.

❖ **CNS Ischemic Response**

- It is activated in response to cerebral ischemia.
- Reduced cerebral blood flow causes CO2 buildup which stimulates vasomotor center thereby increasing arterial pressure.
- It is one of the most powerful activators of the sympathetic vasoconstrictor system.
- CNS Ischemic response is not activated until pressure falls below 60mmHg; greatest activation occurs at pressures of 15-20mmHg.
- Cushing reaction is a special type of CNS ischemic response.
- Prolonged CNS ischemia has a depressant effect on the vasomotor center.

"ومن يستبقْ للعلا غايةً فأولى به من سواه التعبْ"- الرّافعي

بالتوفيق ☺