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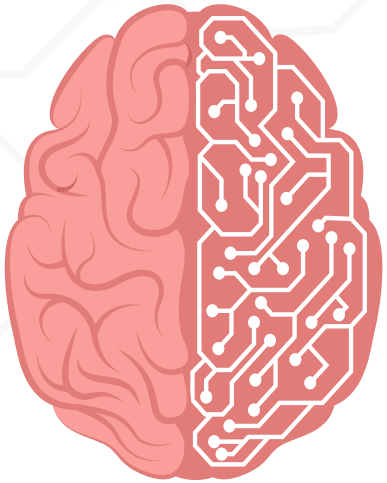

Physiology - CVS

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Blood Pressure Regulation 2

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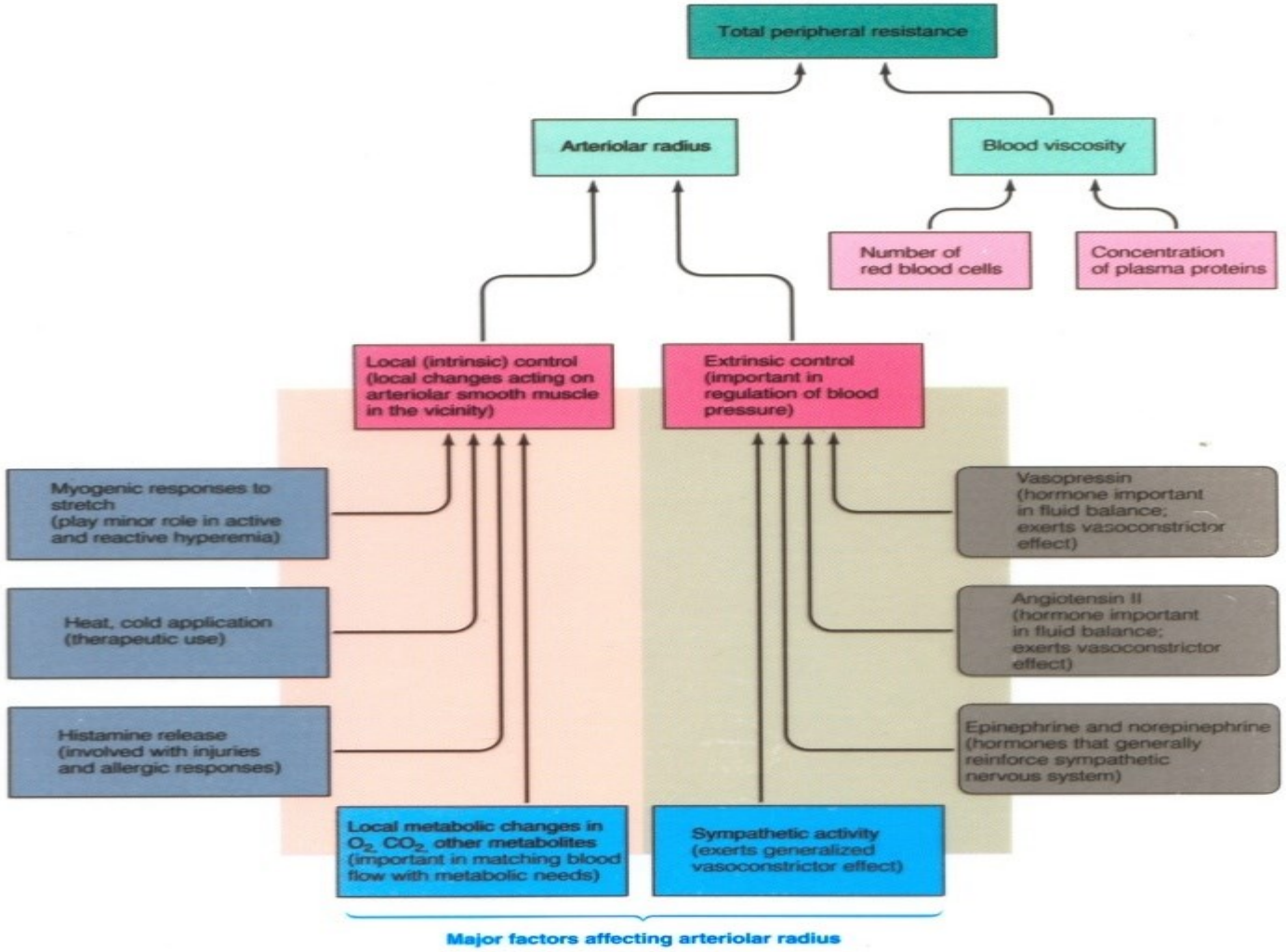
Objectives

- Outline the intermediate term and long term regulators of ABP.
- Describe the role of Epinephrine, Antidiuretic hormone (ADH), Renin-Angiotensin-Aldosterone and Atrial Natriuretic Peptide (ANP) in BP regulation
- Point out the role of Kidney-body fluid system in long term regulation of BP
- Follow up the responses of the circulatory shock

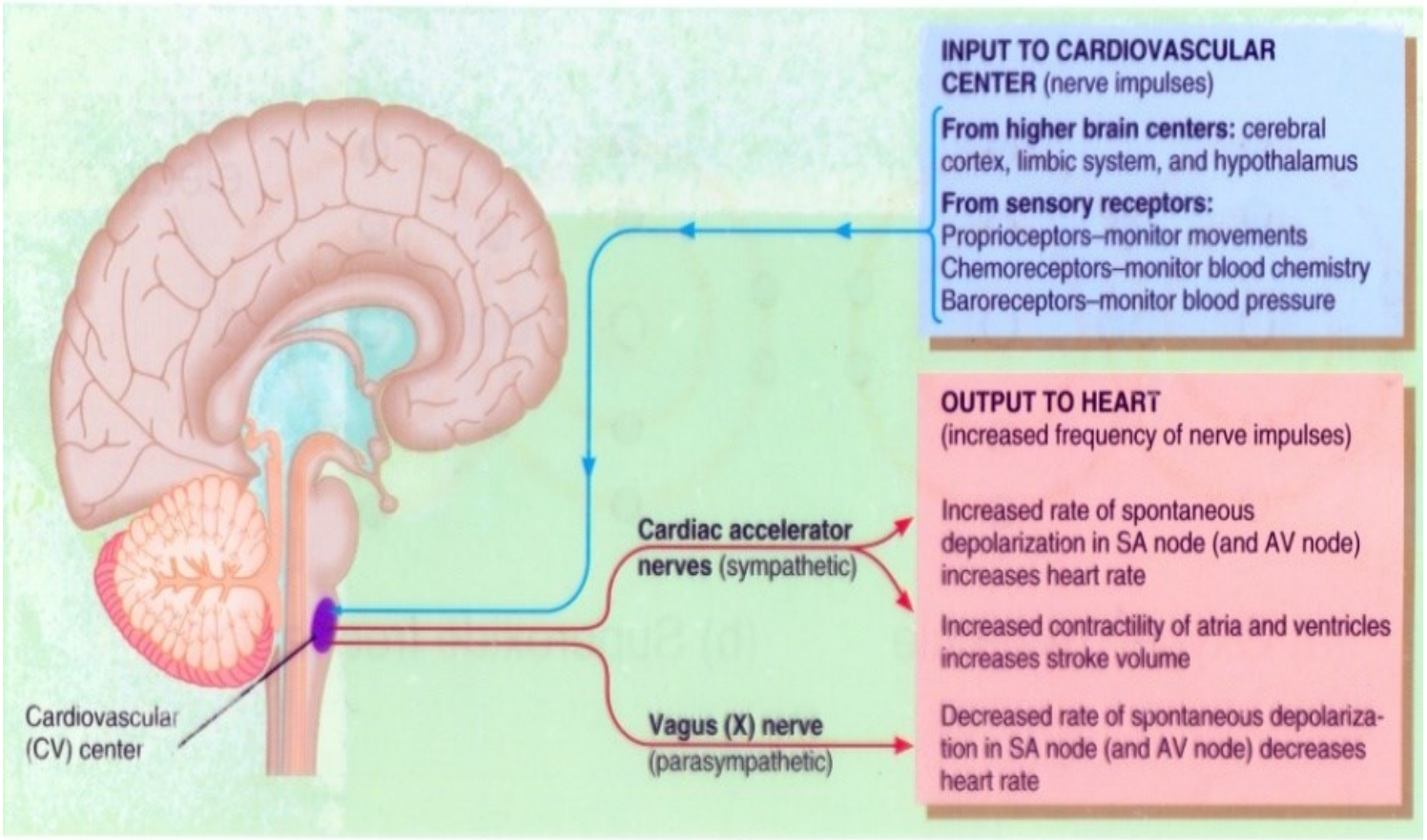
Factors affecting Total Peripheral Resistance

- TPR is mainly affected by the radius because it's inversely proportional to the 4th power of the radius.
- The arteriolar radius is affected by **vasoconstrictors** like vasopressin, angiotensin, Epi and NE, **the sympathetic system,** or **local factors** (to be discussed later)
- The blood viscosity is affected by the number of RBCs and the concentration of plasma proteins



Nervous Control of the Heart

- The cardiovascular center, the cardioaccelerators, and cardioinhibitors are located in the medulla oblongata
- Signals coming from the higher brain centers can affect these things mentioned above



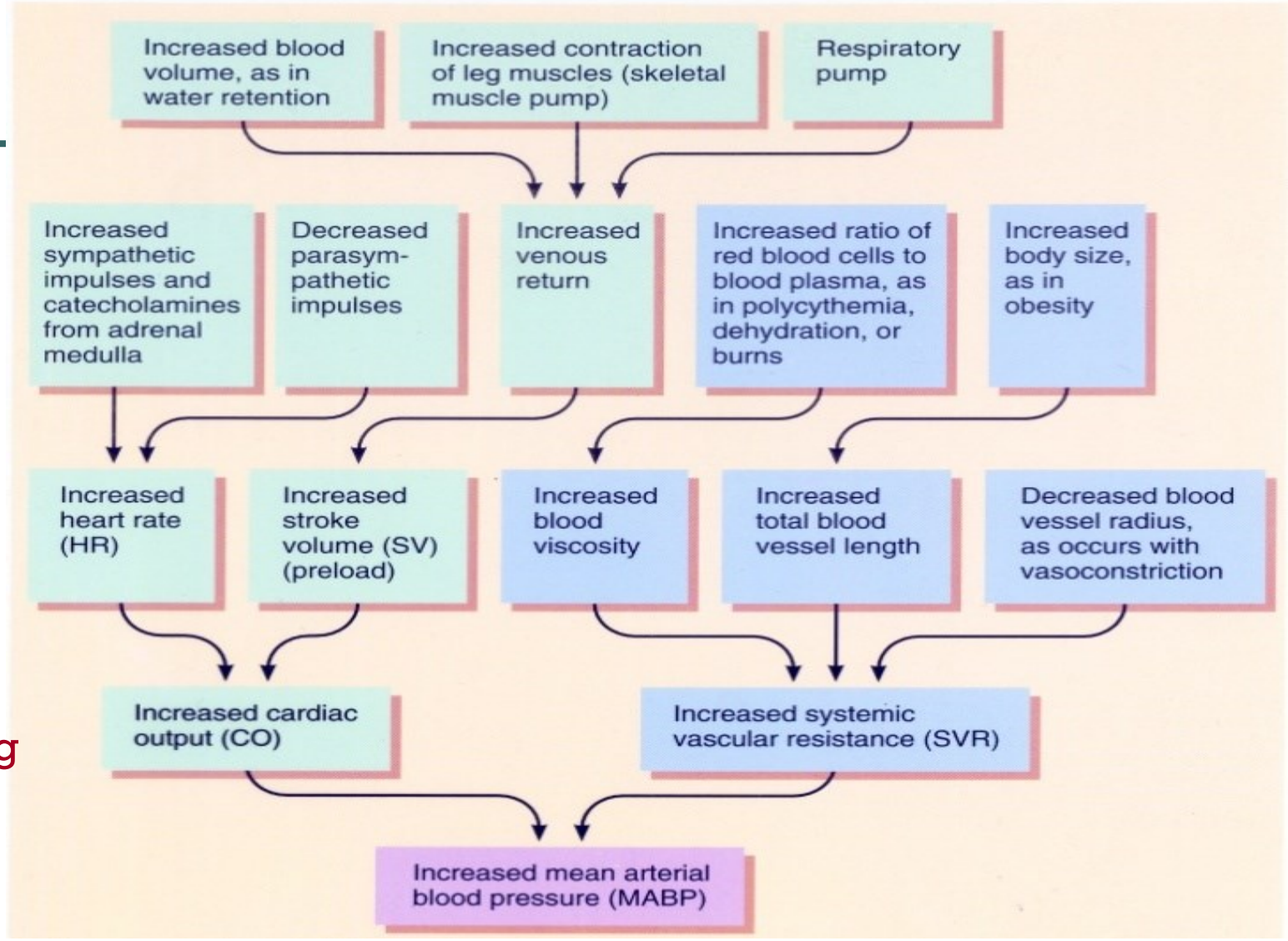
Factors that affect the Mean Arterial Pressure

(Study everything in the figure; it's important and easy because it keeps getting repeated)

<u>Notes not written in the figure:</u>

- Atrial bainbridge reflex affects the HR which affects the CO
- Remember:

1. increased venous return → increased SV (Frank-Starling law)
2. Increased contractility increases SV



Intermediate / Long term Regulation of BP

1. Epinephrine – Adrenal medulla system

   works as intermediate term needs ~ 10 min. to work
   causes vasoconstriction → **increased HR → increased contractility → increased MAP**

2. ADH (vasopressin) system needs ~ 30 min to work
   causes vasoconstriction

Further explanation

- Intermediate regulation occurs when there's bleeding, for example, after a car accident where the blood pressure slowly decreases.
- Like we took before, the first things that try to increase the blood pressure are the baroreceptors; they are very fast, but they're sometimes not enough during a hemorrhage (caused by the car accident in our example)
- **Why does the Epinephrine-Adrenal medulla system need 10 minutes to work?**

✓ Because even though the already existing epinephrine goes out of the adrenal medulla, we need additional amounts of new epinephrine

✓ So, the formation of the new epinephrine is what needs these ten minutes (remember: it's made from the amino acid tyrosine)

- **Why do we say epinephrine, not the sympathetic system?** It's because epinephrine is a chemical that can go **everywhere** while it flows in the blood, unlike the SNS which can only go to the places it supplies.

Further explanation (hang in there)

- Now, if the bleeding continues, and the pressure is still dropping, after 30 minutes, ADH system starts to work, and the decrease in the blood volume(caused by the bleeding) will stimulate the hypothalamus to secrete more and more ADH/vasopressin (which is a vasoconstrictor) therefore, it increases the TPR, maintaining the MAP back to normal.
- ADH also goes to the kidney, reabsorbing more water which increases the extracellular volume, increasing the blood volume, which in turn increases the venous return, the SV, and eventually the CO

Long term Regulation of BP…cont

3. Renin-Angiotensin-Aldosterone system ~ 1 hour to be effective

Angiotensinogen (14 a.a peptide) converted into Angiotensin I (10 a.a peptide) by Renin that come from afferent arteriolar cell, the angiotensin I is converted into angiotensin II (8 a.a peptide) by Angiotensin converting enzyme mainly in the lungs.

① Angiotensin II (A II) is very potent vasoconstrictor. AII also ② stimulates aldosterone synthesis and secretion from the adrenal cortex (Zona glomerulosa), aldosterone increases Na^+ reabsorption from the renal nephrone and so water.

③ AII is also a positive inotropic agent **(increases contractility → increases SV)**

Remember:
The three layers of the adrenal cortex are GFR [glomerulosa →mineralocorticoids (aldosterone), fasciculata →glucocorticoids(cortisol) , and reticularis → androgens]

Further explanation

- So again, if there is a decrease in pressure that stays for more than one hour, the afferent arteriolar cells secrete Renin, a peptidase that works on angiotensinogen in the kidney (α2 globulin/precursor formed in the liver) and turns it into a decapeptide called angiotensin I (obviously).
- This angiotensin I circulates not only, but mainly in the lung where angiotensin converting enzyme (ACE) is found in the lung epithelium to convert angiotensin I to angiotensin II since angiotensin I isn't a vasoconstrictor.
- Angiotensin II goes everywhere (as a vasoconstrictor), increasing the TPR, trying to increase the MAP back to normal.
- **As a summary for the RAAS,** after increased Renin causes increased A II through multiple steps, A II stimulates aldosterone, which goes to the kidney, especially to the distal nephron, and reabsorbs sodium (and water); this increases the ECF volume → increased blood volume → increased VR → increased SV→ EVENTUALLY INCREASED CO WHICH INCREASES THE PRESSURE
- Remember that the urine output is very low here (because of the water retention)

Long term Regulation of BP …cont

Works opposite to the other systems

4. Atrial Natriuretic peptide (ANP): A 28 a.a peptide released mainly from the Rt. Atrium (but is also secreted from the Lt. Atrium) in response to stretch . It causes increase in GFR (glomerular filtration rate) so increase Na^+ and water. Its concentration decreases when BP is low and its concentration increases if BP is high, mainly due volume overload

Further explanation

- The most active part of the ANP is the end pentapeptide (last 5 AAs).
- ANP is released in response to increase in pressure, so it causes vasodilation in the afferent arterioles, which increases the GFR, and increases sodium (and water) *excretion* → decreases the ECF volume → decreases venous blood volume → decreases VR → decreases SV → decreases CO and eventually decreases pressure (you should have this cascade memorized by now from the million times we've repeated it).
- So, we conclude that ANP can be used as a treatment for hypertension since it works to decrease pressure in case of its increase.

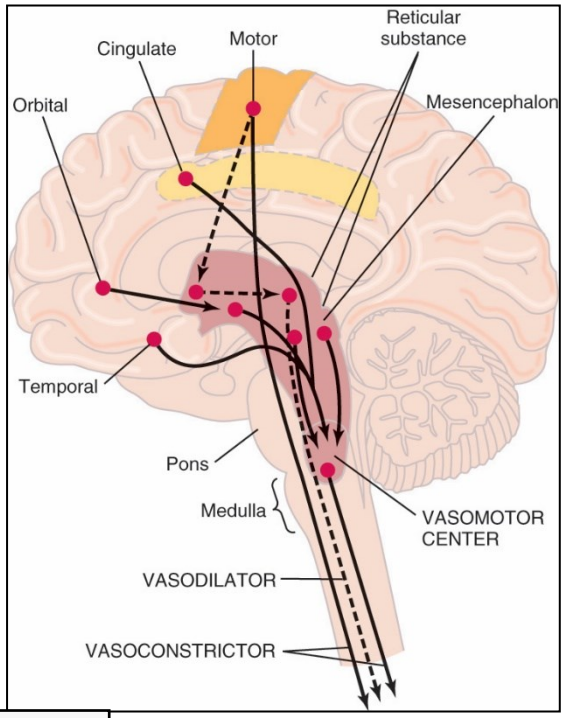
Overall summary:

- If there's an increase in pressure → low epinephrine, low renin (so also low A II and aldosterone) BUT high ANP.
- If there's a decrease in pressure like in hemorrhages, the opposite happens.

CNS Ischemic Response

It's neural but doesn't work that fast, it works when the MAP goes below 60 mmHg which will lead to ischemia in the CNS

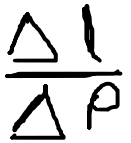
- CNS Ischemic response is activated in response to cerebral ischemia.
- Reduced cerebral blood flow causes CO2 buildup which stimulates vasomotor center thereby increasing arterial pressure.
- CNS Ischemic response is one of the most powerful activators of the sympathetic vasoconstrictor system.



Cerebral Ischemia → ↑CO_2 → **Vasomotor Center** → ↑**Sympathetic Activity** → ↑ **Arterial Pressure**

Further explanation

- The CNS blood flow usually is controlled locally to keep the blood flow to the brain constant regardless of the MAP unless it decreases below 60 mmHg.
- If you remember, the baroreceptors work when the pressure is between 60-180, above that, their work will be minimal and below it also their work will be minimal and needs to be around 100
- The first part of response is extensive stimulation of the sympathetic nervous system, and it occurs because of ischemia to the CNS, this stimulation goes to every part of our body to save the life of that patient
- This is called " the last ditch stand" " the last chance" for the patient .
- The patient undergoes a shock when the blood pressure decreases and we call it hemorrhagic shock , circulatory shock or volume loading shock , and we call the shock that the patient suffers from after 10 -30 minutes of compensation(to be saved) compensatory shock or reversible shock (trying to maintain the pressure) , if the pressure falls below 60 and the CNS response fails after the ischemia, there will be suppression of the CNS which will lead to death (irreversible shock which means death) or the patient might live with certain organ failure

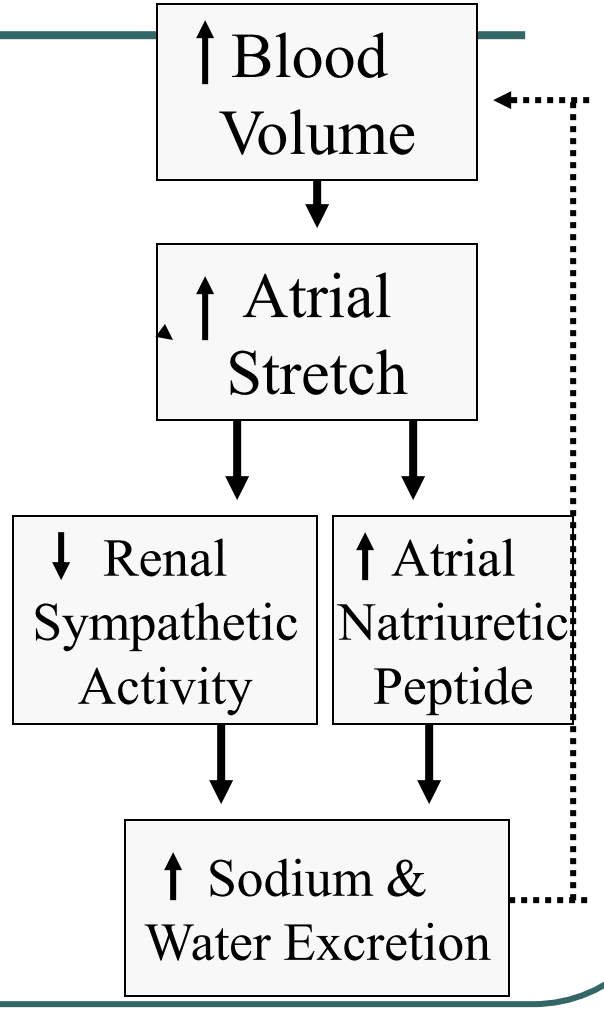


CNS Ischemic Response

- 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.

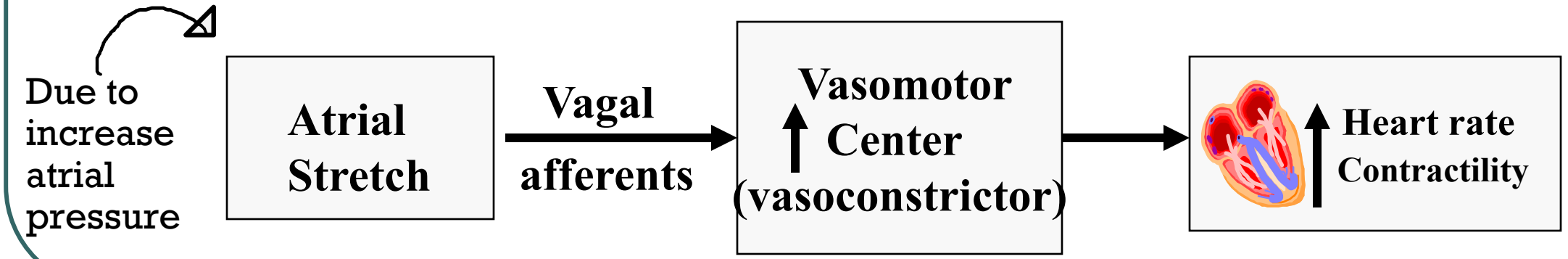
Atrial and Pulmonary Artery Reflexes

- Low pressure receptors in atria and pulmonary arteries minimize arterial pressure changes in response to changes in blood volume.
- Increases in blood volume activates low pressure receptors which in turn lower arterial pressure.
- Activation of low pressure receptors enhances Na^+ and water by:
  - Decreasing rate of antidiuretic hormone(atrio-hypothalamic reflex)
  - Increasing glomerular filtration rate(atrio-renal reflex) (vasodilation and vasoconstriction of afferent arteriole) (increasing urine formation)
  - Decreasing Na^+ reabsorption (increase Na+ excretion)



Bainbridge Reflex

- Prevents damming of blood in veins atria and pulmonary circulation.
- Increase in atrial pressure increases heart rate.
- Stretch of atria sends signals to VMC via vagal afferents to increase heart rate and contractility.



Blood Pressure Regulation

- Mean Arterial Pressure (MAP) = 1/3 systolic pressure + 2/3 diastolic pressure

Or Diastolic pressure + 1/3 of pulse pressure

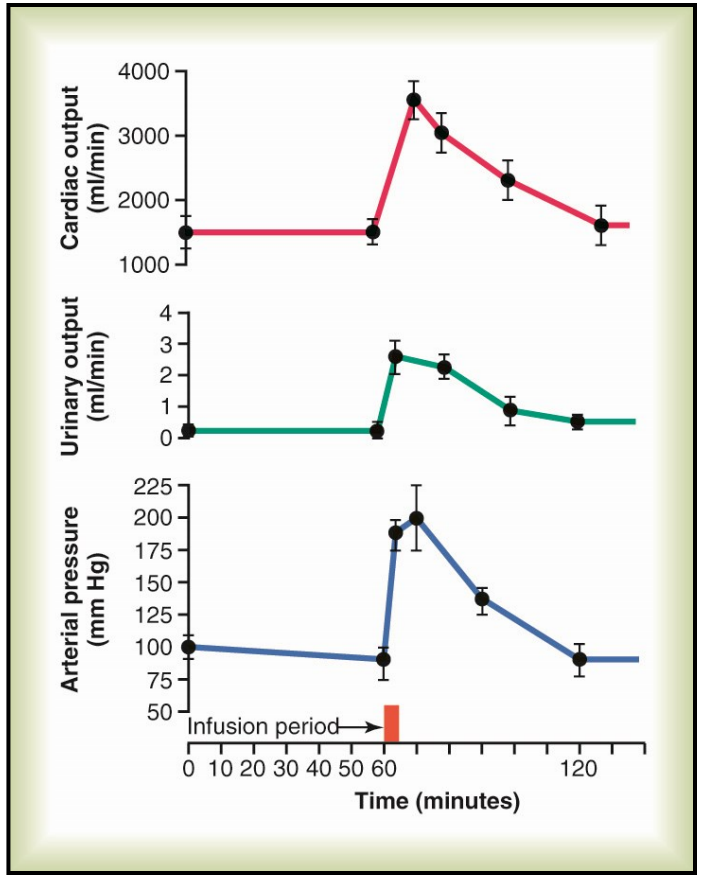
$$CO = \frac{MAP}{TPR}$$

$$MAP = CO * TPR$$

Renal Body Fluid System for Long Term Arterial Pressure Control

Depends mainly on the kidney and ECF

- Plays a dominant role in long term pressure control.
- As extracellular fluid volume increases arterial pressure increases.
- The increase in arterial pressure causes the kidneys to lose Na and water which returns extracellular fluid volume to normal. (pressure diuresis)



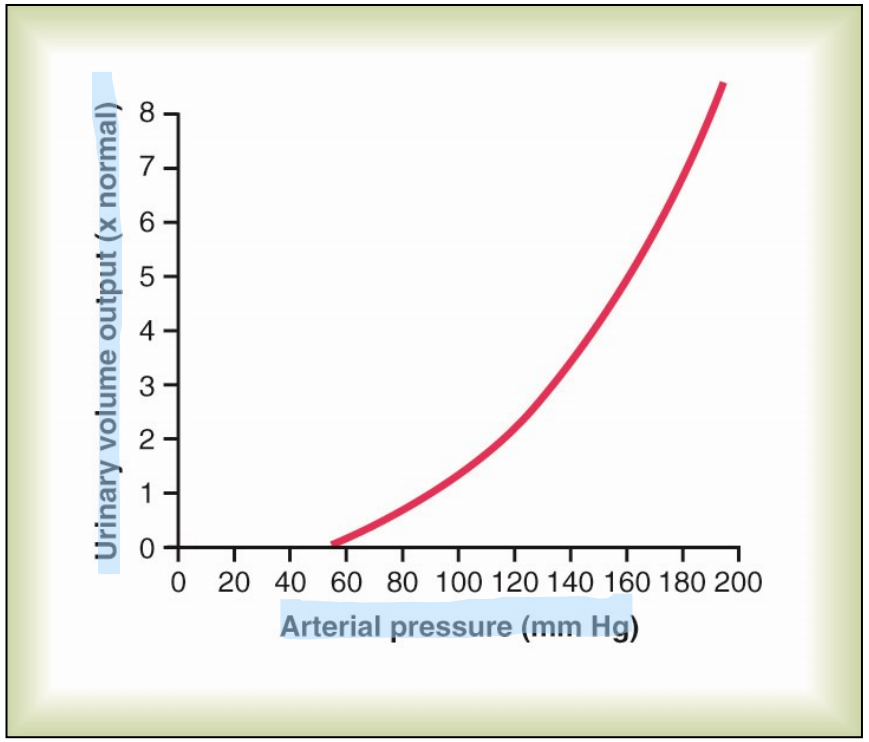
Explanation for the previous curves

- We added fluid to the system
- By that, you increase venous return by which CO will increase and that will lead to an increase in the MAP (The pressure will work on the kidney to increase the urine output to decrease this excess pressure)

Pressure Natriuresis and Diuresis

- The effect of pressure to increase water excretion is called pressure diuresis.
- The effect of pressure to increase Na excretion is called pressure natriuresis.

- This is the kidney function curve
- Whenever the pressure increases there is increase in urine output. (Pressure diuresis curve or normal kidney function curve)
- The effect of pressure is to increase water excretion or sodium excretion.
- Atrial natriuretic hormone also increases sodium excretion.



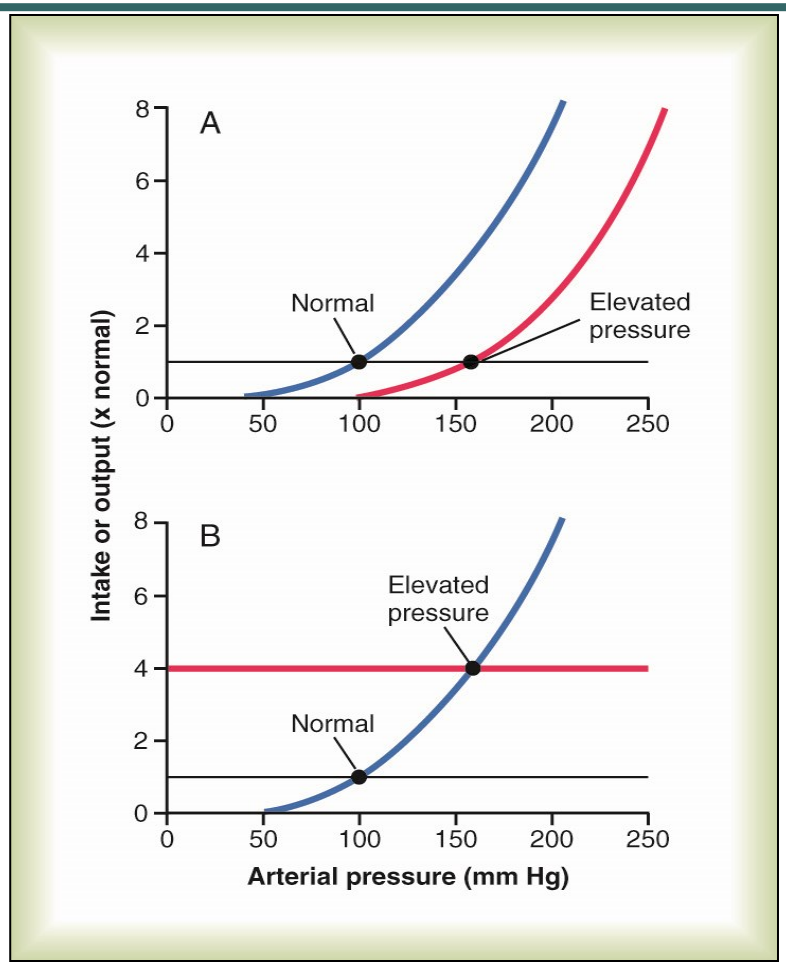
Graphical Analysis of Renal Body Fluid Mechanism

The most common cause of secondary hypertension is kidney damage

- The major determinants of long-term arterial pressure control.
  - Based on renal function curve
  - Salt and water intake line
- Equilibrium point is where intake and output curves intersect.

MAP is mainly controlled by intake and output

- Renal body fluid feedback system has an infinite gain.



Explanation of previous figure

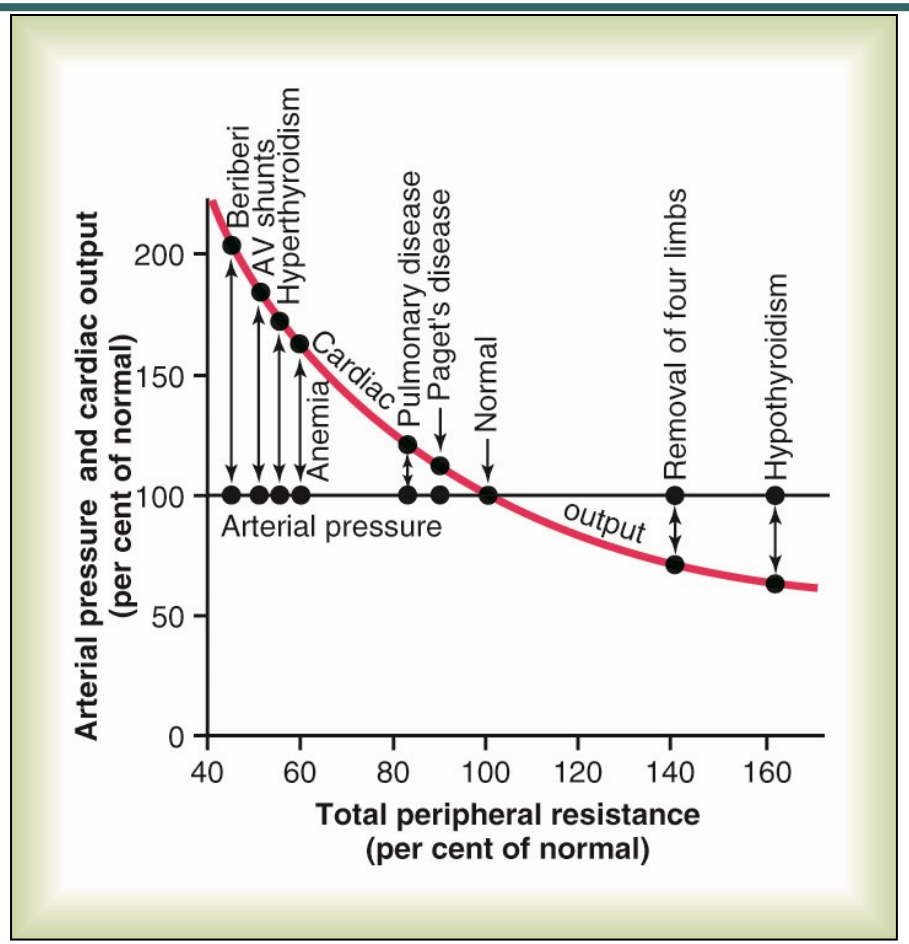
- You can increase the pressure by two things, you increase the intake or the uptake.
- This increased intake means chronic intake, and increased salt intake leads to drinking excess amounts of water. Increased salt intake will lead to increased blood volume, increased mean systemic filling pressure, and increased venous return and increased stroke volume and then the cardiac output. This leads to an increase in pressure.
- That's why patients with hypertension are advised to decreased salt intake or not to eat salt at all, because the main cation in the extracellular fluid is sodium.
- The intake of salt might be normal but there might be kidney dysfunction.

Explanation of previous figure

- The first curve shows that there is an increase to pressure even with constant intake and output due to abnormal kidney function (shift to the right)
- The second curve shows normal kidney function but there's high intake for a prolonged period of time which will lead to an increase in the pressure
- Remember that baroreceptors adapt and their gain is low that's why they lose importance in long term regulation

Failure of Total Peripheral Resistance to Elevate Long-term Arterial Pressure

- Changes in TPR does not affect long-term arterial pressure level.
- One must alter the renal function curve in order to have long-term changes in arterial pressure.
- Changing renal vascular resistance does not lead to long-term changes in arterial pressure .



- Decreasing and increasing the resistance is important for acute control, but if someone had a long-term condition such as hyperthyroidism, it decreases the resistance, and as a compensation there is an increase in the cardiac output so that the MAP remains constant. If someone has hypothyroidism which increases the resistance this would cause decreased cardiac output.

- In beri-beri (thiamine (B1) deficiency) there is an abnormality in the subcutaneous tissue of the vessels which causes their relaxation and decreases the resistance and decreases the CO.

- If you want to change the pressure for someone on the long-term, then changing the resistance is not enough, you cannot discharge them after giving them only a vasodilator, this will only work acutely.
- You have to give them something that decreases the fluid (volume), such as a diuretic, or changes the renal function curve.

Sodium is a Major Determinant of ECFV

- As Na^+ intake is increased; Na^+ stimulates drinking, increased Na^+ concentration stimulates thirst and ADH secretion.
- Changes in Na^+ intake leads to changes in extracellular fluid volume (ECFV).
- ECFV is determined by the balance of Na^+ intake and output.