REGULATION OF RENAL BLOOD FLOW AUTO REGULATION

- The special feature of renal blood flow is auto regulation.
- Auto regulation means the regulation of blood flow to an organ by the organ it self.
- GFR is kept constant at 125ml/min despite wide variation in arterial pressure, this is called auto regulation of GFR.The other organs like brain area heart also have the auto regulation mechanism. But in kidneys, it is highly significant and more efficient.
- Auto regulation means, the **blood** flow to the glomeruli and the **function** of glomerali are not affected if the mean arterial blood pressure falls up to 60 mmHg or rises up to 180 mmHg.
- The normal mean arterial blood pressure is 93 mmHg.
- When the mean arterial blood pressure falls below 60 mmHg or rise above 180mmHg the auto regulation fails.

WHY GFR IS AUTO REGULATED

- If GFR is very slight fluid passes through tubule very slowly all substances are reabsorped kidney fail to eliminate essential waste products.
- If GFR is very high fluid passes through tubule very rapidly kidney are unable glucose.

MECHANISM OF AUTO REGULATION OF GFR

- GFR is auto regulated by "tubulo glomerular feedback" which consist of two mechanism operating at the same time.

AFFERENT ARTERIOLAR VASODILATOR FEED BACK

- When GFR decreases there is over reabsorption of Na^+ and Cl^- in the ascending limb of loop of Henle.
- Decrease Na^+ and Cl^- concentration at macula densa.
- Afferent arteriole dilates.
- Increase blood flow through glomerulus causing.
- Increase glomerular pressure increase GFR.

Efferent arteriolar vasoconstrictor feedback mechanism

- Low GFR results in excess reabsorption of Na+and cl- in the ascending limb of Henle causing reduction in ionic concentration at macula densa
- The Juxtra Glomerular cells release Renin in response to low concof ions.
- Angiotensin 2 is ultimately formedfrom renin which constricts the efferent arterioles and raises the pressure in glomerulus.The increase pressure then brings the GFR BACK TOWARDS NORMAL.

MYOGENIC AUTOREGULATION OF RENAL BLOOD FLOW AND GFR

- Ability of individual blood vessel to resist stretching during increased arterial pressure a phenomenon referred to as the myogenic mechanism. When the blood flow is increased there is vasoconstriction of afferent arteriole.
- Vasoconstriction is because of smooth muscle cells called Juxtra glomerular cells (JG cells) present in the afferent arteriole.
- When the blood pressure is less the blood flow to kidney is reduced, there is vasodilatation and the blood flow is increased.
- Stretch of the vascular wall allows increased movement of calcium ions from the extra cellular fluid into the cells causing them to contract.
- Contraction prevents over distension by raising vascular resistance helps to prevent excessive increase in renal blood flow and GFR when arterial pressure increases.

MYOGENIC AUTOREGULATION OF RENAL BLOOD FLOW AND GFR (CONTINUED)

- Decreased sodium delivery to the macula densa elicits a tubuloglomerular feed back.
- The decreased afferent arteriolar resistance raises renal blood flow and GFR.
- Increased GFR allows sodium excretion at normal level, and increasing the excretion of waste products of protein metabolism as urea.

Tubulo glomerular feed back mechanism

- Involves the Juxtra glomerular apparatus, which is the specialized combination of tubular and vascular cells where the tubules, after having bent back on its self ,passes through the angle formed by the afferent and efferent arterioles as they join the glomerulus.
- The smooth muscle cells within the walls of the afferent arterioles in this region are specialized to form granular cells ,so called because they contain many secretary granules
- Specialized tubular cells in this region are collectively known as the **mecula densa.**

Macula densa

- Macula densa detects changes in the rate at which fluid is flowing past them through the tubule.
- When there is spontaneous decline in GFR accompanying a fall in arterial blood pressure ,these cells bring about afferent arteriolar vaso dilation by altering the rate of secretion of the relevant vasodilator chemicals.
- Elevation in the arterial blood pressure ,more fluid than normal is filtered and reaches the distal tubules ,these cells bring about afferent arteriolar vasoconstriction, reducing GFR and reducing GFR to normal.

Other factors that increase renal blood flow and GFR.

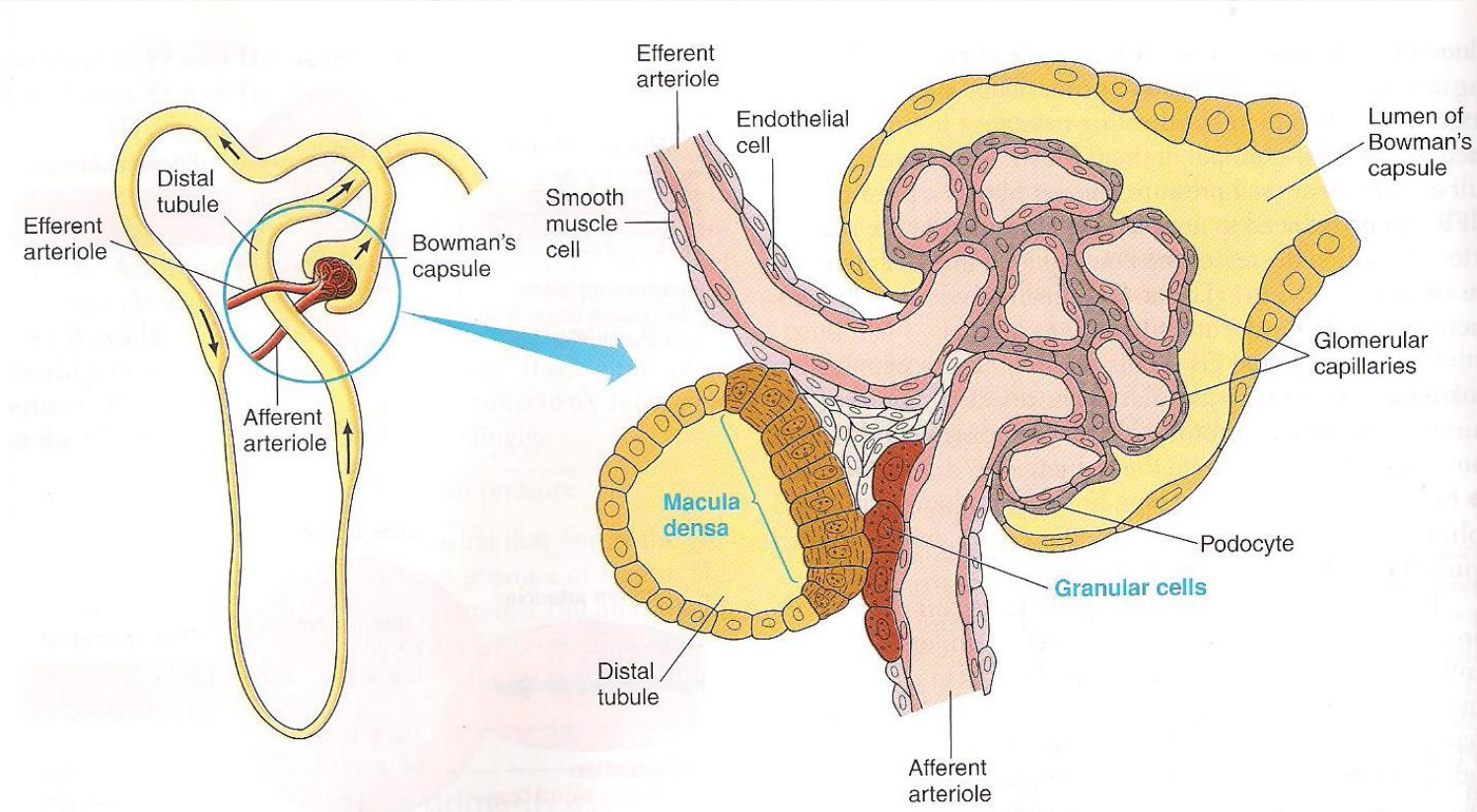
- High protein intake cause GFR and renal blood flow increase 20 to 30 percent with 1 or 2 hours.
- A high prtein meal increases release of aminoands into the blood, which are reaborbed in the proximal tubule.
- Amino acids and sodium are reabrorbed together also stimulates sodium reaborption.

IN UNCONTROLLED DIABETES MELLITUS

- Increase in blood glucose leads to increase in renal blood flow and GFR.
- Glucose is also reabsorbed along with sodium in the proximal tubule.
- Increased glucose delivery to the tubules causes to readbsorb excess sodium this in turn decreases delivery of sodium to mecula densa activating tubuloglomerular feed back mechanism.

JUXTRA GLOMERULAR APPARATES

➢Juxtra glomerular apparatus is a specialized organ situated near the glomerulus of each nephron (juxtra = near).



STRUCTURE OF JUXTRA GLOMERULAR APPARATUS

- The juxtra glomerular apparatus is formed by three different structures.
- Mecula densa
- Extraglomerular mesengial cells.
- Juxtra glomerular cells.

MACULA DENSA

- The end portion of thick ascending segment in each nephron runs in between afferent and efferent arterioles of the same nephron.
- The cuboidal epithelial cells are lightly packed, this thick ascending segment is called macula densa.

EXTRA GLOMERULAR MESENGIAL CELLS

- These cells are situated in the triangular region bound by afferent arteriole, efferent arteriole and macula densa.
- They are phagocytic and secrete prostaglanding.

JUXTRA GLOMERULAR CELLS

- The wall of the afferent arteriole before entering the glomerulus is thickened like a cuff. This is called Juxtra glomerular cells (JG cells).
- JG cells are specialized type of smooth muscle cells.

FUNCTIONS OF JUXTRA GLOMERULAR APPARATUS

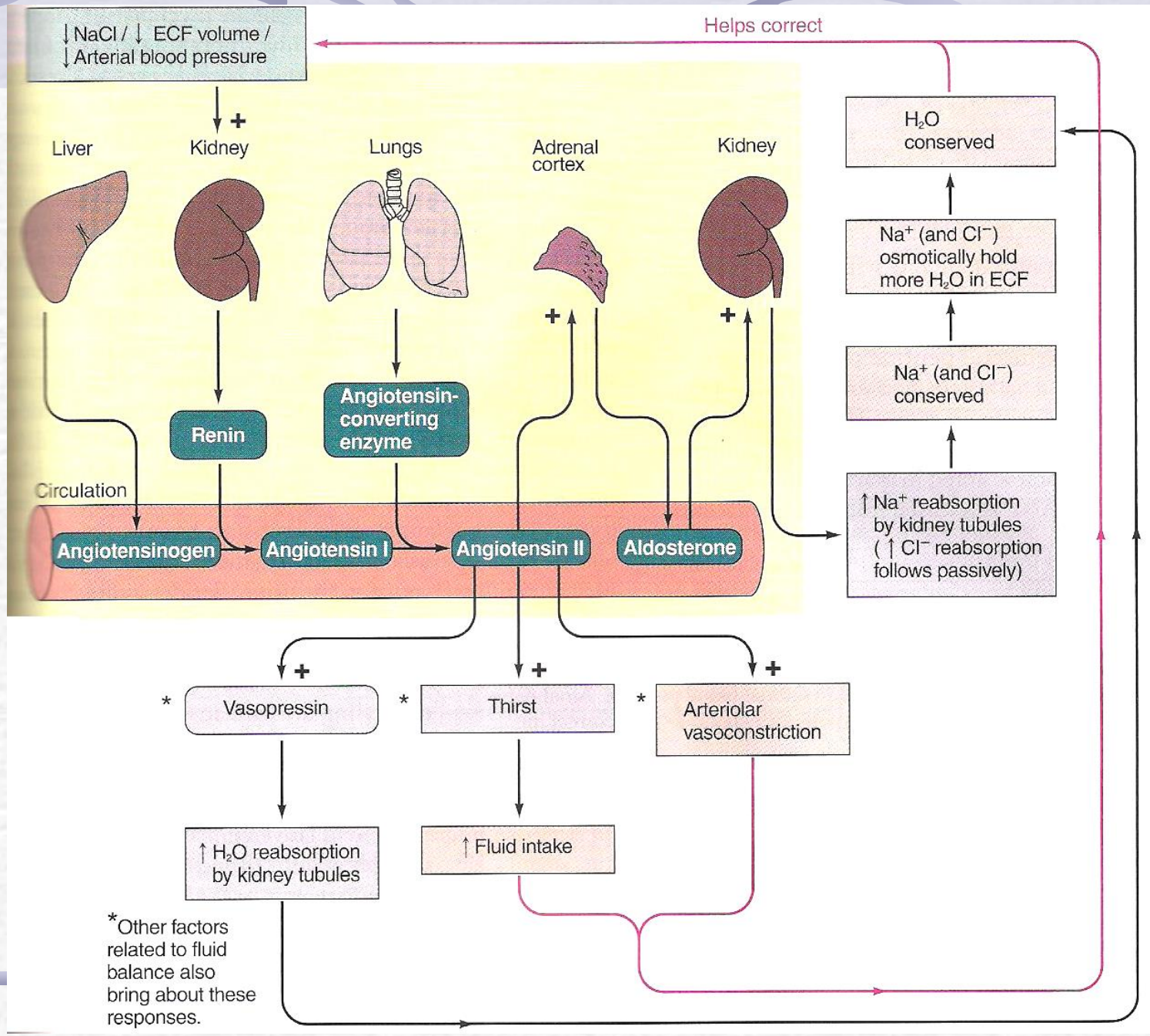
- Secretion of hormonal substance.
- It also regulates the glomerular blood flow and glomerular filtrate rate.

SECRETION OF RENIN

- Granular cells (JG cells) of juxtra glomerular apparatus secrete the hormone Renin.
- Renin is a glycoprotein with 340 amino acids.
- Renin secretion is inversely proportional to the rate of transport of Na^+ and Cl^-.

ACTION OF RENIN

- Renin when released into the blood it act on a specific plasma protein called angiotensinogen or renin substrate.
- By the activity of Renin, the angiotensinogen is converted into a deca peptide called angiotensin I.
- Angiotensin I is converted into angiotensin II by the activity of angiotensin converting enzyme (ACE) secreted by lungs.
- Angiotensin 1 is physiologically inactive and serves only as the precursor of angiotensin II.
- Most of the conversion of angiotensin 1 and angiotensin II takes place when the blood passes through lungs.

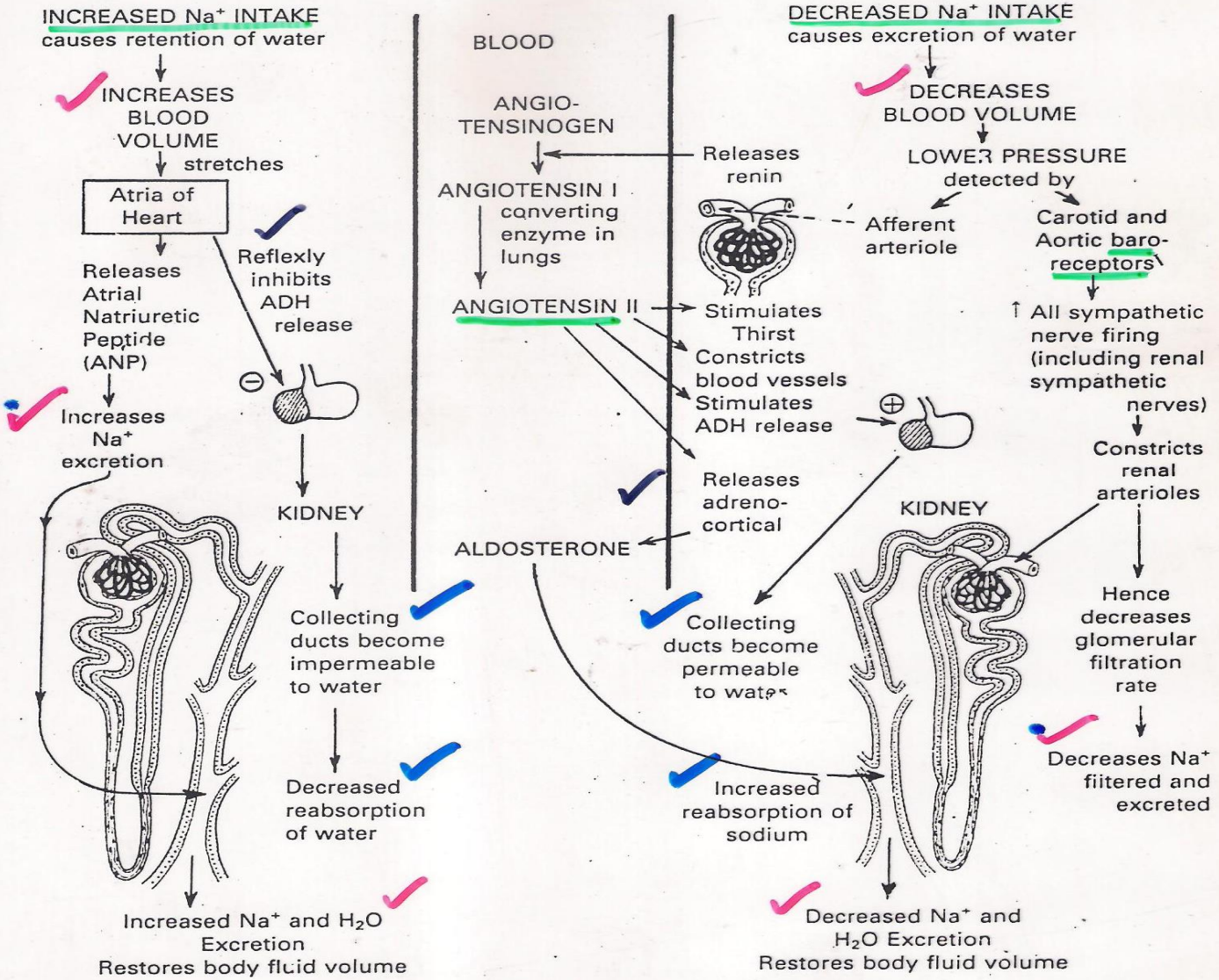

↓NaCl / ↓ ECF volume / ↓Arterial blood pressure
Helps correct
Liver
Kidney
Lungs
Adrenal cortex
Kidney
+
+
+
+
Renin
Angiotensin-converting enzyme
Circulation
Angiotensinogen
Angiotensin I
Angiotensin II
Aldosterone
H_2O conserved
Na^+ (and Cl^-) osmotically hold more H_2O in ECF
Na^+ (and Cl^-) conserved
↑ Na^+ reabsorption by kidney tubules (↑ Cl^- reabsorption follows passively)
+
+
+
* Vasopressin
* Thirst
* Arteriolar vasoconstriction
↑ H_2O reabsorption by kidney tubules
↑ Fluid intake
*Other factors related to fluid balance also bring about these responses.

ANGIOTENSIN II

- Angiotensin II has a short half life of about 1-2 minutes.
- It is rapidly degraded into a hepta peptide called angiotensin III by angiotensinases which are present in RBCs and vascular beds in many tissues.
- Angiotensin III is converted to angiotensin IV which is hexapeptide.
- Angiotensin II is potent vasoconstrictor of arterioles.
- Angiotensin II causes constriction of systemic arterioles leading to elevation of blood pressure. Indirectly by increasing the release of naradrenaline from post ganglionic sympathetic fibers. Naradrenaline is a general vasoconstrictor.
- It stimulates the adrenal cortex to scerete aldosterone Aldosterone resulting in sodium retension.
- It helps to maintain the glomerular filtration rate.

DEFENCE OF BODY FLUID VOLUME

The **volume** of the extracellular fluid (ECF) is determined mainly by the amount of osmotically active solute it contains. Na^+ is the most important active solute in the body, hence mechanisms that control Na^+ balance will also control ECF volume.



Control of vasopressin (ADH) release by changes in volume overrides its control by osmotic changes.

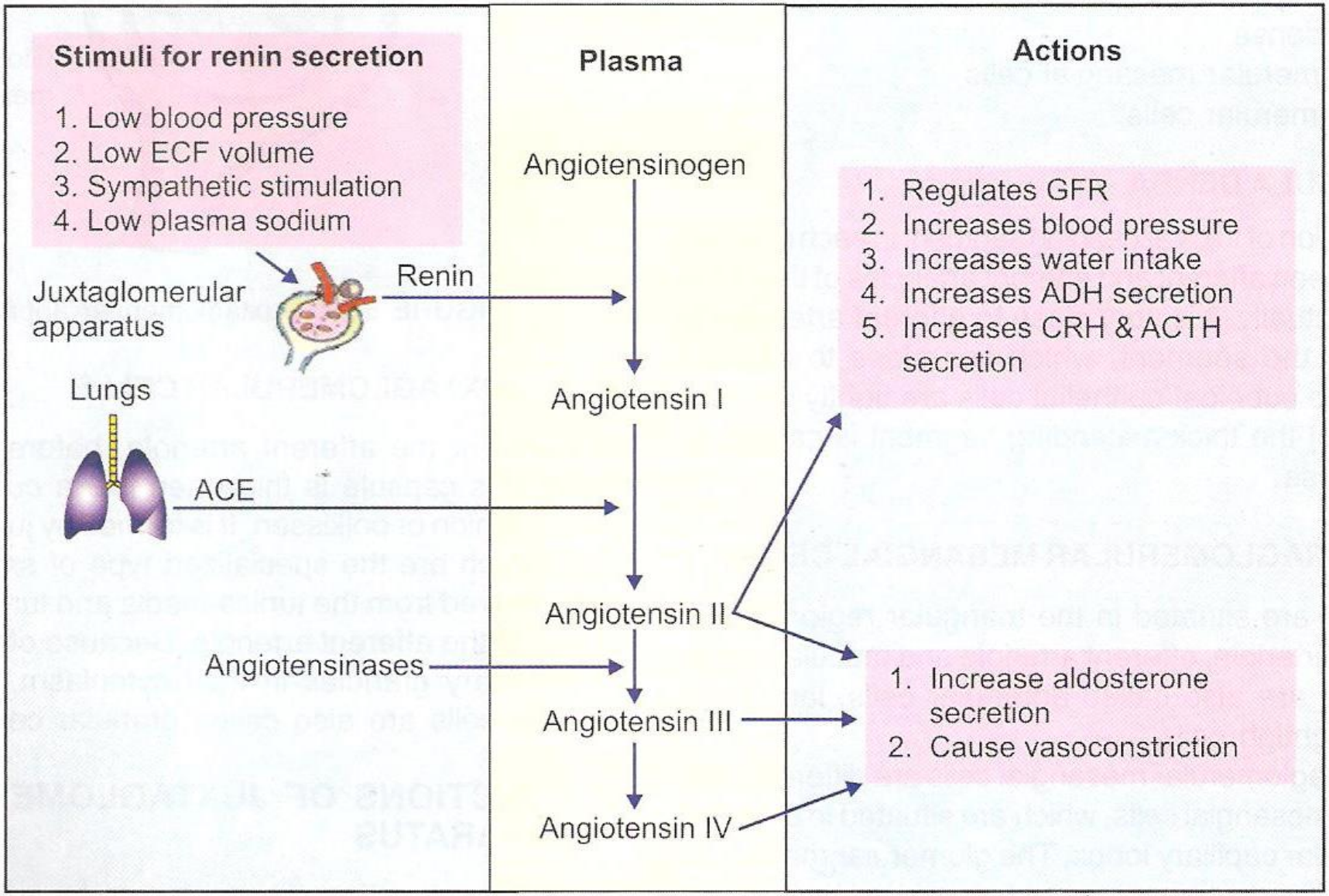
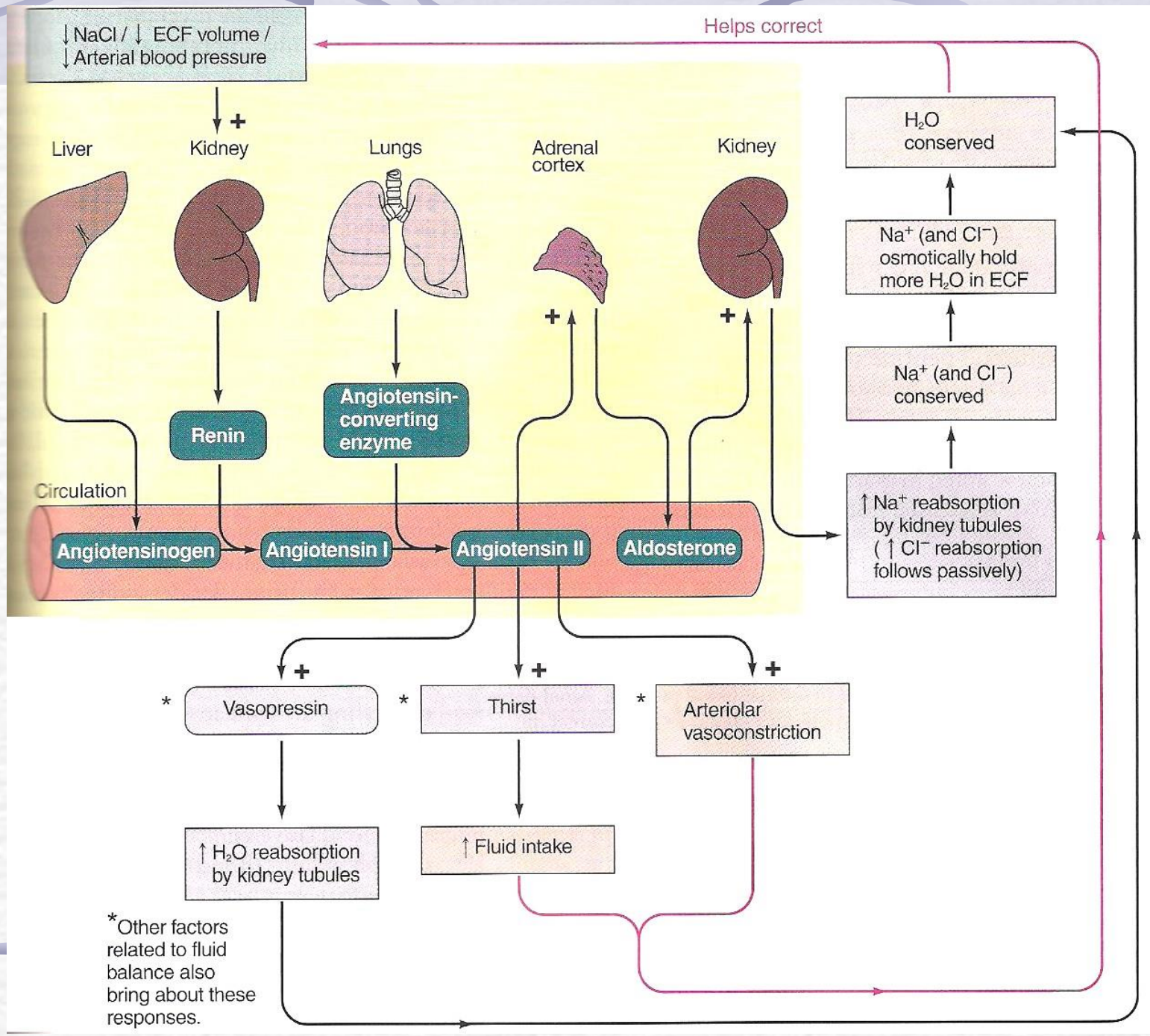


FIGURE 50-2: Renin–angiotensin system

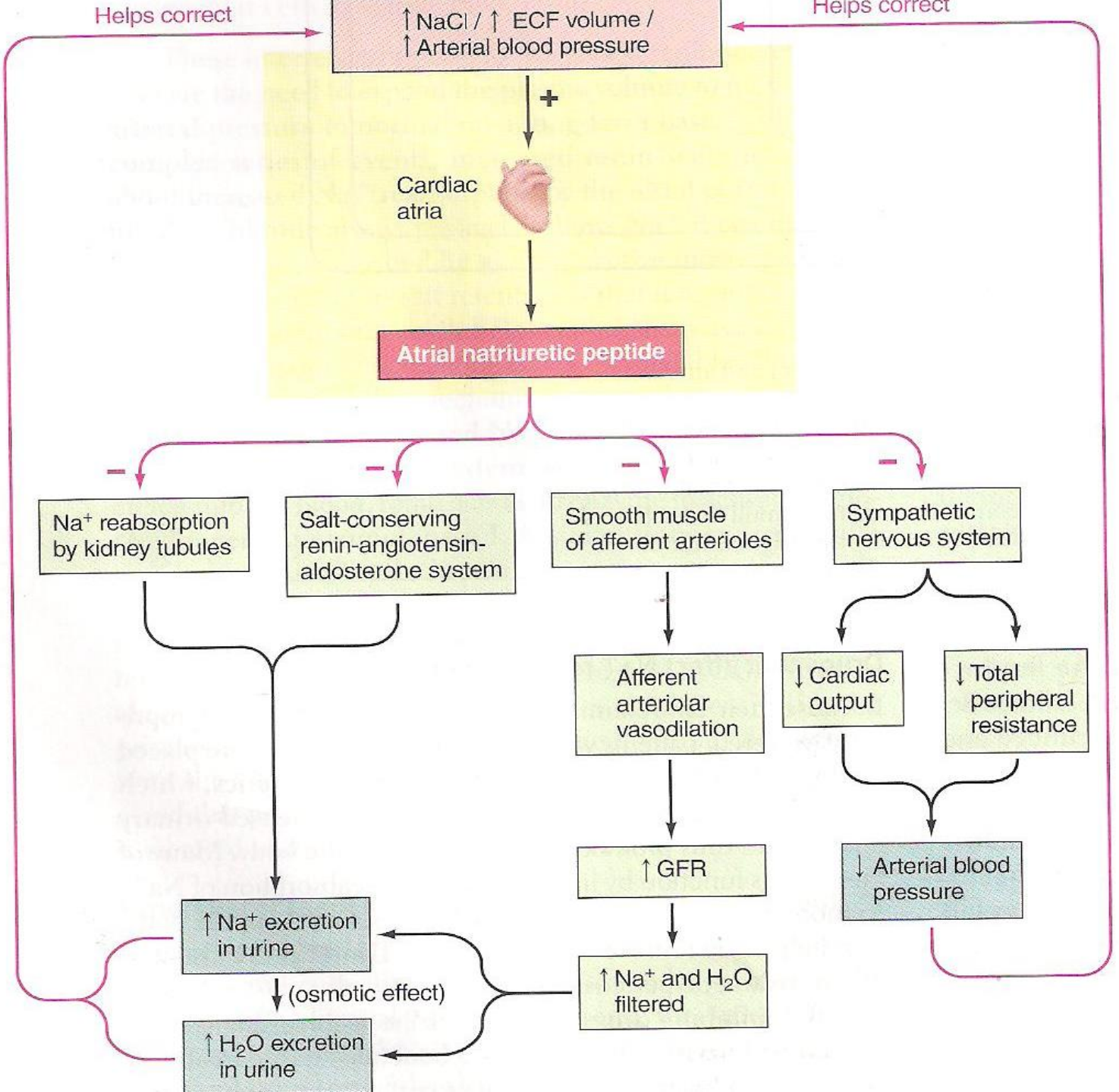

↓NaCl / ↓ ECF volume /
↓Arterial blood pressure
Helps correct
Liver
Kidney
Lungs
Adrenal cortex
Kidney
+
+
+
+
Renin
Angiotensin-converting enzyme
Circulation
Angiotensinogen
Angiotensin I
Angiotensin II
Aldosterone
H_2O conserved
Na^+ (and Cl^-) osmotically hold more H_2O in ECF
Na^+ (and Cl^-) conserved
↑ Na^+ reabsorption by kidney tubules (↑ Cl^- reabsorption follows passively)
+
+
+
* Vasopressin
* Thirst
* Arteriolar vasoconstriction
↑ H_2O reabsorption by kidney tubules
↑ Fluid intake
*Other factors related to fluid balance also bring about these responses.

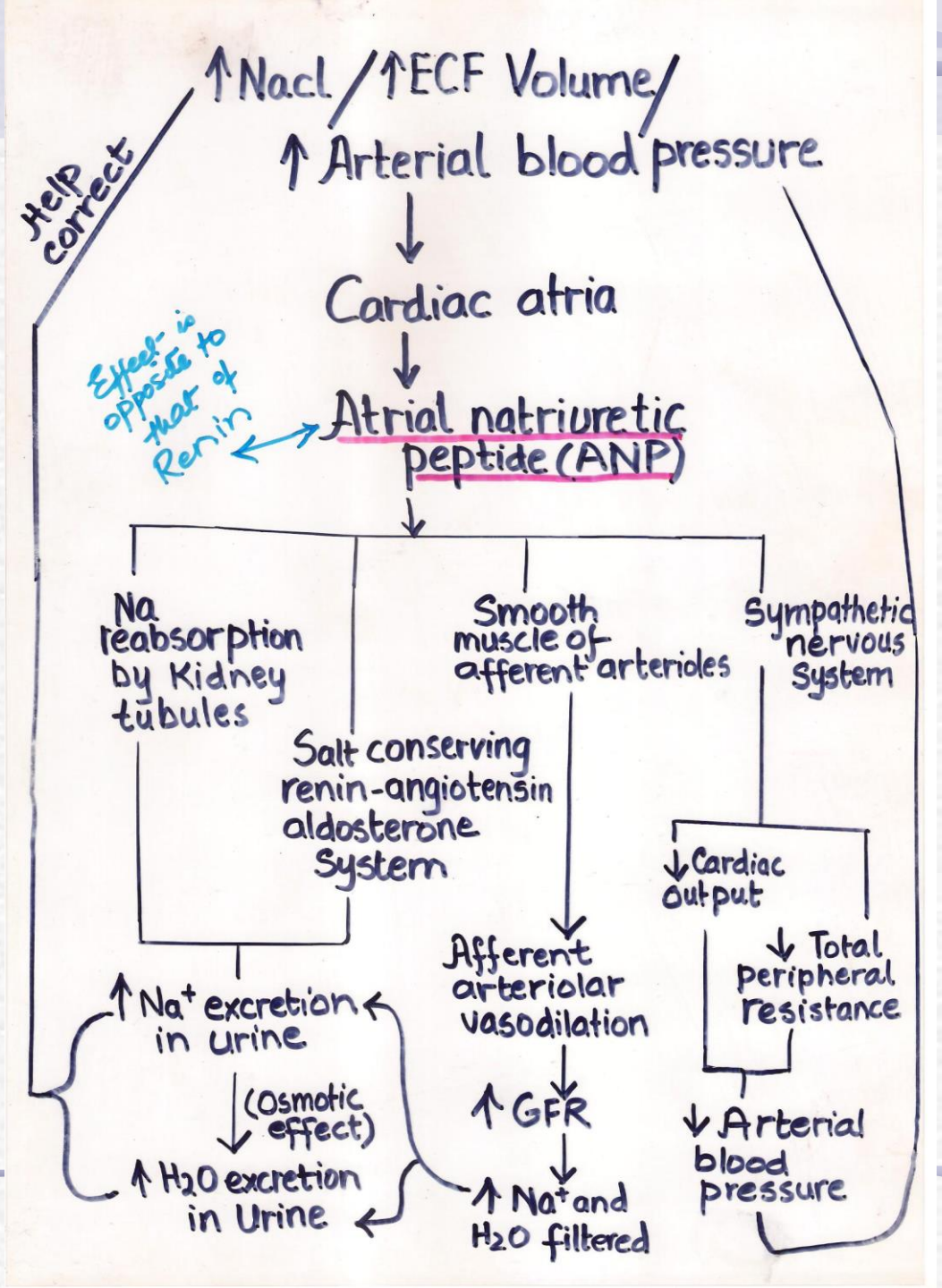
STIMULI THAT INCREASE RENIN SECRETION

- Sodium depletion(decrease Na).
- Diuretics(enhances the output of urine).
- Hypotension(decrease blood pressure).
- Hemorrhage(decrease blood pressure)
- Upright posture.
- Dehydration (water loss).
- Constriction of the renal artery or aorta(decrease blood flow to kidney).
- Cirrhosis (impaired liver function).
- Sympathetic nerve activity and circulating catecholamines(causes constriction of vessels).
- Prostaglandins.

ATRIAL NATRIURETIC PEPTIDE(ANP)

1. Natriuretic hormone.Natrium means SODIUM and uresis means WATER.
2. Increase in the blood volume
3. Increase in the venous return
4. Stretches the atria.
5. Stimulates the release of ANP
6. ADH from post pitutary is inhibited.
7. Increase ANP together with decrease ADH,leads to greater excretion of salt and water in urine.
8. This act as a negative feed back correction to lower blood volume and thus maintain heamostasis.
9. ANP function as an endogenous diuretic.


Helps correct
↑ NaCl / ↑ ECF volume /
↑ Arterial blood pressure
Helps correct
+
Cardiac atria
Atrial natriuretic peptide
−
−
−
−
Na+ reabsorption by kidney tubules
Salt-conserving renin-angiotensin-aldosterone system
Smooth muscle of afferent arterioles
Sympathetic nervous system
Afferent arteriolar vasodilation
↓ Cardiac output
↓ Total peripheral resistance
↑ GFR
↓ Arterial blood pressure
↑ Na+ excretion in urine
(osmotic effect)
↑ H2O excretion in urine
↑ Na+ and H2O filtered


↑Nacl / ↑ECF Volume
↑ Arterial blood pressure
Help correct
Cardiac atria
Effect is opposite to that of Renin
Atrial natriuretic peptide (ANP)
Na reabsorption by Kidney tubules
Salt conserving renin-angiotensin aldosterone System
Smooth muscle of afferent arterioles
Sympathetic nervous System
↓Cardiac output
↓ Total peripheral resistance
↑ Na+ excretion in urine
(Osmotic effect)
↑ H2O excretion in Urine
Afferent arteriolar vasodilation
↑ GFR
↑ Na+ and H2O filtered
↓ Arterial blood pressure

STIMULI THAT INHIBIT RENIN SECRETION

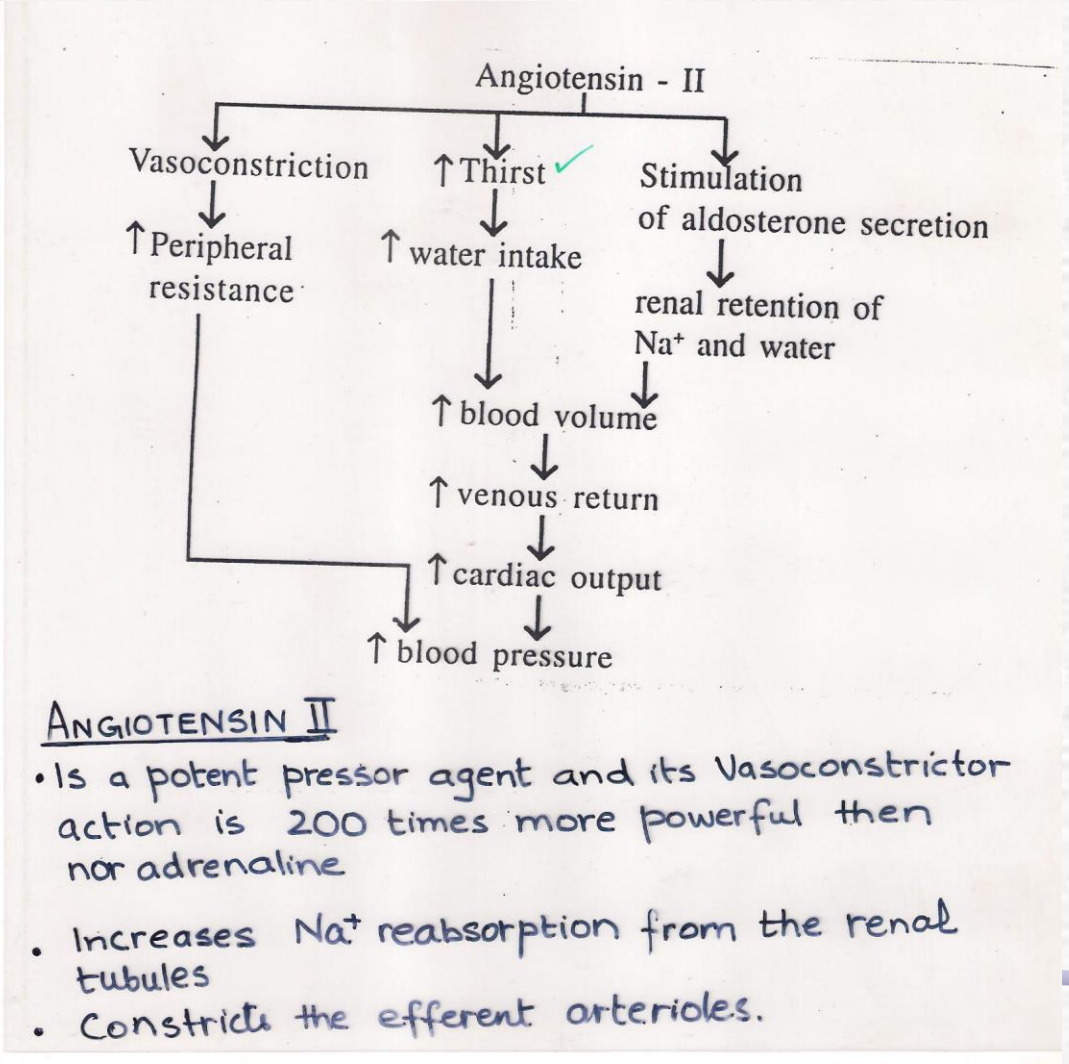
- Increased Na+Cl- reabsorbtion across mecula densa.
- Angiotensin II.
- Vasopressin.
- Increased stretch of JG cells.

ROLE OF ANGIOTENSIN II IN CONTROLLING RENAL EXCRETION

- Change in Na and fluid intake(Angiotensin formation)
- Sodium intake is elevated above normal
- Renin secretion is decreased.
- Decreased angiotensin II formation.
- Decreased tubular reabsorbtion of Sodium and water.
- Increasing kidney excretion of sodium and water.
- Minimize the rise in extracellular fluid volume.
- Decreased blood pressure.

ANGIOTENSIN II

- ANGIOTENSIN II IS ONE OF THE MOST POWERFUL SODIUM AND WATER RETAINING HORMONE



ANTI DIURETIC HARMONE OR VASOPRESSIN

- Is harmone of posterior pitutary gland it prevents excessive urine production.

SITE OF FORMATION:

- Supra optic nuclei of hypothalamus.

TRANSPORT:

- ADH is transported from supra optic nuclei to nerve ending in posterior pitutary gland by carrier proteins called neurophysins.

SECRETION:

- By nerve ending in post pitutary gland.

NATURE:

- Polypeptide containing amino acids.

HALF LIFE:

- 15-20 min.

FACTORS INCREASING ADH SECRETION:

- Increased Na conc or ↑ Osmolality of extracellular fluid.
- Low blood volume, low blood pressure.
- Decreased extracellular fluid volume.
- Pain, emotion, exercise, anxiety.
- Nausea, vomitting.
- Angiotensin II
- **Drugs:** Morphine, nicotine, barbiturates and anasthesia.
- Factors dereasing ADH secretion:
- ↓Na concentration.
- ↓ Osmolality of extracellular fluid.
- Alcohol
- ↑B.P
- ↑Blood volume.

ACTIONS OF ADH: ON KIDNEYS:

- Increases permeability of the collecting tubules and ducts to water.
- ↑ water absorption from lumen of colecting tubules and ducts.
- Conserves water in the body less water passes in urine.

ON VASCULAR SMOOTH MUSCLE:

- Constriction of arterioles → ↑ B.P (vaso = vessel Pressin = constriction, with pressure).
- **DISORDER RELATED TO ADH (DIABETES INSPIDUS):**
- Syndrome characrerized by passage of large volume of dilute urine due to the absence of ADH.
- Lesions of supra optic nuclei.
- Tumors of hypothalamus.
- Meningitus – destruction of part of hypothalamus.

ALDOSTERONE ESCAPE

- Increase or decrease in Angiotensin II has no large effect on extracellular cell fluid volume or blood volume
- Increase level of Angiotensin II causes sodium and water retension
- Increase in Extracellular cellular fluid volume
- Increase blood pressure
- Increase the kidney output of Na and water.
- Reestablishing balance, this balance is called ALDOSTERONE ESCAPE.

ALDOSTERONE ESCAPE

- Means that the kidneys begins to excrete an amount of Na+ equally to the daily intake despite the continued presence of ALDOSTERONE.

PRESSURE DIURESIS

- Increased output of water in urine caused by increased arterial pressure diuresis.

PRESSURE NATRIURESIS

- Increased output of sodium(natrium)in urine caused by increased arterial pressure is called pressure natriuresis.