THE RENAL SYSTEM(L4)

Prof. Dr. Azza Sajid
Department :Pharmacology & toxicology
Pharmacy College

2nd stage

PHYSIOLOGY #II
University of Basra

Control of urine production.

- The body needs to control:
- Your **blood volume** = reduce water loss when dehydrated; increase loss when over-hydrated. This is mainly due to **ADH** and to **aldosterone/ ANH**, but is affected by **blood pressure** (through ultrafiltration process).

- The **amount of salts in the blood** and therefore lost in the urine e.g. Na^+, K^+. This is mainly controlled by **aldosterone** and **ANH**.

ADH

- **ADH** is secreted by the **hypothalamus** and stored and released from the posterior pituitary, in response to either **high blood OP** or **low blood pressure** detected by the hypothalamus (both indicate dehydration).

- **ADH** makes the **walls of the collecting duct permeable to water**, so that a total of 99% of the water in the urine is reabsorbed.
- When over-hydrated: the absence of ADH results in 20% water loss (= 19% from the collecting duct + the 1% unrecoverable water).

Controlling sodium chloride by Aldosterone + ANH.

- A **low blood pressure** results in the **juxtamedullary apparatus** (attached to the glomerulus) releasing the enzyme **renin** into the blood. This activates the hormone **angiotensin**, which cause the adrenal glands to release **aldosterone**.
- **Aldosterone** increases **reabsorption of sodium ions from the distal tubule and collecting duct** (Note: the Na^+ pumps in the proximal tubule and loop of Henle are unaffected). As well as increasing blood Na^+, it increases the blood volume by increasing reabsorption of water alongside with the Na+

- If **blood pressure is high**, then no aldosterone is secreted. Instead, **cardiac cells in the heart secrete ANH (atrial natriuretic hormone)**, which inhibits absorption of sodium from the urine. The resulting high sodium in the filtrate increases its osmotic pressure, so less water is reabsorbed from the filtrate and thus **more water is excreted** in the urine.
- Aldosterone and ANH are thus antagonistic hormones responsible for controlling blood sodium, but in doing so, they alter water reabsorption by the kidney.

Antidiuretic hormone (ADH) mechanism
The increase in blood volume (pressure) is detected by baroreceptors.

Decreased ADH secretion results.

Decreased ADH decreases the permeability of the distal tubules and collecting ducts to water. Less water returns to the blood and more water is lost in the urine.

Atrial natriuretic hormone (ANH) mechanism
The increase in blood volume (pressure) is detected by atrial cardiac muscle cells.

Increased ANH secretion results.

Decreased aldosterone and increased ANH decrease Na^+ reabsorption in the distal tubules and collecting ducts; more Na^+ and water are lost in the urine.

Renin–angiotensin–aldosterone (ADH) mechanism
The increase in blood volume (pressure) is detected by the juxtaglomerular apparati.

Inhibition of the renin–angiotensin–aldosterone mechanism decreases aldosterone secretion.

Sympathetic division response
The increase in blood volume (pressure) is detected by baroreceptors.

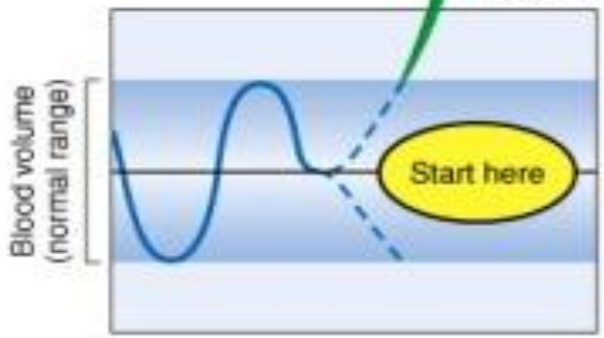
Decreased sympathetic stimulation results in vasodilation of renal arteries.

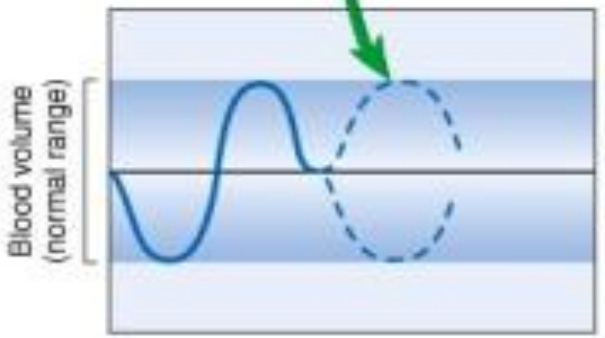
Increased renal blood flow increases the rate of filtrate formation and more water is lost in the urine.

An increase in blood volume occurs (usually results in an increase in blood pressure).

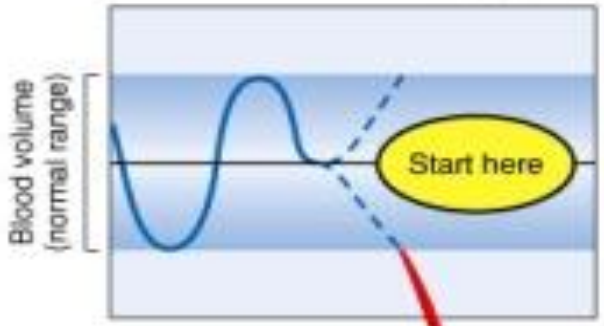
A decrease in blood volume (blood pressure) results from increased water and Na^+ loss in the urine.

Follow the green arrows when blood volume increases.





Blood volume homeostasis is maintained.



Follow the red arrows when blood volume decreases.

A decrease in blood volume occurs (usually results in a decrease in blood pressure).

Sympathetic division response
The decrease in blood volume (pressure) is detected by baroreceptors.

→ Increased sympathetic stimulation results in vasodilation of renal arteries.

→ Decreased renal blood flow decreases the rate of filtrate formation and less water is lost in the urine.

Renin–angiotensin–aldosterone (ANH) mechanism
The decrease in blood volume (pressure) is detected by the juxtaglomerular apparati.

→ Stimulation of the renin–angiotensin–aldosterone mechanism increases aldosterone secretion.

Atrial natriuretic hormone (ADH) mechanism
The decrease in blood volume (pressure) is detected by artrial cardiac muscle cells.

→ Decreased ANH secretion results.

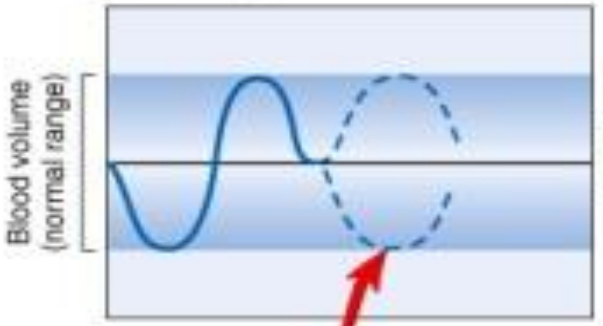
→ Increased aldosterone and decreased ANH increase Na^+ reabsorption in the distal tubules and collecting ducts; less Na^+ and water are lost in the urine.

Antidiuretic hormone (ADH) mechanism
The decrease in blood volume (pressure) is detected by baroreceptors.

→ Increased ADH secretion and increased thirst result.

→ • Increased ADH increases the permeability of the distal tubules and collecting ducts to water. More water returns to the blood and less water is lost in the urine.

An increase in blood volume (blood pressure) results from decreased water and Na^+ loss in the urine.



Blood volume homeostasis is maintained.

Thirst center in hypothalamus.

- Overall control of water balance is by the hypothalamus. The Thirst center in the hypothalamus responds to:
- Low blood pressure.
- High osmotic pressure of the blood.
- Dehydration of the mucosa of the mouth.
- These all stimulate the feeling of “thirst” so you drink water and increase your blood volume.

Blood pressure

- When there are temporary changes in blood pressure, the afferent arteriole in to the renal corpuscle stabilises ultrafiltration by constricting when pressure rises and dilating when pressure drops.
- However, the arteriole is also controlled by the sympathetic nervous system from the hypothalamus (measuring the overall blood pressure). If there is a **severe drop in pressure** due to heavy bleeding or extensive inflammation, **increased sympathetic stimulation** increases vasoconstriction to reduce filtration and thus reduce further urine loss. This also happens during **intense physical activity**, when there is a high blood pressure, in order to maintain the high pressure and thus rapid O_2 transport.
- Conversely, **continuous high pressure** (when not active) **decreases sympathetic stimulation** → vasodilation → greater urine production → reduced blood volume and thus pressure.

- **Regulation of ions (summary).**
- **Sodium ions.**
- This is the major cation in the extracellular fluid and thus gives 90% of its OP. Low bp → increased angiotensin → increased **aldosterone** → increased reabsorption in the distal tubules and collecting ducts, so less Na^+ is lost. High bp → increased **ANH** → opposite effect.
- Some Na^+ is also lost during **sweating,** but the concentration varies depending on body availability.

- **Potassium ions.**
- Extracellular K^+ must be kept low to maintain the resting potential of the body cells, but is required inside the cell. Dehydration increases the conc of plasma K^+, which must thus be excreted.
- Aldosterone $\rightarrow$ increased loss from the distal tubules and collecting ducts (at the same time as Na^+ is reabsorbed).

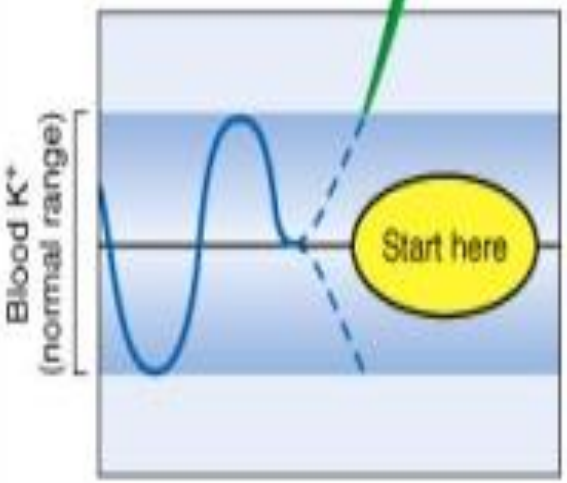
Increased blood levels of K^+ act on the adrenal cortex to increase aldosterone secretion.

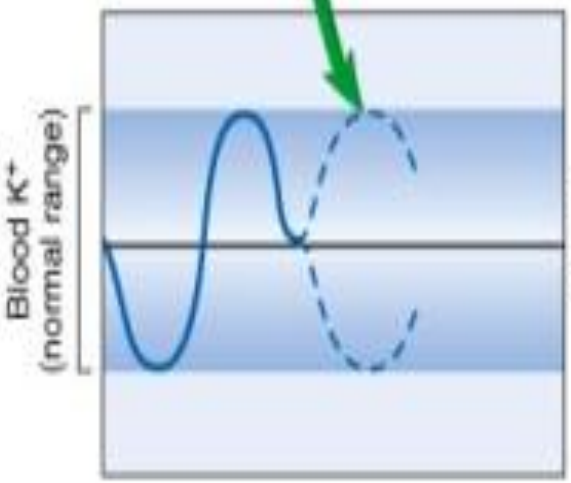
Increased aldosterone increases the rate of K^+ secretion from the distal tubules and collecting ducts of the kidney into the urine.

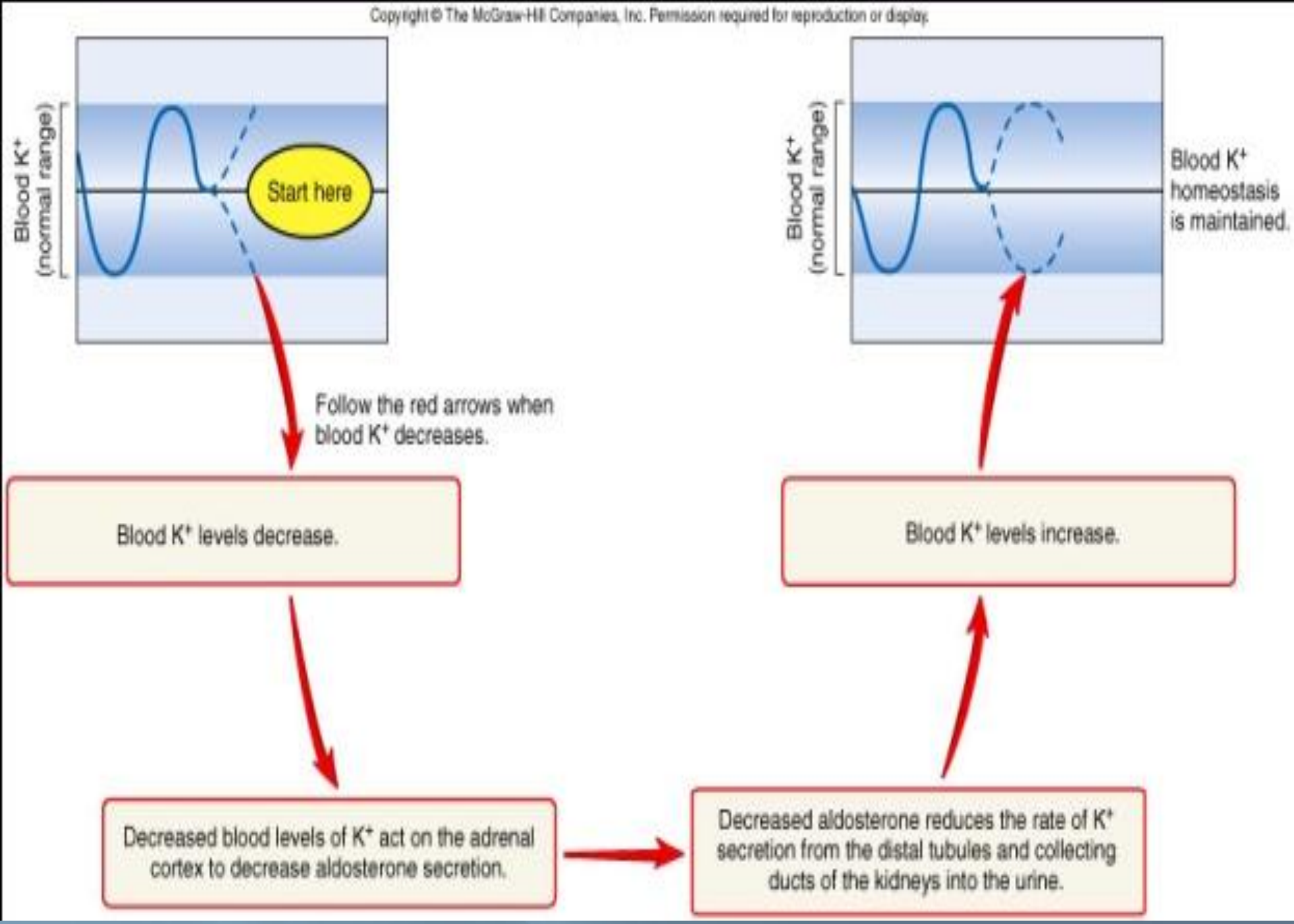
Blood K^+ levels decrease.

Blood K^+ levels increase.

Follow the green arrows when blood K^+ increases.







Calcium ions.

- Ca^{2+} conc. is of major importance in nerves(especially the synapses) and muscles, and affects the permeability of the cell membrane to Na^{+} and so is closely controlled.
- Parathyroid hormone increases as Ca^{2+} decreases to:
- 1- Stimulate osteoclasts to release Ca^{2+} from bones,
- 2- Reduce loss in the urine
- 3- Increase uptake from the gut (by stimulating vitamin D).
- Excessive Ca^{2+} reduces PTH but increases calcitonin to reverse these 3 processes.

Calcitonin mechanism
The parafollicular cells of the thyroid gland detect the increase in blood Ca^{2+} levels.

Increased calcitonin secretion by the parafollicular cells results.

Decreased breakdown of bone matrix by osteoclasts results in the decreased release of Ca^{2+} from bones.

PTH mechanism
The parathyroid gland cells detect the increase in blood Ca^{2+} levels.

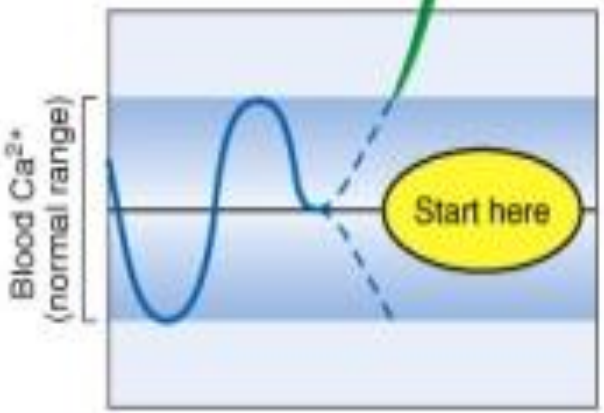
Decreased PTH secretion from the parathyroid glands results.

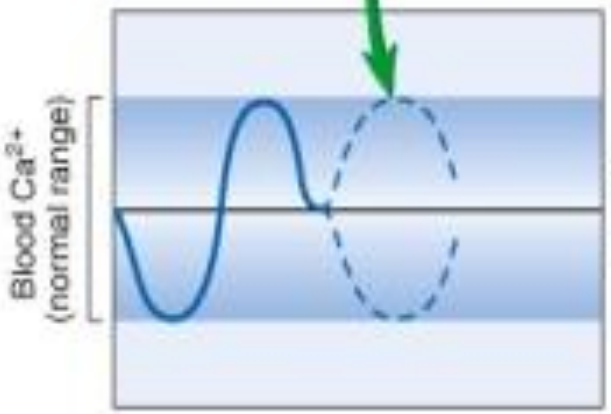
- Decreased breakdown of bone matrix by osteoclasts results in the decreased release of Ca^{2+} from bones.
- Decreased reabsorption of Ca^{2+} by the kidneys results in increased Ca^{2+} loss in the urine.
- Decreased synthesis of active vitamin D by the kidneys results in decreased Ca^{2+} absorption from the small intestine.

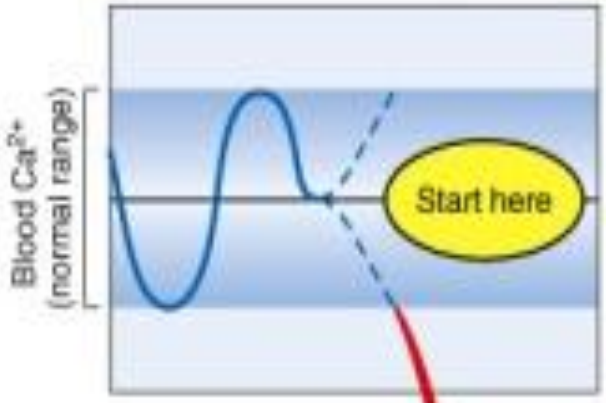
Blood Ca^{2+} levels increase.

A decrease in blood Ca^{2+} levels occurs because fewer Ca^{2+} enter the blood than leave the blood.

Follow the green arrows when blood Ca^{2+} increases.







Follow the red arrows when blood Ca^{2+} decreases.

Blood Ca^{2+} levels decrease.

PTH mechanism
Parathyroid gland cells detect the decrease in blood Ca^{2+} levels.

Increased PTH secretion from the parathyroid glands results.

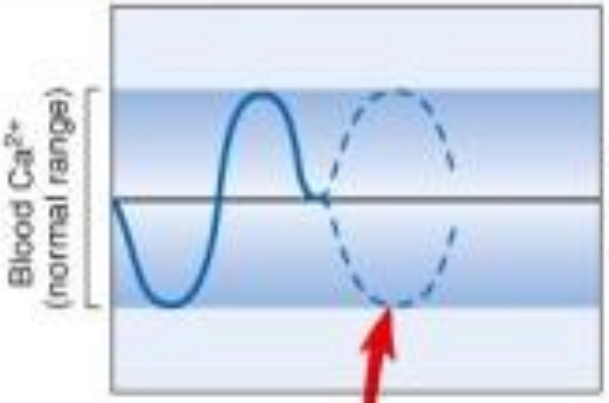
- Increased breakdown of bone matrix by osteoclasts results in the increased release of Ca^{2+} from bones.
- Increased reabsorption of Ca^{2+} by the kidneys results in decreased Ca^{2+} loss in the urine.
- Increased synthesis of active vitamin D by the kidneys results in increased Ca^{2+} absorption from the small intestine.

Calcitonin mechanism
Parafollicular cells of the thyroid gland detect the decrease in blood Ca^{2+} levels.

Decreased calcitonin secretion by the parafollicular cells results.

Increased breakdown of bone matrix by osteoclasts results in the increased release of Ca^{2+} from bones.

An increase in blood Ca^{2+} levels occurs because more Ca^{2+} enter the blood than leave the blood.



Blood Ca^{2+} homeostasis is maintained.

Urine collection and Micturition

Passage of urine from kidney to bladder

- Urine moves from the **collecting ducts** of the renal tubules to the **renal pelvis** by **hydrostatic pressure.**
- Urine moves from the **pelvis** into the **ureter** by the **smooth muscles contraction.**
- The **peristaltic wave** which propagates along the ureters length propels urine into the bladder to store the urine.

Micturition

•The flow of urine to the urinary bladder is relatively continuous.

•The urinary bladder acts as a reservoir for urine until it can be eliminated at appropriate time.

•The bladder can distend to accommodate the large volume of fluid .The maximum volume it can contain is **1L,** and discomfort begins when urine volume exceeds **500ml.**

•The capacity of the urinary bladder to distend is due to the following factors:

•The walls of the bladder contain large folds, which unfold to enlarge the lumine of the urinary bladder.

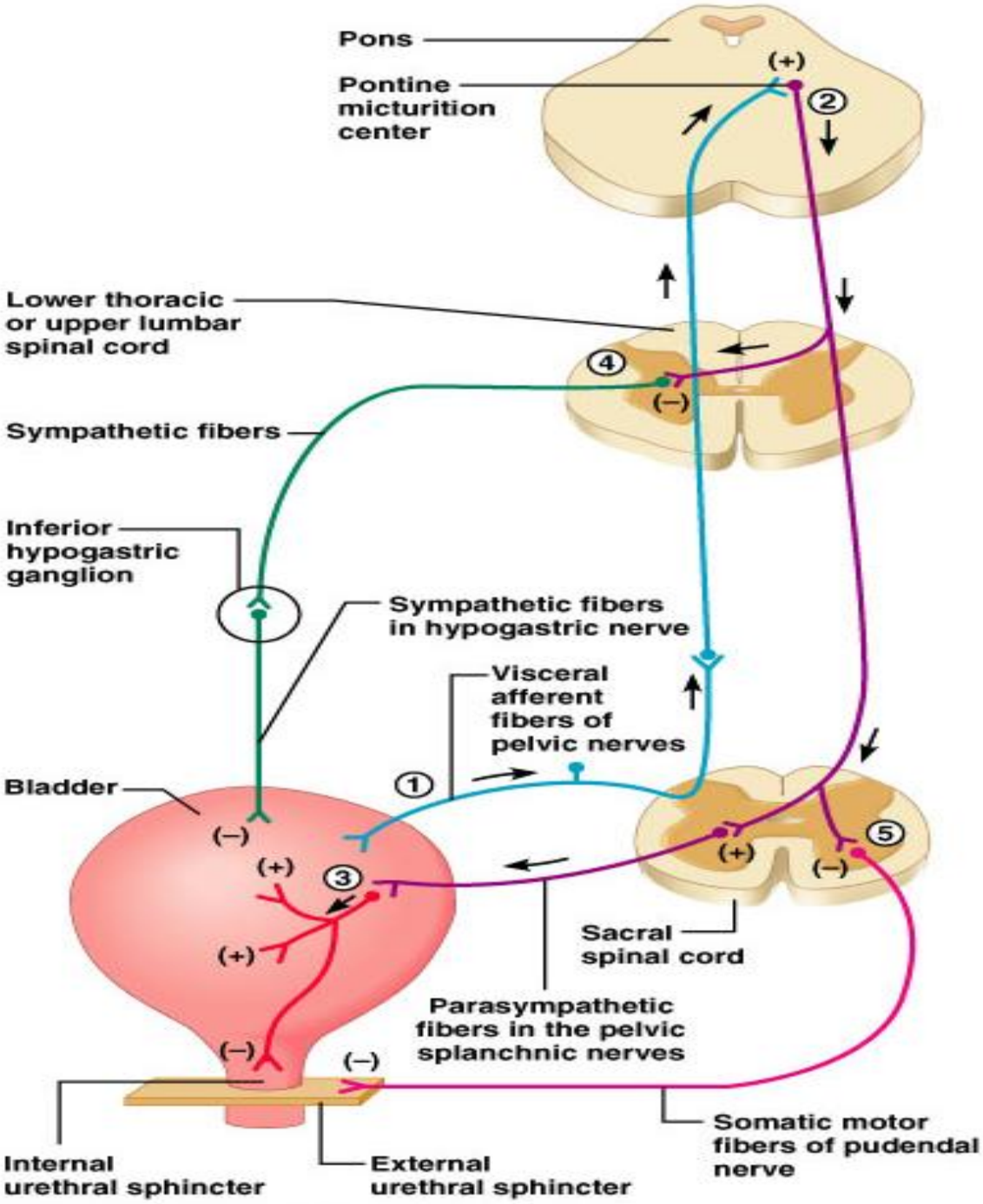
•The lining of urinary bladder is stretchable transitional epithelium.

•Smooth muscle wall of the urinary bladder stretch to accommodate the fluid volume.

•The bladder expands as the urine flows into it , but the internal pressure does not increase(because its structure) until the bladder volume becomes large.

Micturition reflex

- Micturition reflex is activated when the bladder wall is stretched resulting in elimination of urine from the urinary bladder **(micturition).**
- Integration of the micturition reflex occurs in the **sacral region** of the spinal cord and modified in the pons of cerebrum.
- When urine fills the bladder stimulates **stretch receptors** which produce action potential.
- Action potential is carried by sensory neurons to **spinal cord** through the **pelvic nerves.**
- Action potential is carried to the bladder through parasympathetic fibers
    - **Parasympathetic stimulation** causes contraction of smooth muscles of the bladder and decrease somatic motor action potentials causing the **external urinary sphincter** to relax.
- Urine flows from the bladder to the **urethra** by increase the pressure.
- The micturition reflex produces a series of contractions of the urinary bladder.


Pons
Pontine micturition center
(+)
②
Lower thoracic or upper lumbar spinal cord
④
(–)
Sympathetic fibers
Inferior hypogastric ganglion
Sympathetic fibers in hypogastric nerve
Visceral afferent fibers of pelvic nerves
①
Bladder
(–)
(+)
③
(+)
(–)
(–)
(+)
(–)
⑤
Sacral spinal cord
Parasympathetic fibers in the pelvic splanchnic nerves
Somatic motor fibers of pudendal nerve
Internal urethral sphincter
External urethral sphincter

THANKS