Renal System
Part II

Physiology

Pharmacy stage II, Semester I

2025-2026

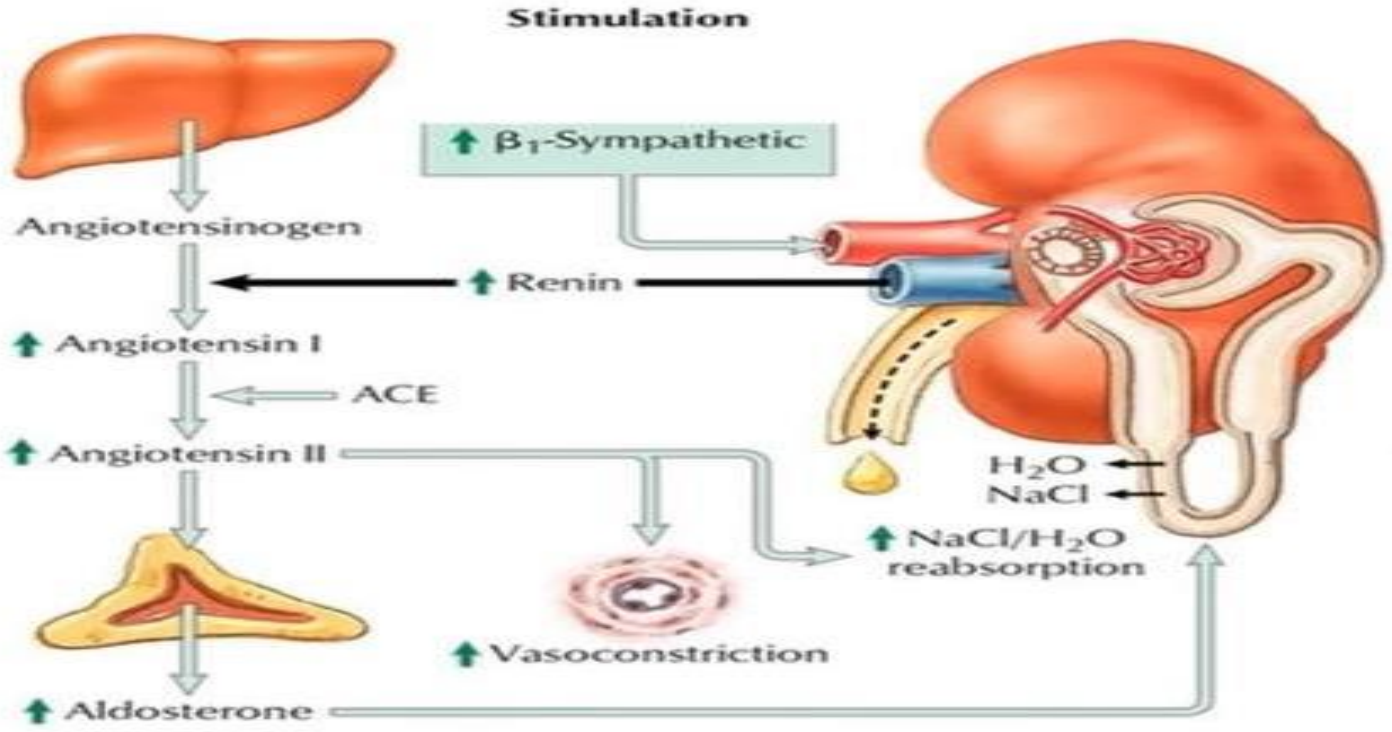
Factors affect the rate of tubular reabsorption of fluid

These factors play a significant role in determining the rate of fluid volume excretion (i.e. the urine). They are:

[1] Osmotic diuresis: An important example on the osmotic diuresis is the diabetes mellitus in which the proximal tubules fail to reabsorb all the glucose, as normally occurs. Instead, the nonabsorbed glucose passes the entire distance through the tubules and carries with it a large portion of the tubular water. Osmotic diuresis also occurs when substances that are poorly or cannot be reabsorbed by the tubules are filtered in excessive quantities from the plasma into glomerular filtrate. Examples of such substances are sucrose, mannitol, and urea.

[2] Plasma colloid osmotic pressure: A sudden increase in plasma colloid osmotic pressure instantaneously decreases the rate of fluid volume excretion. The cause of this is due to (A) a **decrease in GFR** and (B) an **increase tubular reabsorption**.

[3] Sympathetic stimulation: Sympathetic stimulation causes constriction of the afferent arterioles via β_1 receptors stimulation. It greatly decreases the glomerular pressure and simultaneously decreases GFR. At the same time, the blood flow into the peritubular capillaries is decreased and consequently, the capillary pressure is decreased, thus increasing tubular reabsorption. Also sympathetic stimulation stimulate juxtaglomerular complex (via β_1 receptors) to release renin.



[4] Arterial pressure: Under normal condition (when the renal autoregulatory mechanism is intact), a change in blood pressure causes a slight change diuresis and natriuresis. Unlike in renal diseases (when the renal autoregulatory mechanism is impaired), small increase in arterial pressure often causes marked increase in urinary excretion of Na and water. This results from **two separate effects**:

(A) The increase in arterial pressure increases glomerular pressure, which in turn increases GFR, thus leading to increased urine output.

(B) The increase in arterial pressure also increases the peritubular capillary pressure, thereby decreasing tubular reabsorption.

[5] Hormonal control: Such as:

- **ADH:** When excess antidiuretic hormone is secreted by the posterior pituitary gland, the effect is to increase the water permeability of the distal tubule, collecting tubule and collecting duct with a consequent decrease the urinary volume output acutely. However, when excess ADH is secreted for long periods of time, the acute effect of decreasing urinary output is not sustained. The reason is that other factors, such as the arterial pressure, colloid osmotic pressure, and concentrations of the osmolar substances in the glomerular filtrate all change in the direction that leads eventually to a urinary volume output equal to the daily need.
- ADH release is also controlled by cardiovascular reflexes that respond to decreases in blood pressure and/or blood volume. Whenever blood pressure and blood volume are reduced, such as occurs during hemorrhage, increased ADH secretion causes increased fluid reabsorption by the kidneys, helping to restore blood pressure and blood volume toward normal.
- **Aldosterone:** This is secreted by the zona glomerulosa cells of the adrenal cortex by its action on the principal cells (P Cells) of the cortical collecting tubule to increase Na reabsorption and to increase K secretion.

➢ **Angiotensin II:**

[1] It stimulates aldosterone secretion, which in turn increases Na and water reabsorption.

[2] It constricts the efferent arterioles and consequently increases Na and water reabsorption through the following mechanisms:

A- When the angiotensin constricts the efferent arterioles, this reduces the peritubular capillary pressure causing an increase in the rate of reabsorption of water and electrolytes from the tubular system especially from the proximal tubule, because the balance forces at the capillary membrane is now in favor of absorption.

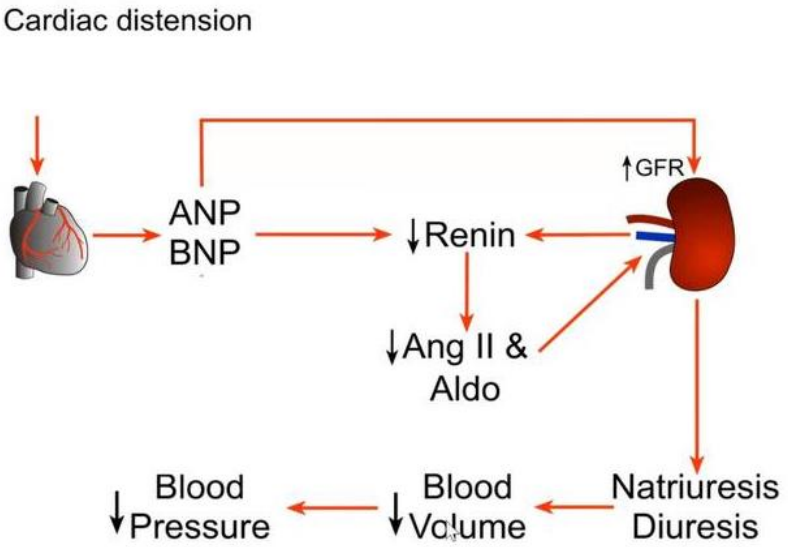
B - Because of the constriction of the efferent arterioles, the blood flow through glomeruli is decreased while the GFR is still near normal. This will lead that a very high proportion of plasma fluid to filter through the glomerular membrane into tubules. Therefore, the concentration of the plasma proteins in the blood leaving the glomeruli becomes very high and this concentrated plasma flows on into the peritubular capillaries. As the result, the colloid osmotic pressure in these capillaries is greatly increased, which is an additional factor that enhances reabsorption of water and salt.

C - There is evidence that angiotensin also has a direct effect on the distal tubules in causing increased active reabsorption of Na.

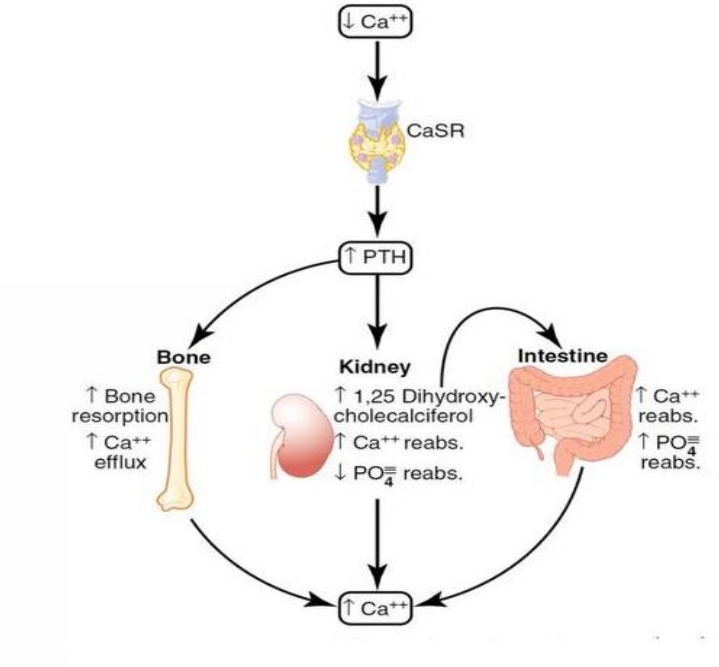
[3] It act directly especially on the proximal tubule to increase Na and water reabsorption (by stimulating *Na-K ATPase pump* at the basolateral membrane of the tubular cell) and *Na-H exchange* (at the luminal side of the tubular cell).

[4] Mesangial cells constrict in response to angiotensin II and reduce the capillary filtration coefficient resulting in an overall decrease in GFR.

- **Atrial natriuretic peptide:** It is released from specific cells of the cardiac atria upon distension as a result of plasma volume expansion. It inhibits the reabsorption of Na and water by the renal tubules especially in the collecting ducts with consequent increase in the urinary output.



- **Parathyroid hormone**: It increases the reabsorption of Ca and Mg ions from the ascending limb of loop of Henle and distal tubule. It inhibits the reabsorption of phosphate from the proximal tubule.



Regulation of Tubular Reabsorption and Glomerulus Filtration

- **Autoregulation of GFR & Renal Blood Flow (RBF)**

Autoregulation is an **intrinsic negative-feedback system** in the kidneys that keeps **renal blood flow (RBF ≈ 1200 mL/min)** and **glomerular filtration rate (GFR ≈ 125 mL/min)** relatively constant **despite changes in arterial pressure** (effective range ~**80–180 mmHg**). This stability prevents large errors in salt/water loss or waste retention.

- **Why it matters:**
  Even a ~**±5%** change in GFR can cause either excessive loss of water/solutes (if too high) or inadequate excretion of wastes (if too low).
- **The three cooperating mechanisms:**

A) <u>Tubuloglomerular Feedback (TGF)</u>

B) <u>Myogenic mechanism:</u>

C) <u>Glomerulotubular balance</u>

A) Tubuloglomerular Feedback (TGF)

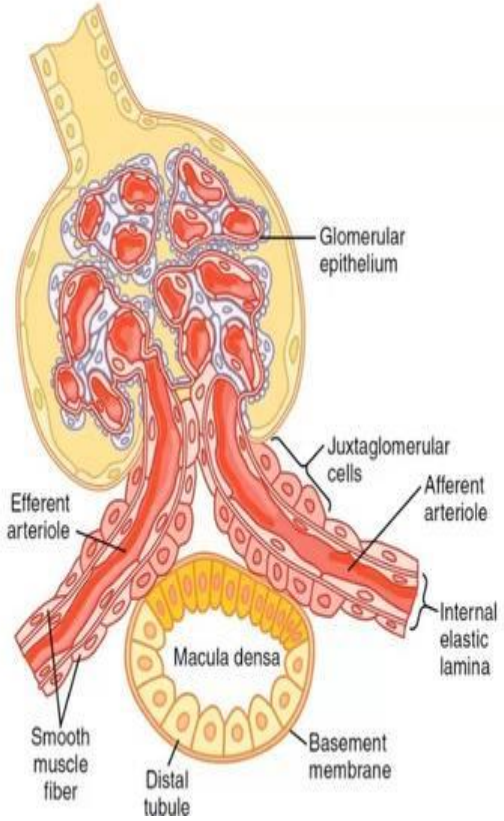
The **macula densa** within the **juxtaglomerular complex (JG complex)** senses **sodium/chloride (NaCl)** delivery (via **Na-K-2Cl cotransporter, NKCC2**) and drives two coordinated feedbacks to stabilize **glomerular filtration rate (GFR)** and **renal blood flow (RBF)**:

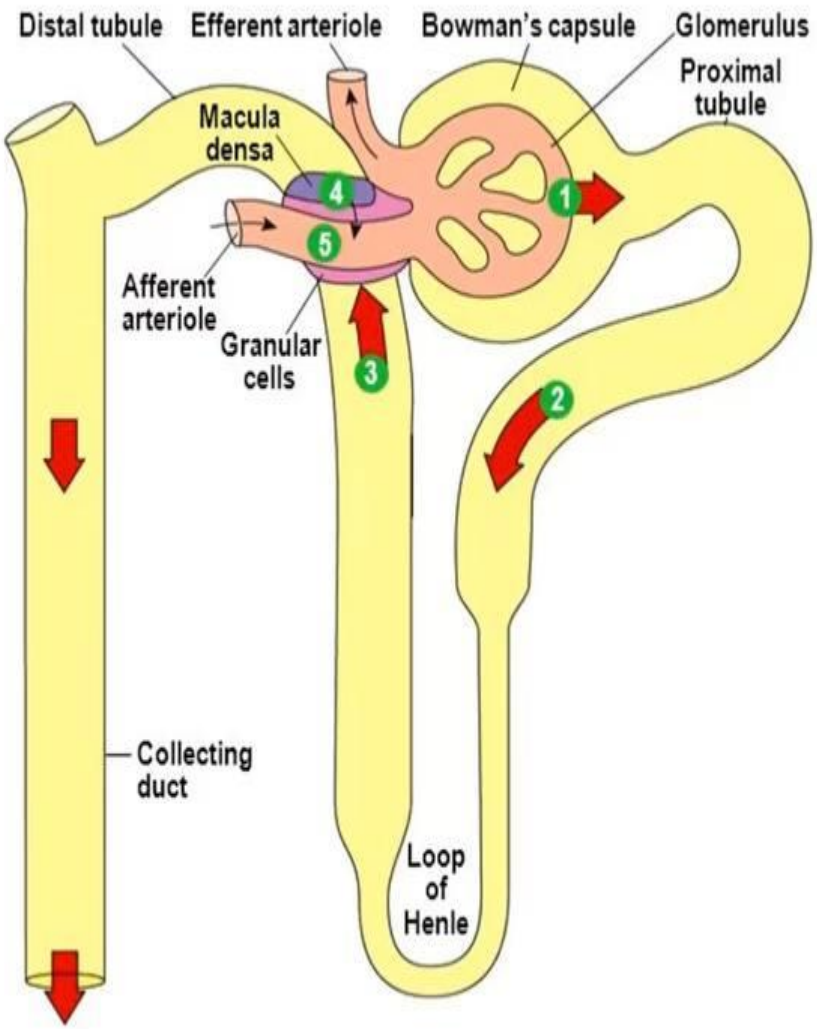
1) Afferent arteriolar vasodilator/vasoconstrictor feedback

- **When GFR is low**
- Tubular flow slows; the **thick ascending limb of the loop of Henle** reabsorbs more **NaCl → low NaCl at the macula densa**.
- The macula densa releases **nitric oxide (NO)** and **prostaglandin E_2 (PGE_2)** and reduces **adenosine**.
- **Outcome: Afferent arteriole dilates → glomerular capillary hydrostatic pressure (P_GC) increases → GFR rises** toward normal.
- In parallel, signaling to **juxtaglomerular cells (JG cells)** increases **renin**, priming the efferent mechanism.
- **When GFR is high**
- Faster tubular flow delivers **more NaCl** to the macula densa → **high NaCl** there.
- The macula densa releases **ATP/adenosine (A1 receptors)** and lowers **NO**.
- **Outcome: Afferent arteriole constricts → P_GC falls → GFR decreases** toward normal; **renin** is suppressed.

Regulation of Tubular Reabsorption and glomerular filtration

1. Tubuloglomerular Feedback





1. GFR increases.
2. Flow through tubule increases.
3. Flow past macula densa increases.
4. Paracrine diffuses from macula densa to afferent arteriole.
5. Afferent arteriole constricts.

Resistance in afferent arteriole increases.

Hydrostatic pressure in glomerulus decreases.

GFR decreases.

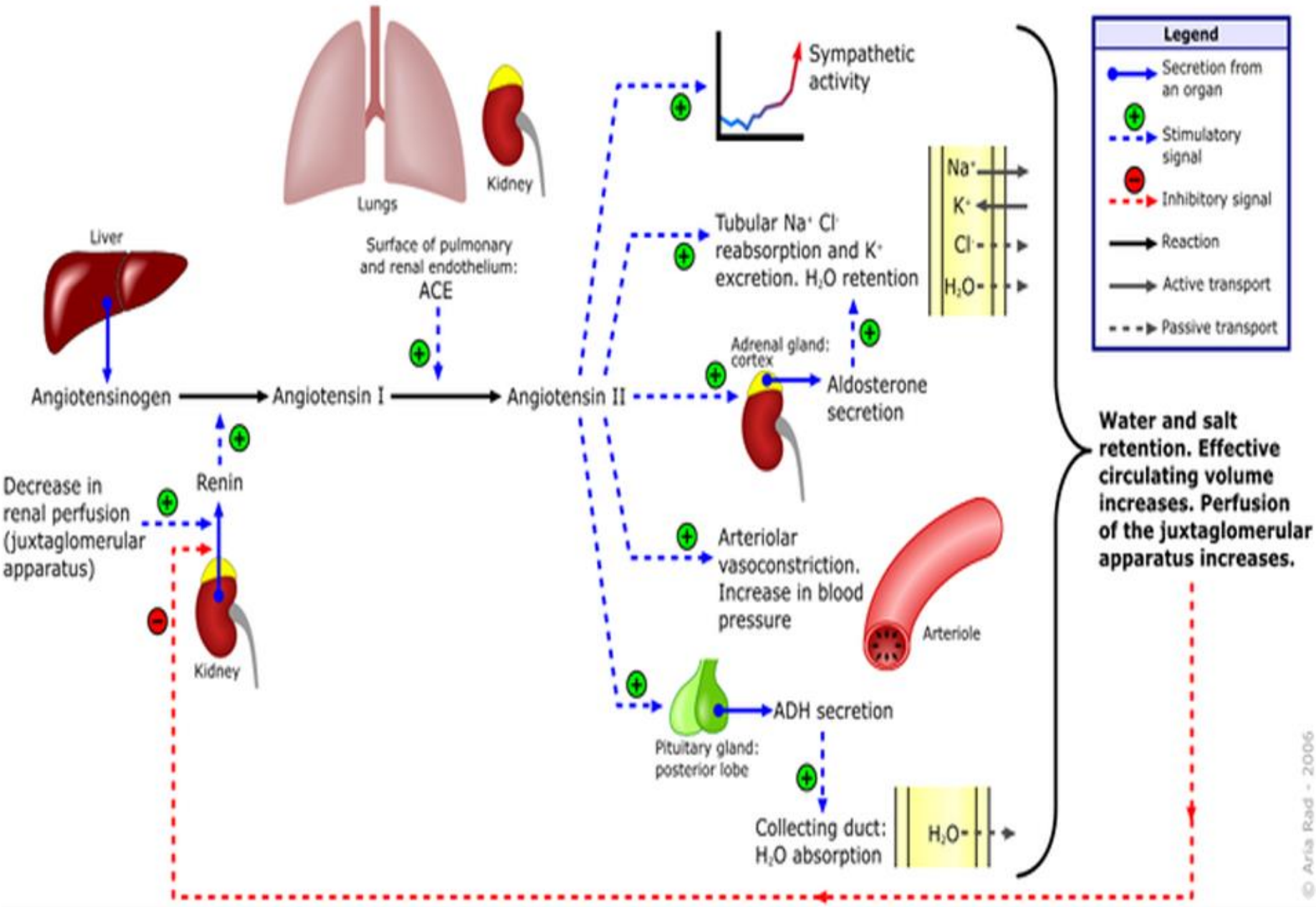
2) Efferent arteriolar vasoconstrictor feedback via Renin–Angiotensin–Aldosterone System (RAAS)

Trigger

- **Low NaCl at the macula densa** or **renal perfusion pressure** or **renal flow is decrease** or **stimulation of renal nerves** or Blood Pressure drops (as measured by the stretch of the afferent arteriole) → **renin release (**from renal juxtaglomerular.cells)
- **Renin** cleaves **angiotensinogen** (liver) to **angiotensin I**; **angiotensin-converting enzyme (ACE)** converts it to **angiotensin II** and perform several function :

1. Constricts mainly the efferent arterioles (much more than the afferent arterioles). Therefore, the constriction of the efferent arterioles causes the pressure in the glomerulus to rise leading to increase in GFR back to normal**.** .
2. Potent vasoconstrictor → total peripheral resistance ↑ → arterial blood pressure ↑.
3. Stimulates aldosterone release from the adrenal cortex (zona glomerulosa) → sodium (Na^+) reabsorption ↑ via epithelial Na^+ channels (ENaC) and Na^+/K^+-ATPase; water follows osmotically → extracellular fluid volume ↑ / blood pressure ↑.
4. Stimulates antidiuretic hormone (ADH, vasopressin) from the posterior pituitary → aquaporin-2 insertion in collecting duct → water reabsorption ↑ (urine concentrates).
5. Promotes thirst (hypothalamic centers) → fluid intake ↑ → supports blood volume and pressure.

Renin-angiotensin-aldosterone system

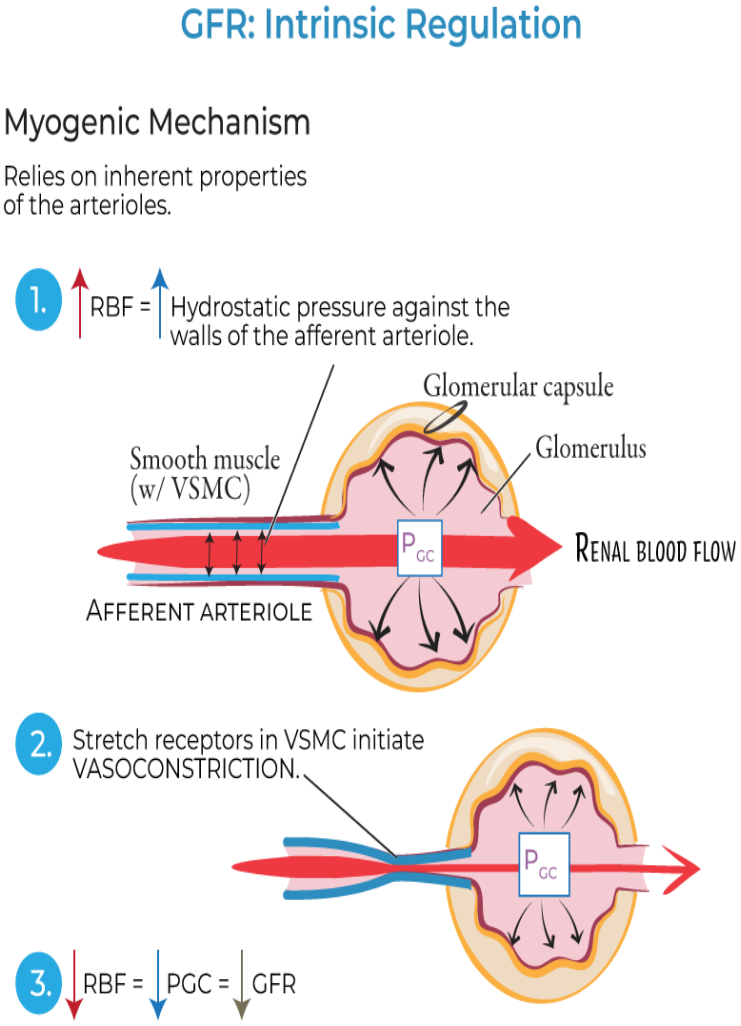


[B] Myogenic mechanism:

This mechanism of stabilizing the GFR is based on the tendency of smooth muscle to contract when stretched.

When the arterial pressure rises, it stretches the wall of the arteriole, and this in turn causes a secondary contraction of the arteriole. This decreases the renal blood flow and GFR back toward normal, thus opposing the effect of the rising arterial pressure to increase the flow.

Conversely, when the pressure falls too low, an opposite myogenic response allows the artery to dilate and therefore increases the flow and GFR.



[C] Glomerulotubular balance

- It is the ability of the tubules to increase reabsorption rate in response to increased tubular load, which means that when the GFR increases, the rate of tubular reabsorption increases in exact proportion to the increase in filtration.

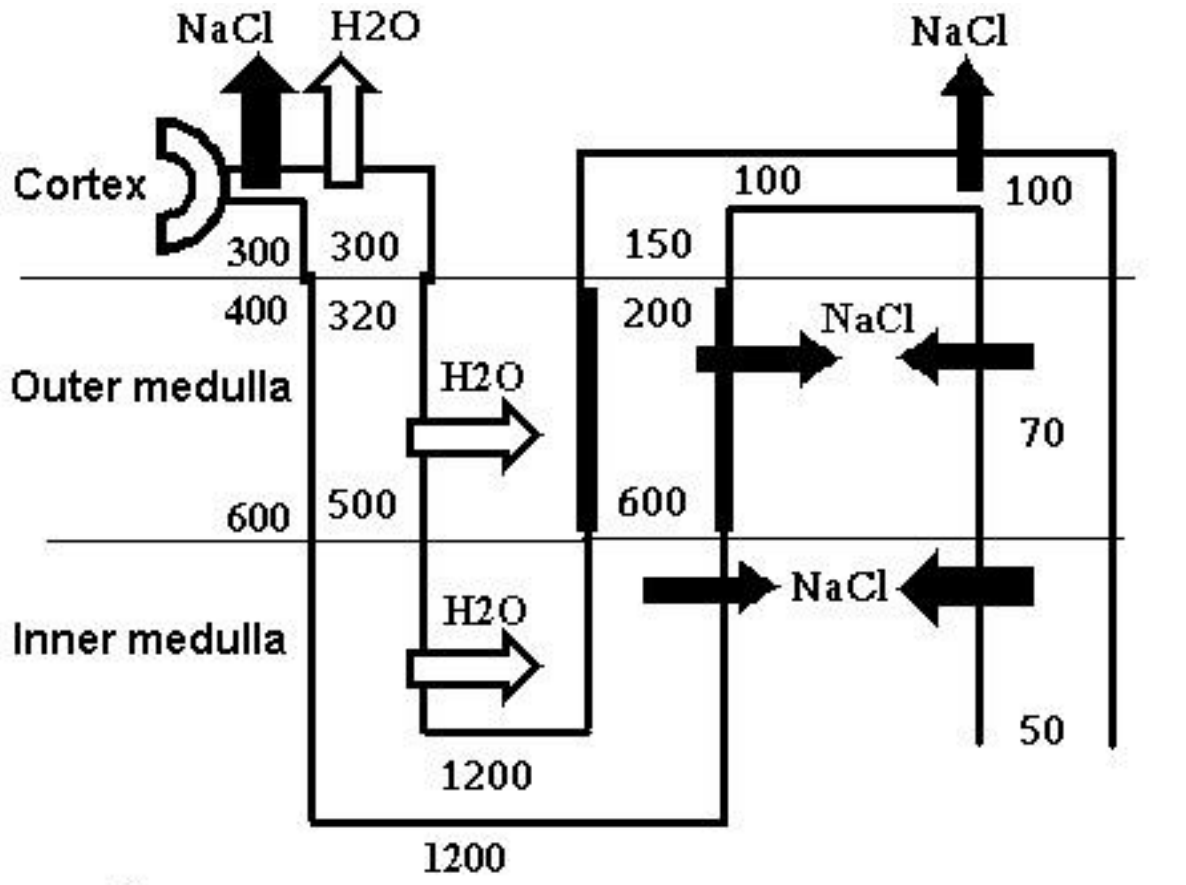
- Glomerulotubular balance is especially **good** in the proximal tubules and loop of Henle and **less effective** in the more distal segments of the tubular system. This slight lack of glomerulotubular balance in the distal tubular segments can lead to a tremendous increase in urine output when the GFR is increased.

- Also, very slight changes in rate of reabsorption of tubular fluid can cause equally as great alteration in urine output.

Renal Mechanisms for excreting diluted or concentrated urine

[1] Making dilute urine

- **Proximal tubule:** reabsorbs **water and solutes proportionally** → tubular fluid stays **iso-osmotic ≈300 mOsm/L**.
- **Thin descending limb: permeable to water, not salt** → water leaves to hyperosmotic medulla → fluid becomes **more concentrated**.
- **Thick ascending limb (and early distal tubule): reabsorbs $Na^+/K^+/Cl^-$ (NKCC2)** but is **water-impermeable** → fluid becomes **dilute** (to **~100 mOsm/L** by early distal tubule).
- **Late distal tubule/cortical collecting duct (no ADH):** continue **NaCl reabsorption** with **low water permeability** → urine can reach **~50 mOsm/L**.
- **Key point:** "Diluting segments" = **thick ascending limb + early distal tubule** (salt out, water stays).



Active reabsorption

Passive movement by osmosis

Renal mechanism for excreting a dilute urine (this occurs in the absence of ADH).

[2] Making concentrated urine

- **Two requirements:**

1- High Antidiuretic Hormone (ADH / vasopressin):

- ↑ water permeability in **late distal tubule** and **collecting duct** (Aquaporin-2 insertion).
- ↑ **urea permeability** in inner medullary collecting duct → **urea recycling** augments medullary gradient.

2- Hyperosmotic renal medulla (corticomedullary gradient):

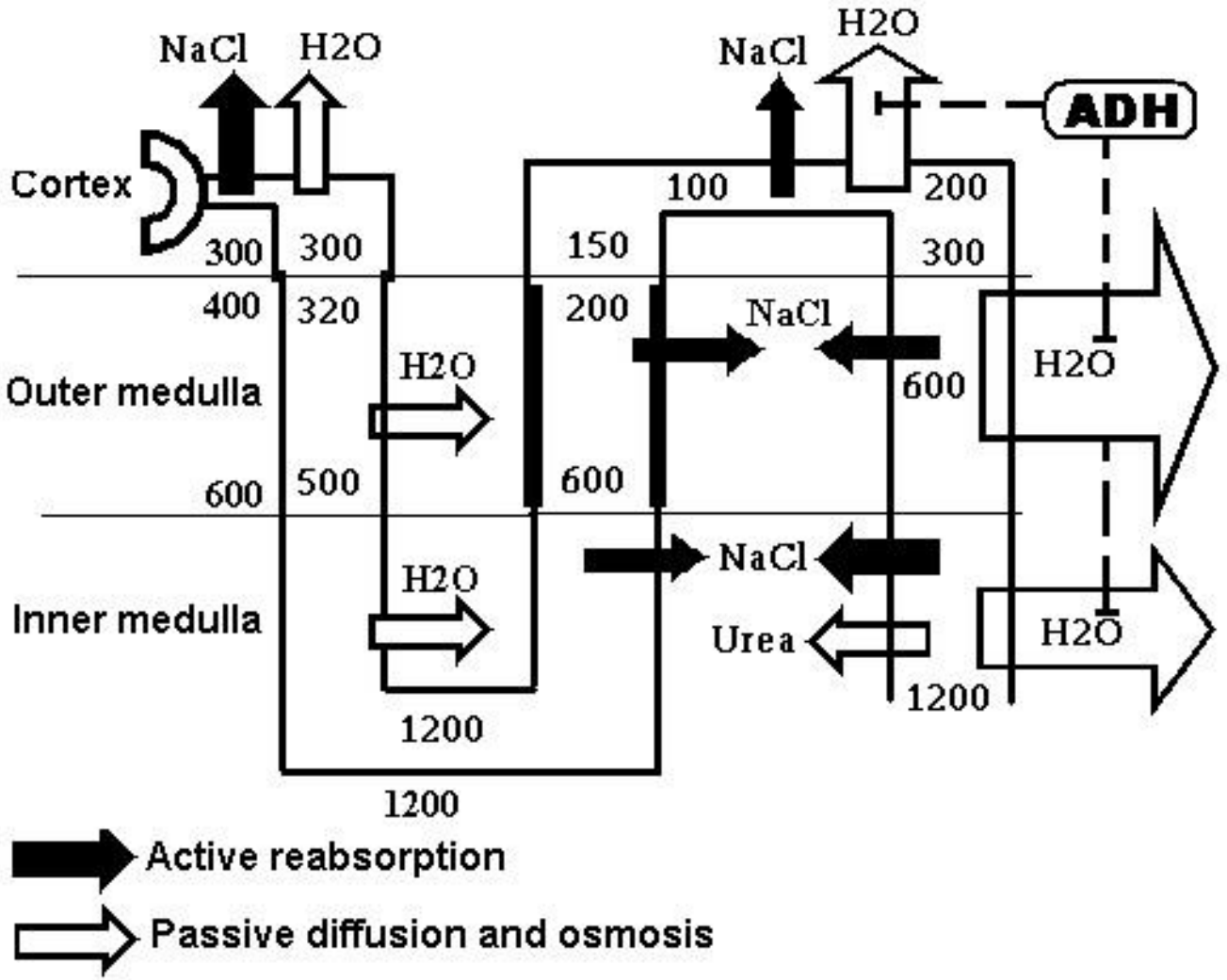
- Cortex ~**300**, outer medulla ~**600–800**, inner medulla **~1200–1400 mOsm/L**.
- Built by **countercurrent multiplication** (loops of Henle) and **maintained** by **countercurrent exchange** (vasa recta) + **low medullary blood flow** + **urea recycling**.

- **Countercurrent multiplication (loops of Henle)**

1- Thick ascending limb: actively pumps NaCl out (via NKCC2) and is **water-tight** → creates a small **transverse gradient**.

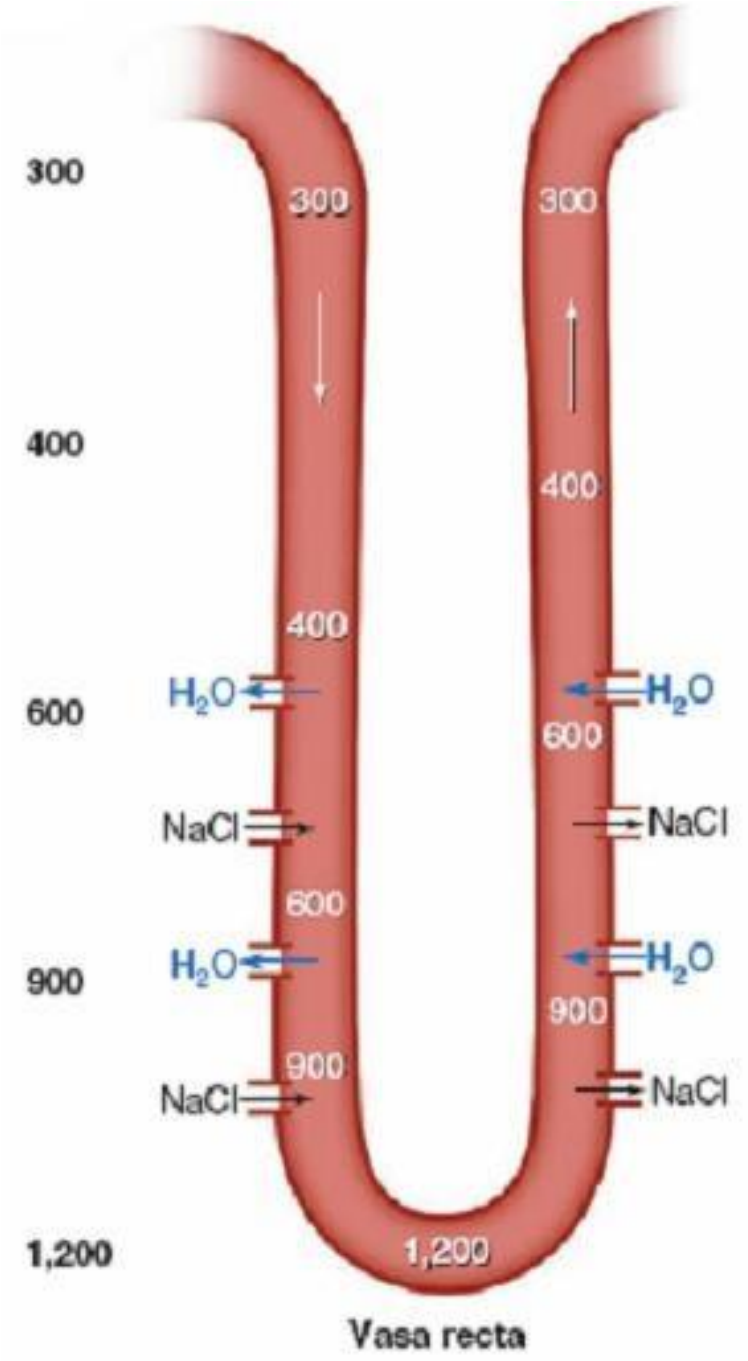
2- Thin descending limb: water-permeable → water exits osmotically into hypertonic interstitium.

3- Continuous inflow/outflow shifts and **multiplies** the small gradient along the length of the loops, generating a **steep longitudinal gradient** in the medulla.



Renal mechanism for excreting a concentrated urine (in the presence of high concentration of ADH).

- **Countercurrent exchange (vasa recta)**
- **Slow medullary blood flow** (<2% of RBF) and **hairpin loops** allow passive **exchange** with interstitium:
  1- Descending limb of vasa recta: **gains solute, loses water** in the deep medulla.
  2- Ascending limb: **gives back solute, re-gains water** on the way out.
  3- Net effect: delivers nutrients **without washing out** the medullary gradient.
- **With high ADH**, water is reabsorbed osmotically from the collecting duct into the hyperosmotic medulla → **small volume, concentrated urine**.



Role of urea

- **Core idea:** Urea is not just a waste; it is a **key osmotic contributor** that helps the kidney make **concentrated urine**. Its handling is **segment-specific** and **controlled by antidiuretic hormone (ADH, vasopressin)** in the collecting duct.
- **ADH dependence in collecting duct**

1. **Without ADH:** collecting duct is **nearly impermeable** to **water** and **urea** → little urea leaves the lumen → urine stays **dilute**.
2. **With ADH:** collecting duct water permeability ↑ (Aquaporin-2) and **inner medullary collecting duct** urea permeability ↑ → **urea reabsorption** ↑ into the medullary interstitium.

- **Segmental handling**

1. **Proximal tubule:** **~40%** of filtered urea **reabsorbed**; because **60–80% water** is also reabsorbed, the **tubular urea concentration rises** to **~2–3× plasma** by the end of proximal tubule.
2. **Thin descending limb / loop of Henle:** somewhat **permeable to urea**; high medullary interstitial urea **diffuses into the lumen**.
3. **Thick ascending limb, distal convoluted tubule, cortical & outer medullary collecting duct: low urea permeability** → as water is reabsorbed here, **urea concentrates** in the lumen.
4. **Inner medullary collecting duct (with ADH): permeable to urea** → urea **diffuses out** to the interstitium (where **urea supplies ≈½** of the high osmolality), then **re-enters** the **thin limb** → **urea recycling**.

- **Urea recycling (the "urea cycle")**

1. **Path:** Inner medullary collecting duct → **interstitium** → **thin limb of Henle** → up through distal/collecting segments → back to **inner medullary collecting duct**.
2. **Purpose: Trap/recirculate urea** in the medulla, **preserving the corticomedullary gradient** (NaCl + urea) → enables **small-volume, concentrated urine** when **ADH is high**.

- **Vasa recta (countercurrent exchange)**

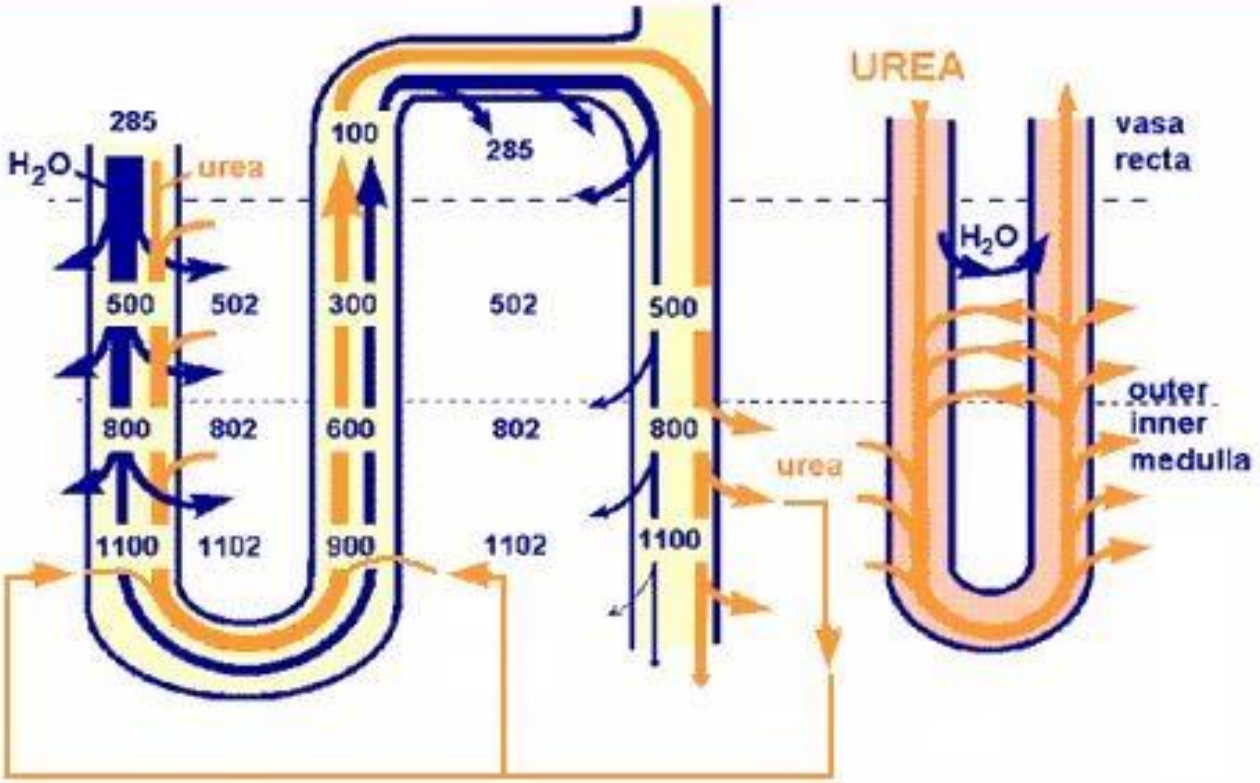
Very low flow (<2% RBF) and **hairpin loops** allow solute/water exchange **without washing out** the gradient: descending vasa recta **gain solute/lose water**; ascending limbs **return solute and regain water** → medullary gradient **maintained**.

- **Special notes**

1. **Water diuresis (low ADH):** collecting duct stays **urea-tight** → **less urea** enters interstitium → medullary osmolality falls to ~**600 mOsm/kg** → urine **dilute**.
2. **Dietary protein: High protein → more urea → better concentrating ability**; **protein restriction → poor concentrating ability**.
3. **Urea excretion determinants: Plasma urea concentration** and **GFR**. Typically **~40–60%** of filtered urea is excreted. With **low GFR** (renal disease), urea accumulates until higher plasma urea × GFR restores excretion.

Bottom line: With **ADH** and a **strong medullary gradient** (built by **NaCl** and **urea**, preserved by **vasa recta**), urea **recycling** lets the kidney conserve water (concentrated urine). Without ADH, the system is urea-tight and urine remains **dilute**.

COUNTERCURRENT CONCENTRATION OF UREA

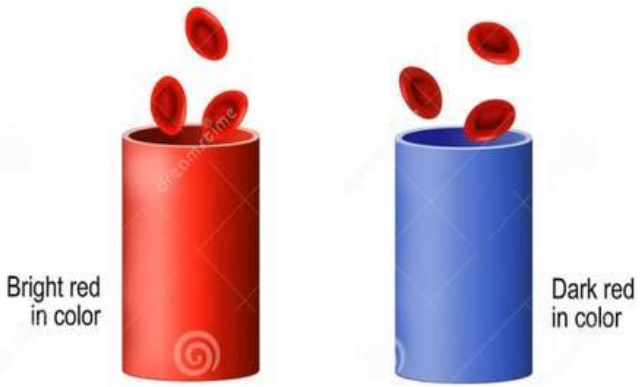


- **Vasa recta:** Blood flowing into the medulla picks up urea from the concentrated medullary ISF. As that concentrated blood flows up from the papilla it loses urea to the medullary ISF.
- **Urea,** reabsorbed from the collecting tubule, is thus recycled and trapped within the medulla.

Acid-Base Regulation

- Precise H^+ regulation is essential
- H^+ concentration of the body fluids normally is kept at a low level.
- Acids: release H^+ ion (H_2CO_3) if increased→ acidosis
- Bases: accept H^+ ion (HCO_3^-, $HPO_4^=$ and proteins (Hb)) if increased→ alkalosis
- The normal pH is 7.4
- pH is inversely related to the H^+ concentration $pH = -\log [H^+]$

Normal pH in the body

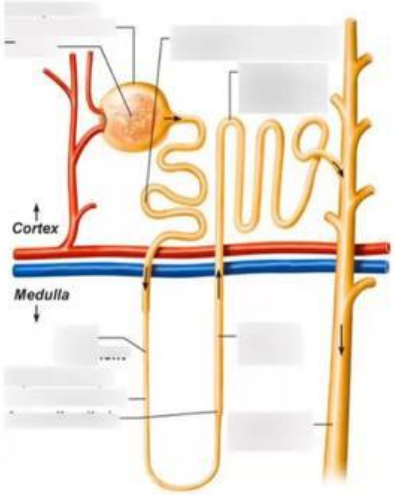


- The normal pH of arterial blood is 7.4,
- The pH of venous blood and interstitial fluids is about 7.35
- The lower limit of pH is about 6.8, and the upper limit is about 8.0
- The pH of intracellular fluid range between 6.0 and 7.4.
- The pH of urine can range from 4.5 to 8.0

Defending Against Changes in H^+ Concentration

1. the *chemical acid-base buffer systems of the body fluids,* (within seconds)
2. the ***respiratory center,*** which regulates the removal of CO_2 (within a few minutes);
3. the ***kidneys,*** which can excrete either acid or alkaline urine. (over a period of hours to several days). <u>It is slow but it is the most powerful.</u>

Buffering of H^+ in the Body Fluids



- Bicarbonate Buffer System
- *carbonic anhydrase* is essential
- In the walls of the lung alveoli, and the epithelial cells of the renal tubules

respiratory acidosis

Metabolic alkalosis

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

respiratory alkalosis

metabolic acidosis

the most powerful extracellular buffer

Phosphate Buffer System

- It plays a major role in buffering *renal tubular fluid* and *intracellular fluids*.
- The main elements of the phosphate buffer system are $H_2PO_4^-$ and $HPO_4^=$.

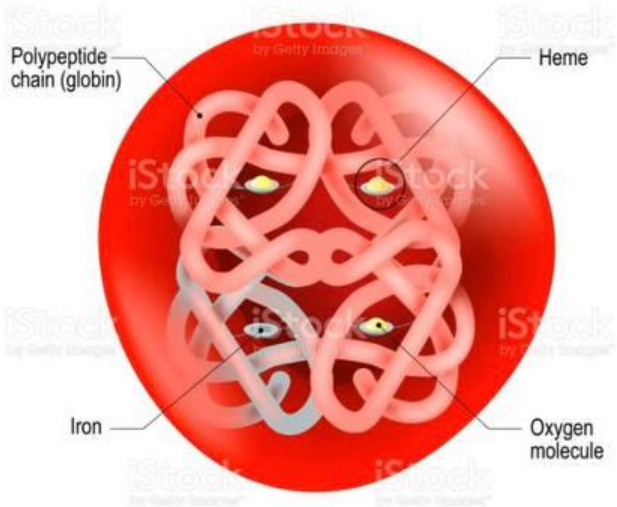
$$H^+ + HPO_4^= \leftrightarrow H_2PO_4^-$$

$$OH^- + H_2PO_4^- \leftrightarrow HPO_4^= + H_2O$$

Proteins Are Important Intracellular Buffers

- Proteins are among the most plentiful buffers in the body
- In the red blood cell, hemoglobin (Hb) is an important buffer, as follows:

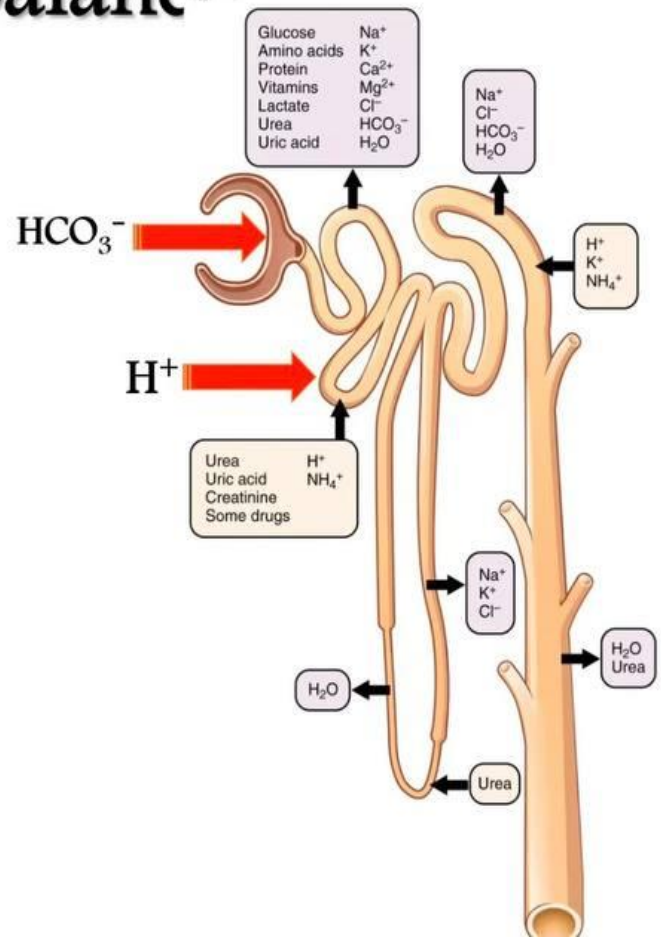
  - $H^+ + Hb \leftrightarrow HHb$



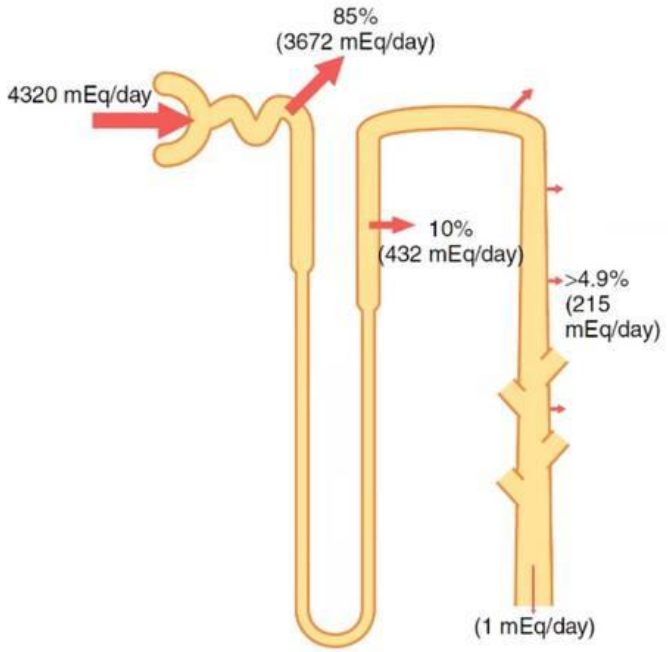
Renal Control of Acid-Base Balance

- by excreting either acidic or basic urine
- the kidneys regulate extracellular fluid H+ concentration through three fundamental mechanisms:

1. secretion of H^+,
2. reabsorption of filtered $HCO3^-$,
3. production of new $HCO3^-$.



Secretion of H^+ and Reabsorption of HCO_3^- by the Renal Tubules



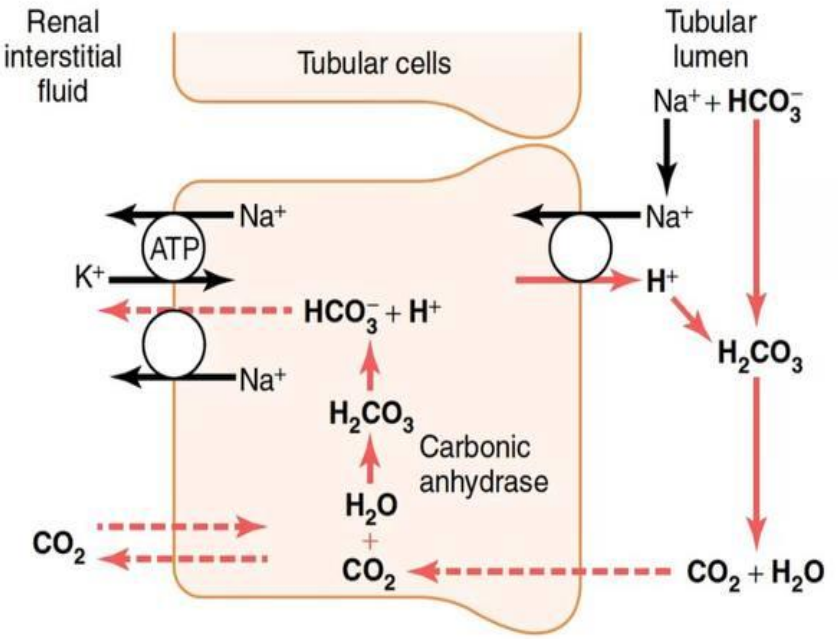
- for each HCO3− reabsorbed, a H+ must be secreted.

- H^+ is secreted along the nephron (PT, TAL, and especially α-intercalated cells in the collecting duct).
- Filtered HCO_3^- is "reabsorbed" in PT/TAL by titrating it with secreted H^+ (then returning HCO_3^- to blood), and *new* HCO_3^- is added to plasma by α-intercalated cells in the collecting duct.

H^+ is Secreted by Secondary Active Transport in the Early Tubular Segments

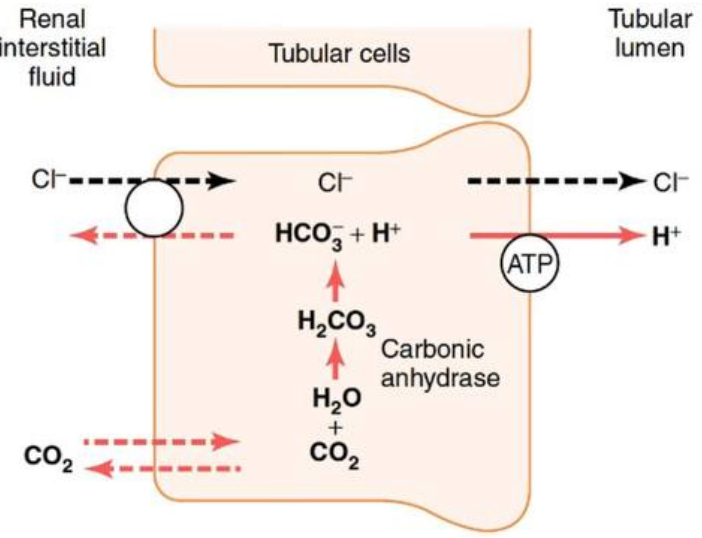
- By the sodium-hydrogen exchanger protein
- The net result is that for every H^+ secreted into the tubular lumen, an HCO_3^- enters the blood.
- The transport of HCO_3^- across the basolateral membrane is facilitated by two mechanisms:

1. Na^+-HCO_3^- co-transport
2. Cl^--HCO_3^- exchange



Secretion of H^+ in the Intercalated Cells of Late Distal and Collecting Tubules

- By a hydrogen-transporting ATPase.



- In order to maintain the normal pH (acid-base balance) of the blood, the cells of the proximal convoluted tubules secrete hydrogen ions in the filtrate, they combine with buffers;
- Bicarbonate, forming carbonic acid ($H^+ + HCO_3^-$ H_2CO_3)
- Ammonia, forming ammonium ions ($H^+ + NH_3$ NH_4^+)
- Hydrogen phosphate, forming dihydrogen phosphate($H^+ + HPO_4^{2-}$ H_2PO_4).

Carbonic acid is converted to carbon dioxide (CO_2) and water (H_2O), and the CO_2 is reabsorbed maintaining the buffering capacity of the blood.

Hydrogen ions are excreted in the urine as ammonium salts and hydrogen phosphate.

- The normal pH of urine varies from 4.5 to 7.8 depending on diet, time of day and a number of other factors.
- **Individuals whose diet contains a large amount of animal proteins tend to produce more acidic urine (lower pH) than vegetarians do.**

Micturition: Is the process by which the urinary bladder empties when it becomes filled. The principal nerve supplies to the bladder are:

[1] The pelvic nerves which connect with spinal cord through the sacral plexus (S-2 and S-3) with the bladder. The pelvic nerves are both sensory and motor nerve fibers. The sensory fibers mainly detect the degree of stretch of the bladder walls. The motor nerve fibers transmitted in the pelvic nerves are parasympathetic fibers. These terminate on ganglion cells located in the wall of the bladder. Short postganglionic nerves then innervate the detrusor muscle.

[2] Motor somatic fibers are also transmitted to the bladder through pudendal nerve to innervate the skeletal muscle fibers of external bladder sphincter.

[3] The hypogastric nerve fibers which connect the spinal cord (L2 spinal segment) with the bladder and carry the sympathetic fiber mainly to the blood vessel and have very little to do with micturition, but they do mediate the contraction of the bladder muscle that prevents semen from entering the bladder during ejaculation. Some sensory fibers (for pain and fullness sensation) also pass by way of the sympathetic nerves.

The micturition reflex: As the bladder fills, it stretches the bladder wall, thus stimulating stretch receptors especially in the bladder neck. The first urge to void is felt at a bladder volume of about 150 ml, and a marked sense of fullness at about 300-400 ml. Then, sensory signals are conducted to the sacral segments of the spinal cord through the pelvic nerves and then back again to the bladder through the parasympathetic fibers in these same nerves initiating micturition contraction of the detrusor muscles.

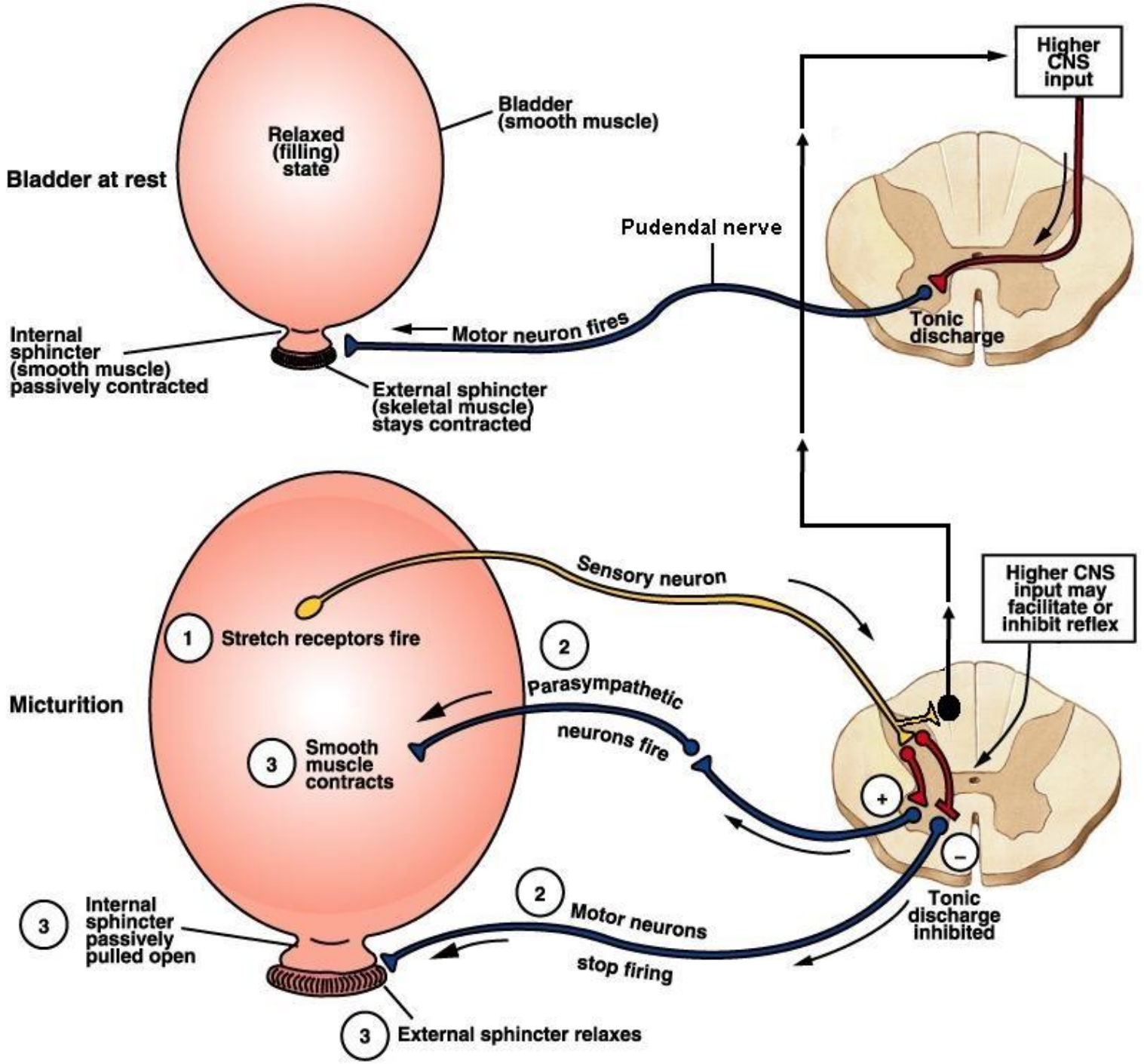
Once a micturition reflex begins, it is self-regenerative and the high pressure inside the bladder forces the bladder neck to open against its tonic contraction. Stretching the bladder neck exacerbates the intensity of the micturition reflex and also activates another reflex.

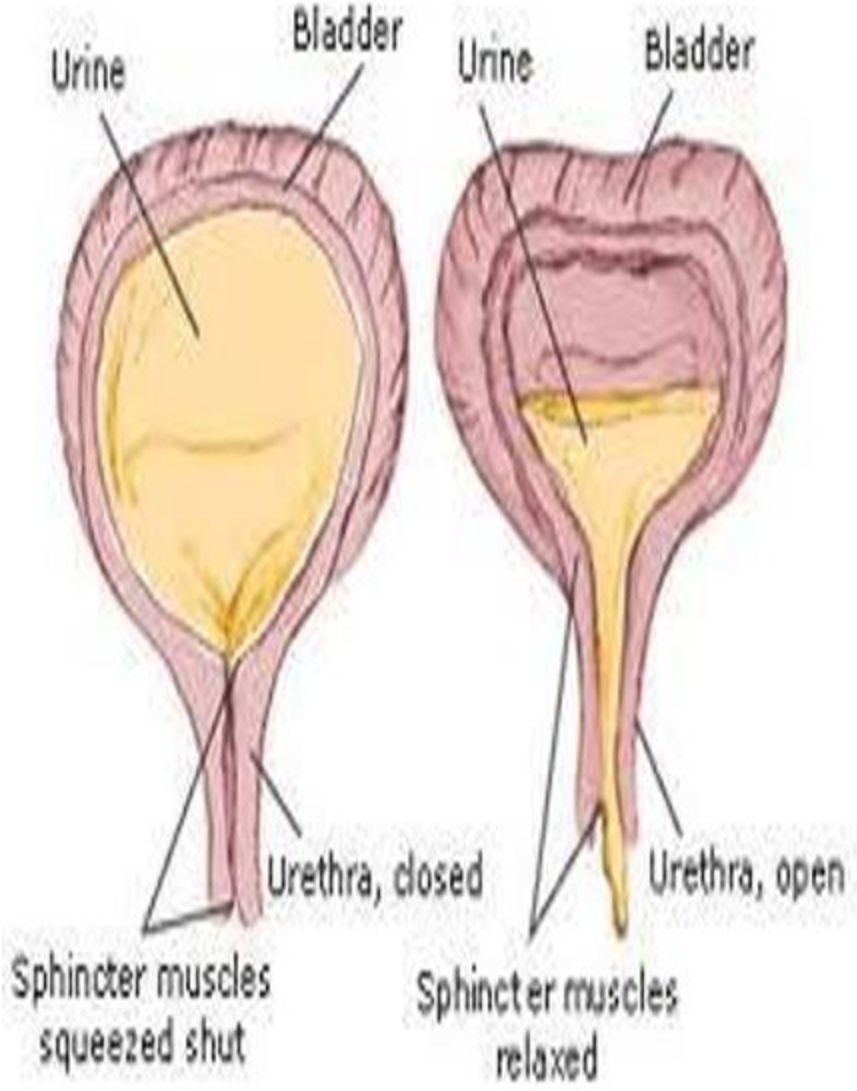
This reflex passes to the sacral portion of the spinal cord and then back through the pudendal nerve to the external sphincter to inhibit it. If this inhibition is more potent than the voluntary constrictor signals from the brain, then urination will occur. Then after a few seconds to more than a minute, the reflex begins to fatigue allowing rapid reduction in bladder contraction.

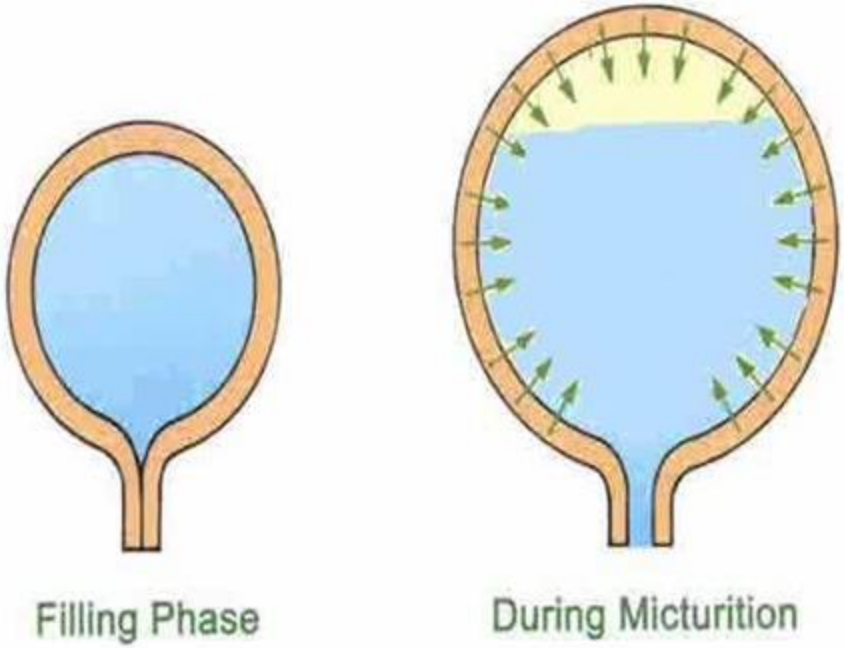
The micturition reflex can be controlled by higher brain centers in the following ways:

1 - The higher centers keep the micturition reflex partially inhibited all the time except when it is desired to micturate.
2 - The higher centers prevent micturition, even if a micturition reflex occurs by continual tonic contraction of the external bladder sphincter until a convenient time presents itself.
3 - When the time to urinate arrives, the cortical centers can (a) facilitate the sacral micturition centers to help initiate a micturition reflex. (b) Inhibit the external urinary sphincter so that urination can occur.

The threshold for the micturition reflex (like any other stretch reflex) can be adjusted by the activity of facilitatory (in pons) and inhibitory (in the midbrain) centers in the brain stem.


Bladder at rest
Relaxed (filling) state
Bladder (smooth muscle)
Higher CNS input
Pudendal nerve
Tonic discharge
Motor neuron fires
Internal sphincter (smooth muscle) passively contracted
External sphincter (skeletal muscle) stays contracted
Micturition
Sensory neuron
1 Stretch receptors fire
2 Parasympathetic neurons fire
3 Smooth muscle contracts
Higher CNS input may facilitate or inhibit reflex
+
–
Tonic discharge inhibited
2 Motor neurons stop firing
3 Internal sphincter passively pulled open
3 External sphincter relaxes





MECHANISM OF MICTURITION ACCORDING TO THE ISLAMIC SCHOLARS

Micturition Reflex (Summary)

Sensors & first urges

Bladder filling stretches the wall (especially the **bladder neck**).

First urge ≈ 150 mL; **strong fullness ≈ 300–400 mL**.

Reflex arc (spinal, S2–S4)

Stretch receptors → **pelvic afferents** → **sacral cord (S2–S4)**.

Return via **parasympathetic pelvic efferents** → **detrusor muscle** contracts.

Once triggered, the reflex is **self-regenerative**: rising intravesical pressure opens the **bladder neck** (overcoming its tonic tone).

External sphincter control

Stretch of the neck also activates a pathway: sacral cord → **pudendal nerve** → **inhibition** of the **external urethral sphincter**.

If this reflex inhibition **exceeds voluntary contraction** from the brain, **urination occurs**.

After seconds to >1 min, the reflex **fatigues**, detrusor pressure falls, and filling resumes if voiding doesn't happen.

Higher centers (brain)

Baseline inhibition of the spinal reflex until voiding is appropriate.

Can **maintain continence** by tonic activation of the **external sphincter**.

When it's time to void: **facilitate sacral centers** (pontine micturition center) **and inhibit** the external sphincter → coordinated voiding.

Threshold is modulated by **facilitatory centers (pons)** and **inhibitory centers (midbrain)**.

Clinical applications:

Abnormalities of micturition:

[1] The atonic bladder: It is due to destruction of the sensory fibers from the bladder to the spinal cord which prevents transmission of stretch signals from the bladder and therefore, prevents micturition reflex contraction. Therefore, instead of emptying periodically, the bladder fills to capacity and overflows a few drops at a time through urethra (overflow dribbling or incontinence*).*

[2] The automatic bladder: If the spinal cord is damaged above the sacral region but the sacral cord segments are still intact, typical micturition reflexes can still occur. However, they are no longer controlled by the brain.

[3] The neurogenic bladder: It results in frequent and relatively uncontrolled micturition. This condition derives from partial damage in the spinal cord or the brain stem that interrupts most of the inhibitory signals. Therefore, facilitatory impulses passing continually down the cord keep the sacral centers so excitable that even a small quantity of urine will elicit an uncontrolled micturition reflex, and thereby promote frequent urination.

- **Dysuria;** difficulty or pain in urination. Possibly from kidney or bladder stones caused by “precipitation” of chemicals in the urine to form crystals
- **Polyuria;** frequent urination
- **Nocturnal enuresis;** bed-wetting—vasopression (hormone that decreases urine production) secretion does not increase at night as it should

Effect of spinal cord transection:

During spinal shock, the bladder is flaccid and unresponsive. It becomes overfilled, and urine dribbles through the sphincters (overflow incontinence). After spinal shock has passed, the voiding reflex returns, although there is, of course, no voluntary control and no inhibition or facilitation from higher centers when the spinal cord is transected.

Diuretics:

A substance that increases the rate of urine volume output by decreasing the rate of Na reabsorption from the tubules, which in turn causes natriuresis (increased Na output) and this in turn causes diuresis (increased water output or also called polyuria). The increased water output, in most cases, occurs secondary to inhibition of tubular Na reabsorption because Na remaining in the tubules acts osmotically to decrease water reabsorption. Because the renal tubular reabsorption of many solutes, such as K, Cl, Mg, and Ca, is also influenced secondarily by Na reabsorption, many diuretics raises renal output of these solutes as well. Diuresis is also associated with substances that are not easily reabsorbed by the renal tubules or filtered in excess such as urea, mannitol, sucrose, and glucose. These substances cause a marked increase in the concentration of osmotically active molecules or ions in the tubules. The osmotic pressure of these solutes then greatly reduces water reabsorption, flushing large amounts of tubular fluid on into the urine.

The effect of most diuretics on renal output of salt and water subsides within a few says. This is due to activation of other compensatory mechanisms initiated by decreased extracellular fluid volume such as reduced arterial blood pressure with consequent reduction of GFR and increases renin secretion. All these responses together override the chronic effects of the diuretics on urine output.

Diabetes insipidus:

- A disease associated with the inadequate secretion or action of ADH. When the secretion of ADH is adequate, due to a genetic defect in the ADH receptors or the aquaporin channels renders the kidneys incapable of responding to ADH, the condition is called nephrogenetic diabetes insipidus. Without proper ADH secretion or action, the collecting ducts are not very permeable to water, and so a large volume (5 to 10 L per day) of dilute urine is produced.
- The dehydration that results causes intense thirst, but a person with this condition has difficulty drinking enough to compensate for the large volumes of water lost in the urine. In this **case the specific gravity and the osmolarity of the urine are very low.**