# Counter-Current System Regulation of Renal Functions

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This presentation includes only the most important terms and facts. Its content by itself is not a sufficient source of information required to pass the Physiology exam.

A40. Water resorption, hyper- and hypotonic urine. Counter-current system.
A41. Osmotic, water and pressure diuresis
A39. Urea formation, physiological role in kidney

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A36. Renal blood flow and its autoregulation
A37. Glomerular filtration, principals and regulation, juxtaglomerular apparatus.
A38. Renal $Na^+$, $K^+$, $Cl^-$ transports, their regulation.
A44. Metabolic and endocrine renal function.

B65. Formation and secretion of posterior pituitary hormones
B70. Adrenal cortex. Functions, malfunctions.
B74. Natriuretic peptides
B84. Regulation of body fluid volume
B85. Regulation of constant osmotic pressure

# Water Transport in Tubules

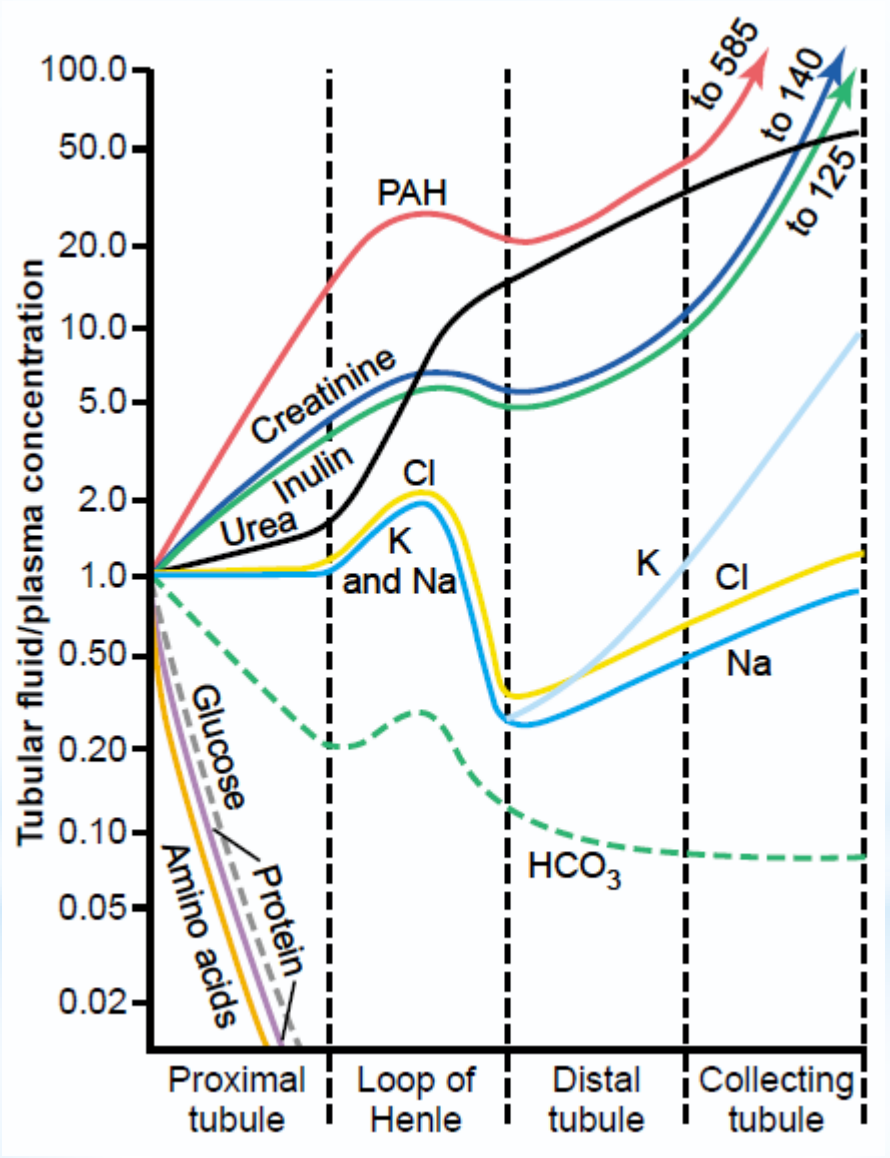
GFR 180 l/day

UFR ~1 l/day

UFR 0.5 l/day
(1400 mosm/l)

up to

UFR 23.3 l/day
(30 mosm/l)

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pronounced secretion in comparison with $H_2O$

pronounced reabsorption in comparison with $H_2O$

# Water Transport in Tubules

## *Proximal Tubule*

Intensive transport of solutes from the tubule to the intersticium forms an osmotic gradient which drives the water reabsorption.

The water reabsorption is facilitated by water channels in apical membranes of epithelial cells (protein aquaporin 1, not guided by ADH!).

From the proximal tubule, isoosmotic fluid outflows, its volume is notably decreased compared to the glomerular ultrafiltrate - 60-70% of solutes and water were reabsorbed.

# Water Transport in Tubules

## *Loop of Henle*

1) thin descending part - passive reabsorption of water (osmosis)
2) thick ascending part – impermeable for water, intensive reabsorption of solutes

From the thick ascending loop of Henle, hypotonic fluid outflows, its volume is notably decreased.

# Water Transport in Tubules

## *Distal Tubule*

1) the first part – analogical to the thick ascending loop of Henle – impermeable for water, reabsorption of solutes (reabsorption of $Na^+$ varies, regulated by aldosteron)
2) the next part – analogical to the cortical part of collecting duct – water reabsorption regulated by ADH (aquaporin 2)

Tonicity of the outflowing fluid depends on the actual level of ADH, may be even isotonic (dependent on the tonicity of the neighbouring tissue, the renal cortex is isotonic).

# Water Transport in Tubules

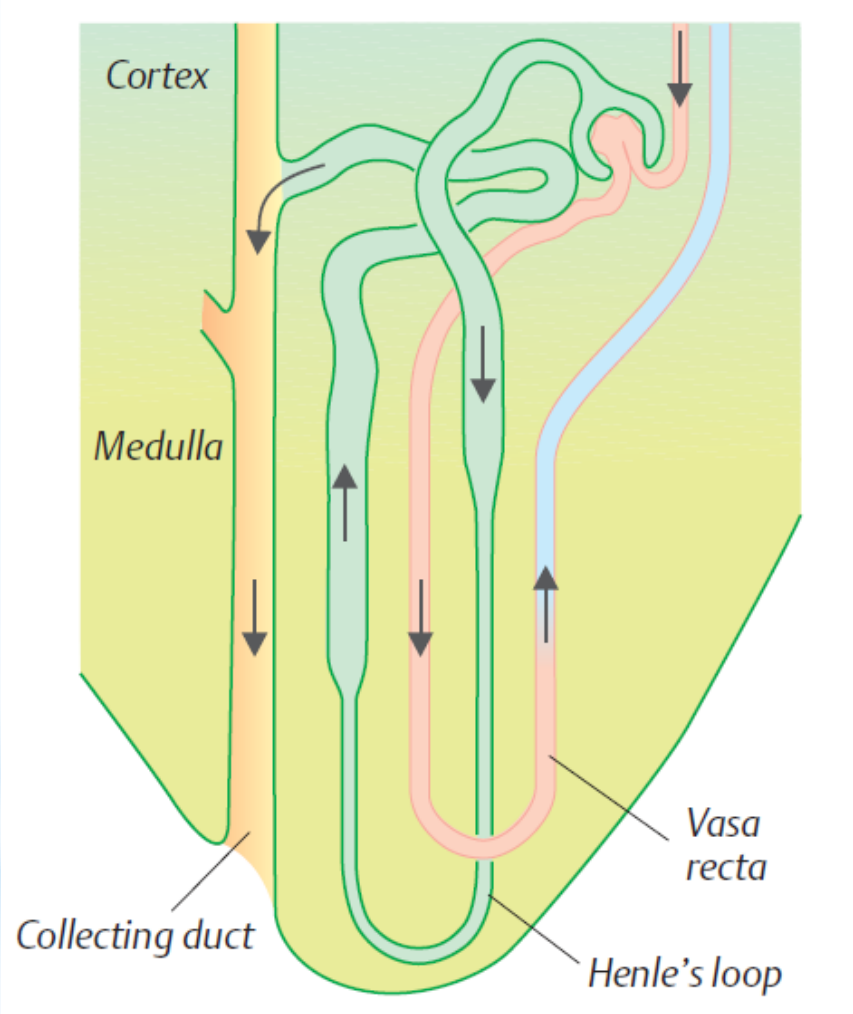
## *Collecting Duct*

1) the cortical part – water reabsorption regulated by ADH (aquaporin 2), isotonic intersticium

1) the medullar part – water reabsorption regulated by ADH (aquaporin 2), hypertonic intersticium

Tonicity of the outflowing fluid depends on the actual level of ADH, may be even hypertonic (dependent on the tonicity of the neighbouring tissue, the renal medulla is hypertonic); in the absence of ADH, notably hypotonic.

# Counter-Current System in Kidneys

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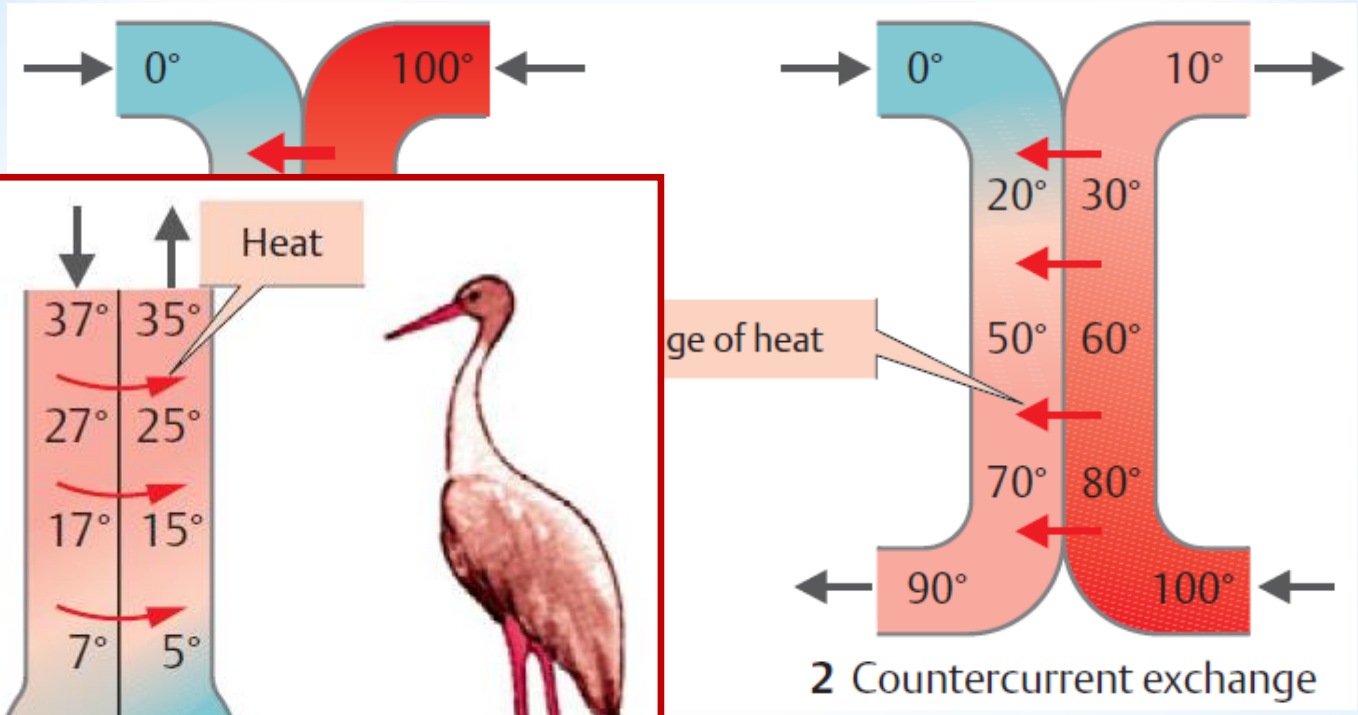
# Counter-Current System in Kidneys




2 Countercurrent exchange

3 Countercurrent exchange (heat) in loop

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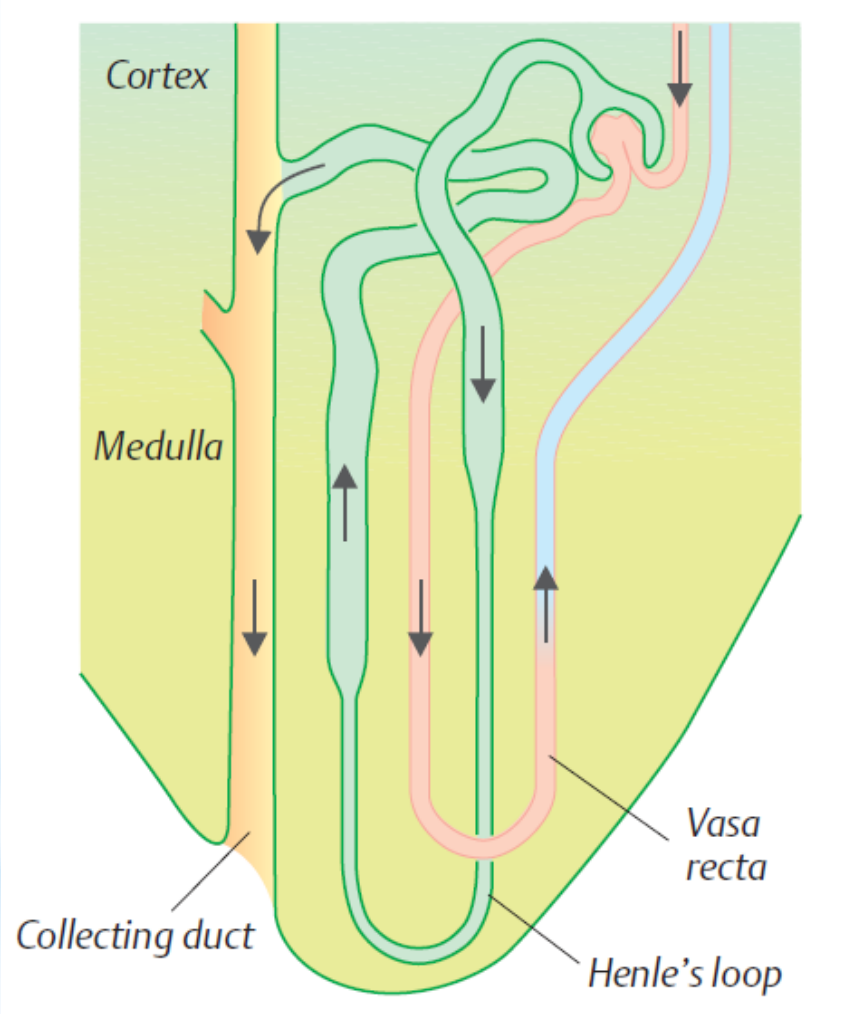
# Counter-Current System in Kidneys

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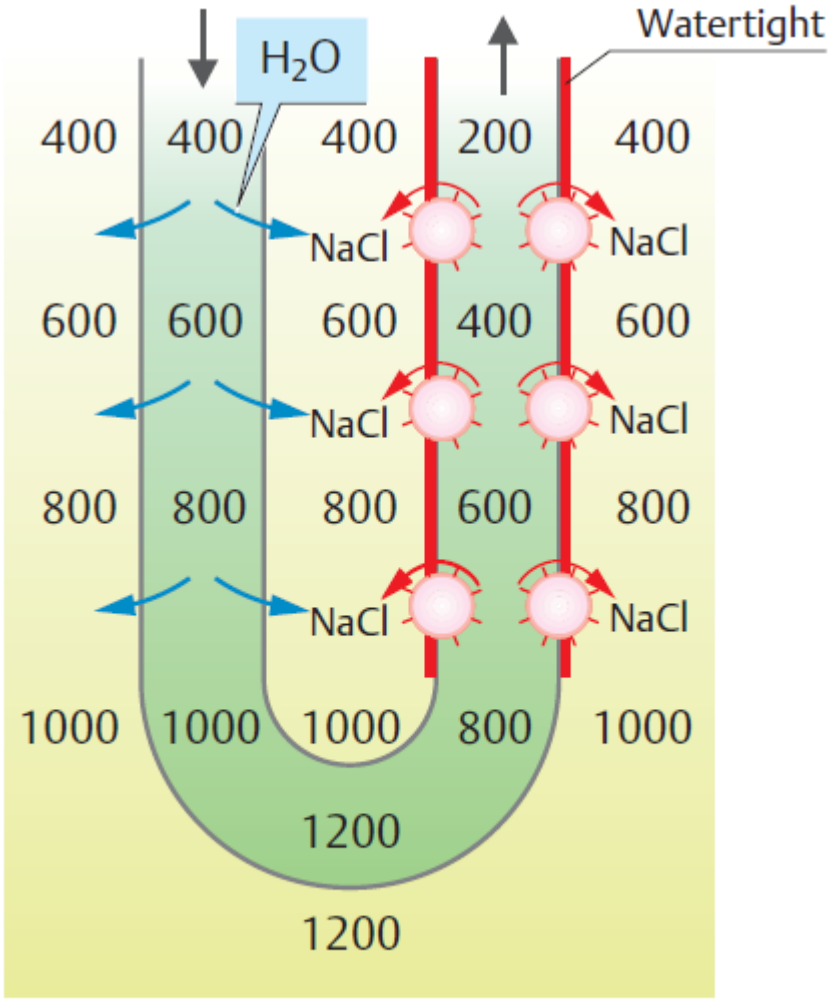
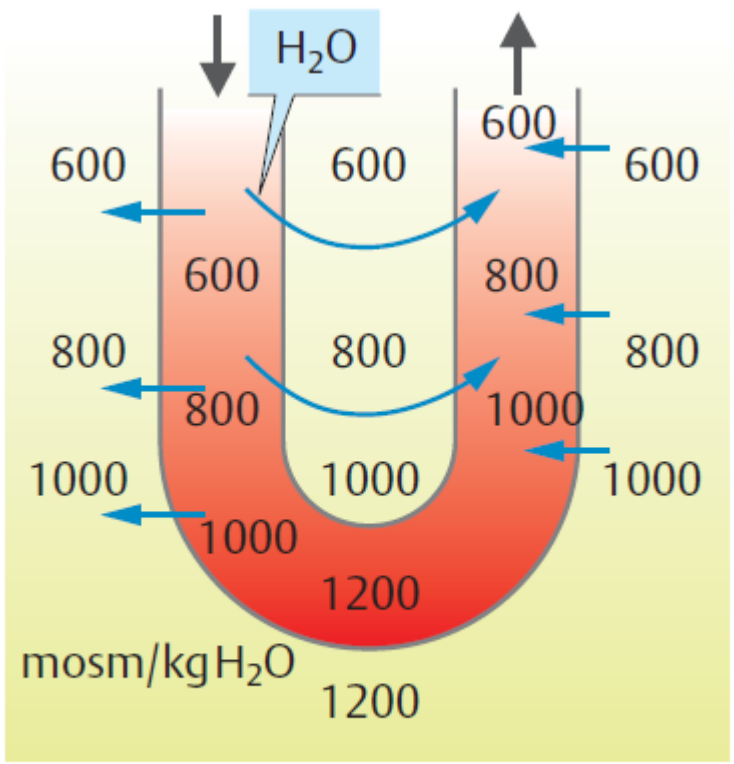
# Counter-Current System in Kidneys




**5** Countercurrent multiplier (Henle's loop)



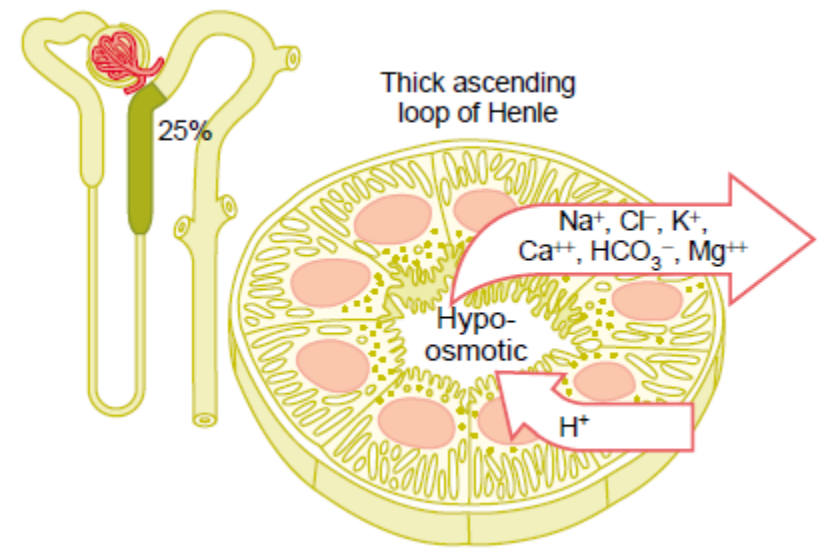

**4** Countercurrent exchange (water) in loop (e.g. vasa recta)

# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Loop of Henle*

1) Active transport of $Na^+$, co-transport of $Na^+$ with $K^+$ and $Cl^-$ from ascending loop of Henle; gradient even 200 mOsm/l

2) Impermeability of ascending loop of Henle for water

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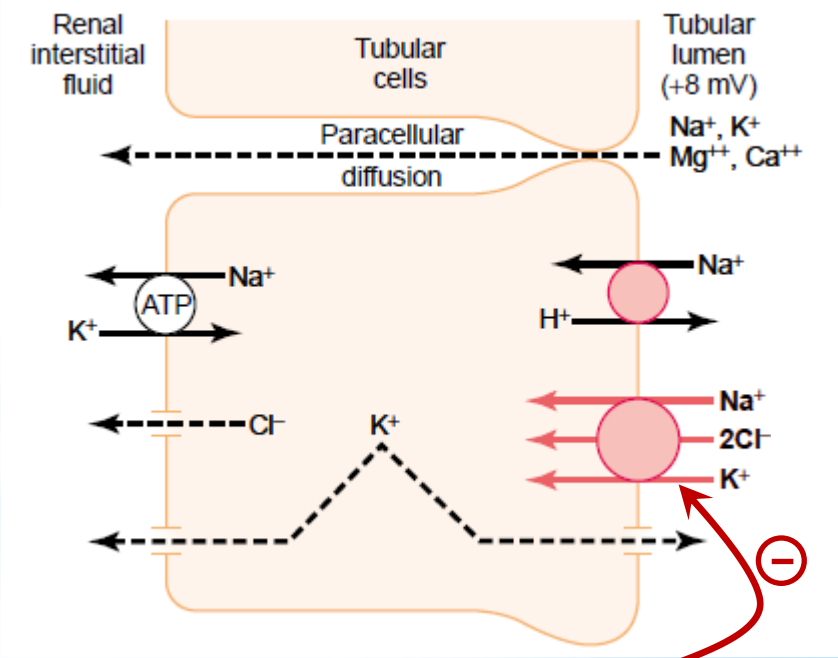
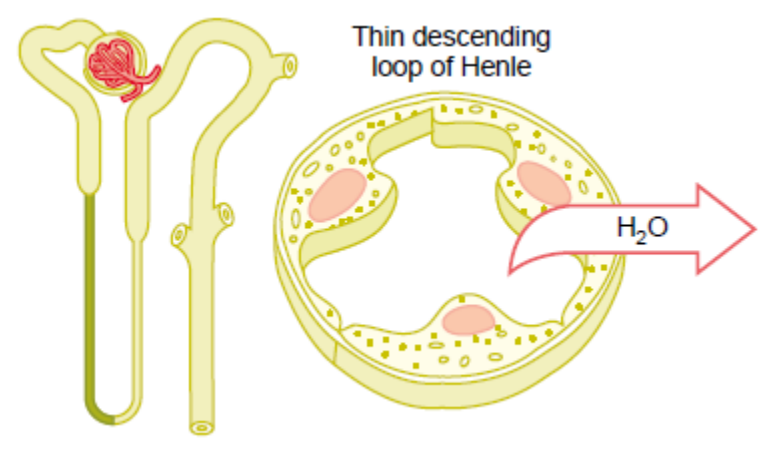



diuretics (*e.g.* furosemid)

# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Loop of Henle*

1) Active transport of $Na^+$, co-transport of $Na^+$ with $K^+$ and $Cl^-$ from ascending loop of Henle; gradient even 200 mOsm/l
2) Impermeability of ascending loop of Henle for water
3) Permeability of descending loop of Henle for water

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# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Loop of Henle*

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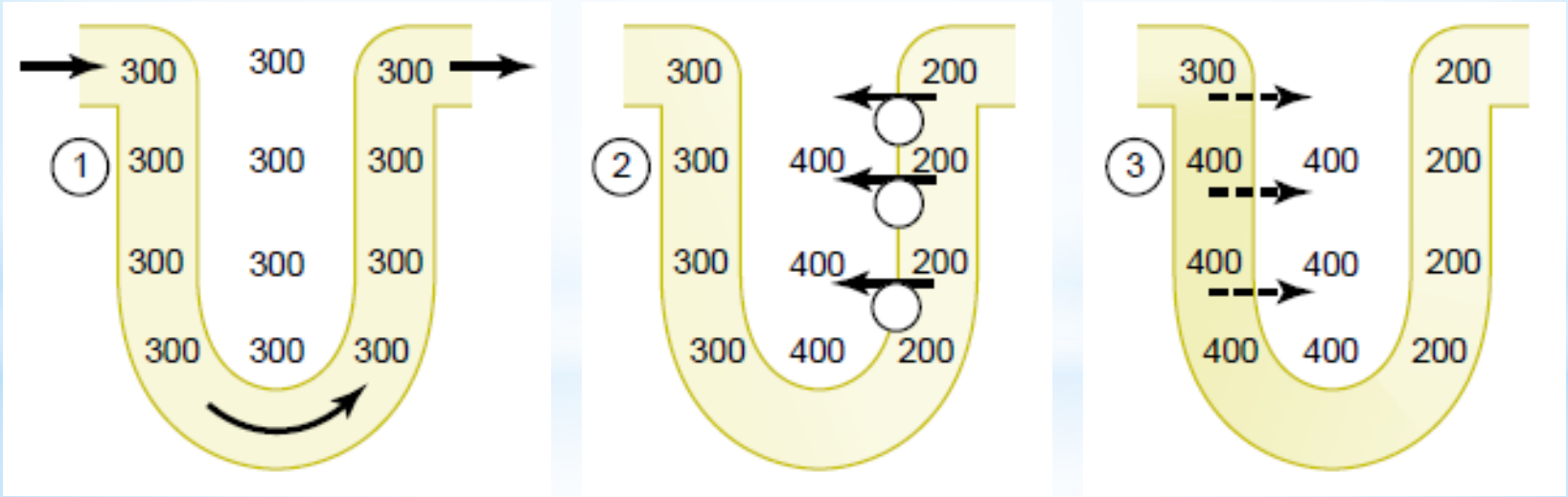


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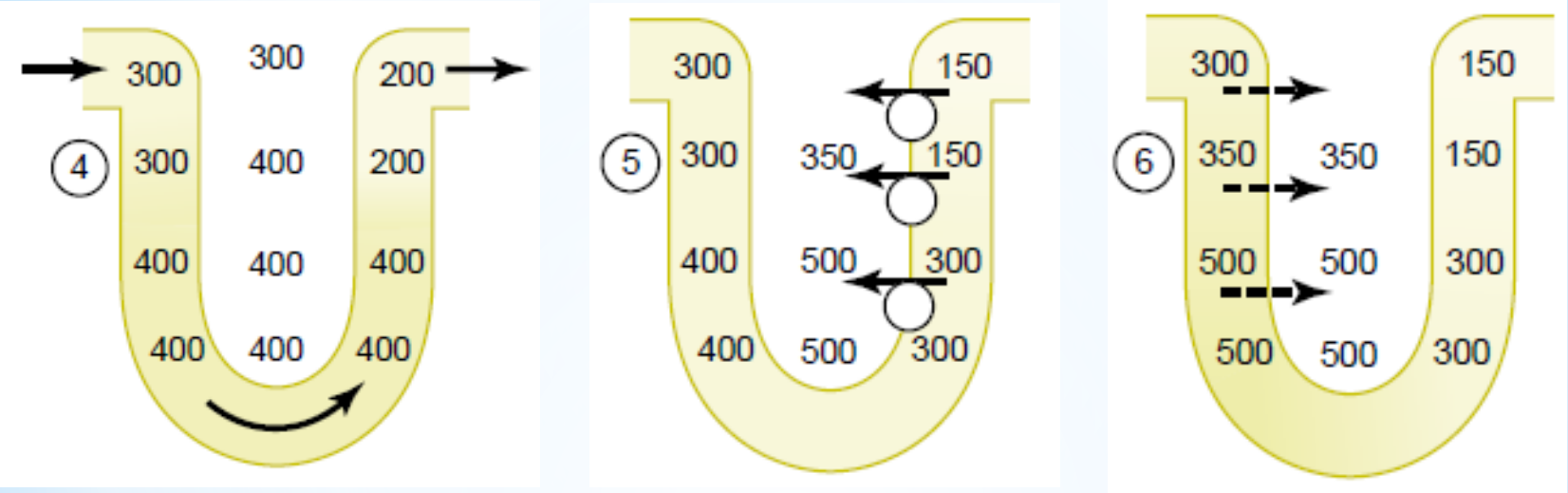
# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla - Role of Loop of Henle*

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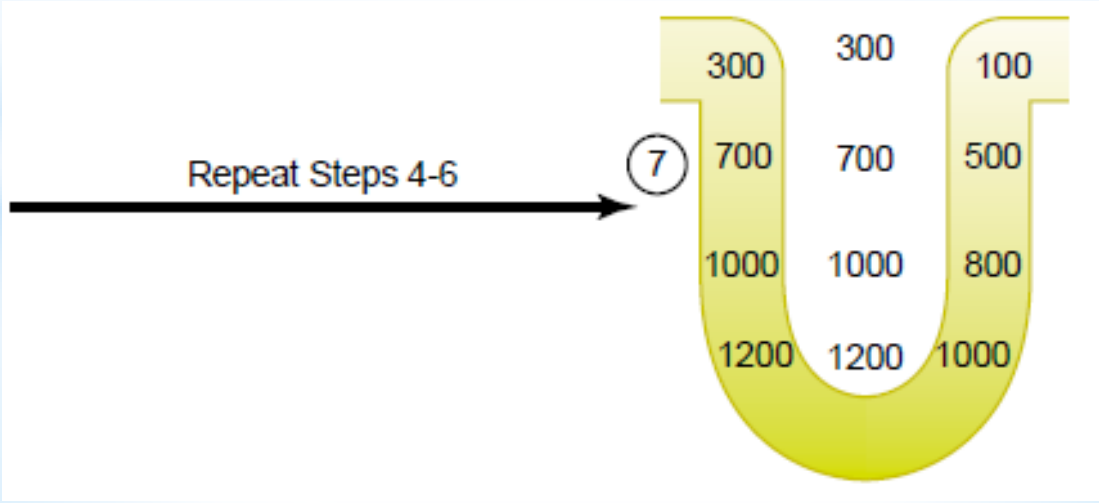
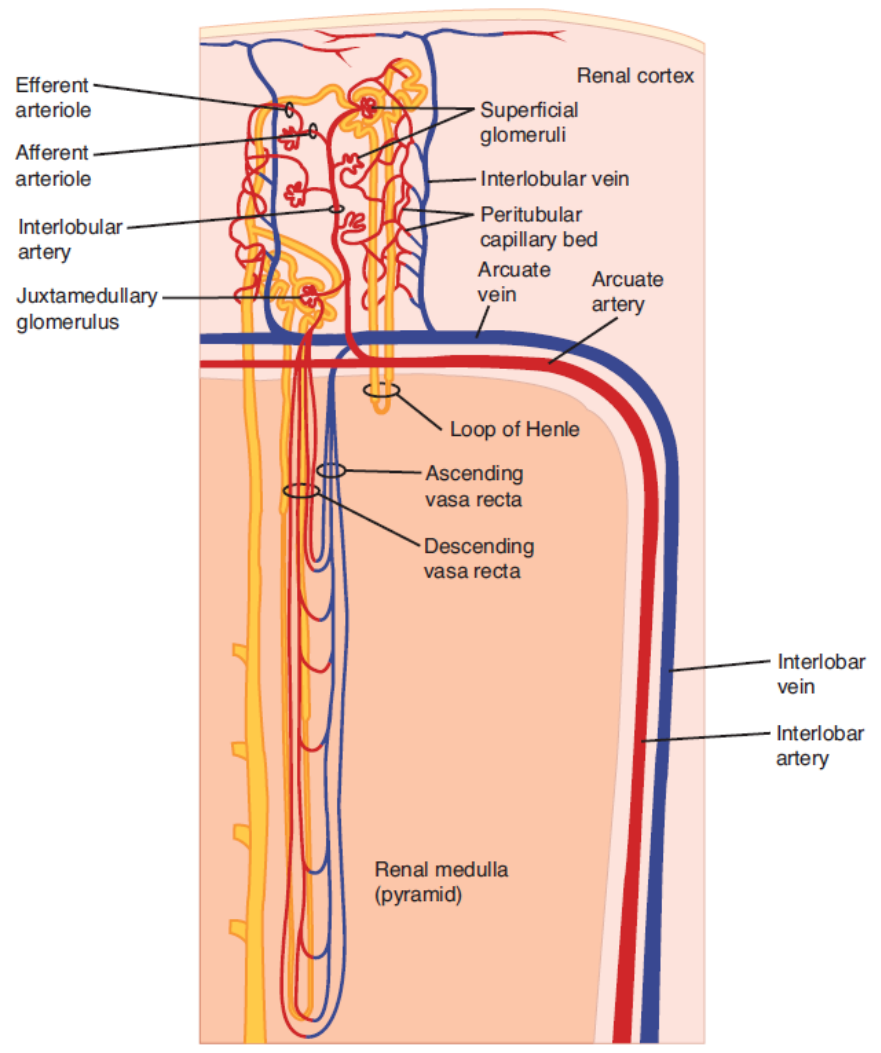


# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Vasa Recta*

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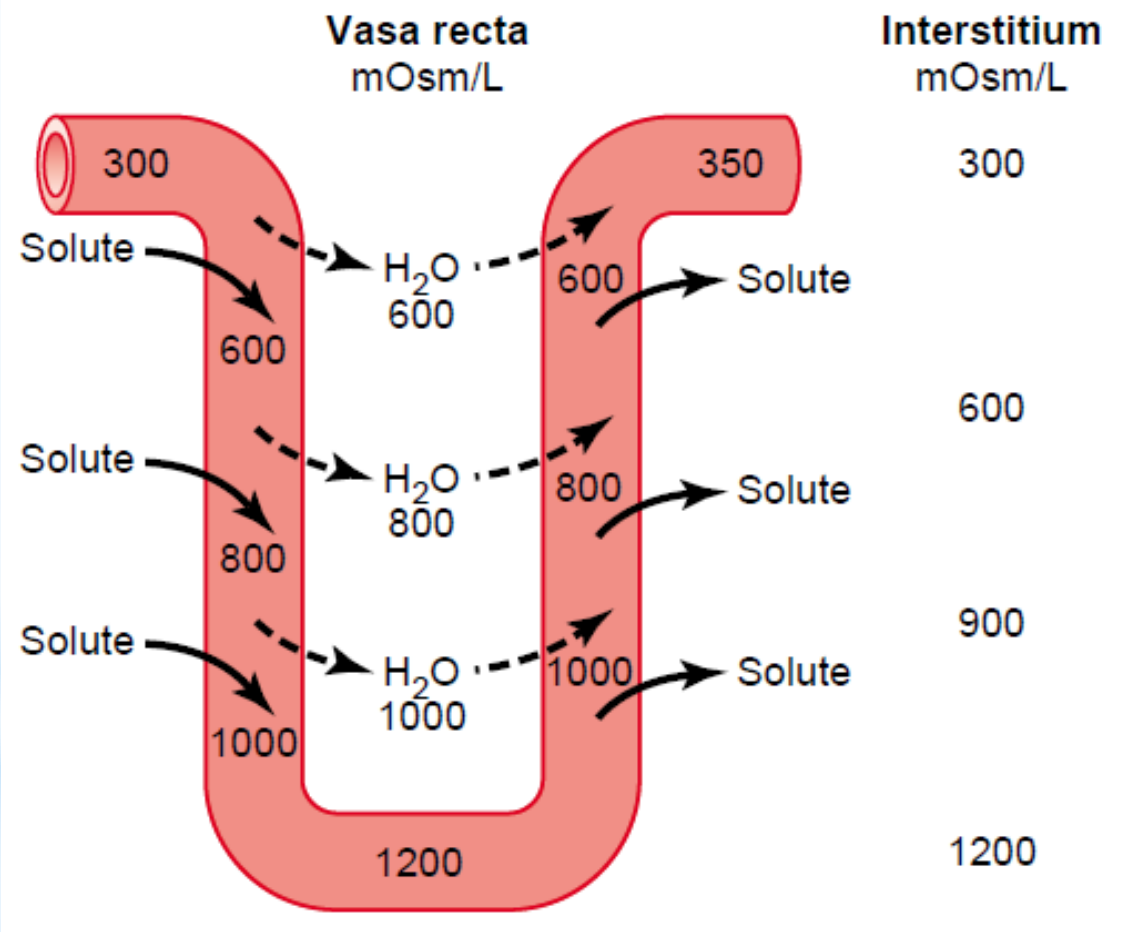
# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Vasa Recta*

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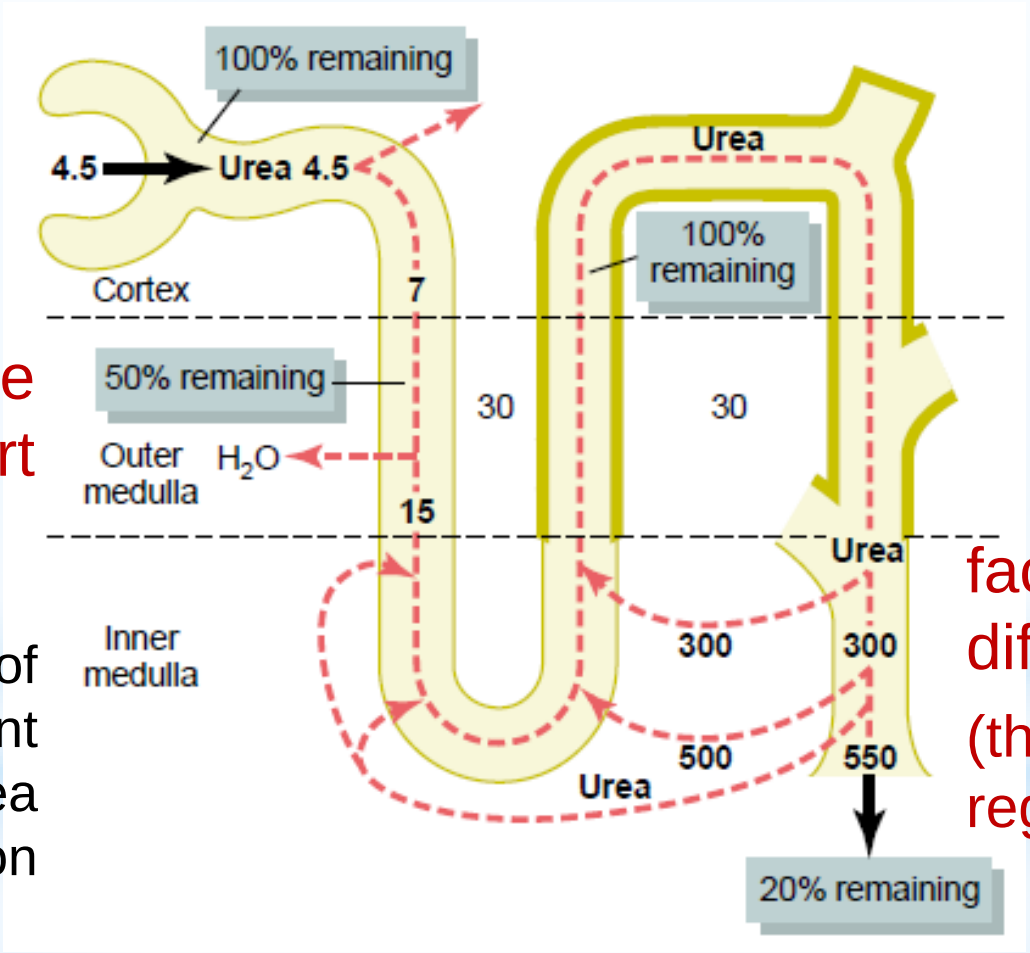
# Counter-Current System in Kidneys

## *Hyperosmotic Renal Medulla – Role of Urea*

passive transport

following parts of tubulus resistant to urea reabsorption




facilitated diffusion

(through UT-A1 - regulated by ADH)

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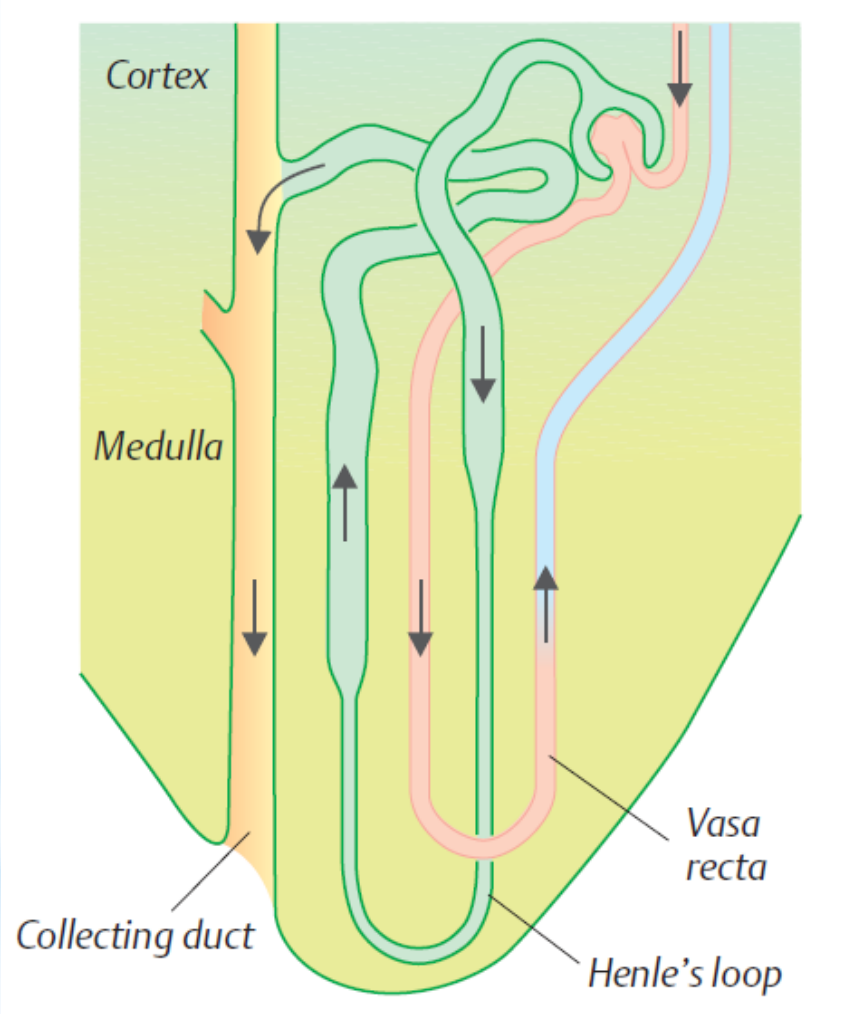
# Counter-Current System in Kidneys

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# *Water Diuresis*

- following drinking of a higher amount of hypotonic fluid
- starts ~15 min after drinking, maximum reached within ~40 min
- drinking itself → slightly ↓ ADH secretion
- water reabsorption in the intestine → ↓ plasma osmolarity – osmoreceptors in the hypothalamus → notable ↓ ADH secretion → ↓ water reabsorption in tubulus → ↑ diuresis

# *Water Diuresis*

- following drinking of a higher amount of hypotonic fluid

# *Water Intoxication*

- the water intake per time > the amount of water which can be excreted (maximal diuresis ~16 ml/min)
- hypotonic fluid from plasma to cells → cellular edema, symptoms of water intoxication (convulsions, coma even death due to the brain edema)
- iatrogenic – not restricted water intake after application of exogenic ADH or during its higher secretion induced by non-osmotic stimuli (*e.g.* surgery)

# *Osmotic Diuresis*

- induced by presence of non-absorbed osmotically active solutes in renal tubules
- non-absorbed solutes (*e.g.* glucose - *diabetes mellitus*) in the proximal tubules → osmotic effect – water retained in the tubulus

- ↓ transepithelial gradient for $Na^+$ ($Na^+$ in the tubule in a higher amount of water) → inhibition of $Na^+$ reabsorption in the proximal tubule → $Na^+$ retained in the tubule ~ further osmotic load → further retaining of water in the tubule

# *Osmotic Diuresis*

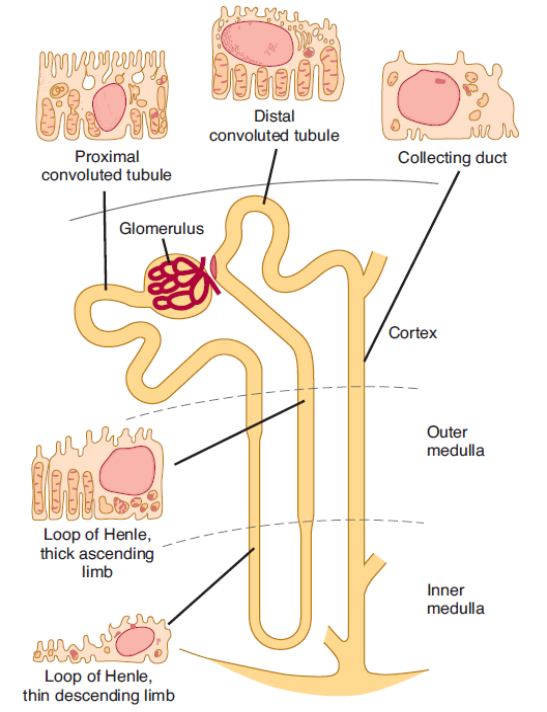
- induced by presence of non-absorbed osmotically active solutes in renal tubules

- more isotonic fluid with higher total amount of $Na^+$ into the loop of Henle → ↓ reabsorption of solutes in the ascendent loop of Henle after reaching the borderline concentration gradient for $Na^+$ reabsorption → ↓ hypertonicity of the renal medulla

- more fluid flows through other parts of tubulus + ↓ hypertonicity of the renal medulla → ↓ water reabsorption in the collecting duct → ↑ diuresis, urine with an increased amount of solutes

# Regulation of Renal Functions

## Regulation of Renal Blood Flow

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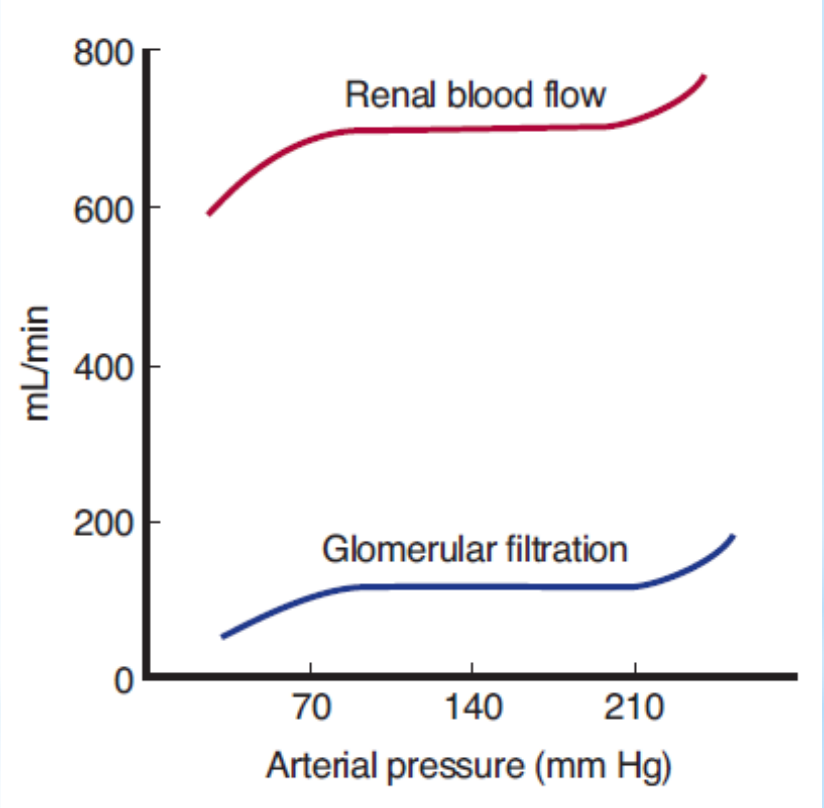
# Regulation of Renal Blood Flow

1) Myogenic Autoregulation
2) Neural Regulation
3) Humoral Regulation

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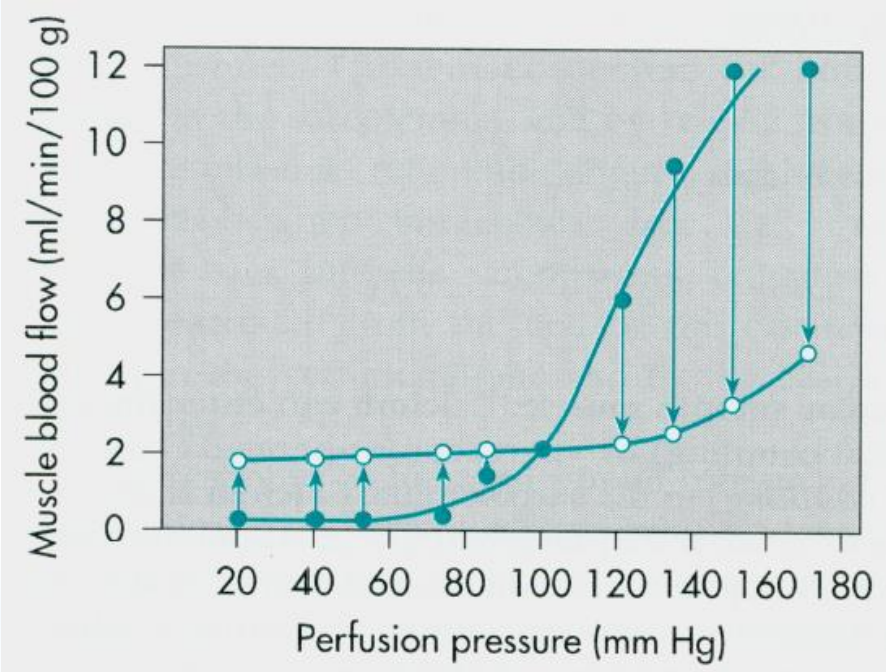
# Regulation of Renal Blood Flow

## 1) Myogenic Autoregulation

- dominates
- provides stable renal activity by maintaining stable blood flow at varying systemic pressure (stable glomerular pressure and, thus, also stable glomerular filtration rate)



# Regulation of Renal Blood Flow

## 2) Neural Regulation

- conformed to demands of systemic circulation
- renal blood flow forms 25% of the cardiac output, thus, it considerably influence BP
- **sympathetic system - norepinephrine**

  light exertion (both emotional and physical) + upright body posture → ↑ sympathetic tone → ↑ tone of *v. aff.* and *eff.* → ↓ renal blood flow but without ↓ GFR (↑ FF)

  higher ↑ of sympathetic tone - during anesthesia and pain - GFR may already ↓

  in healthy people – minor impact

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

- contribute to regulation of systemic BP and regulation of body fluids
- **norepinephrine, epinephrine** (from adrenal medulla)
  $\rightarrow$ constriction of aff. and eff. arterioles $\rightarrow \downarrow$ renal blood flow and GFR
  in agreement with $\uparrow$ activity of sympathetic system
  (small impact with the exception of serious conditions, for example serious bleeding)

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

- contribute to regulation of systemic BP and regulation of body fluids
- **norepinephrine, epinephrine** (from adrenal medulla)

  $\rightarrow$ constriction of aff. and eff. arterioles $\rightarrow \downarrow$ renal blood flow and GFR
- **endothelin**

  constriction of aff. and eff. arterioles $\rightarrow \downarrow$ renal blood flow and GFR

  released locally from the impaired endothel (physiological impact - hemostasis; pathologically increased levels at the toxemia of pregnancy, acute renal failure, chronic uremia)

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

- contribute to regulation of systemic BP and regulation of body fluids
- **NO** (from the endothel)

  continual basal production → vasodilation in the kidney → stable renal blood flow and GFR

- **prostanglandins ($PGE_2$, $PGI_2$), bradykinin**

  → vasodilation

  minor impact under physiological conditions

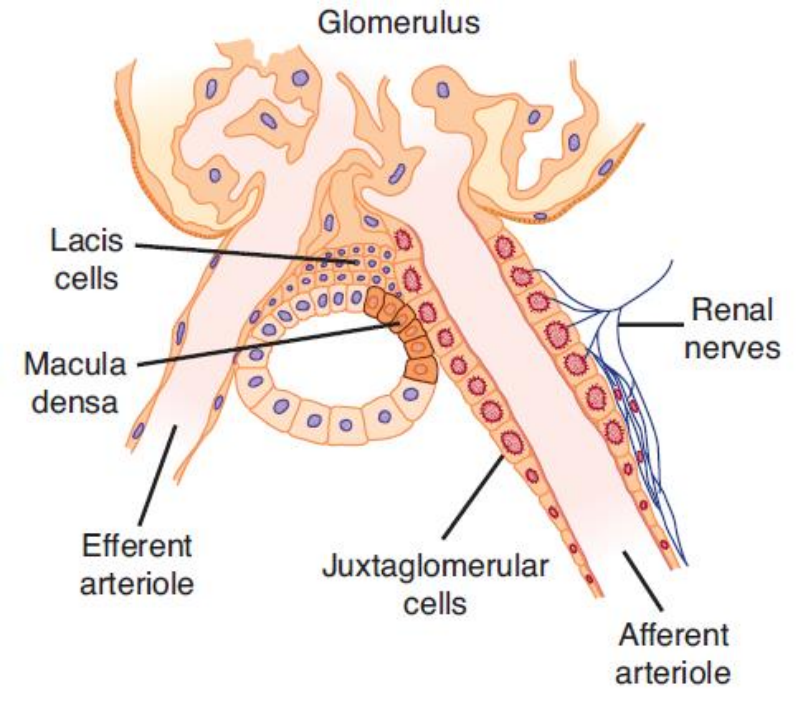
  decrease the effect of vasoconstrictive substances which reduce marked ↓ of renal blood flow and GFR

  non-steroidal anti-inflammatory agents during stress (surgery, ↓ fluid volume) may → notably ↓ GFR

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

- contribute to regulation of systemic BP and regulation of body fluids
- **Renin-Angiotensine System**

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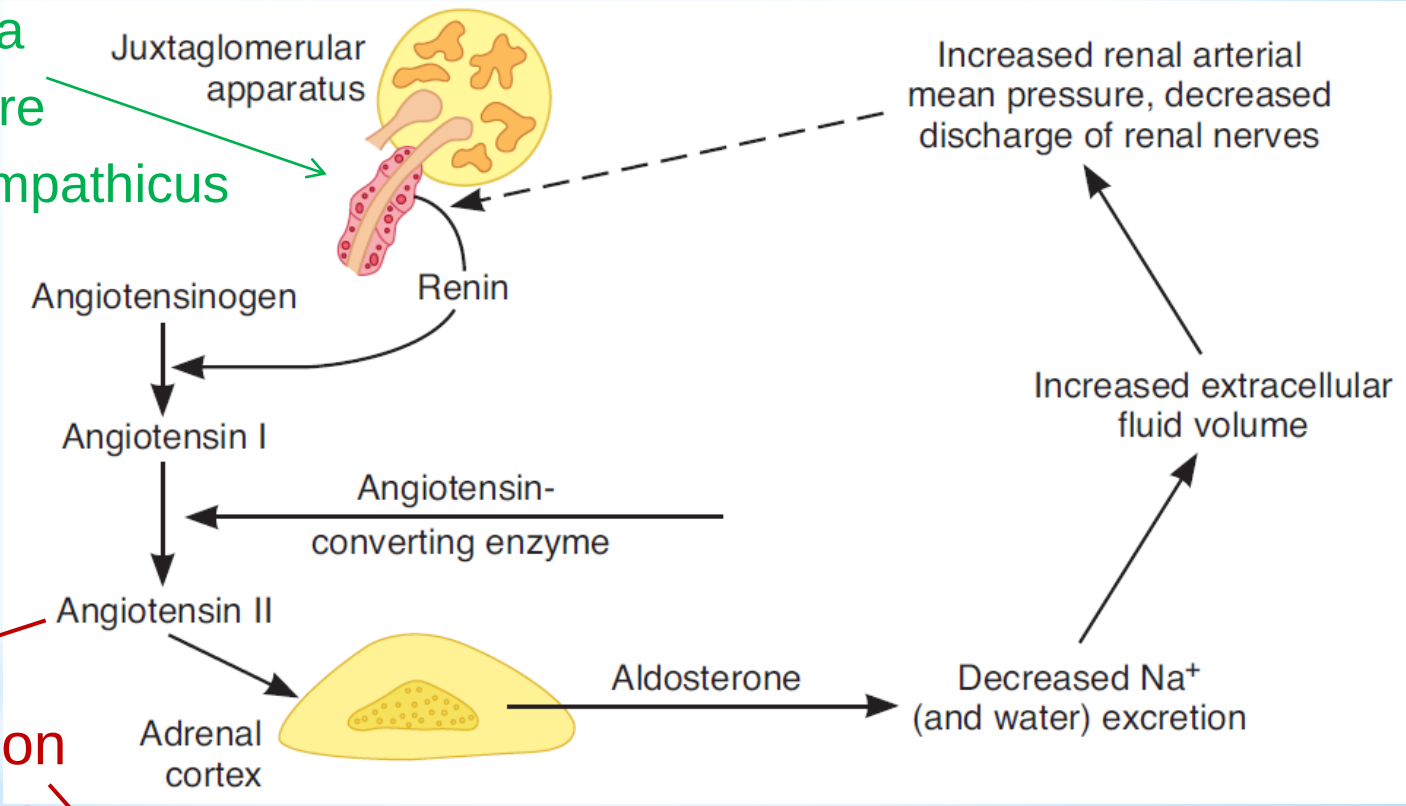
# Regulation of Renal Blood Flow

## *Renin-Angiotensine System*

↓ $Na^+$ in plasma

↓ blood pressure

↑ activity of sympathicus (β rec.)




vasoconstriction (more in eff. a.)

thirst, ADH

↓ renal blood flow but ↑ GFR

(usually during ↓ BP or fluid depletion – prevention of ↓ GFR + ↑ tubular reabsorption of $Na^+$ and water due to ↓ $P_c$ in peritubular capillaries)

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

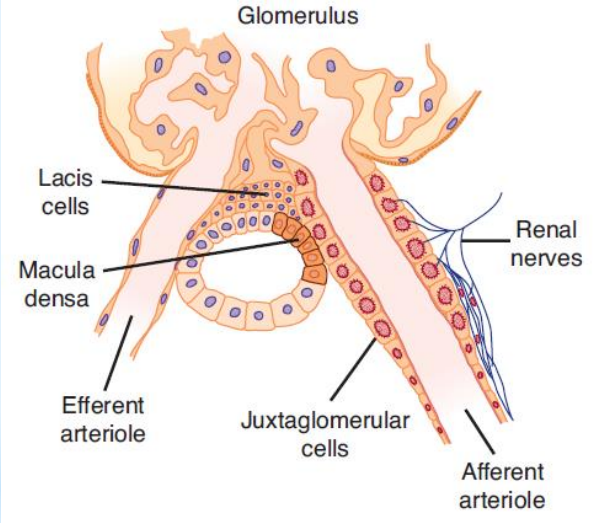
### *Tubuloglomerular Feedback*

- provides constant NaCl load in the distal tubule, prevents excessive changes of renal excretion

# Regulation of Renal Blood Flow

## 3) Humoral Regulation

### *Tubuloglomerular Feedback*

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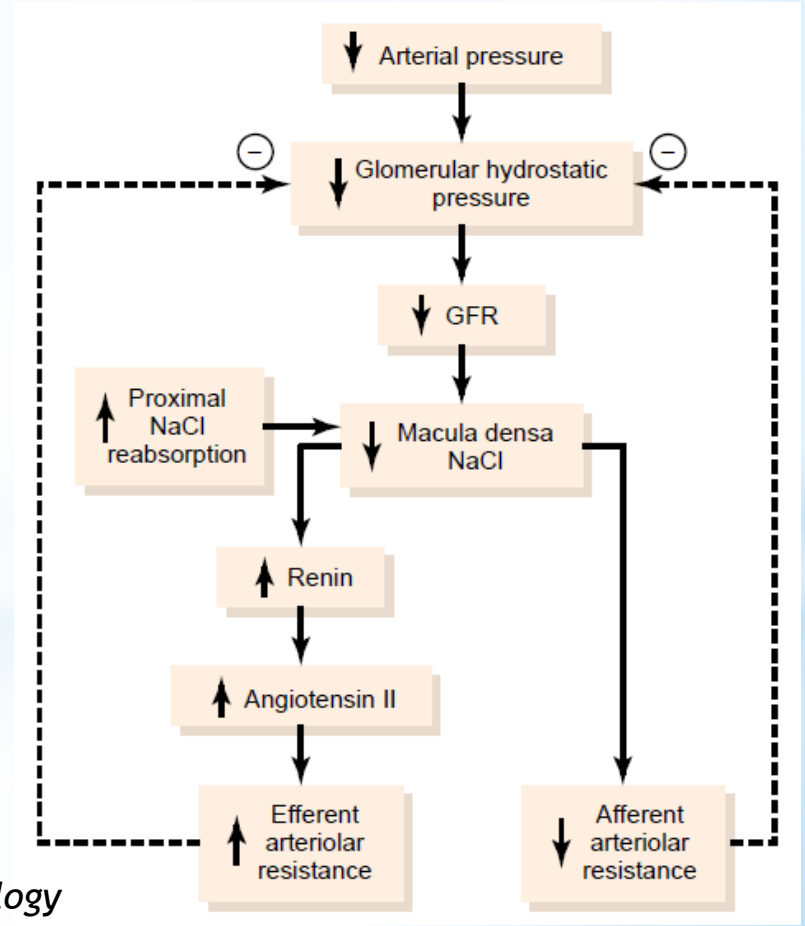


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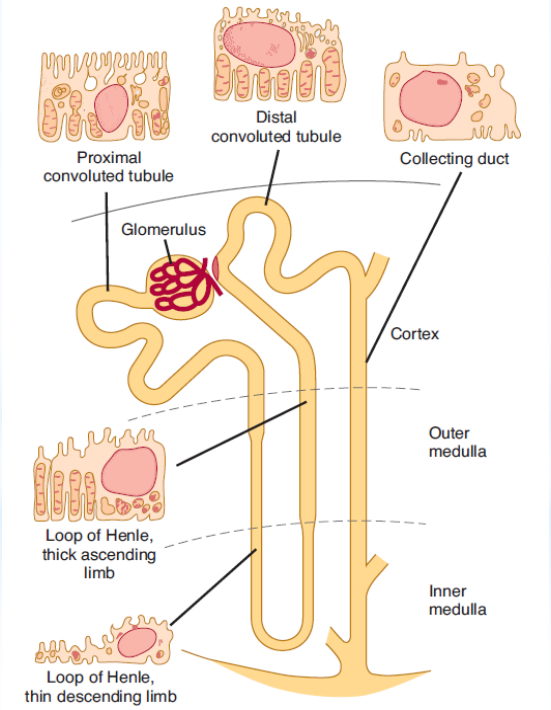
# Regulation of Renal Functions

## Regulation of Glomerular Filtration
## Regulation of Tubular Reabsorption

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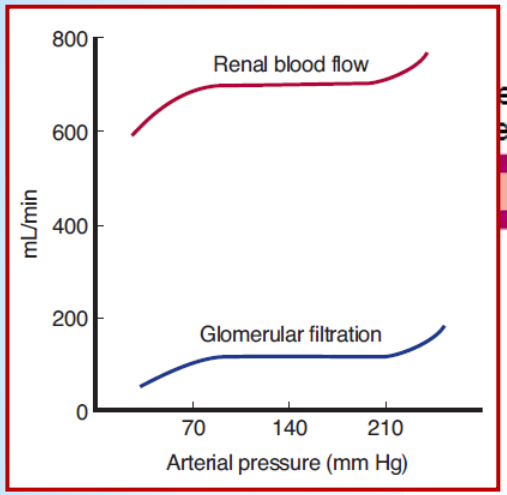
# Regulation of Glomerular Filtration

GFR = $K_f$ · net filtration pressure

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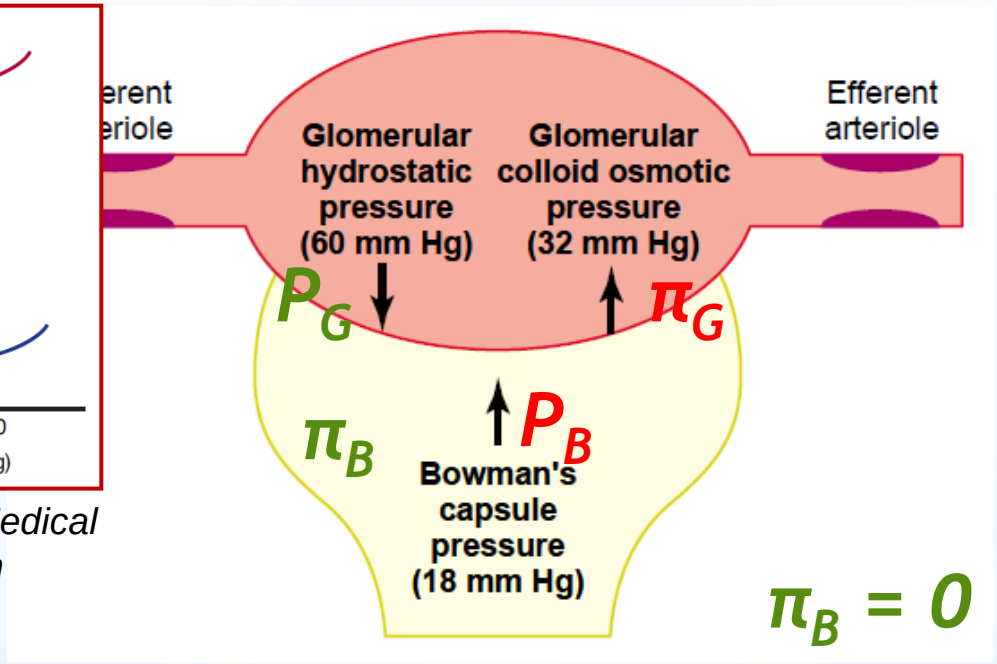


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Under physiological conditions:

net filtration pressure = $P_G + \pi_B - P_B - \pi_G = 60 + 0 - 18 - 32 = 10$ mmHg

$$GFR = K_f \cdot (P_G + \pi_B - P_B - \pi_G)$$

# Regulation of Tubular Reabsorption

- controls balance between the glomerular filtration and tubular reabsorption

1) Local Regulation
2) Neural Regulation
3) Humoral Regulation

*Glomerulotubular Balance*

- ↑ tubular reabsorption rate at ↑ load of fluid flowing through tubules (prevention of overload of distal parts of tubulus)
- namely in the proximal tubule
- local mechanisms (present even in isolated proximal tubule)
- mechanisms not fully known (changes of physical forces?)

# Regulation of Tubular Reabsorption

1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Intersticium*

- tubular reabsorption is controlled by hydrostatic and coloid osmotic forces (similary to GFR)

$$GFR = K_f \cdot \text{net filtration pressure}$$

$$TRR = K_f \cdot \text{net reabsorptive force}$$

# Regulation of Tubular Reabsorption

1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Intersticium*

$K_f$ - $\uparrow K_f \rightarrow \uparrow$ TRR and *vice versa*

- rather stable under physiological conditions

# Regulation of Tubular Reabsorption

1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Intersticium*

- tubular reabsorption is controlled by hydrostatic and coloid osmotic forces (similary to GFR)

$$GFR = K_f \cdot \text{net filtration pressure}$$

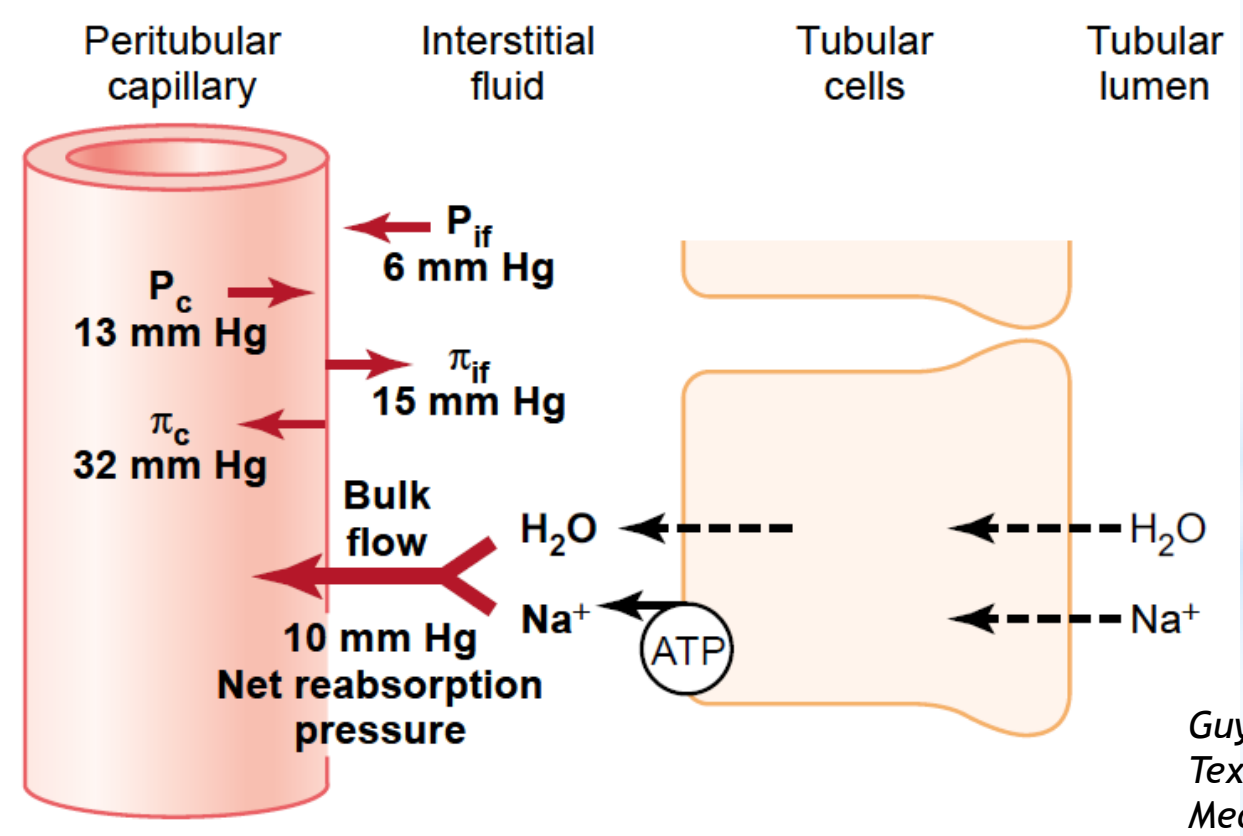
$$\downarrow$$

$$TRR = K_f \cdot \text{net reabsorptive force}$$

# Regulation of Tubular Reabsorption

1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Interstitium*

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# Regulation of Tubular Reabsorption

1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Intersticium – renal haemodynamics influence*

$P_c$ - **BP** (↑ BP → ↑ $P_c$ → ↓ TRR) *autoregulation!*

- **resistance of aff. and eff. arterioles**

  (↑ resistance → ↓ $P_c$ → ↑ TRR)

  (↑ resistance of eff. a. → ↓ $P_c$ + ↑ $P_g$ → ↑ TRR + ↑ GFR )

$\pi_c$ - **π in plasma**(↑ π → ↑ $\pi_c$ → ↑ TRR)

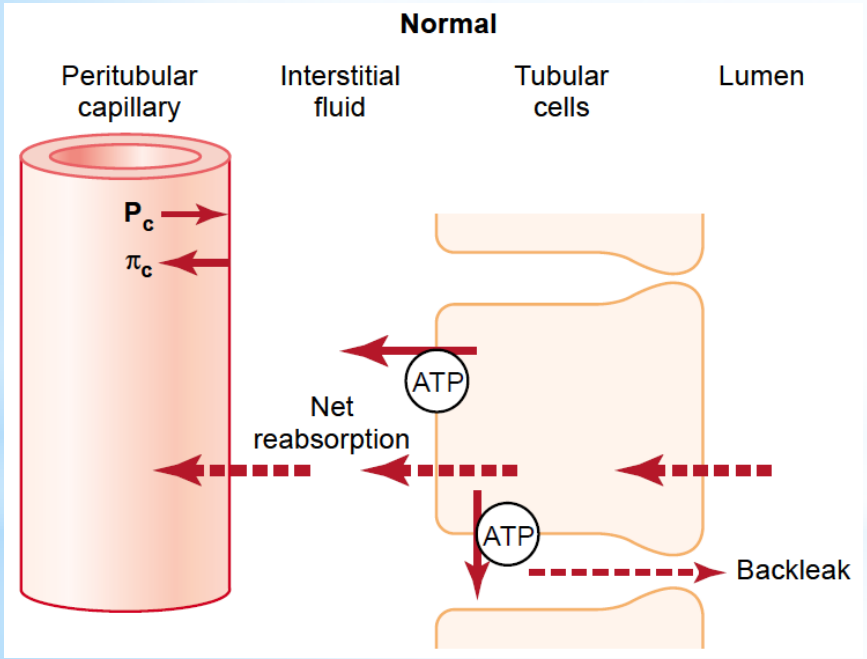
- **fitration fraction** (↑ FF → ↑ $\pi_c$ → ↑ TRR)

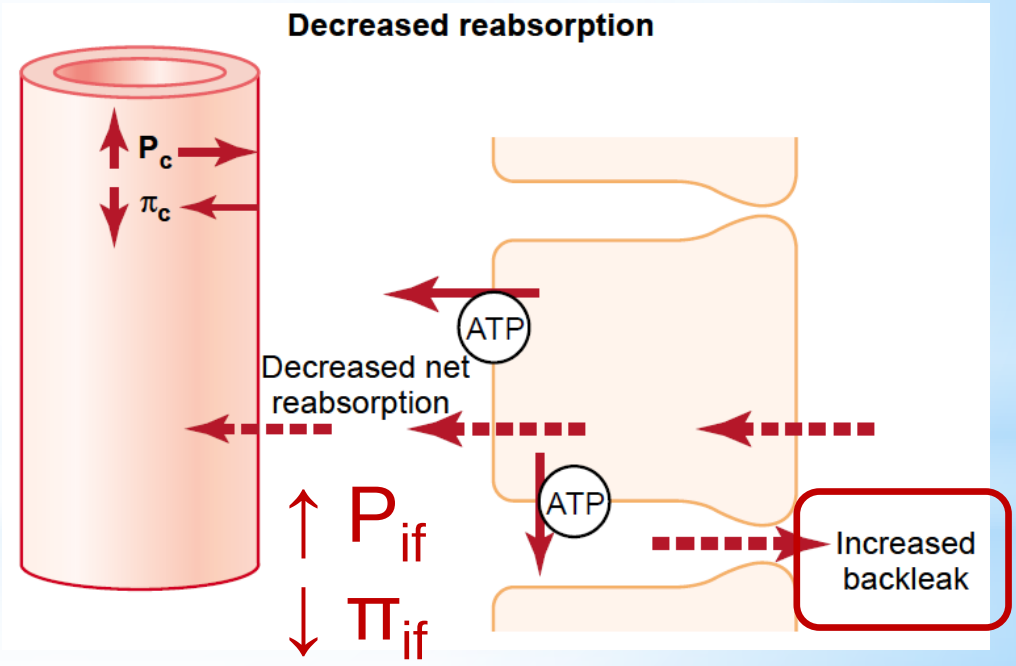
  (FF = GFR /renal plasma flow)

# Regulation of Tubular Reabsorption

## 1) Local Regulation

*Physical Forces in Peritubular Capillaries and in Renal Intersticium – changes in intersticium ($P_{if}$, $\pi_{if}$)*

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↑ reabsorption → ↓ $P_{if}$ a ↑$\pi_{if}$ → ↓ *backleak*

# Regulation of Tubular Reabsorption

## 1) Local Regulation

*Pressure Natriuresis and Pressure Diuresis*

- increased excretion of salt and water at ↑ BP
- mechanisms:

↑ GFR

physiologically at common BP (75-160 mmHg)
slight effect on diuresis due to autoregulation of renal blood flow and GFR

*vs.* impaired autoregulation (renal diseases)

# Regulation of Tubular Reabsorption

## 1) Local Regulation

*Pressure Natriuresis and Pressure Diuresis*

- increased excretion of salt and water at ↑ BP
- mechanisms:

↑ GFR

↓ TRR

↑ BP → slight ↑ $P_c$ → ↑ $P_{if}$ → ↑ *backleak* → ↓ TRR

↓ formation of angiotensine II

↑ BP → ↓ secretion of renin → ↓ formation of angiotensine II → ↓ reabsorption of $Na^+$ (both directly and through ↓ secretion of aldosteronu)

# Regulation of Tubular Reabsorption

## 2) Neural Regulation

***Sympathicus***

→ ↑ reabsorption of salt and water

- during a small ↑ of its activity (α-rec. in epithelia):

  directly through ↑ reabsorption of $Na^+$ in the proximal tubule, in the ascending loop of Henle and may be also in the distal parts of tubulus

- during a notable ↑ of its activity indirectly:

  → constriction of aff. and eff. arterioles → ↓ renal blood flow → ↓ $P_c$ → ↑ TRR

# Regulation of Tubular Reabsorption

3) Hormonal Regulation

- impact – separate regulation of reabsorption/excretion of particular solutes (other mechanisms are nonspecific – influence the total TRR)

*Aldosteron*

*Angiotensine II*

*Natriuretic peptides (namely ANP)*

*Antidiuretic hormone*

*Parathormone, …*

*Urodilatin (renal NP)*

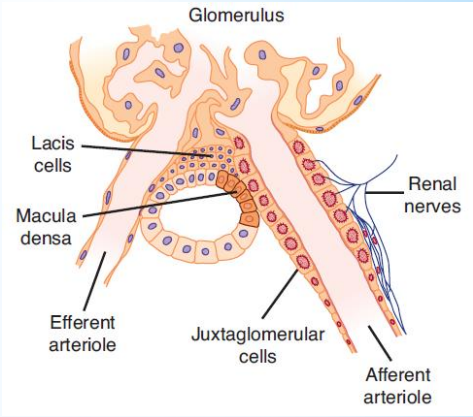
# Regulation of Tubular Reabsorption

## 3) Hormonal Regulation

***Aldosteron***

***Angiotensine II***

- RAS

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***Aldosteron***

- principal cells of the distal tubule and of the cortical part of collecting duct
- stimulation of activity and number of $Na^+/K^+$ ATPases + ↑ permeability of the luminal membrane for $Na^+$ (epithelial $Na^+$ channels)

  → ↑ reabsorption of $Na^+$ (and water)

  → ↑ secretion of $K^+$

# Regulation of Tubular Reabsorption

3) Hormonal Regulation

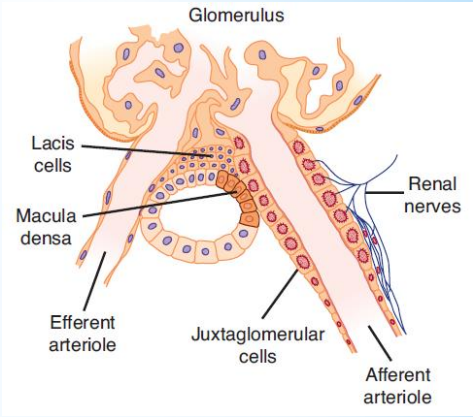
***Aldosteron***

***Angiotensine II***

- RAS

***Angiotensine II***

- shifts BP and extracellular volume back to normal

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# Regulation of Tubular Reabsorption

## 3) Hormonal Regulation

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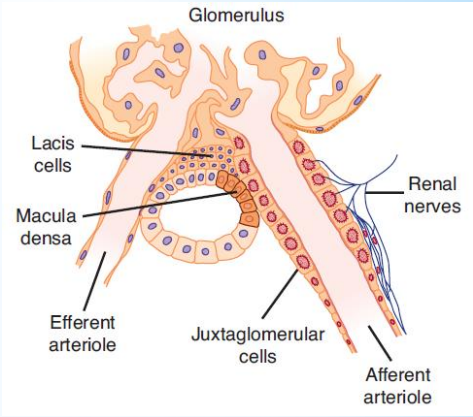


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***Angiotensine II***

→ ↑ reabsorption of $Na^+$ (and water):

a) stimulation of aldosteron secretion

b) constriction of eff.a.

→↓$P_c$ → ↑ TRR (namely in the proximal tubule)

→ ↓ blood flow → ↑ FF → ↑ $\pi_c$ → ↑ TRR

c) direct stimulation of $Na^+$ reabsorption in the tubulus ($Na^+/K^+$, $Na^+/H^+$, $Na^+/HCO_3^-$)

# Regulation of Tubular Reabsorption

## 3) Hormonal Regulation

***Natriuretic peptides (namely ANP)***

increased tension of atrial cardiomyocytes

→ ↑ secretion of ANP:

→ ↓ reabsorption of salt and water directly (namely in the collecting ducts)

→ ↓ secretion of renin → ↓ angiotensine II → ↓ TRR

The level of ANP chronically increased at congestive heart failure which helps to reduce retention of salt and water.

# Regulation of Tubular Reabsorption

## 3) Hormonal Regulation

***Antidiuretic hormone (ADH)***

- controls excretion of water

↑ osmolality of plasma (osmoreceptors)

→ ↑ secretion of ADH – $V_2$ receptors in the final part of the distal tubule and in the collecting ducts → fusion of the vesicles with water channels (aquaporins 2) with the luminal membranes of epithelial cells

→ ↑ reabsorption of water by osmosis

# Regulation of Tubular Reabsorption

## 3) Hormonal Regulation

*Parathormone*

- controls excretion of $Ca^{2+}$

↓ calcemia

→ ↑ secretion of parathormone:

→ ↑ tubular reabsorption of $Ca^{2+}$
(namely in the distal tubule)

→ ↓ tubular reabsorption of phosphate in the proximal tubule

→ ↑ tubular reabsorption of $Mg^{2+}$ in the loop of Henle

# Filling and emptying of the bladder

## cystometrogram