

Renal cortex receives ~**90%** of the blood supply to the kidneys.  
Renal medulla is relatively ischemic because blood supply is reduced (**10%** of blood supply to the kidneys)

# ПРОЦЕССЫ

- Фильтрация



клубочек

- Реабсорбция



каналец

- Секреция

# ФУНКЦИИ

1. Поддержание водно-электролитного равновесия.
2. Выведение токсинов.
3. Регуляция обмена кальция и фосфора.
4. Поддержание кислотно-щелочного равновесия.
5. Стимуляция эритропоэза.

# Фильтрация

СКФ = 90 – 120 мл/мин

## Легко фильтруются - < 70 кДа (~ 3,6 нм)

- большинство электролитов
- мочевины, креатинин (**100%**)
- глюкоза, ас, органические кислоты: мочевины, кетоновые тела и др.
- НМ протеины: инсулин (5808 Да), миоглобин (17 кДа)
- инулин, р-аминогиппуровая кислота

## Плохо фильтруются

- альбумин (из-за заряда), глобулины (из-за ММ)
- липофильные вещества – т.к. транспортируются белками (непрямой билирубин, гормоны)

# Оценка СКФ

- ❑ По клиренсу креатинина (проба Реберга - Тареева)
- ❑ По клиренсу инулина

## По специальным формулам:

1. Шварца (у детей)
  2. Кокрофта-Голта (оценивает клиренс креатинина)
  3. MDRD (у пациентов с СД)
  4. СКД-ЕРІ (у пациентов с ССЗ)
- + уровень **цистатина С**

Name	Equation	Units	Comments
Clearance	$C_x = \frac{[U]_x \dot{V}}{[P]_x}$	mL/min	x is any substance
Clearance ratio	Clearance ratio = $\frac{C_x}{C_{\text{inulin}}}$	None	Also means fractional excretion of x
Renal plasma flow	$RPF = \frac{[U]_{\text{PAH}} \dot{V}}{[RA]_{\text{PAH}} - [RV]_{\text{PAH}}}$	mL/min	
Effective renal plasma flow	Effective RPF = $\frac{[U]_{\text{PAH}} \dot{V}}{[P]_{\text{PAH}}}$	mL/min	Underestimates RPF by 10%; equals $C_{\text{PAH}}$
Renal blood flow	$RBF = \frac{RPF}{1 - \text{Hct}}$	mL/min	1 minus Hct is fraction of blood volume that is plasma
Glomerular filtration rate	$GFR = \frac{[U]_{\text{inulin}} \dot{V}}{[P]_{\text{inulin}}}$	mL/min	Equals $C_{\text{inulin}}$
Filtration fraction	$FF = \frac{GFR}{RPF}$	None	
Filtered load	Filtered load = $GFR \times [P]_x$	mg/min	
Excretion rate	Excretion = $\dot{V} \times [U]_x$	mg/min	
Reabsorption or secretion rate	Reabsorption or secretion = Filtered load – Excretion	mg/min	If <i>positive</i> , net reabsorption If <i>negative</i> , net secretion
Free-water clearance	$C_{\text{H}_2\text{O}} = \dot{V} - C_{\text{osm}}$	mL/min	If <i>positive</i> , free water is excreted If <i>negative</i> , free water is reabsorbed

?

**SAMPLE PROBLEM.** In a 24-hour period, 1.44 L of urine is collected from a man receiving an infusion of inulin. In his urine, the [inulin] is 150 mg/mL and the  $[\text{Na}^+]$  is 200 mEq/L. In his plasma, the [inulin] is 1 mg/mL and the  $[\text{Na}^+]$  is 140 mEq/L. *What is the clearance ratio for  $\text{Na}^+$ , and what is the significance of its value?*



**SOLUTION.** The clearance ratio for  $\text{Na}^+$  is the clearance of  $\text{Na}^+$  relative to the clearance of inulin. The clearance equation for any substance is  $C = [U] \times \dot{V} / [P]$ . All of the values needed are provided in the description, although urine flow rate ( $\dot{V}$ ) must be calculated.

$$\begin{aligned}\dot{V} &= \text{Urine volume/time} \\ &= 1.44 \text{ L}/24 \text{ hr} \\ &= 1440 \text{ mL}/1440 \text{ min} \\ &= 1.0 \text{ mL}/\text{min}\end{aligned}$$

$$\begin{aligned}C_{\text{Na}^+} &= \frac{[U]_{\text{Na}^+} \times \dot{V}}{[P]_{\text{Na}^+}} \\ &= \frac{200 \text{ mEq/L} \times 1 \text{ mL}/\text{min}}{140 \text{ mEq/L}} \\ &= 1.43 \text{ mL}/\text{min}\end{aligned}$$

$$\begin{aligned}C_{\text{inulin}} &= \frac{[U]_{\text{inulin}} \times \dot{V}}{[P]_{\text{inulin}}} \\ &= \frac{150 \text{ mg/mL} \times 1 \text{ mL}/\text{min}}{1 \text{ mg/mL}} \\ &= 150 \text{ mL}/\text{min}\end{aligned}$$

$$\begin{aligned}\frac{C_{\text{Na}^+}}{C_{\text{inulin}}} &= \frac{1.43 \text{ mL}/\text{min}}{150 \text{ mL}/\text{min}} \\ &= 0.01 \text{ or } 1\%\end{aligned}$$

The calculated clearance ratio for  $\text{Na}^+$  of 0.01 (or 1%) provides a great deal of information about the renal handling of  $\text{Na}^+$ . Because  $\text{Na}^+$  is freely filtered across the glomerular capillaries, it also must be extensively reabsorbed by the renal tubule, making its clearance much less than the clearance of inulin. The clearance ratio of 0.01 means that only 1% of the filtered  $\text{Na}^+$  is excreted. Stated differently, 99% of the filtered  $\text{Na}^+$  must have been reabsorbed.

$$FENa = [(UNa \times PCr) \div (PNa \times UCr)] \times 100$$

Variable	Prerenal	Intrinsic Renal	Postrenal
Urine osmolality (mOsm/kg)	> 500	< 350	< 350
Urine Na <sup>+</sup> (mEq/L)	< 20	> 40	> 40
FENa	< 1%	> 2%	> 1% (mild) > 2% (severe)
Serum BUN/Cr	> 20	< 15	> 15

баро-

(аорты и каротидных телец)

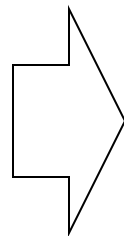
ВОЛЮМО-

(предсердия и полые вены)

осморецепторы

(гипоталамус)

Macula densa



Гемодинамические

механизмы:

изменение СКФ

перитубулярные силы

Нейрогуморальные

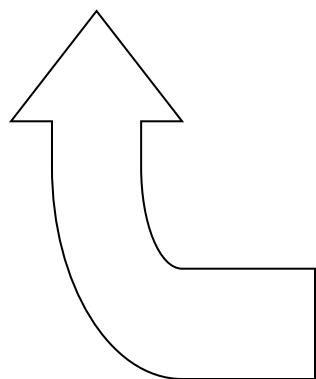
механизмы:

РААС

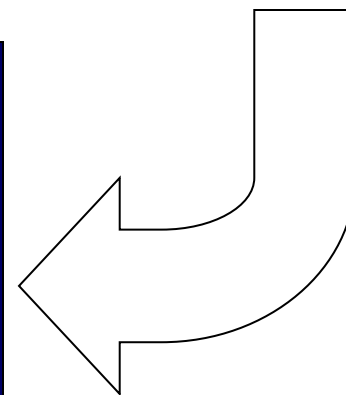
САС

НУП

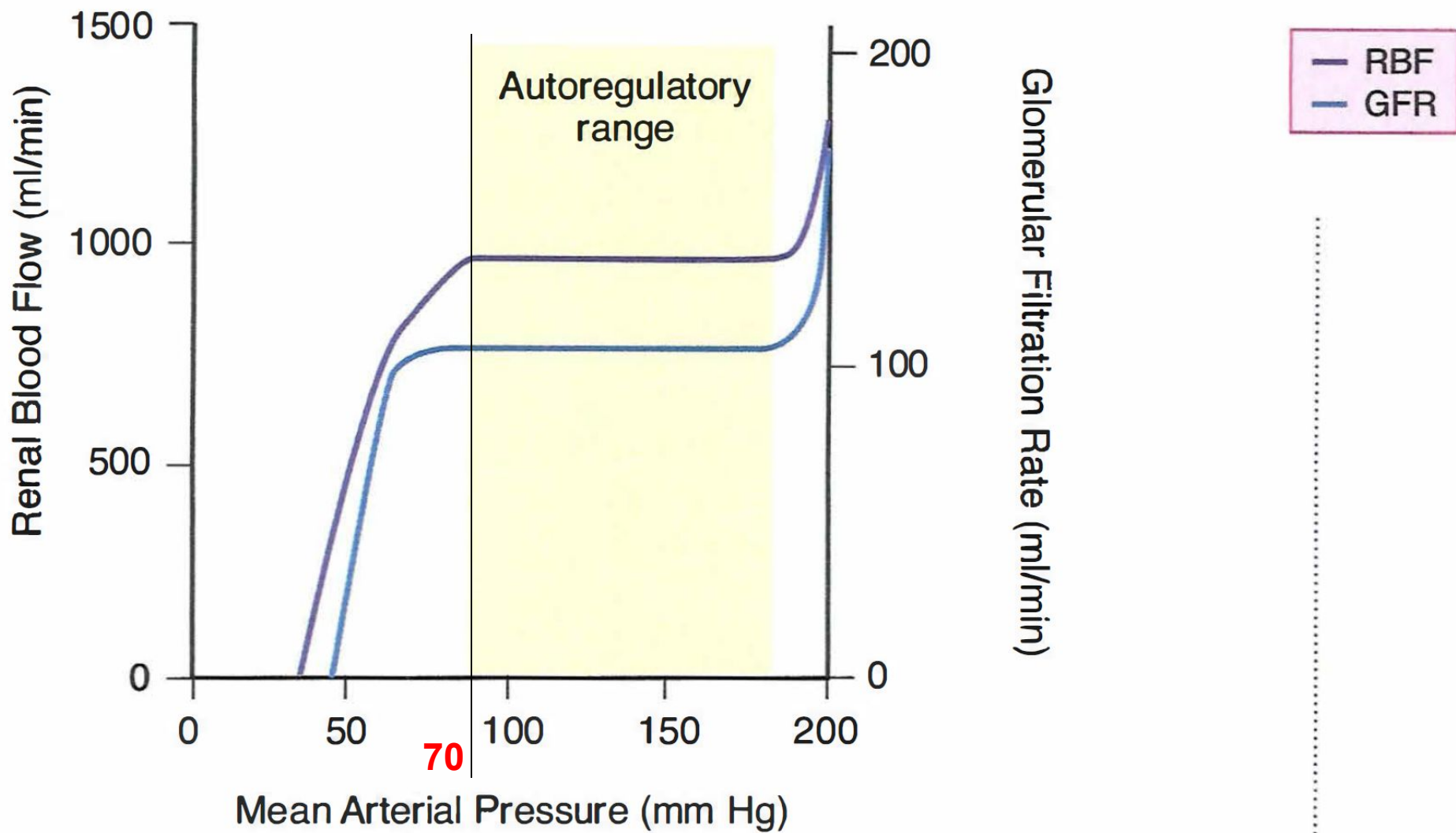
ПгЕ<sub>2</sub>

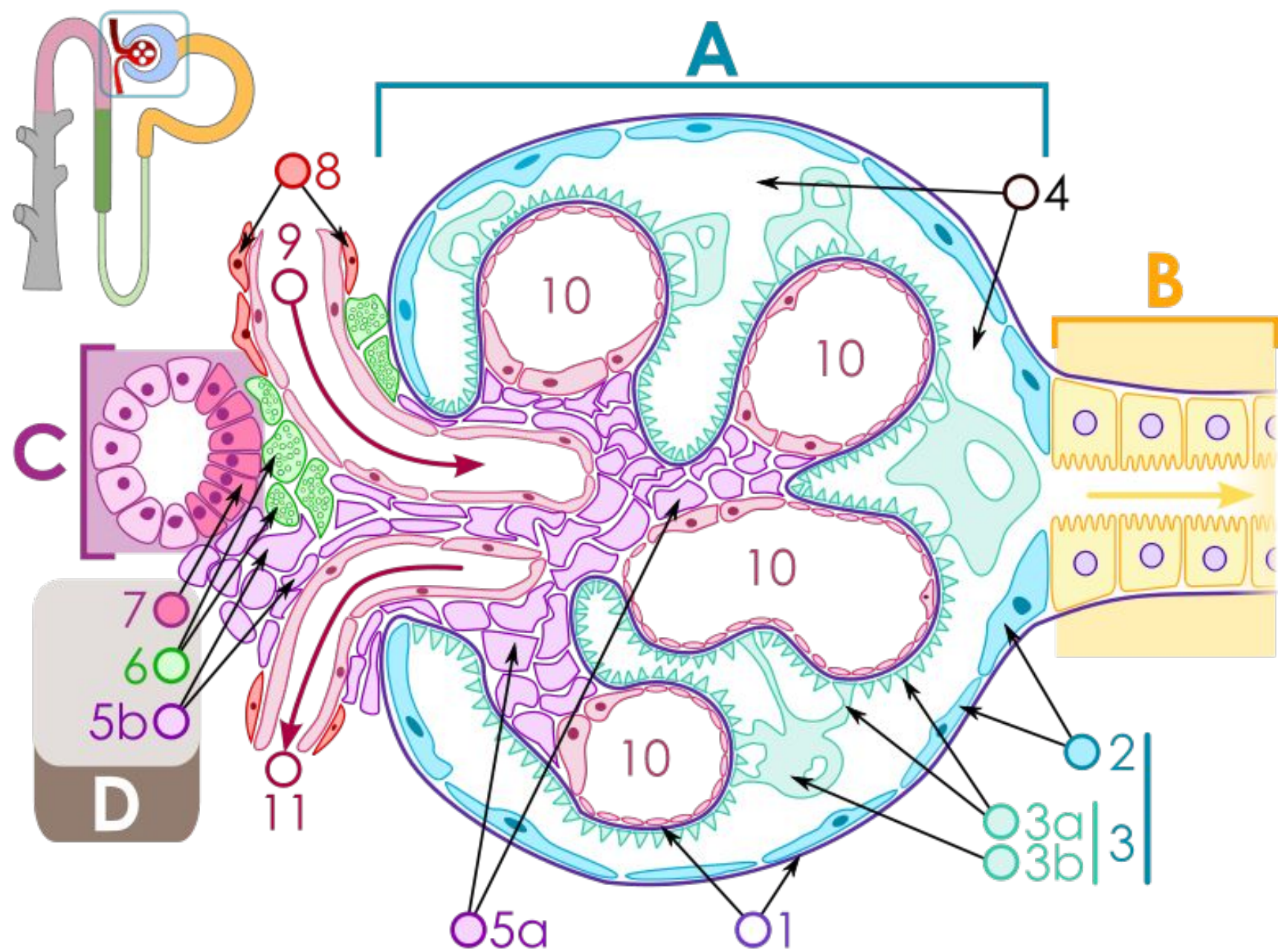


изменение Na  
плазмы и/или  
ОЦК

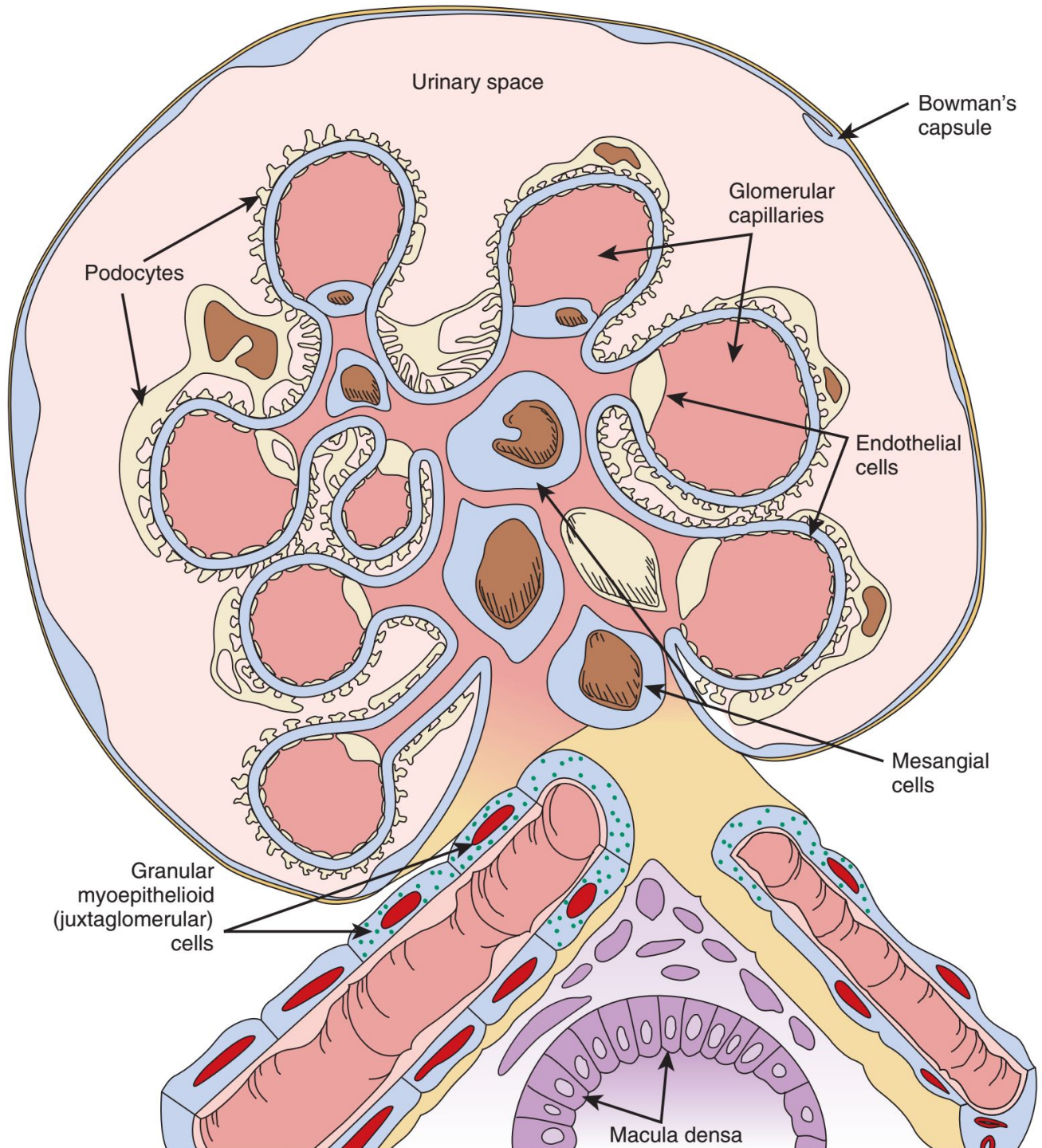


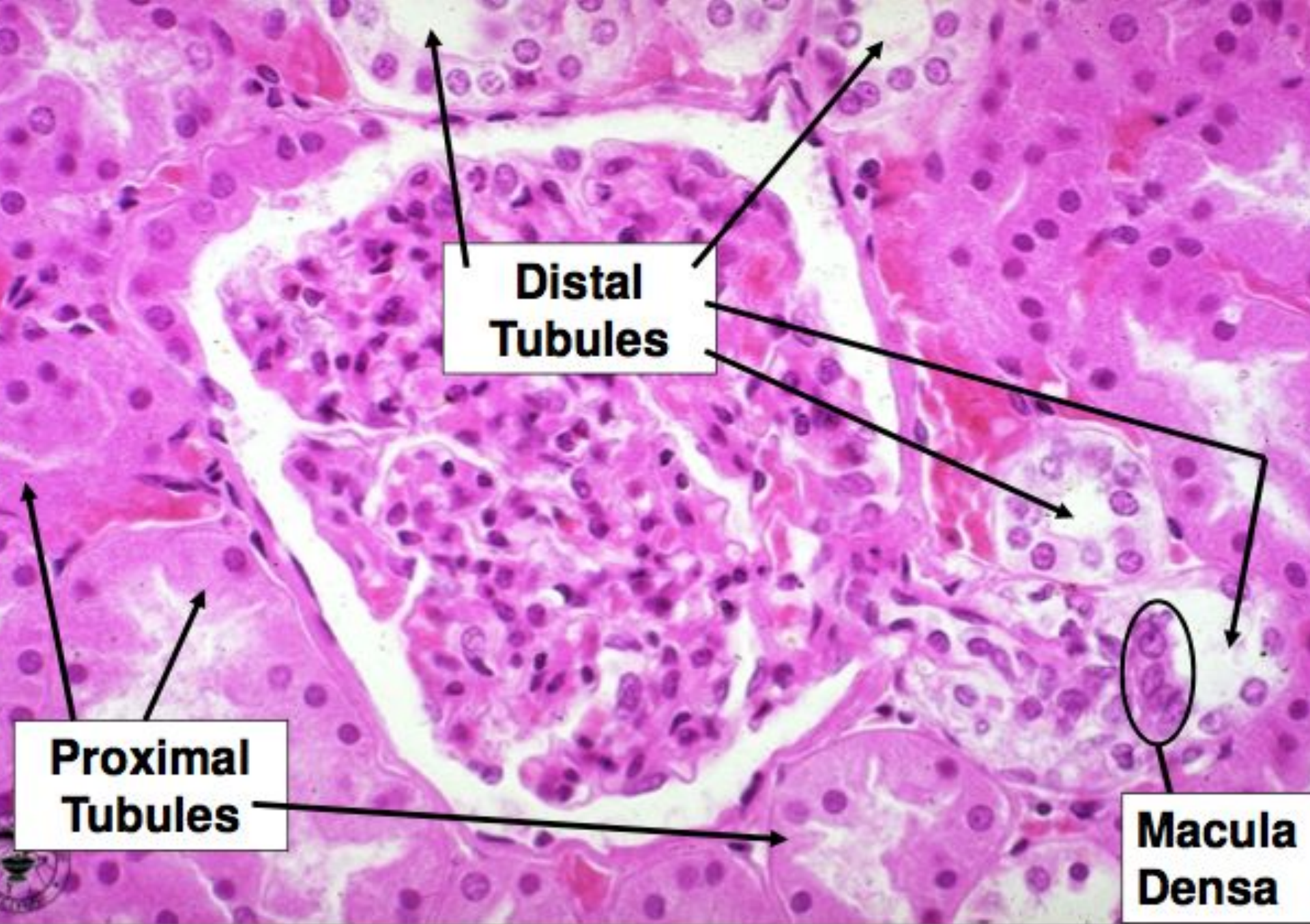
# Ауторегуляция почечного кровотока





A — Почечное тельце B — Проксимальный каналец C — Дистальный извитой каналец D — Юкстагломерулярный аппарат 1. Базальная мембрана 2. Капсула Шумлянского-Боумена — париетальная пластинка 3. Капсула Шумлянского-Боумена — висцеральная пластинка 3а. Подии (ножки) подоцита 3б. Подоцит 4. Пространство Шумлянского-Боумена 5а. Мезангий — Интрагломерулярные клетки 5б. Мезангий — Экстрагломерулярные клетки 6. Гранулярные (юкстагломерулярные) клетки 7. Плотное пятно 8. Миоцит (гладкая мускулатура) 9. Приносящая артериола 10. Клубочковые капилляры 11. Выносящая артериола



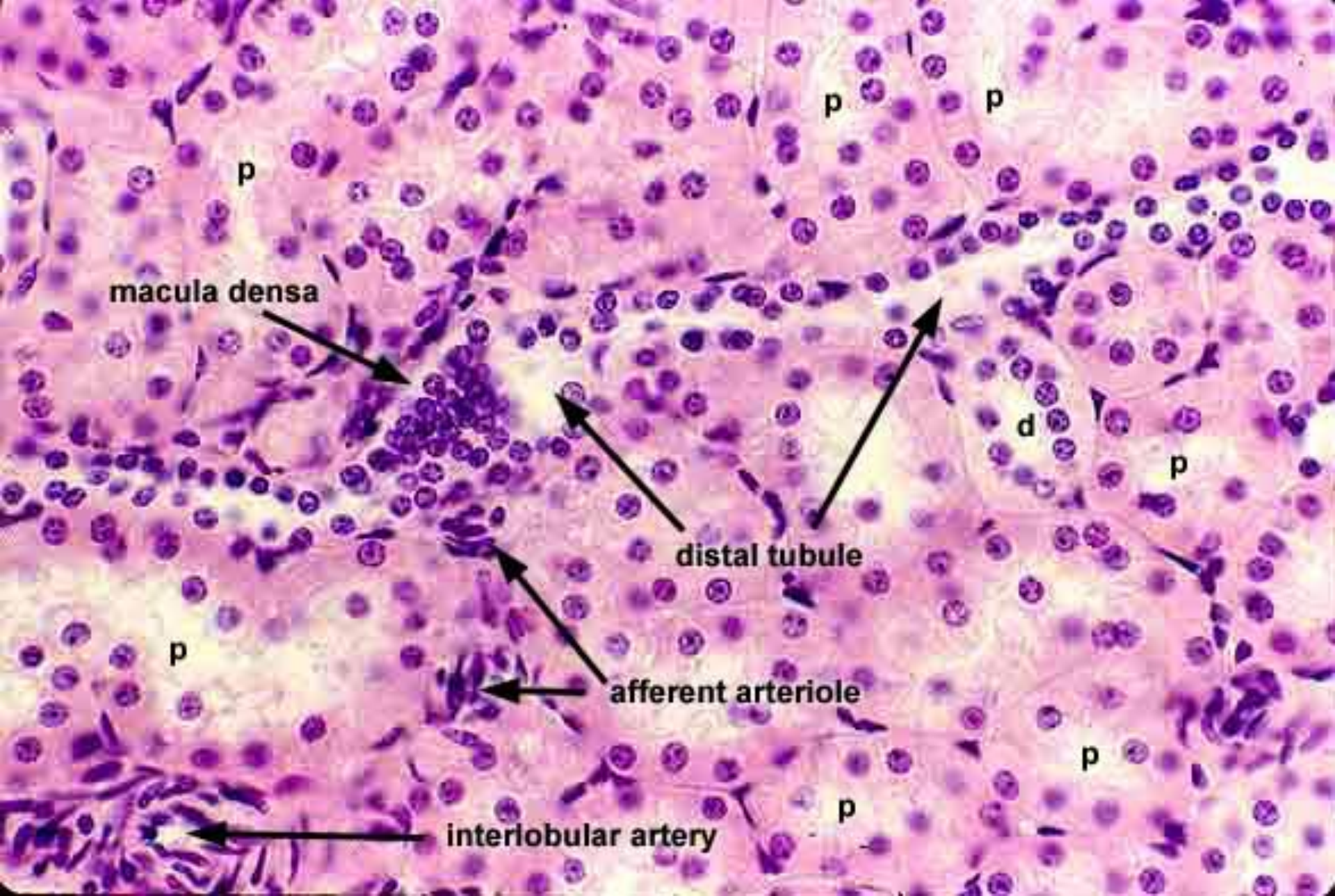


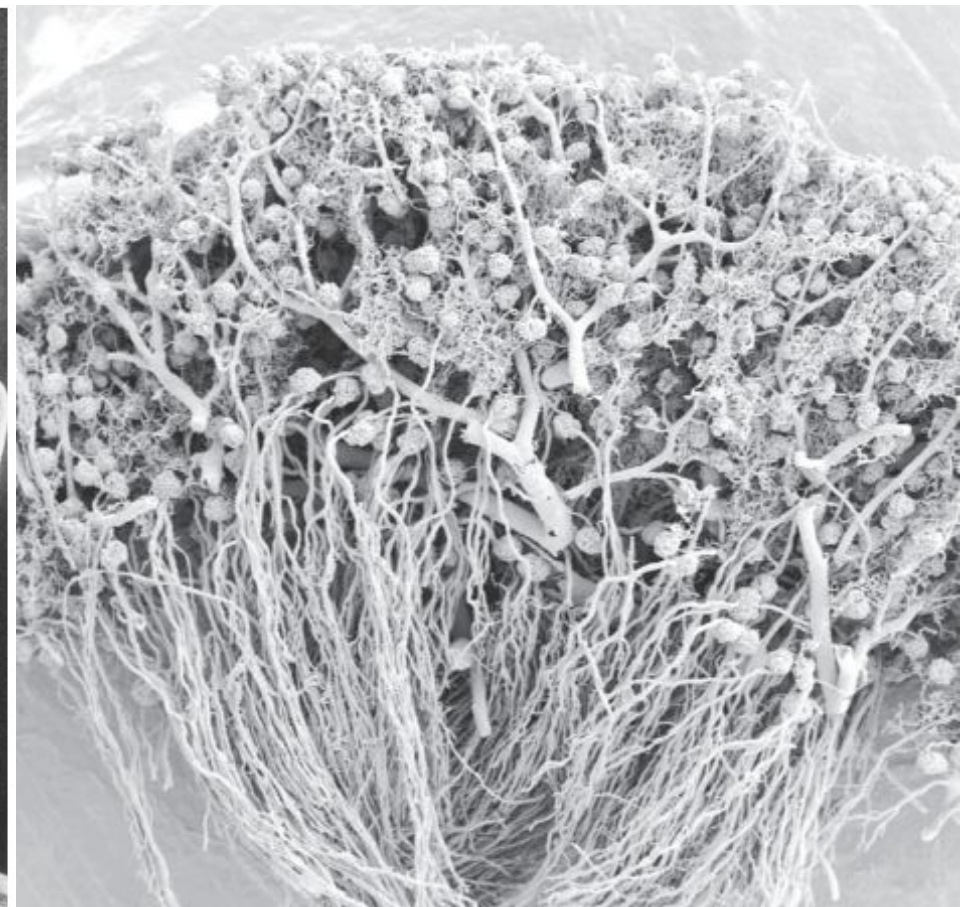
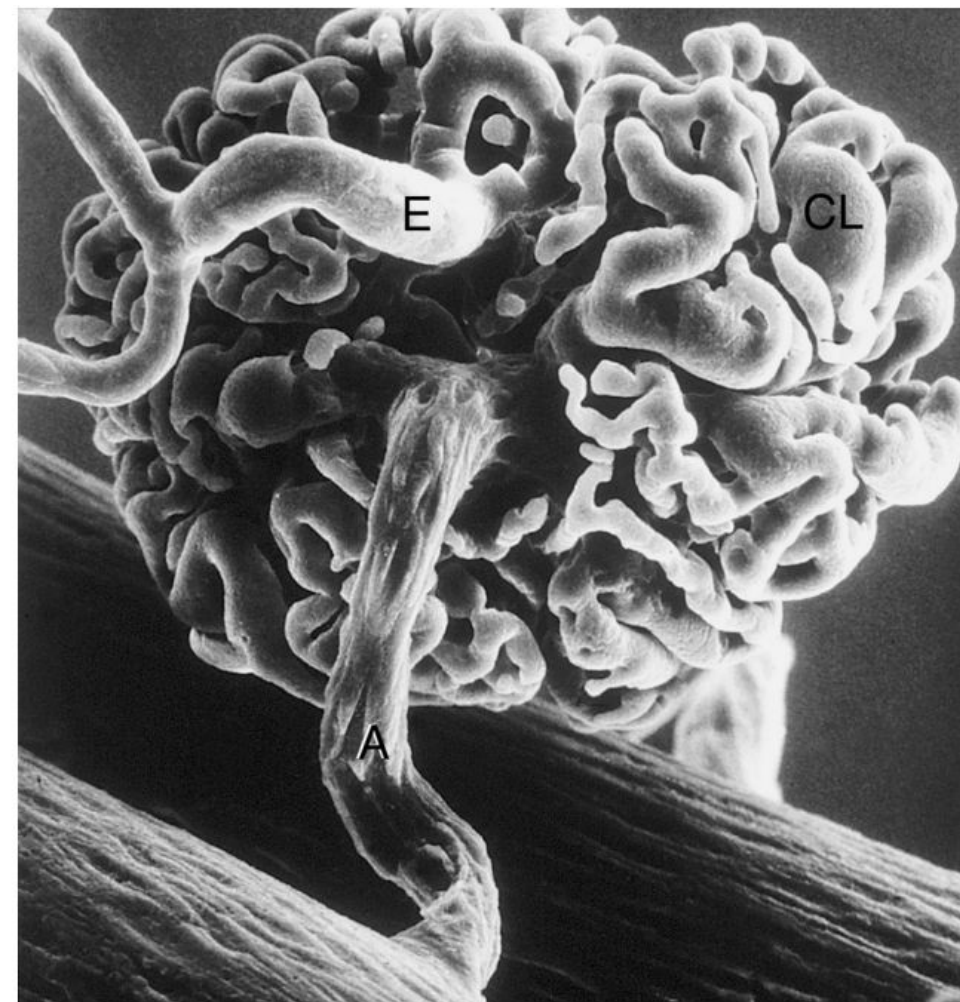
**Distal  
Tubules**

**Proximal  
Tubules**

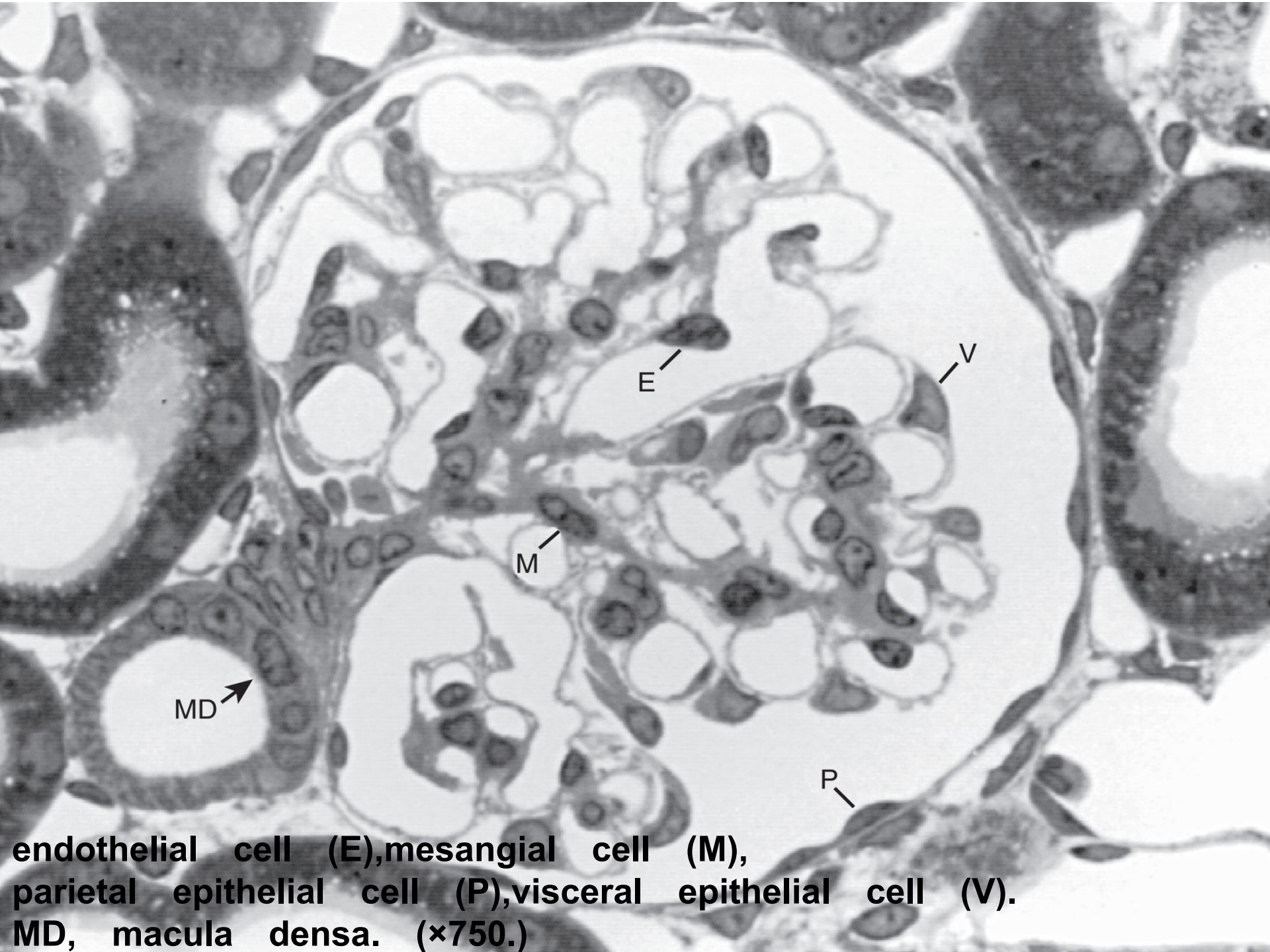
**Macula  
Densa**



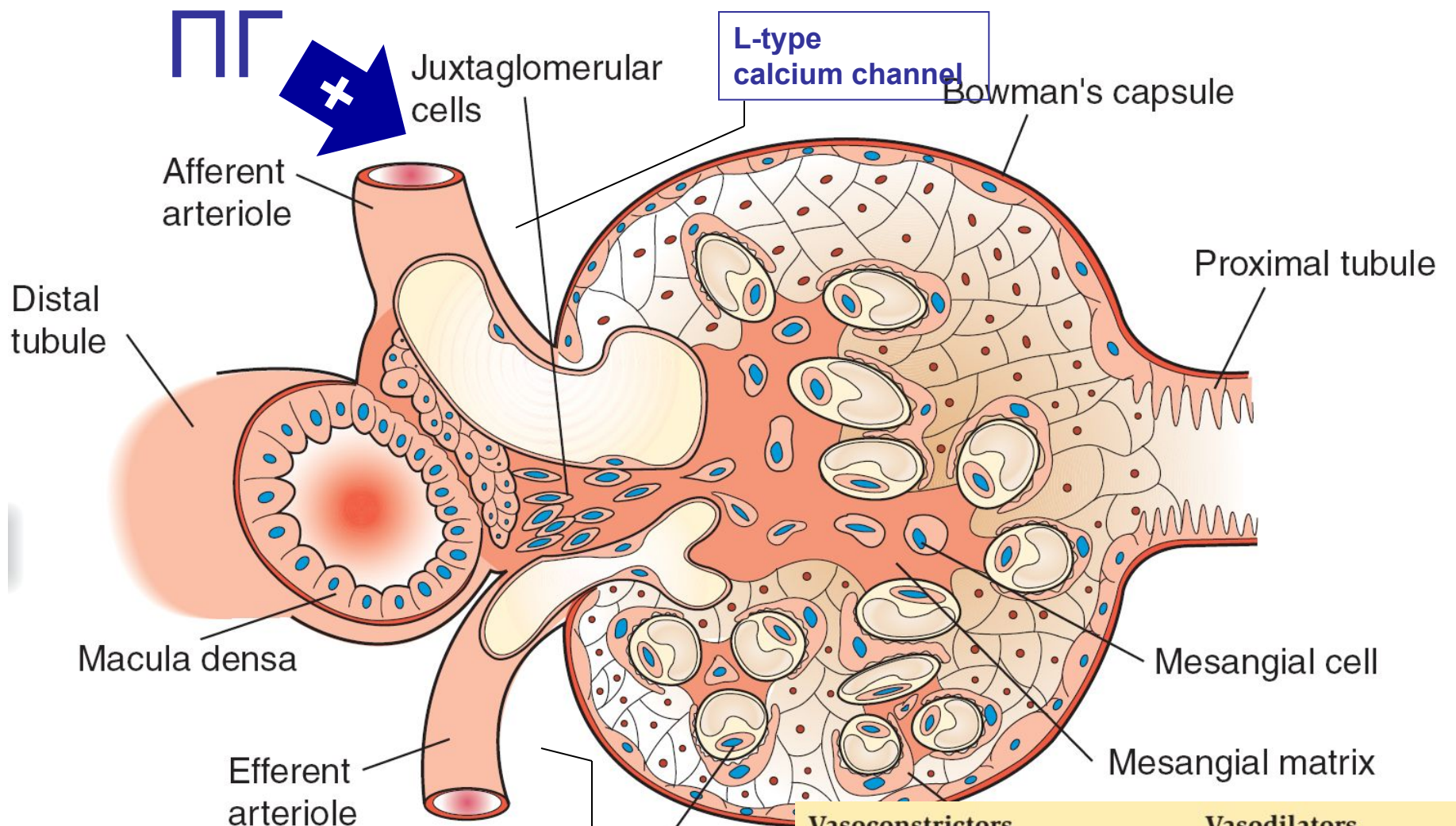




**Figure 3.12** Scanning electron micrograph of a cast of a glomerulus showing the capillary loops (CL) and adjacent renal vessels. The afferent arteriole (A) is shown branching from an interlobular artery. The efferent arteriole (E) branches to form the peritubular capillary plexus (*upper left*). (x300.) (Courtesy Waykin Nopanitaya, PhD.)



**endothelial cell (E), mesangial cell (M),  
parietal epithelial cell (P), visceral epithelial cell (V).  
MD, macula densa. ( $\times 750$ .)**



AT II

Vasoconstrictors	Vasodilators
Sympathetic nerves (catecholamines)	PGE <sub>2</sub>
Angiotensin II	PGI <sub>2</sub>
Endothelin	Nitric oxide
	Bradykinin
	Dopamine
	Atrial natriuretic peptide

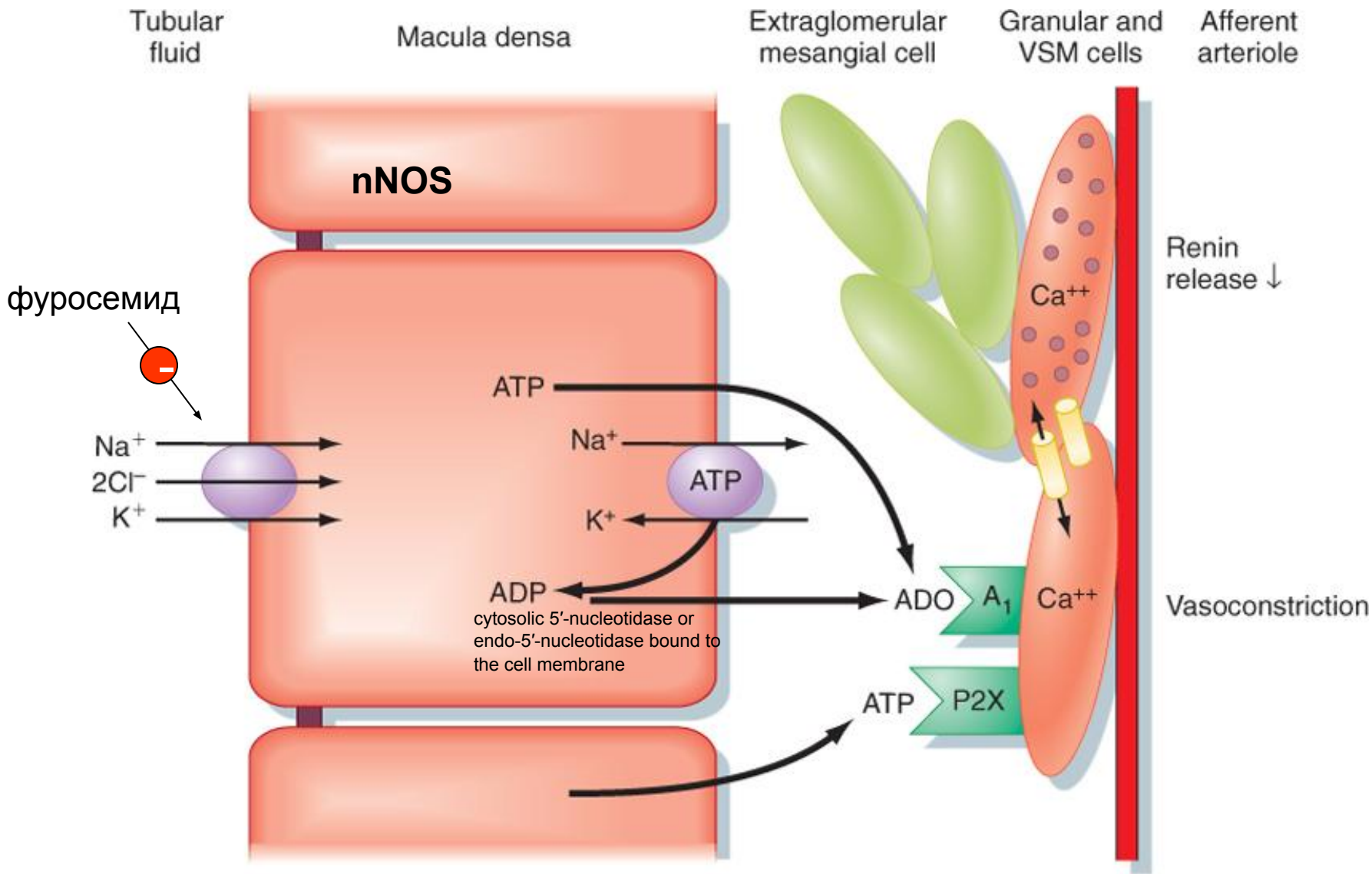


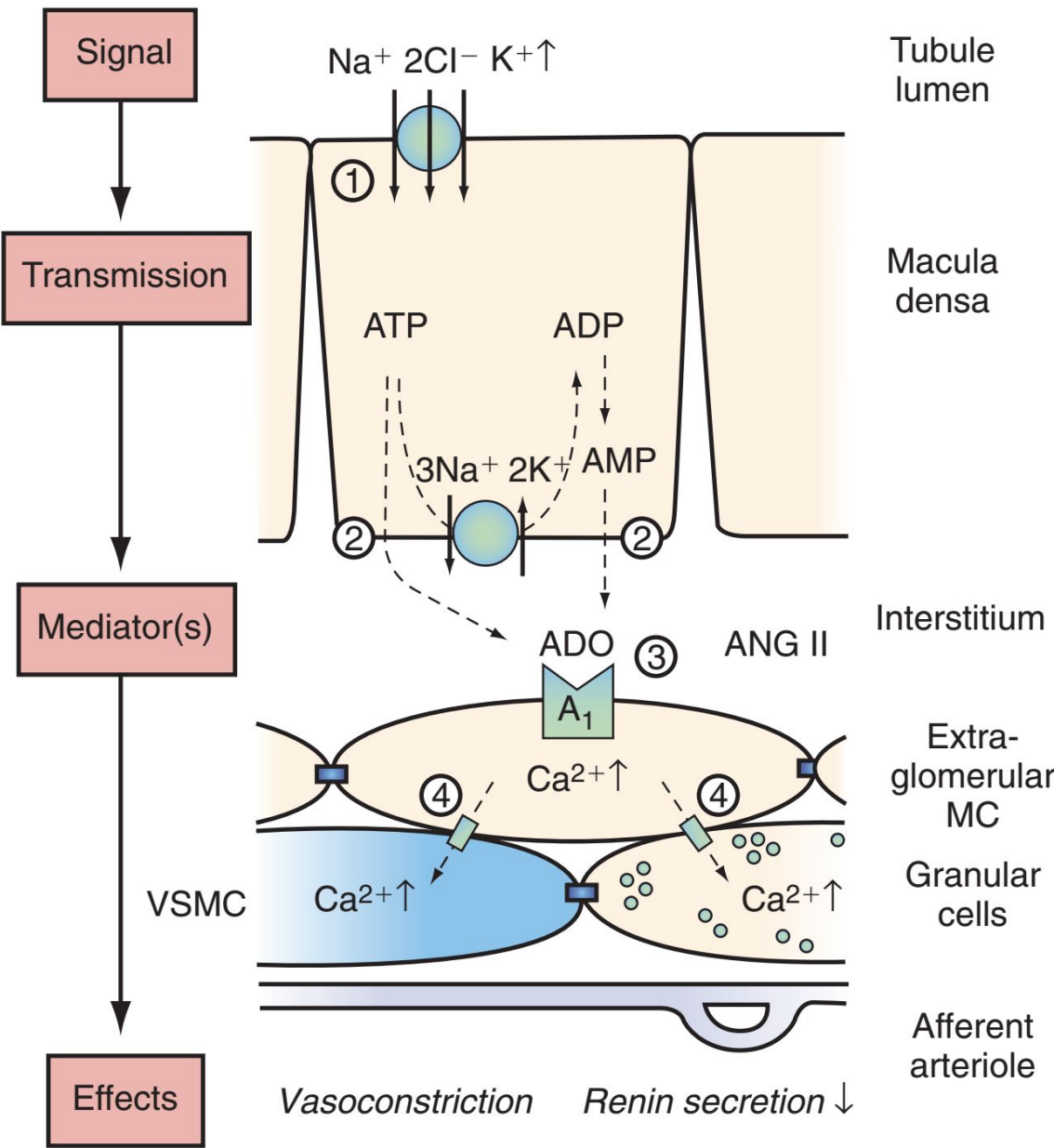
## ПРАКТИЧЕСКИЕ МОМЕНТЫ

Нестероидные противовоспалительные препараты (НПВП) ингибируют образование простагландинов, что может препятствовать расширению приносящей артериолы и, таким образом, вести к снижению СКФ. Эти препараты не должны применяться у пациентов с нарушением функции почек, а также при гиповолемии, когда СКФ поддерживается за счет расширения приносящей артериолы.

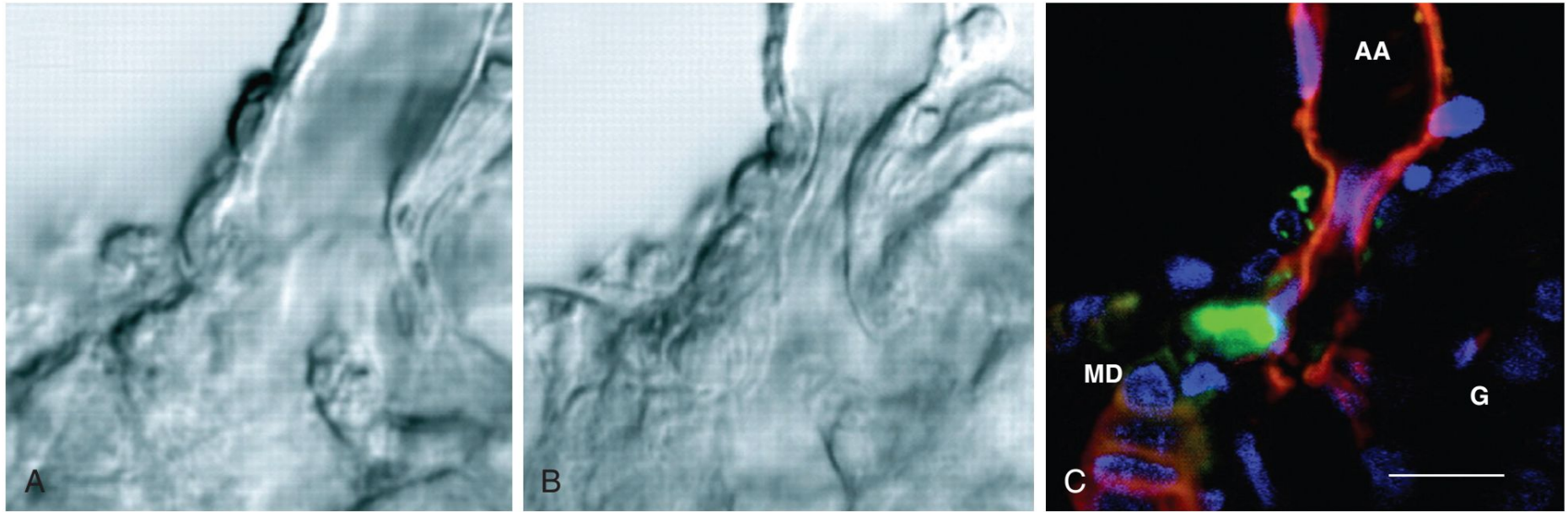
У пациентов со **стенозом почечной артерии** высокое фильтрационное давление в клубочке поддерживается за счет повышенного тонуса выносящей артериолы. **Ингибиторы АПФ** противопоказаны таким пациентам, поскольку они препятствуют констрикции выносящих артериол (ингибируя образование ангиотензина-II), в результате чего резко снижается СКФ, что сопровождается быстрым ухудшением почечной функции.

# Tubuloglomerular feedback





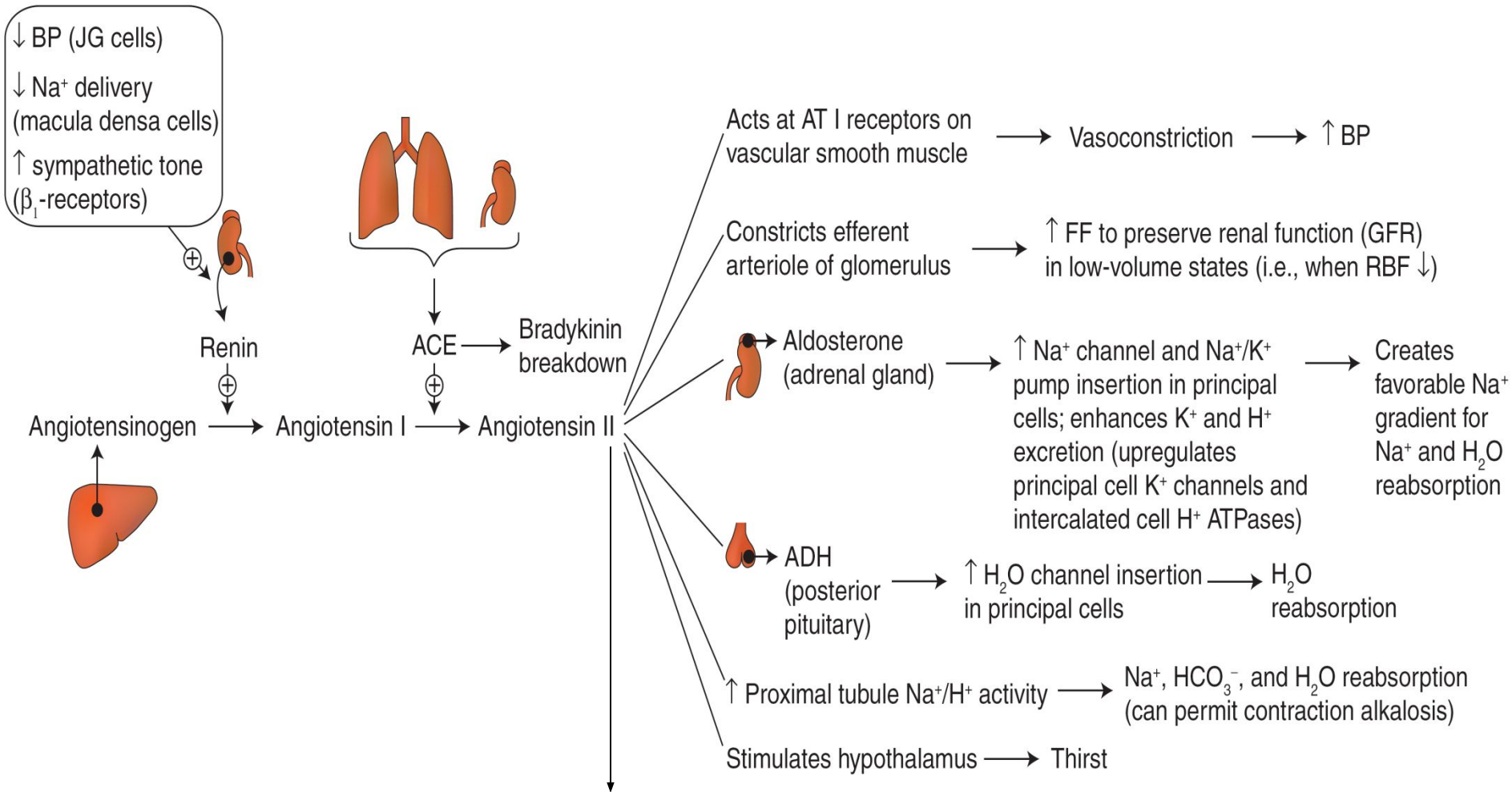
**Figure 3.24** Proposed mechanism of tubuloglomerular feedback (TGF). The sequence of events (*numbers in circles*) are: (1) uptake of  $\text{Na}^+$ ,  $\text{Cl}^-$ , and  $\text{K}^+$  by the  $\text{Na}^+-\text{K}^+-2\text{Cl}^-$  cotransporter on the luminal cell membrane of the macula densa cells; (2) intracellular or extracellular production of adenosine (ADO); (3) ADO activation of adenosine  $\text{A}_1$  receptors, triggering an increase in cytosolic  $\text{Ca}^{2+}$  in extraglomerular mesangial cells (MCs); and (4) coupling between extraglomerular MCs and granular cells (containing renin) and smooth muscle cells of the afferent arteriole (VSMCs) by gap junctions, allowing propagation of the increased  $[\text{Ca}^{2+}]_i$  (intracellular calcium concentration) and resulting in afferent arteriolar vasoconstriction and inhibition of renin release. Local angiotensin II and neuronal nitric oxide synthase (nNOS) activity modulate the response. ADP, adenosine diphosphate; AMP, adenosine monophosphate; ATP, adenosine triphosphate. (From Vallon V: Tubuloglomerular feedback and the control of glomerular filtration rate. *News Physiol Sci* 18:169-174, 2003.)



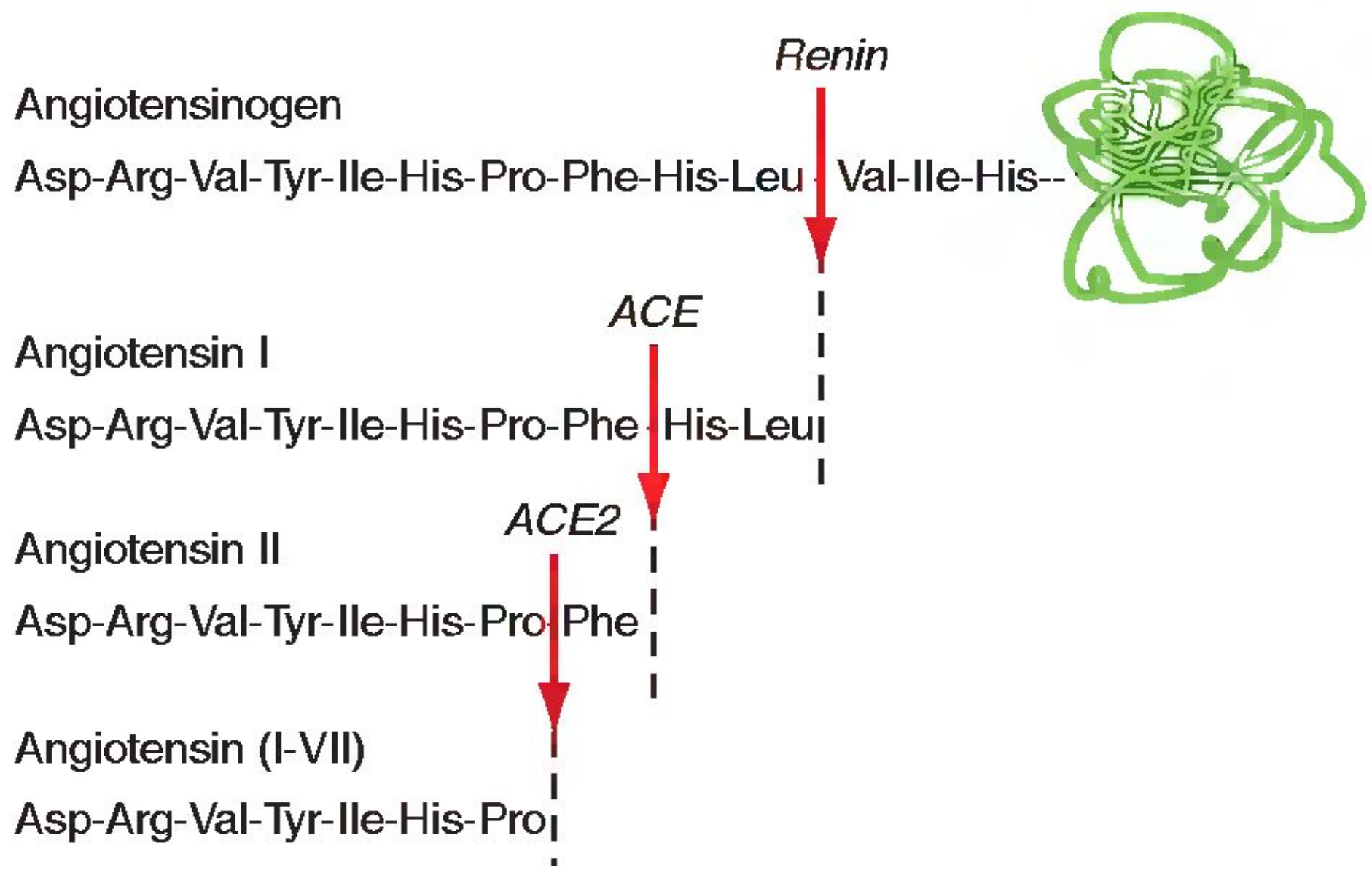
**Figure 3.5** Constriction of the terminal afferent arteriole (AA), an intraglomerular precapillary sphincter, in response to elevations in distal tubular salt content. **A** and **B**, Transmitted light–differential interference contrast (DIC) images. **A**, Control, with NaCl concentration at the macula densa at 10 mM. **B**, NaCl concentration is increased to 60 mM, resulting in an almost complete closure of the AA. **C**, Fluorescence image of the same preparation as shown in **B**. Vascular endothelium and tubular epithelium are labeled with R18 (red), renin granules with quinacrine (green), cell nuclei with Hoechst 33342 (blue). Note that renin-positive granular cells constitute the sphincter. MD, macula densa. Scale bar = 10  $\mu\text{m}$ . (From Peti-Peterdi J: Multiphoton imaging of renal tissues in vitro. *Am J Physiol Renal Physiol* 288:F1079-F1083, 2005.)



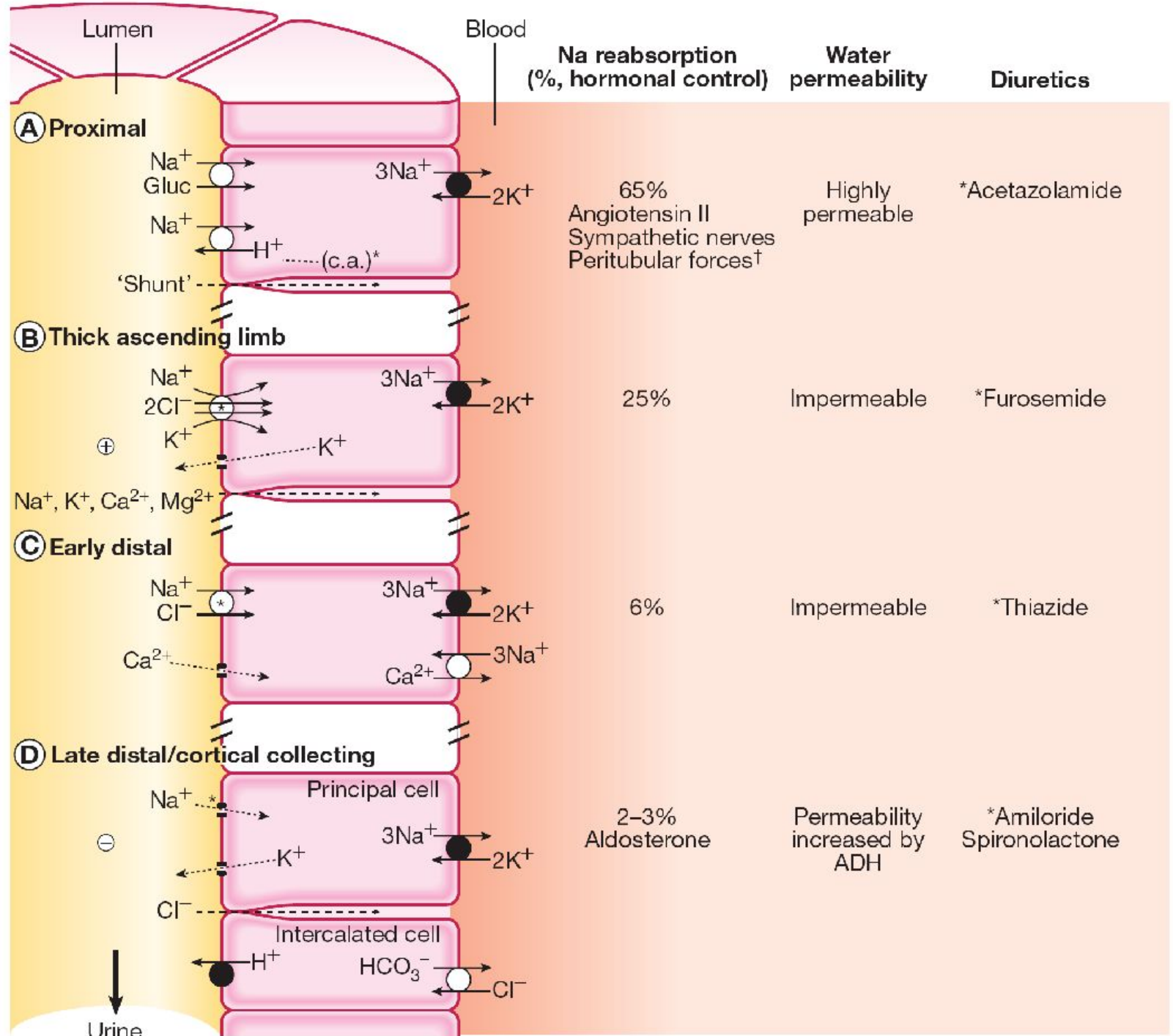
# РААС



ИНСУЛИНОРЕЗИСТЕНТНОСТЬ

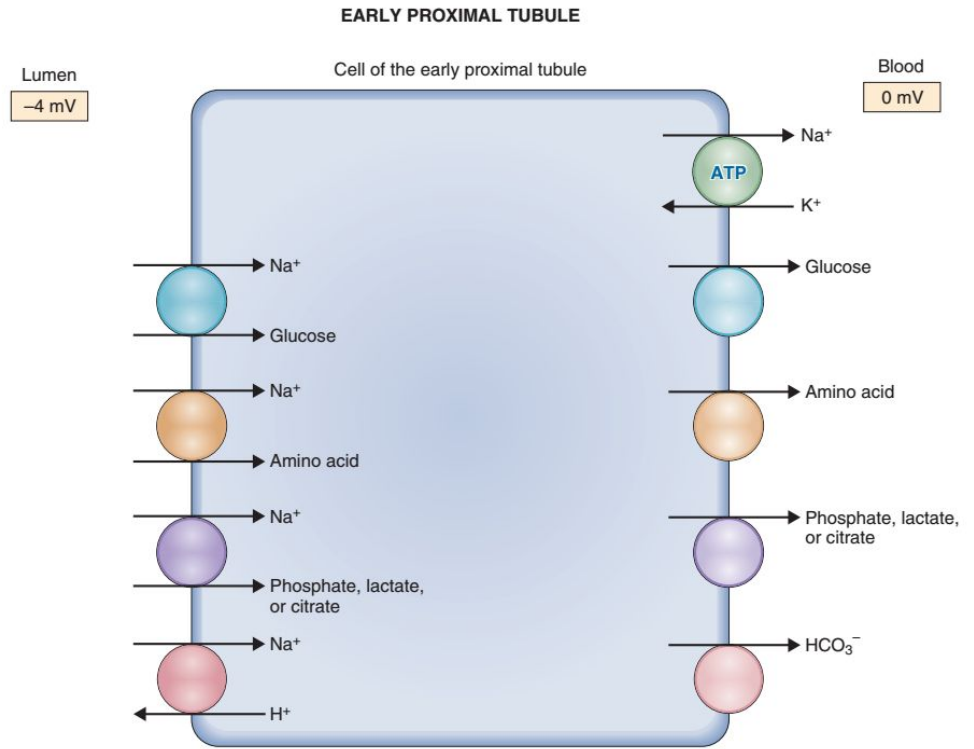


# Реабсорбция



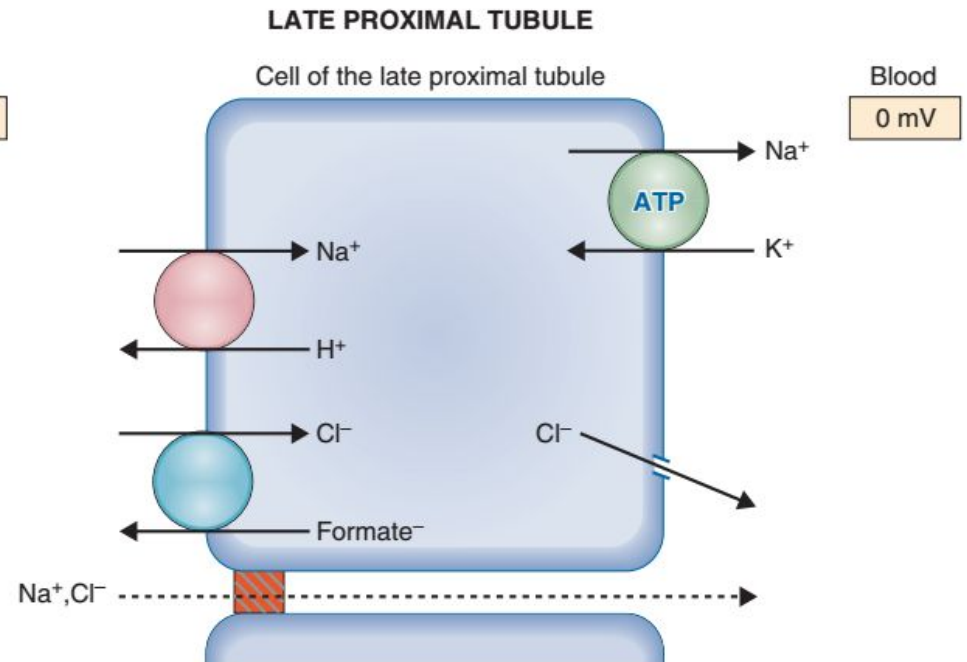
<b>Early Proximal Tubule</b>	Isosmotic reabsorption of solute and water	Na <sup>+</sup> -glucose, Na <sup>+</sup> -amino acid, Na <sup>+</sup> -phosphate cotransport Na <sup>+</sup> -H <sup>+</sup> exchange	PTH inhibits Na <sup>+</sup> -phosphate cotransport Angiotensin II stimulates Na <sup>+</sup> -H <sup>+</sup> exchange	Osmotic diuretics Carbonic anhydrase inhibitors
<b>Late Proximal Tubule</b>	Isosmotic reabsorption of solute and water	NaCl reabsorption driven by Cl <sup>-</sup> gradient	—	Osmotic diuretics
<b>Thick Ascending Limb of the Loop of Henle</b>	Reabsorption of NaCl without water Dilution of tubular fluid Single effect of countercurrent multiplication Reabsorption of Ca <sup>2+</sup> and Mg <sup>2+</sup> driven by lumen-positive potential	Na <sup>+</sup> -K <sup>+</sup> -2Cl <sup>-</sup> cotransport	ADH stimulates Na <sup>+</sup> -K <sup>+</sup> -2Cl <sup>-</sup> cotransport	Loop diuretics
<b>Early Distal Tubule</b>	Reabsorption of NaCl without water Dilution of tubular fluid	Na <sup>+</sup> -Cl <sup>-</sup> cotransport	PTH stimulates Ca <sup>2+</sup> reabsorption	Thiazide diuretics
<b>Late Distal Tubule and Collecting Ducts (principal cells)</b>	Reabsorption of NaCl K <sup>+</sup> secretion Variable water reabsorption	Na <sup>+</sup> channels (ENaC) K <sup>+</sup> channels AQP2 water channels	Aldosterone stimulates Na <sup>+</sup> reabsorption Aldosterone stimulates K <sup>+</sup> secretion ADH stimulates water reabsorption	K <sup>+</sup> -sparing diuretics
<b>Late Distal Tubule and Collecting Ducts (<math>\alpha</math>-intercalated cells)</b>	Reabsorption of K <sup>+</sup> Secretion of H <sup>+</sup>	H <sup>+</sup> -K <sup>+</sup> ATPase H <sup>+</sup> ATPase	— Aldosterone stimulates H <sup>+</sup> secretion	— K <sup>+</sup> -sparing diuretics

There is a **lumen-negative** potential difference across the cells of the early proximal tubule, which is created by  $\text{Na}^+$ -glucose and  $\text{Na}^+$ -amino acid cotransport. These transporters bring net positive charge into the cell and leave negative charge in the lumen. The other transporters are electroneutral (e.g.,  $\text{Na}^+$ - $\text{H}^+$  exchange) and, therefore, do not contribute to the transepithelial potential difference.



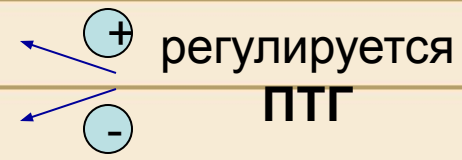
Furthermore, this fluid has a **high  $\text{Cl}^-$  concentration**, although it may not be immediately evident why this is so. The  $\text{Cl}^-$  concentration is high because  $\text{HCO}_3^-$  has been preferentially reabsorbed in the early proximal tubule, leaving  $\text{Cl}^-$  behind in the tubular fluid. As water is reabsorbed isosmotically along with solute, the tubular fluid  $\text{Cl}^-$  concentration increases and becomes higher than the  $\text{Cl}^-$  concentration of the glomerular filtrate and of blood.

In contrast to the early proximal tubule, the late proximal tubule reabsorbs primarily  $\text{NaCl}$  (Fig. 6-21).



**Таблица 1.** Вещества, реабсорбируемые в проксимальном извитом канальце (ПИК)

Вещество	Примерный % реабсорбции в ПИК
Вода	65
Натрий	60
Калий / хлор / бикарбонат	80
Глюкоза	<u>100</u>
Аминокислоты	не менее 7 видов транспортеров 100
Кальций	60
Фосфат	80
Мочевина	50



наследственный дефект всасывания цистина и 2-основных ак (аргинин, лизин, орнитин) – **цистинурия** (не путать с цистинозом), частота - 1:7000, образование камней.

наследственный дефект всасывания нейтральных ак в кишечнике и в канальцах – **болезнь Хартнупа и пеллагра-подобные симптомы**

Disease or Syndrome	Gene
<b>Disorders Involving the Proximal Tubule</b>	
Proximal renal tubular acidosis	Sodium bicarbonate cotransporter ( <i>SLC4A4</i> , 4q21)
Fanconi-Bickel syndrome	Glucose transporter, GLUT2 ( <i>SLC2A2</i> , 3q26.2)
Isolated renal glycosuria	Sodium glucose cotransporter ( <i>SLC5A2</i> , 16p11. )
Cystinuria	
Type I	Cystine, dibasic and neutral amino acid transporter ( <i>SLC3A1</i> , 2p16.3)
Non-type I	Amino acid transporter, light subunit ( <i>SLC7A9</i> , 19q13.1)
Lysinuric protein intolerance	Amino acid transporter ( <i>SLC7A7</i> , 4q11.2)
Hartnup disorder	Neutral amino acid transporter ( <i>SLC6A19</i> , 5p15.33)
Hereditary hypophosphatemic rickets with hypercalcemia	Sodium phosphate cotransporter ( <i>SLC34A3</i> , 9q34)
Renal hypouricemia	
Type 1	Urate-anion exchanger ( <i>SLC22A12</i> , 11q13)
Type 2	Urate transporter, GLUT9 ( <i>SLC2A9</i> , 4p16.1)
Dent disease	Chloride channel, ClC-5 ( <i>CLCN5</i> , Xp11.22)
X-linked recessive nephrolithiasis with renal failure	Chloride channel, ClC-5 ( <i>CLCN5</i> , Xp11.22)
X-linked recessive hypophosphatemic rickets	Chloride channel, ClC-5 ( <i>CLCN5</i> , Xp11.22)

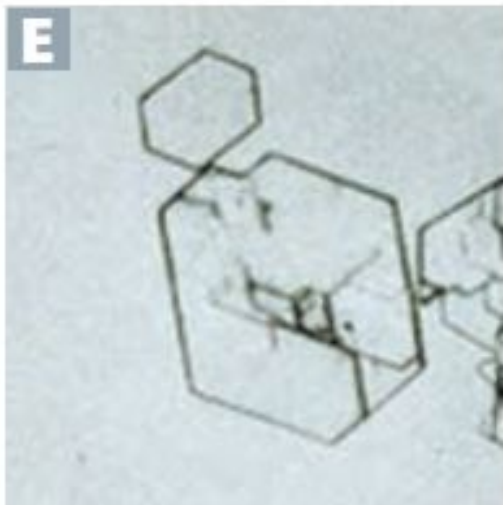


**Cystine**  
**(1%)**

↓ pH

Radiopaque

Hexagonal **E**



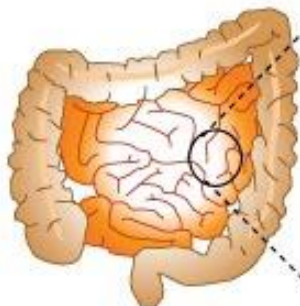
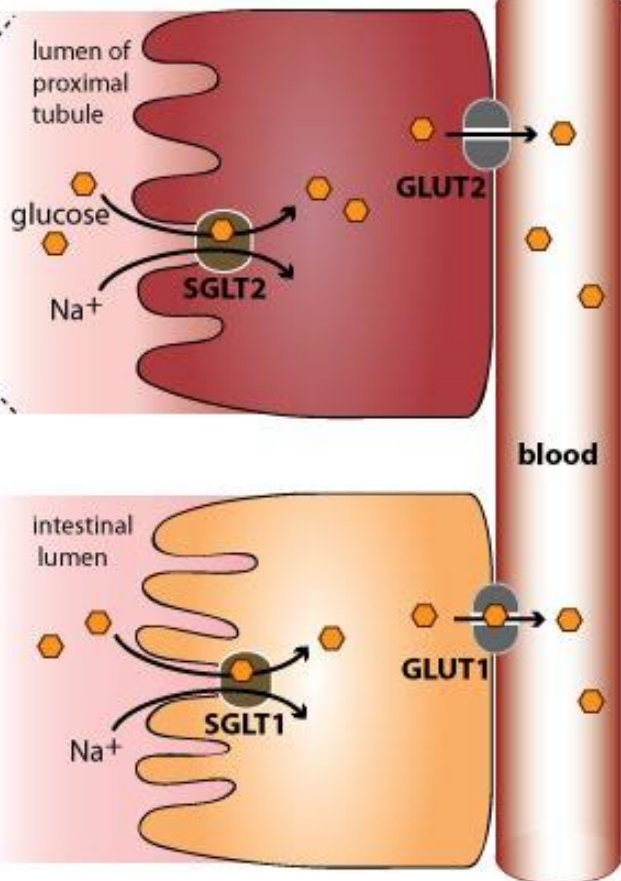
Mostly seen in children, 2° to cystinuria. Can form staghorn calculi. Sodium nitroprusside test ⊕.

Treatment: alkalinization of urine and hydration.

<b>Disorders Involving the Loop of Henle</b>		
Bartter syndrome		
Type 1	Sodium, potassium chloride cotransporter ( <i>SLC12A1</i> , 15q21.1)	241200
Type 2	Potassium channel, ROMK ( <i>KCNJ1</i> , 11q24)	601678
Type 3	Chloride channel, ClC-Kb ( <i>CLCNKB</i> , 1p36)	602023
with sensorineural deafness	Chloride channel accessory subunit, Barttin ( <i>BSND</i> , 1p31)	602522
Autosomal dominant hypocalcemia with Bartter-like syndrome	Calcium-sensing receptor ( <i>CASR</i> , 3q13.33)	601199
Familial hypocalciuric hypercalcemia	Calcium-sensing receptor ( <i>CASR</i> , 3q13.33)	145980
Primary hypomagnesemia	Claudin-16 or paracellin-1 ( <i>CLDN16</i> or <i>PCLN1</i> , 3q27)	248250
Isolated renal magnesium loss	Sodium potassium ATPase, $\gamma_1$ -subunit ( <i>ATP1G1</i> , 11q23)	154020
<b>Disorders Involving the Distal Tubule and Collecting Duct</b>		
Gitelman syndrome	Sodium chloride cotransporter ( <i>SLC12A3</i> , 16q13)	263800
Primary hypomagnesemia with secondary hypocalcemia	Melastatin-related transient receptor potential cation channel 6 ( <i>TRPM6</i> , 9q22)	602014
Pseudoaldosteronism (Liddle's syndrome)	Epithelial sodium channel $\beta$ and $\gamma$ subunits ( <i>SCNN1B</i> , <i>SCNN1G</i> , 16p12.1)	177200
Recessive pseudohypoaldosteronism type 1	Epithelial sodium channel, $\alpha$ , $\beta$ , and $\gamma$ subunits ( <i>SCNN1A</i> , 12p13; <i>SCNN1B</i> , <i>SCNN1G</i> , 16pp12.1)	264350
Pseudohypoaldosteronism type 2 (Gordon's hyperkalemia-hypertension syndrome)	Kinases WNK-1, WNK-4 ( <i>WNK1</i> , 12p13; <i>WNK4</i> , 17q21.31)	145260
X-linked nephrogenic diabetes insipidus	Vasopressin V2 receptor ( <i>AVPR2</i> , Xq28)	304800
Nephrogenic diabetes insipidus (autosomal)	Water channel, aquaporin-2 ( <i>AQP2</i> , 12q13)	125800
Distal renal tubular acidosis		
autosomal dominant	Anion exchanger-1 ( <i>SLC4A1</i> , 17q21.31)	179800
autosomal recessive	Anion exchanger-1 ( <i>SLC4A1</i> , 17q21.31)	602722
with neural deafness	Proton ATPase, $\beta$ 1 subunit ( <i>ATP6V1B1</i> , 2p13.3)	192132
with normal hearing	Proton ATPase, 116-kD subunit ( <i>ATP6VOA4</i> , 7q34)	602722



kidneys



small intestine

**Эмпаглифлозин**  
канаглифлозин  
дапаглифлозин  
ипраглифлозин и др.

Type of SGLT	Major sites	Functions : Transport of
SGLT 1	Small intestine, Heart, Trachea, Kidney(S3)	Na, Glucose Galactose
SGLT 2	Kidney(S1, S2)	Na, Glucose
SGLT 3	Small intestine, Uterus Lung, Thyroid, Testis	Na
SGLT 4	Small intestine, Kidney, Liver, Stomach, Lung	Glucose, Mannose
SGLT 5	Kidney	Unknown
SGLT 6	Spinal cord, Kidney, Brain, Small intestine	Myoinositol, Glucose

# Противоточная система

- Противоточный множитель (петля Генле), обеспечивающий увеличение осмотического градиента по мере продвижения к нижней части петли.
- Противоточный обменник (прямые сосуды), поддерживающий осмотический градиент. Выход воды из собирательных трубочек регулируется АДГ. Иначе осмотический градиент постепенно бы уменьшался из-за реабсорбции воды за счет осмоса.

Градиент осмолярности (мосм/л)

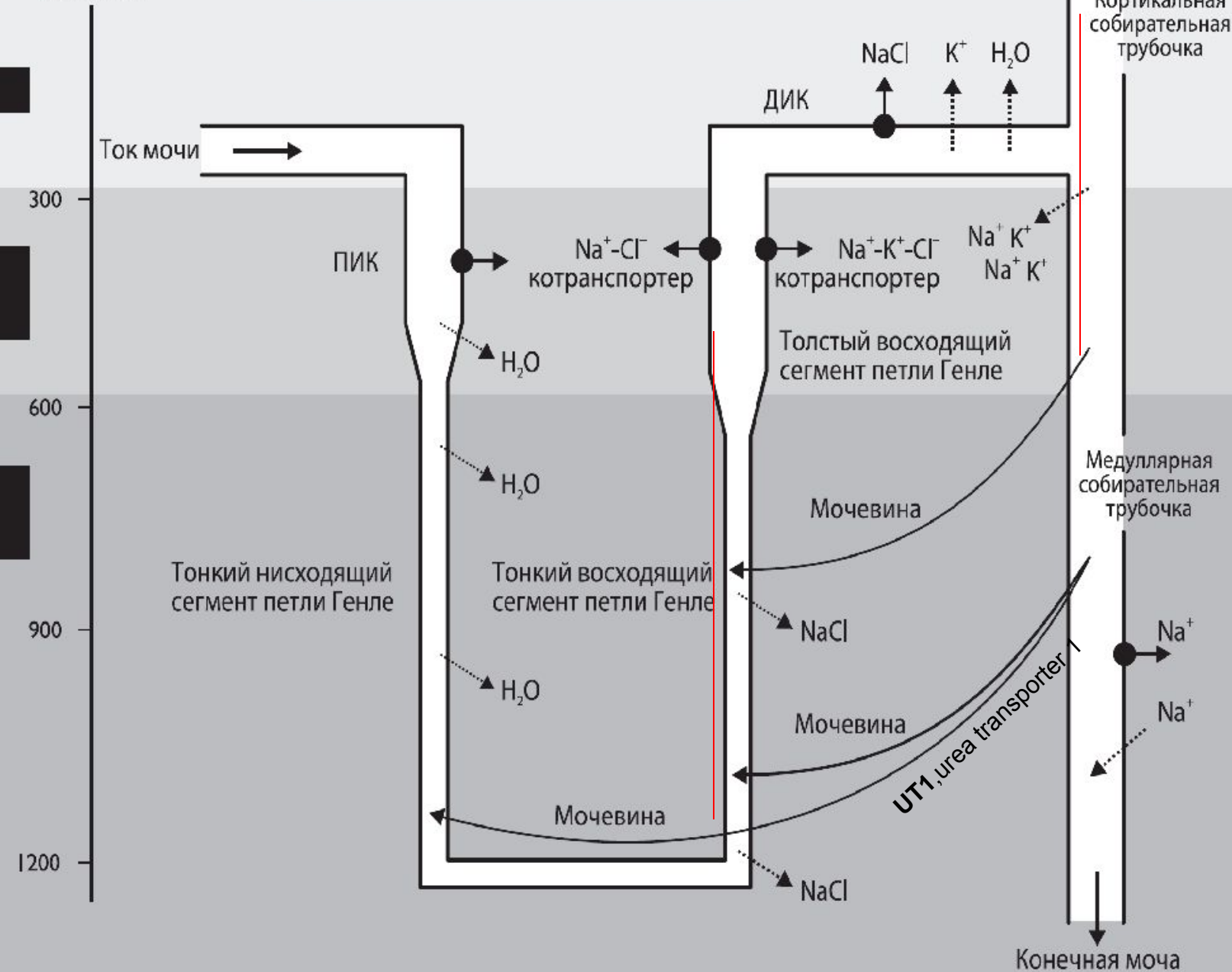
●→ Процесс активного транспорта

⋯→ Пассивная диффузия

Кора

Наружный слой  
мозгового вещества

Внутренний слой  
мозгового вещества



Осмолярность мочи –

**300** мОсм/л

Относительная плотность мочи –

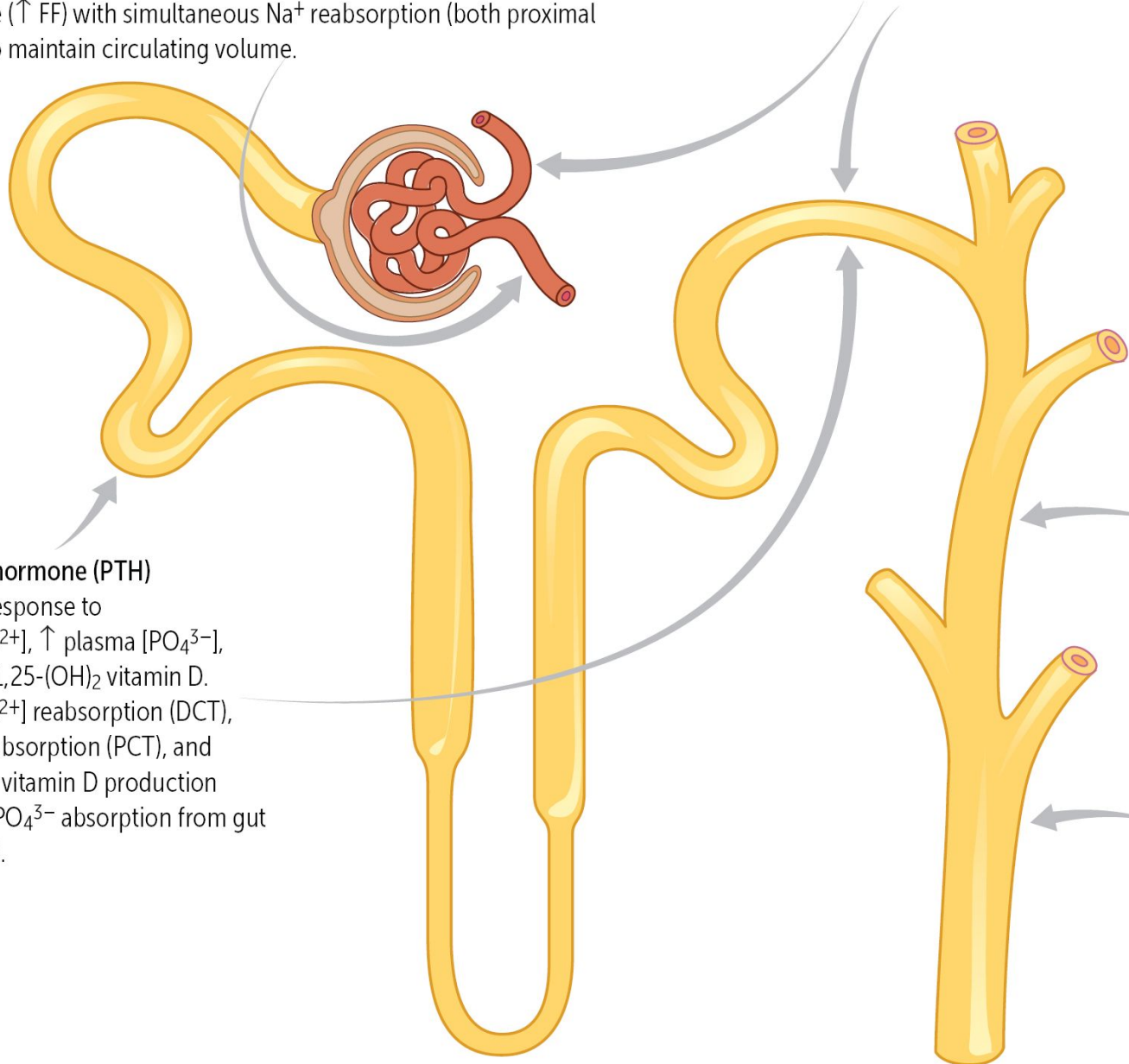
**1010 - 1030**

**Angiotensin II (AT II)**

Synthesized in response to ↓ BP. Causes efferent arteriole constriction → ↑ GFR and ↑ FF but with compensatory Na<sup>+</sup> reabsorption in proximal and distal nephron. Net effect: preservation of renal function in low-volume state (↑ FF) with simultaneous Na<sup>+</sup> reabsorption (both proximal and distal) to maintain circulating volume.

**Atrial natriuretic peptide (ANP)**

Secreted in response to ↑ atrial pressure. Causes ↑ GFR and ↑ Na<sup>+</sup> filtration **with no compensatory Na<sup>+</sup> reabsorption** in distal nephron. Net effect: Na<sup>+</sup> loss and volume loss.



**Parathyroid hormone (PTH)**

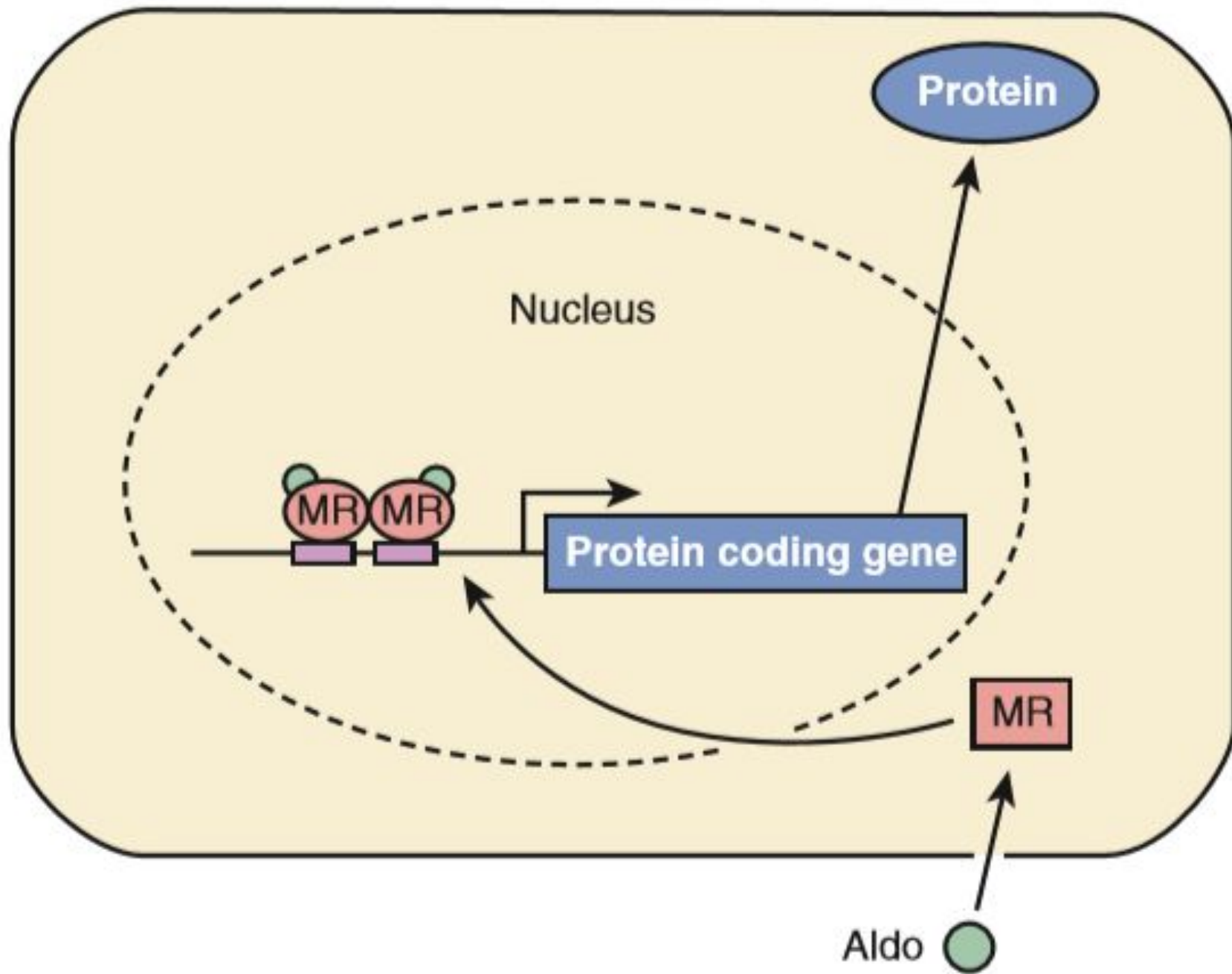
Secreted in response to ↓ plasma [Ca<sup>2+</sup>], ↑ plasma [PO<sub>4</sub><sup>3-</sup>], or ↓ plasma 1,25-(OH)<sub>2</sub> vitamin D. Causes ↑ [Ca<sup>2+</sup>] reabsorption (DCT), ↓ [PO<sub>4</sub><sup>3-</sup>] reabsorption (PCT), and ↑ 1,25-(OH)<sub>2</sub> vitamin D production (↑ Ca<sup>2+</sup> and PO<sub>4</sub><sup>3-</sup> absorption from gut via vitamin D).

**Aldosterone**

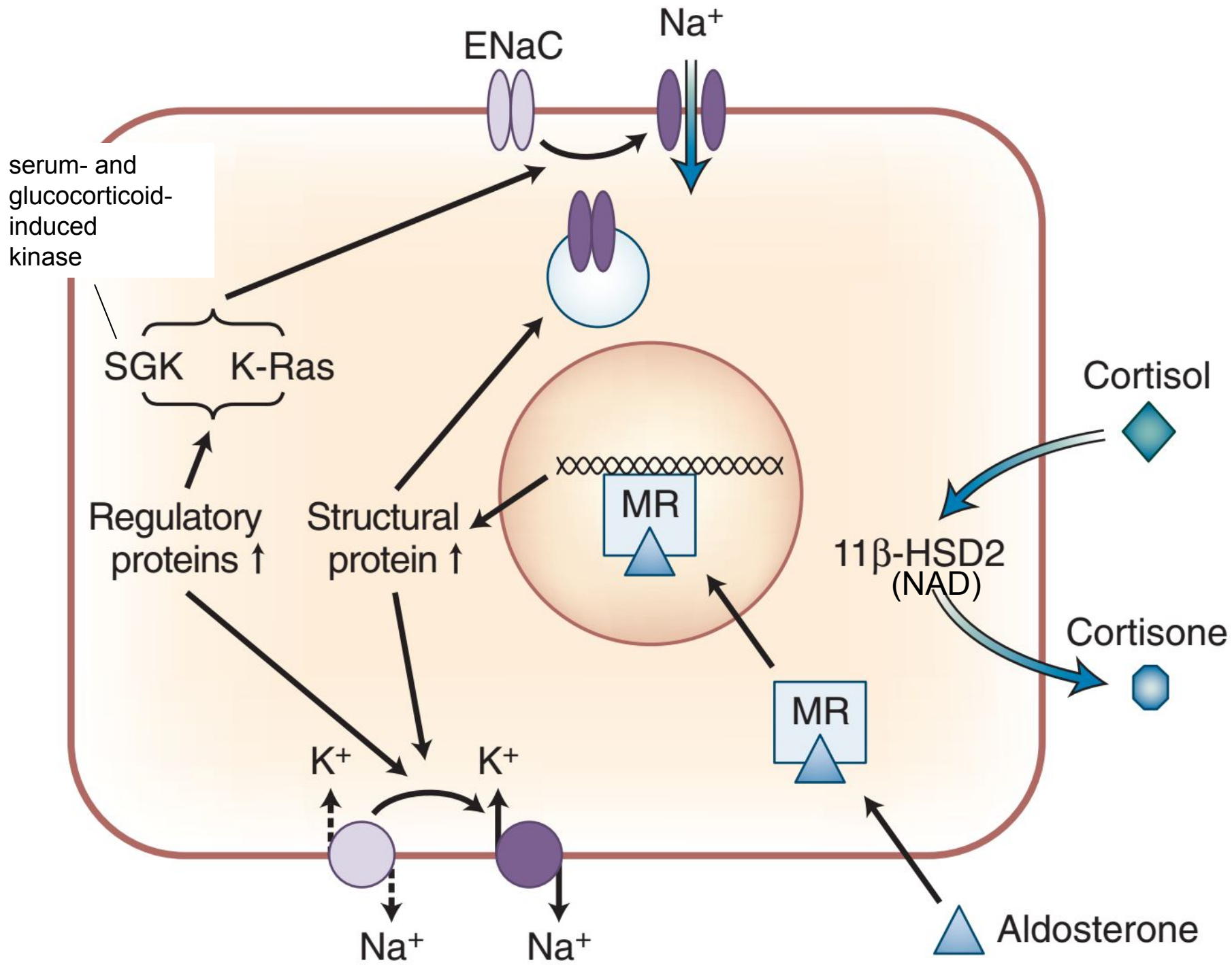
Secreted in response to ↓ blood volume (via AT II) and ↑ plasma [K<sup>+</sup>]; causes ↑ Na<sup>+</sup> reabsorption, ↑ K<sup>+</sup> secretion, ↑ H<sup>+</sup> secretion.

**ADH (vasopressin)**

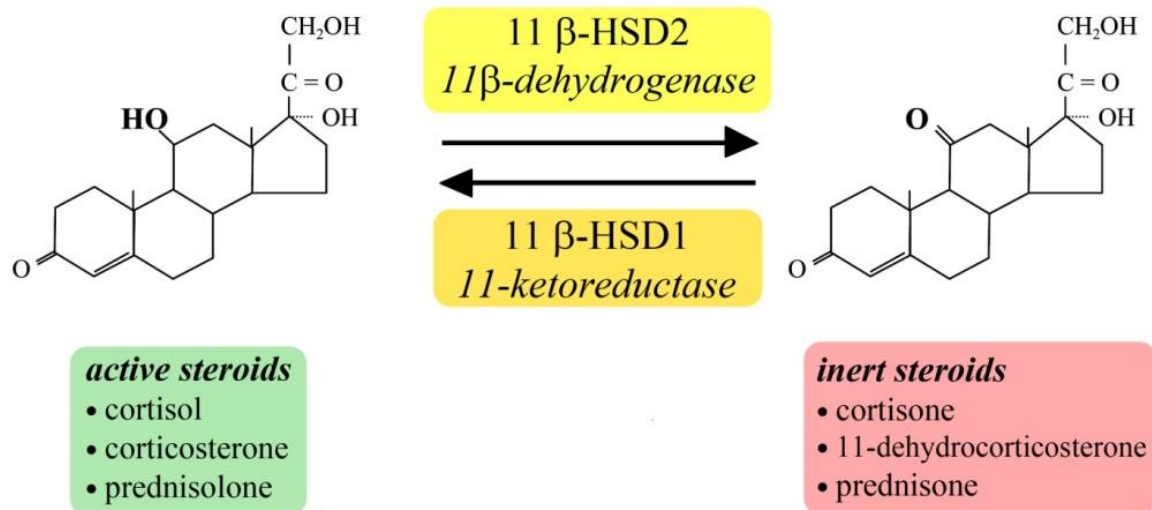
Secreted in response to ↑ plasma osmolarity and ↓ blood volume. Binds to receptors on principal cells, causing ↑ number of water channels and ↑ H<sub>2</sub>O reabsorption.



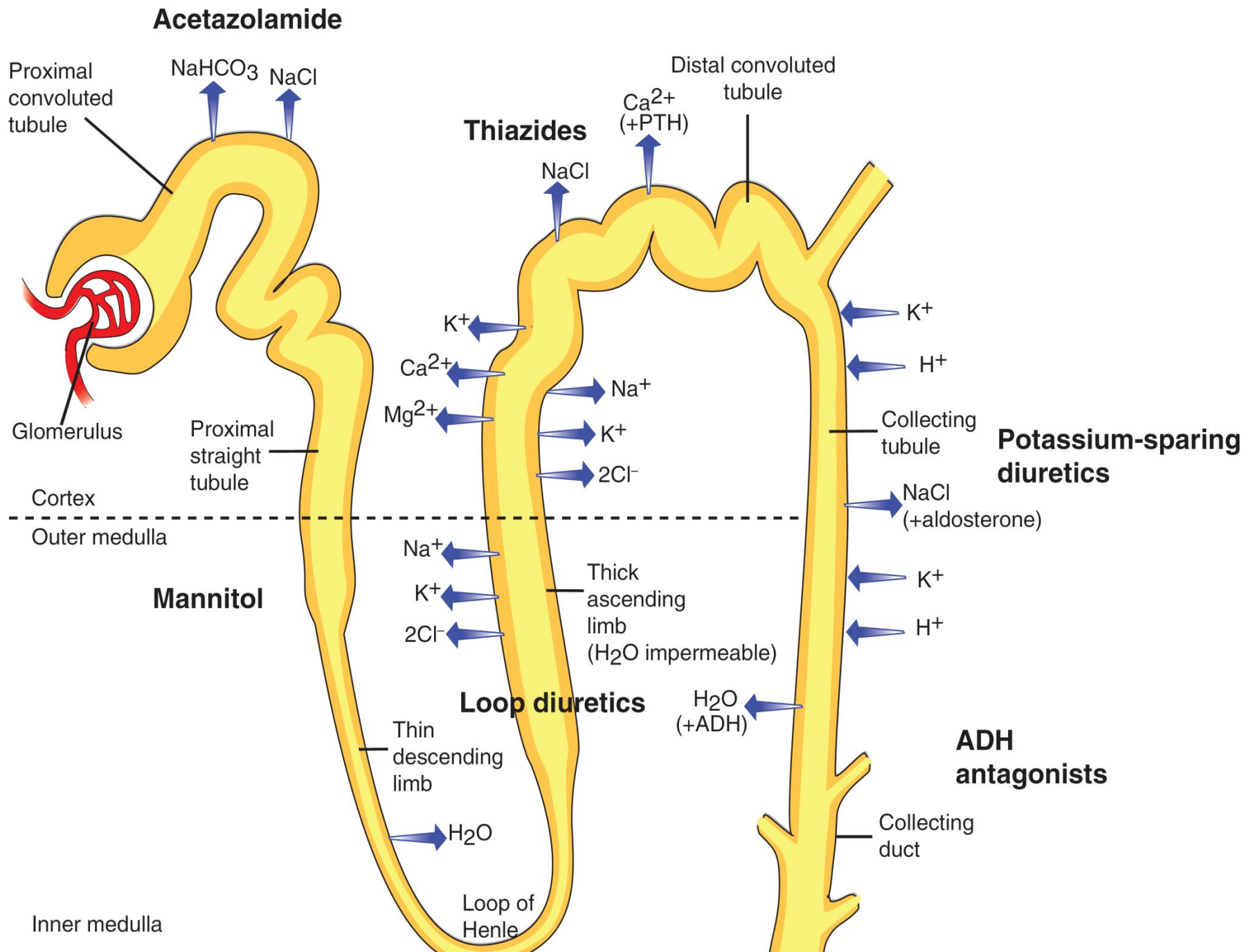




- Синдром кажущегося избытка минералокортикоидов (**SAME**) мутация гена HSD11B2 (гипертензия и гипокалиемия)
- Лакрица (глицирризиновая кислота) – ингибитор 11 $\beta$ -гидроксистероид дегидрогеназы



# Diuretics: site of action



# РОЛЬ АНТИДИУРЕТИЧЕСКОГО ГОРМОНА И РЕНИН-АНГИОТЕНЗИНОВОЙ СИСТЕМЫ В РАЗЛИЧНЫХ ГЕМОДИНАМИЧЕСКИХ РЕАКЦИЯХ:

*1000 мл 0,9% NaCl внутривенно — реакция на небольшое увеличение внутрисосудистого объема*

Это объемная нагрузка изотоническим раствором. Первоначально внутрисосудистый объем увеличивается на 1000 мл, но происходит быстрое перераспределение жидкости во внеклеточных секторах и во внутрисосудистом русле остается около 250 мл, остальной объем наполняет интерстициальное пространство.

- Увеличение объема крови стимулирует кардиопульмональные рецепторы растяжения (правое предсердие).
- Задняя доля гипофиза — снижается секреция АДГ.
- Подавление жажды и активация диуреза.

## *1000 мл крови внутривенно — реакция на значимое увеличение внутрисосудистого объема*

Весь объем остается во внутрисосудистом пространстве.

*Быстрая реакция:*

- Стимуляция барорецепторов артериального русла (каротидный и аортальный синусы) через языкоглоточный и блуждающий нервы.
- Рефлекторное снижение сердечного выброса и сосудистого тонуса.

*Медленная реакция:*

- Подавление ренин-ангиотензиновой системы.
  - Снижение секреции альдостерона.
-

## ***1000 мл 5% глюкозы (внутривенно) или воды (per os) — реакция на снижение осмолярности***

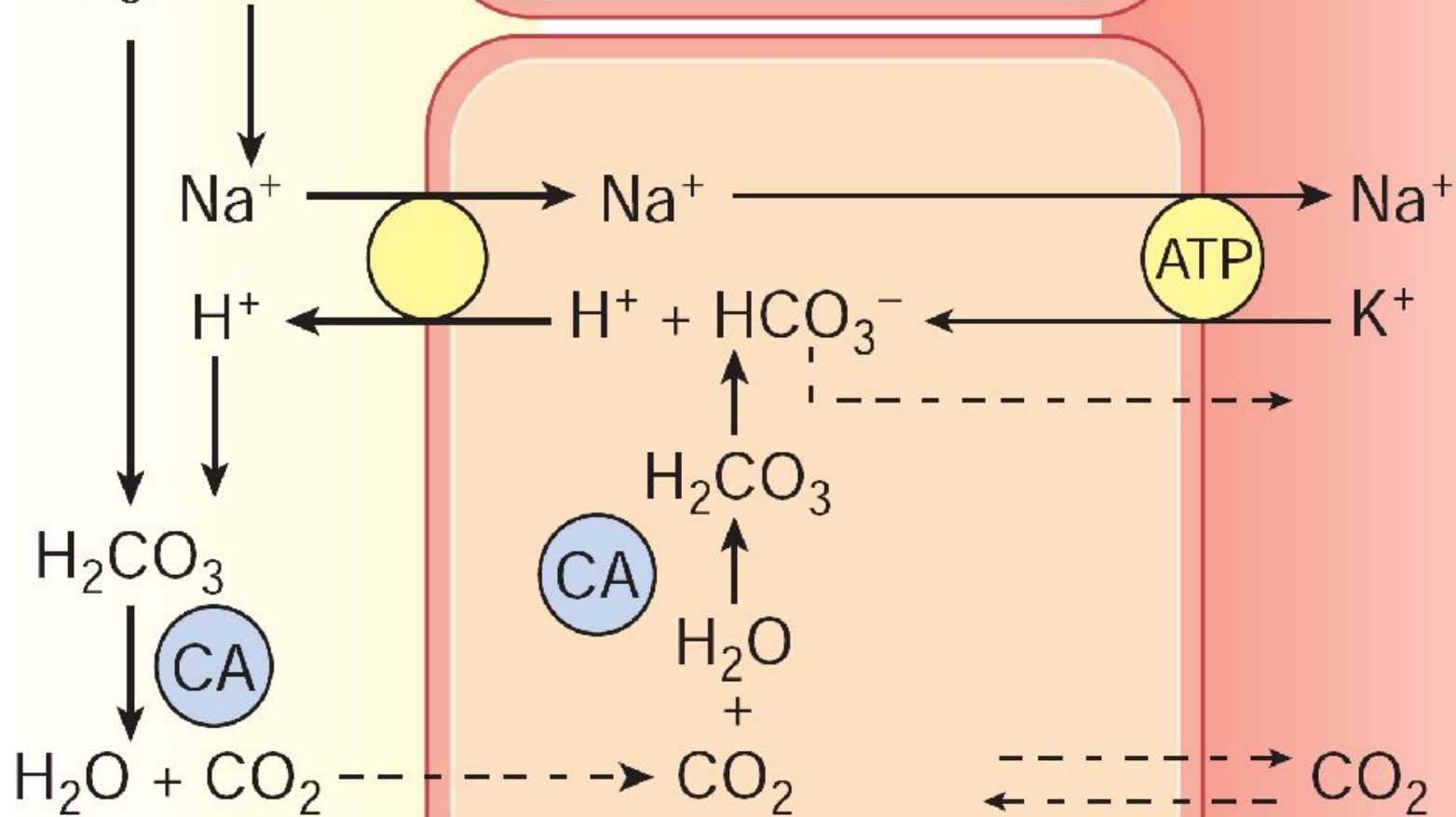
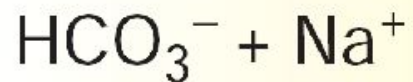
Объемная нагрузка небольшая, так как вода распределяется во всех жидкостных секторах организма и во внутрисосудистом русле остается одна двенадцатая часть (83 мл). Прием воды вызывает схожий эффект, так как она быстро абсорбируется из желудка. При этом происходит разведение плазмы и снижение осмолярности.

- Реакция опосредуется осморецепторами гипоталамуса.
  - Снижение секреции альдостерона.
-

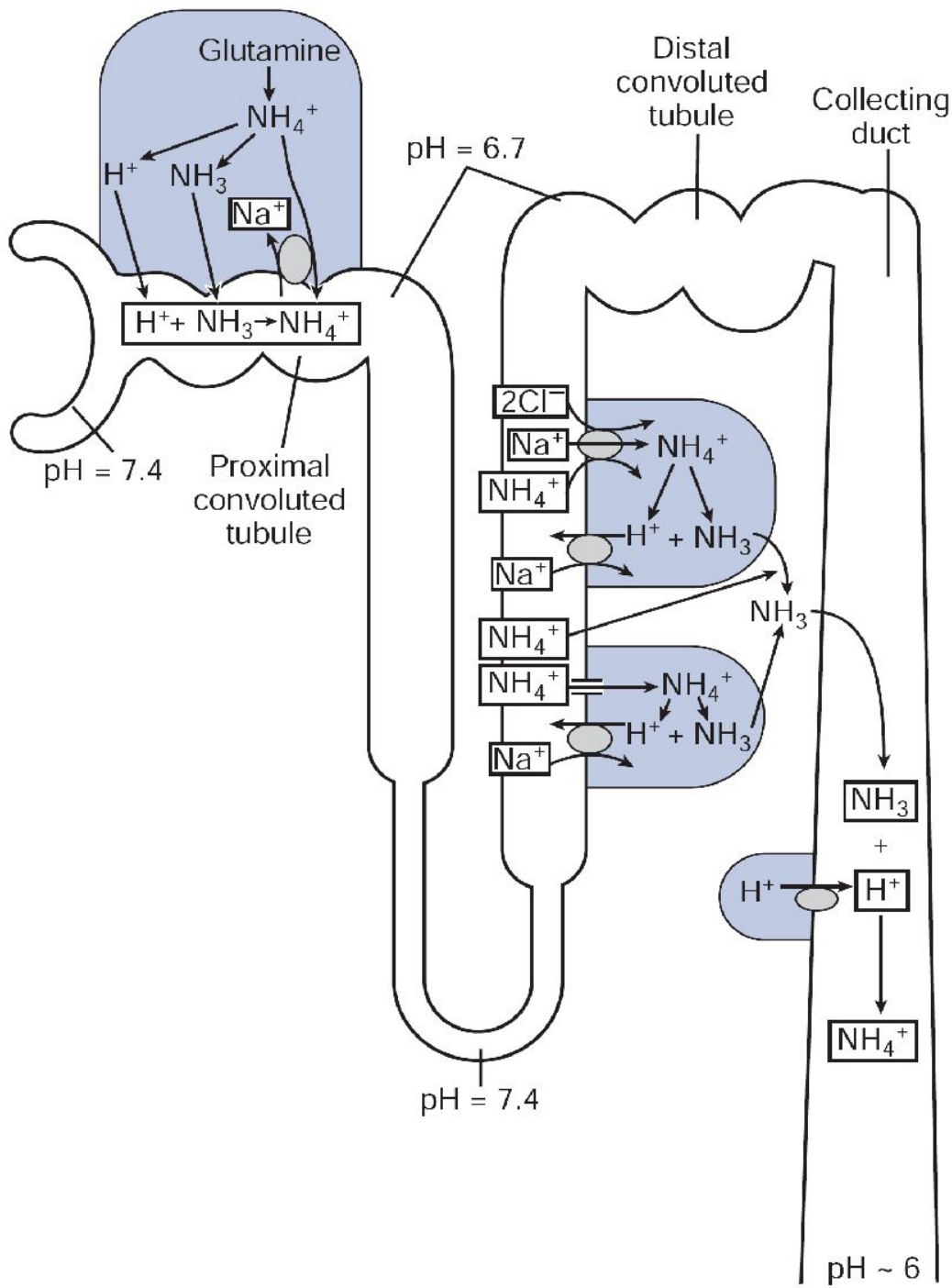
# Почки и КЩС

- Реабсорбция бикарбоната (проксим.)
- Аммонигенез
- НРОЗ
- ацидогенез (дист.)

Почти **100%** бикарбоната  
фильтруется в почках

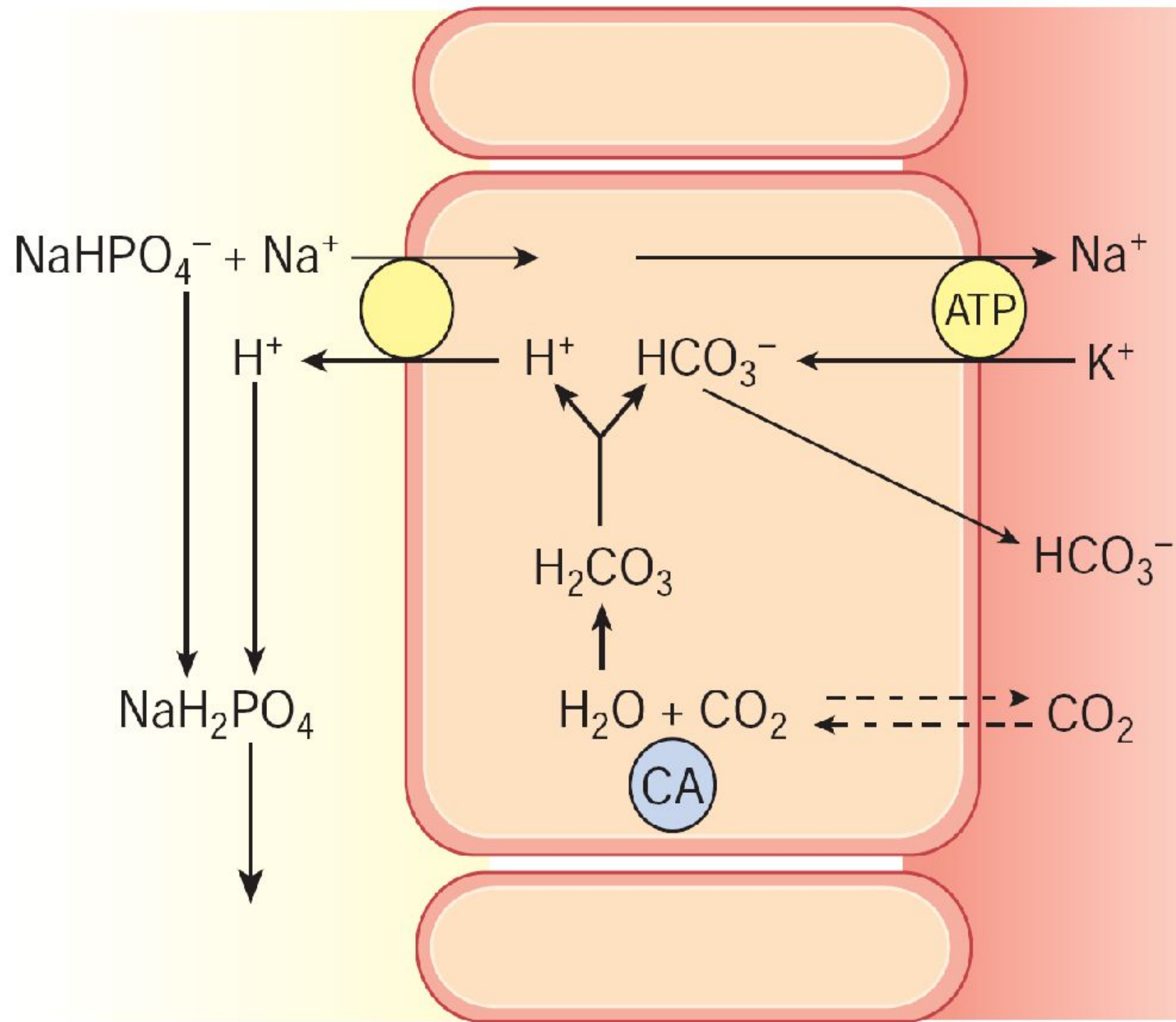






1. The synthesis of ammonium ( $\text{NH}_4^+$ ) from the amino acid glutamine in the proximal tubule
2. The reabsorption and recycling of  $\text{NH}_4^+$  within the medullary portion of the kidney
3. The buffering of  $\text{H}^+$  ions by  $\text{NH}_3$  in the collecting tubules<sup>1,3</sup>

Ammonia ( $\text{NH}_3 + \text{NH}_4$ ) is chiefly produced in proximal tubule cells and is secreted into the tubular urine.  $\text{NH}_4$  is reabsorbed in the thick ascending limb and accumulates in the kidney medulla.  $\text{NH}_3$  diffuses into acidic collecting duct urine, where it is trapped as  $\text{NH}_4$ .



**Type 1**  
**(distal, pH > 5.5)**

Defect in ability of  $\alpha$  intercalated cells to secrete  $H^+$ . Thus, new  $HCO_3^-$  is not generated  $\rightarrow$  metabolic acidosis. Associated with **hypokalemia**,  $\uparrow$  risk for calcium phosphate kidney stones (due to  $\uparrow$  urine pH and  $\uparrow$  bone turnover).

Causes—amphotericin B toxicity, analgesic nephropathy, multiple myeloma (light chains), and congenital anomalies (obstruction) of the urinary tract.

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**Type 2**  
**(proximal, pH < 5.5)**

Defect in proximal tubule  $HCO_3^-$  reabsorption results in  $\uparrow$  excretion of  $HCO_3^-$  in urine and subsequent metabolic acidosis. Urine is acidified by  $\alpha$  intercalated cells in collecting tubule. Associated with **hypokalemia**,  $\uparrow$  risk for hypophosphatemic rickets.

Causes—Fanconi syndrome (c.g., Wilson disease), chemicals toxic to proximal tubule (c.g., lead, aminoglycosides), and carbonic anhydrase inhibitors.

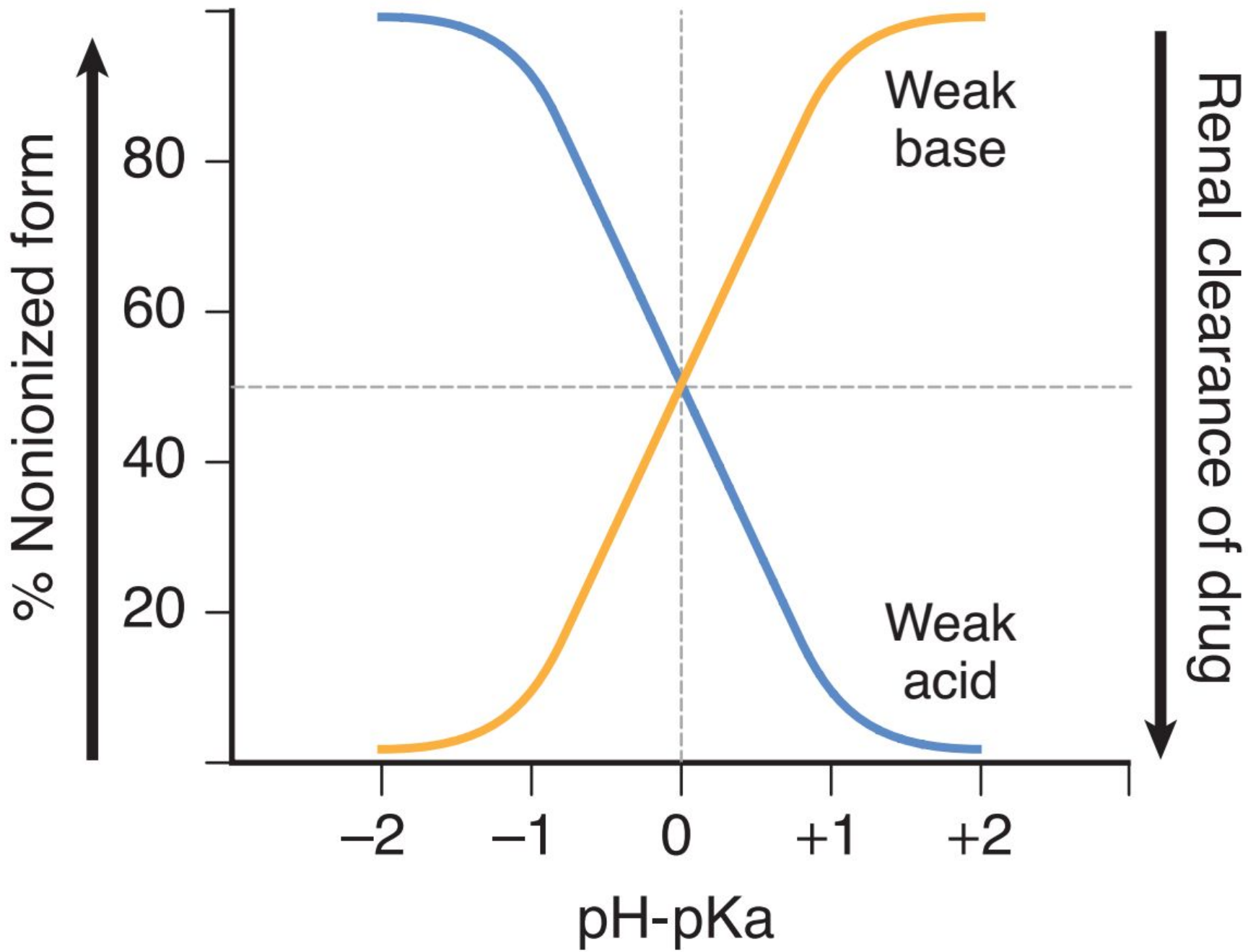
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**Type 4**  
**(hyperkalemic, pH < 5.5)**

Hypoaldosteronism, aldosterone resistance, or  $K^+$ -sparing diuretics. The resulting hyperkalemia impairs ammoniagenesis in the proximal tubule  $\rightarrow$   $\downarrow$  buffering capacity and  $\downarrow$   $H^+$  excretion into urine.

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“**ACID**”azolamide causes **ACID**osis.



**Case:** A 70-year-old woman with a history of osteoarthritis comes to the emergency department because of shortness of breath, tinnitus, and decreased hearing. Her blood gas is initially alkalotic but changes to a pH of 7.28 with a  $p\text{CO}_2$  of 23. Her serum bicarbonate is low, and the anion gap is increased.

1. What is the diagnosis?
2. What is the best initial therapy?
3. How does it work?

# A. Toxicology

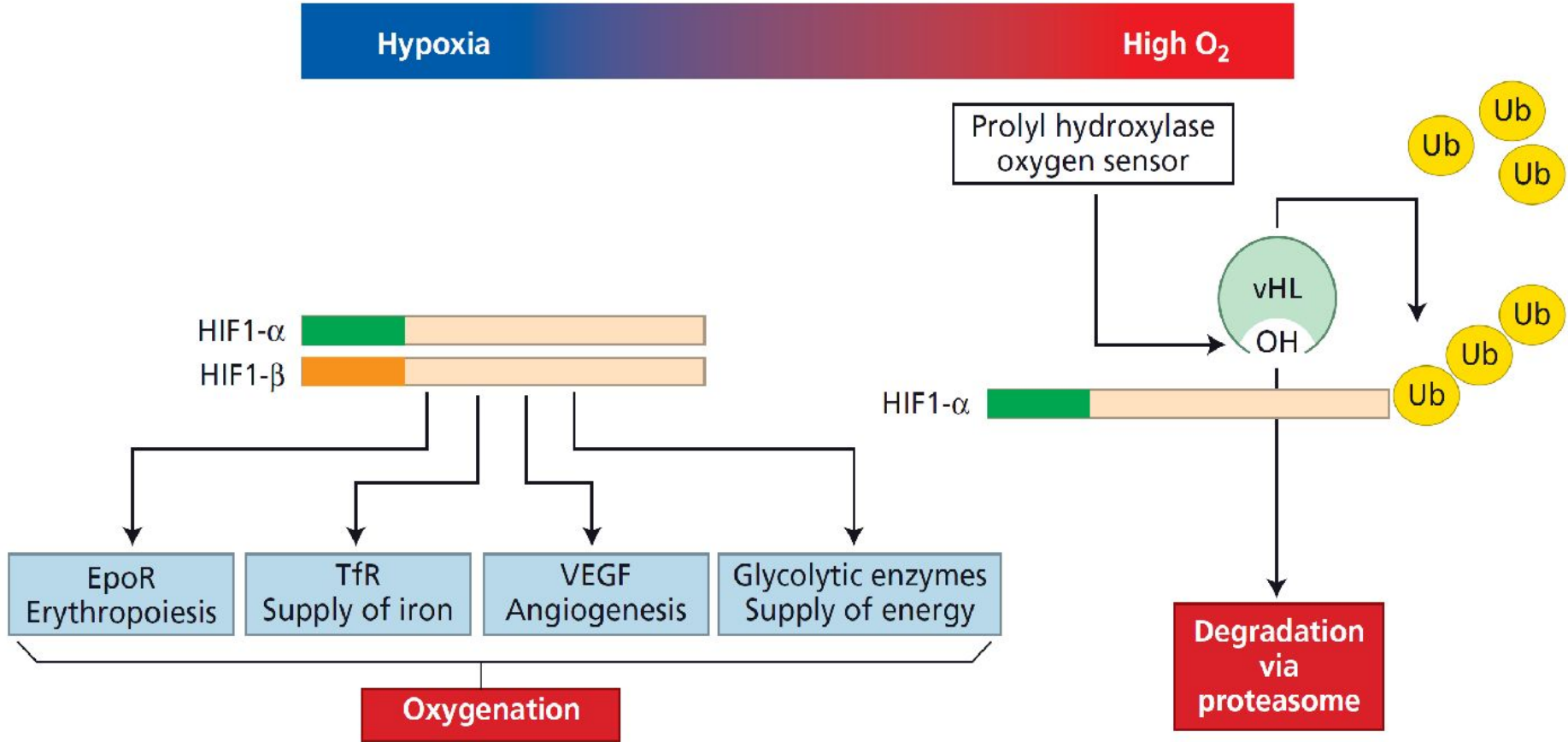
Card 3

1. **Aspirin (salicylate) toxicity** presents with hyperventilation secondary to direct stimulation of the respiratory centers in the brain. In addition, aspirin toxicity can cause tinnitus, encephalopathy, and with severe toxicity pulmonary edema and hyperthermia. In early toxicity, there is respiratory alkalosis from direct stimulation of the brain stem. This is followed by metabolic acidosis, because aspirin poisons the mitochondria and you lose the aerobic metabolism of oxidative phosphorylation. Lactic acidosis accumulates from anaerobic glycolysis.
2. **Bicarbonate** is the best initial therapy for aspirin poisoning.
3. Bicarbonate will **alkalinize the urine**, resulting in increased excretion of aspirin at the kidney tubule.

## Стимулы:

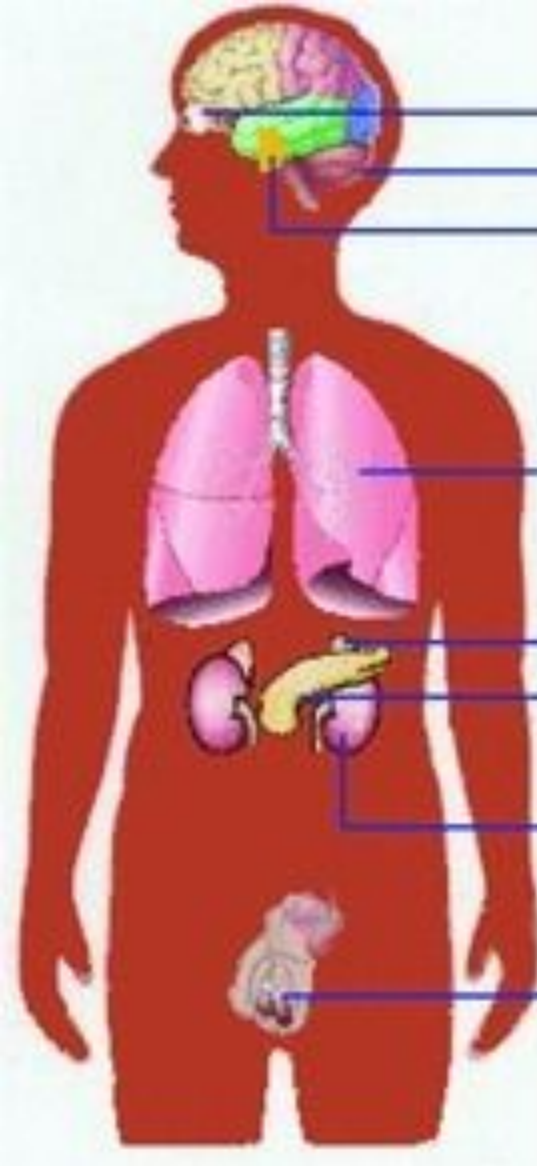
- Снижение числа эритроцитов
- Снижение  $O_2$  в крови
- Повышение потребностей тканей в  $O_2$





The **juxta-tubular cells** of the kidney sense oxygen tension. Proline hydroxylase requires O<sub>2</sub> to hydroxylate a key protein: hypoxia-inducible factor (HIF). This allows the ubiquitination of HIF-alpha by the von Hippel-Lindau factor (VHL) & ubiquitin ligase (UL), resulting in the degradation of HIF in the proteasome. When O<sub>2</sub> is low, HIF activates the gene for EPO and other genes, increasing Hb and encouraging blood vessel formation.





Retinal haemangiomas (70%)

CNS haemangioblastomas (60-84%)

Endolymphatic sac tumours of the middle ear (14%)

Lung cysts (rare, <1%)

Pheochromocytomas (18%)

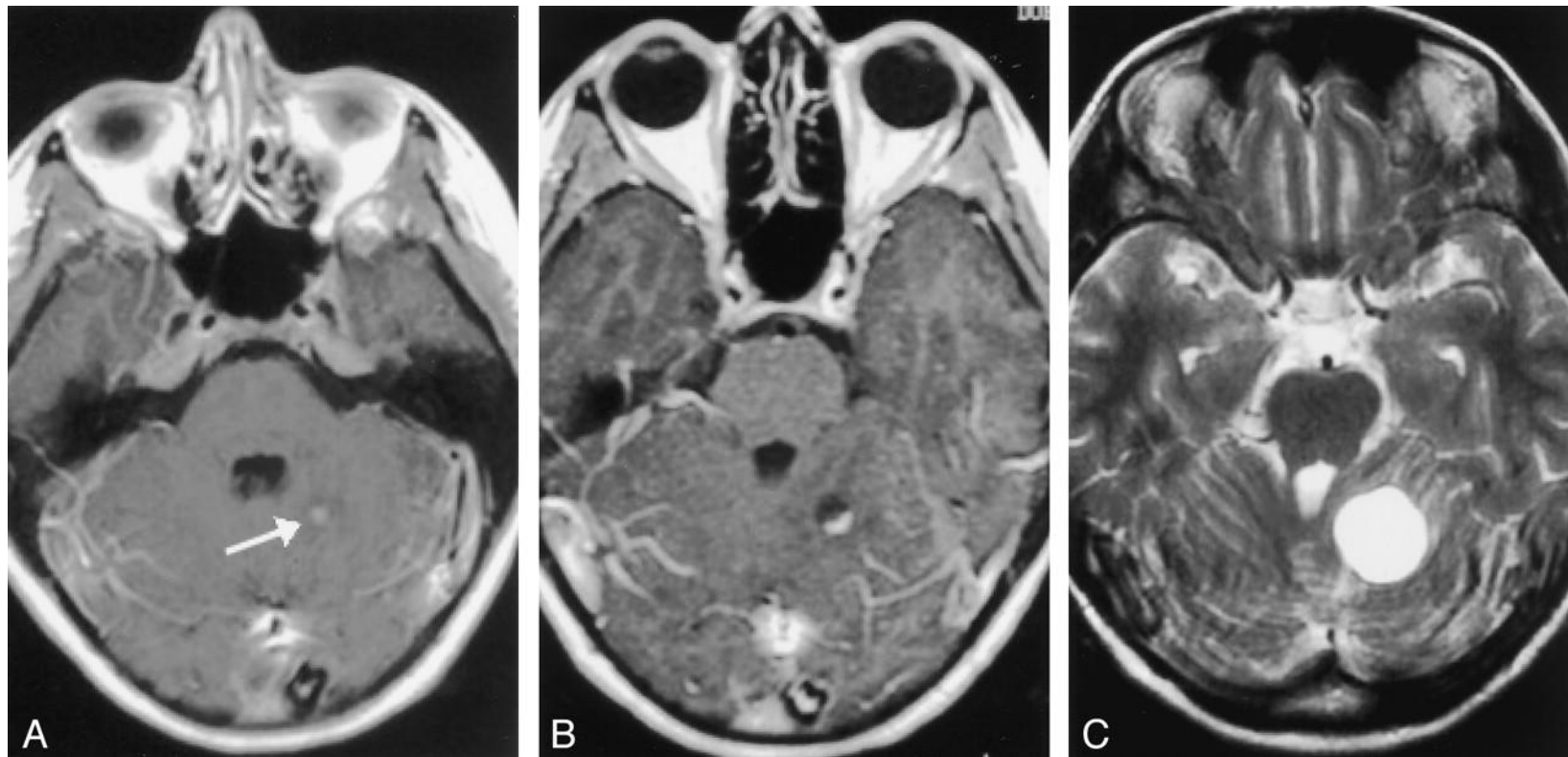
Pancreas: cysts (70%), serous cystadenomas (9%), neuroendocrine tumours (9%)

Kidney: cysts (66%), clear cell renal cell carcinomas (69%)

Epididymal (male, 54%) or broad ligament (female) papillary cystadenomas

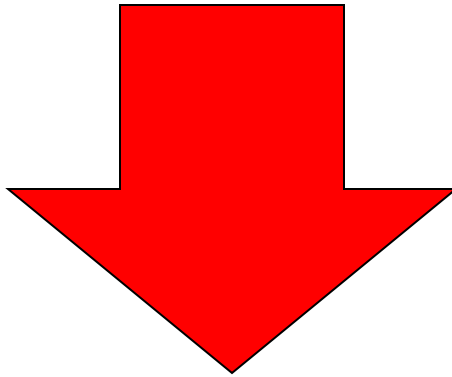


Images in a third patient with a solid cerebellar tumor that progressed to enlarging cyst with the subsequent development of symptoms. A, Contrast-enhanced T1-weighted MR image obtained at presentation shows a tiny enhancing nodule in the left cerebellar hem...

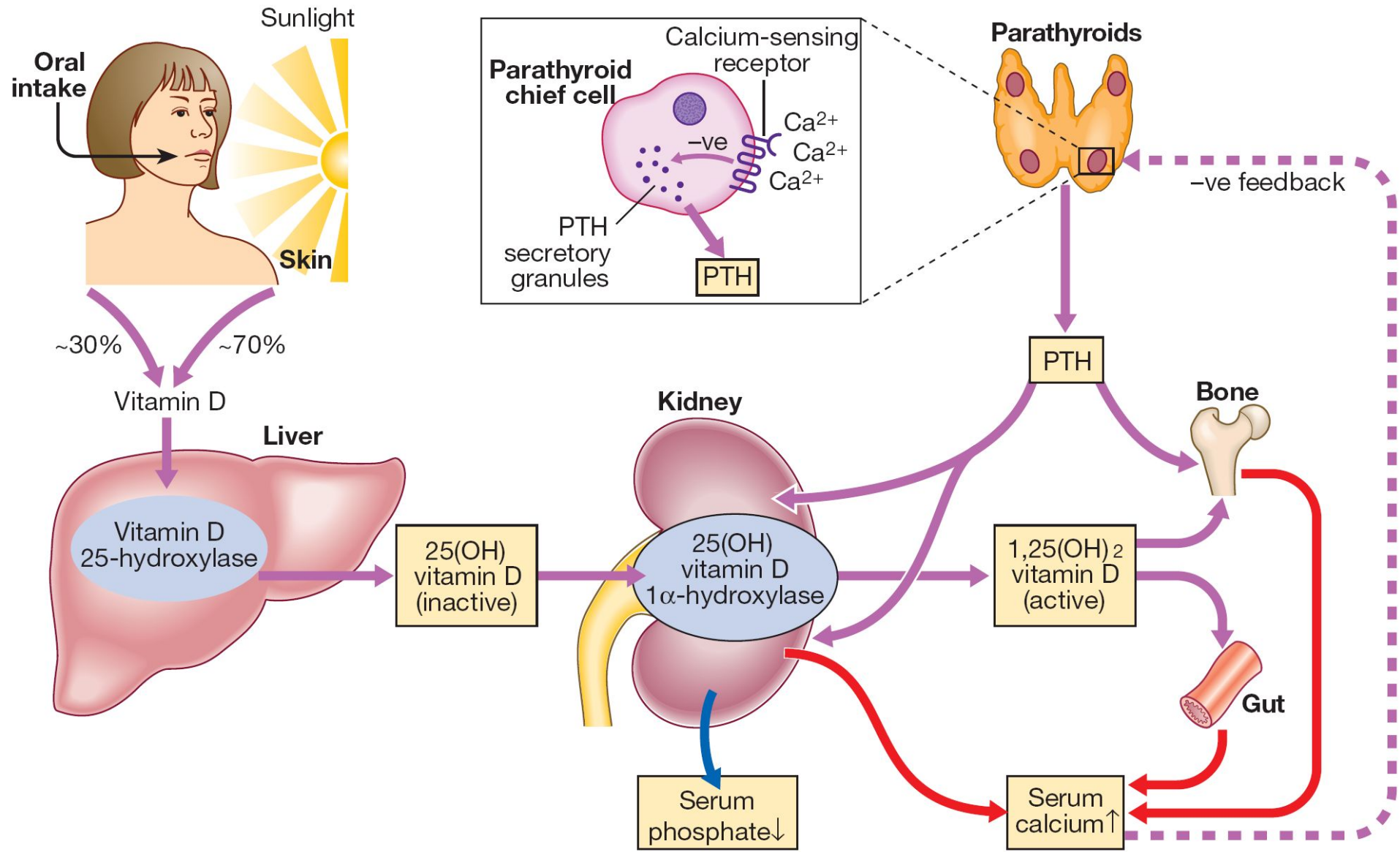


Andrew Slater et al. AJNR Am J Neuroradiol  
2003;24:1570-1574

# Одна из причин эритроцитоза



**! Почечно-клеточный рак !**



**Vitamin D** promotes bone mineralization by stimulating the release of **alkaline phosphatase** from osteoblasts. Alkaline phosphatase hydrolyzes pyrophosphate (removes the phosphate) and **other inhibitors** of calcium-phosphate crystallization