# PHYSIO

## MODIFIED NO. 4


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# Renal Physiology Lect-3
# Guyton chapter 28

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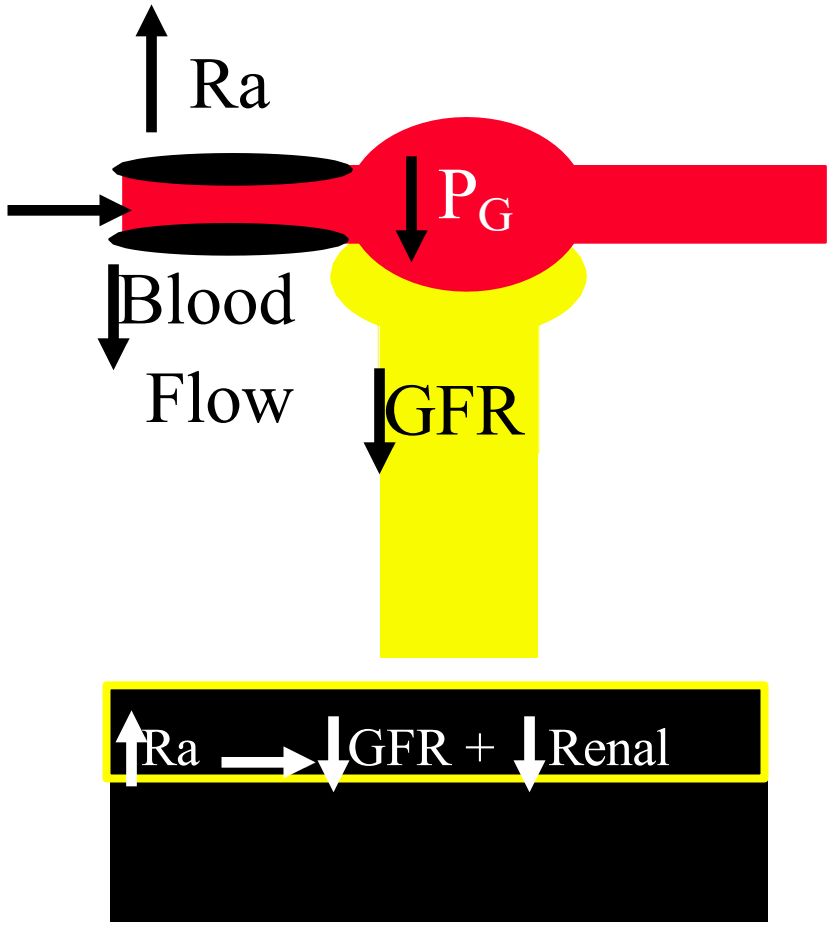
**Color code**

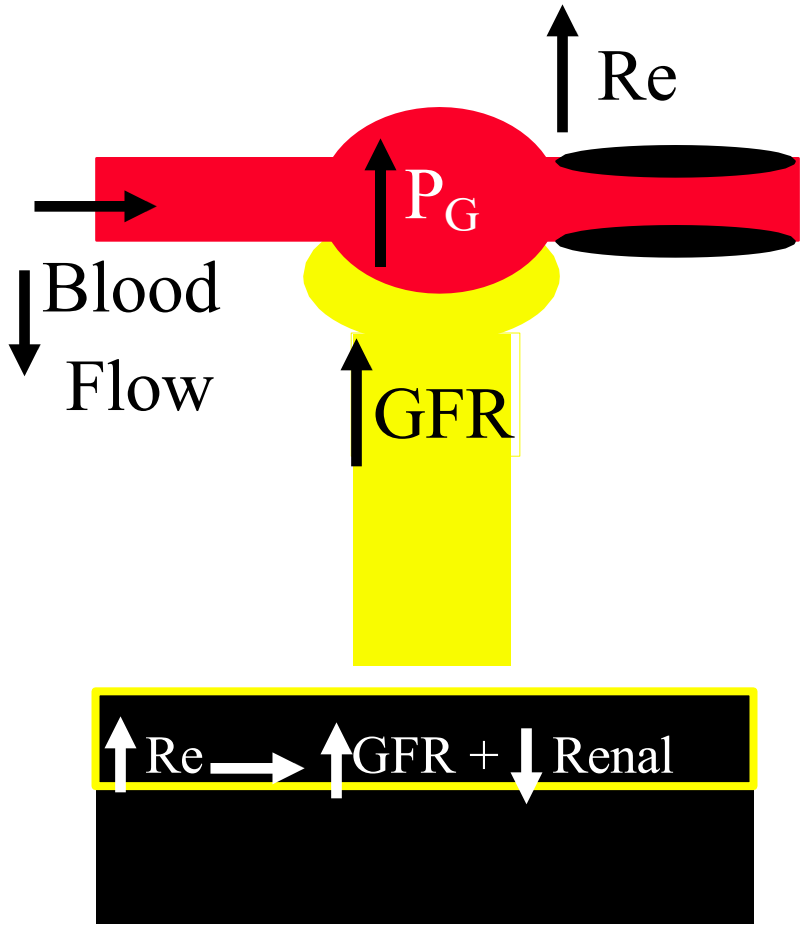
- Slides
- Doctor
- Additional info
- Important

# Effect of afferent and efferent arteriolar constriction on glomerular pressure

A quick revision for the previous lecture

- A modest increase in **efferent** arteriole resistance -> an increase in GFR.
- A modest increase in **afferent** arteriolar resistance -> a decrease in GFR.
- **Both** cases cause a decrease in renal blood flow; because we are impeding blood flow either way.

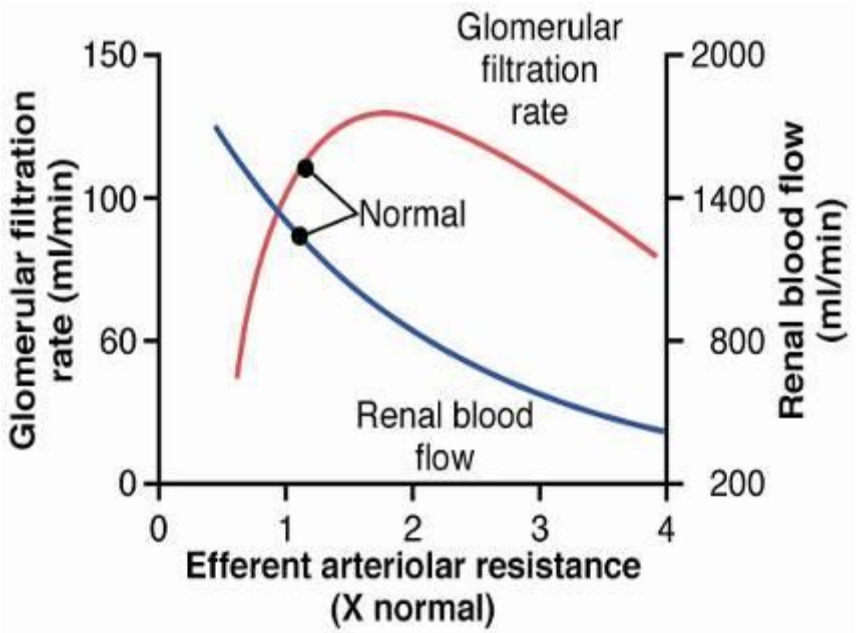


# Effect of changes in afferent arteriolar or efferent arteriolar resistance

Biphasic

When we increase the **afferent** arteriole resistance, we let less blood get into the glomerulus and this obviously will cause less filtration.



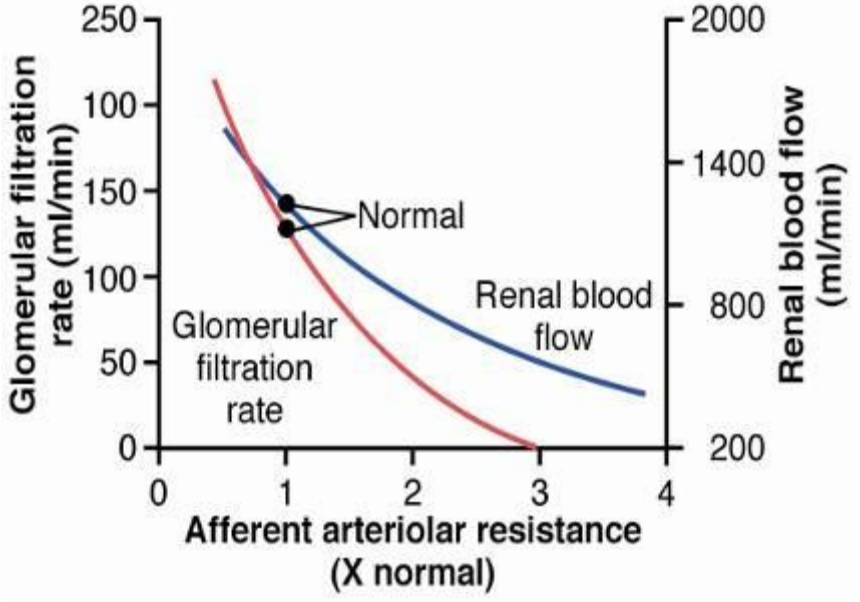
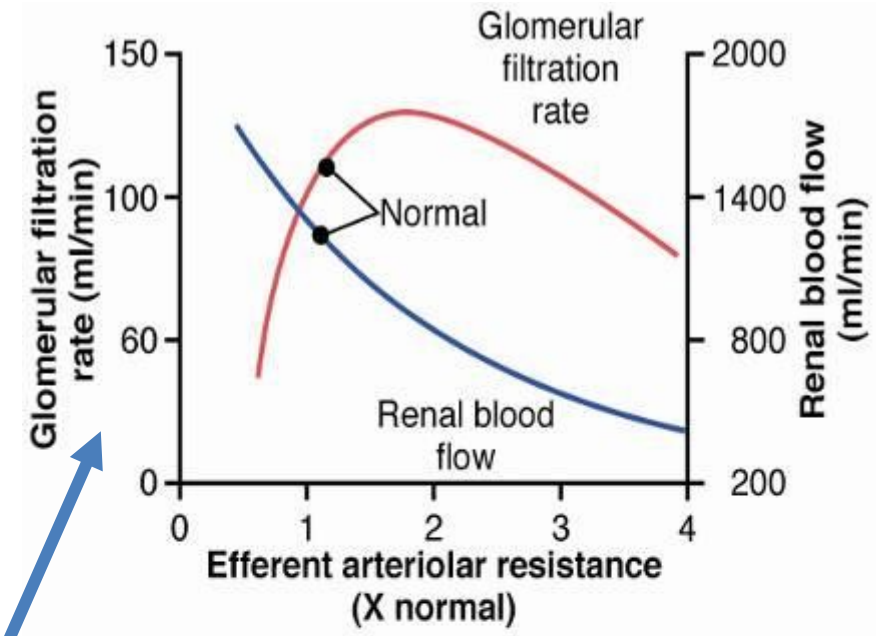



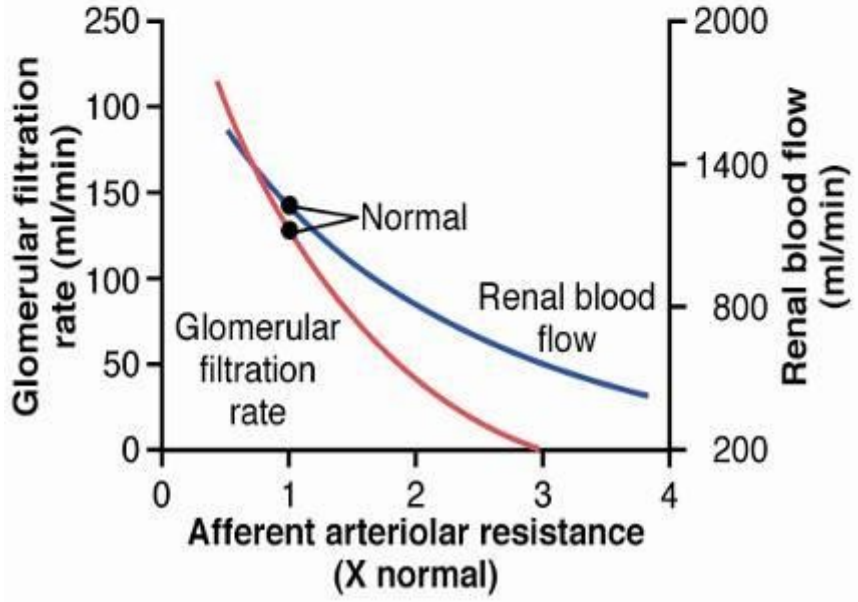

Figure 26-15

Biphasic

When we increase the **efferent** arteriole, we will get a biphasic response :

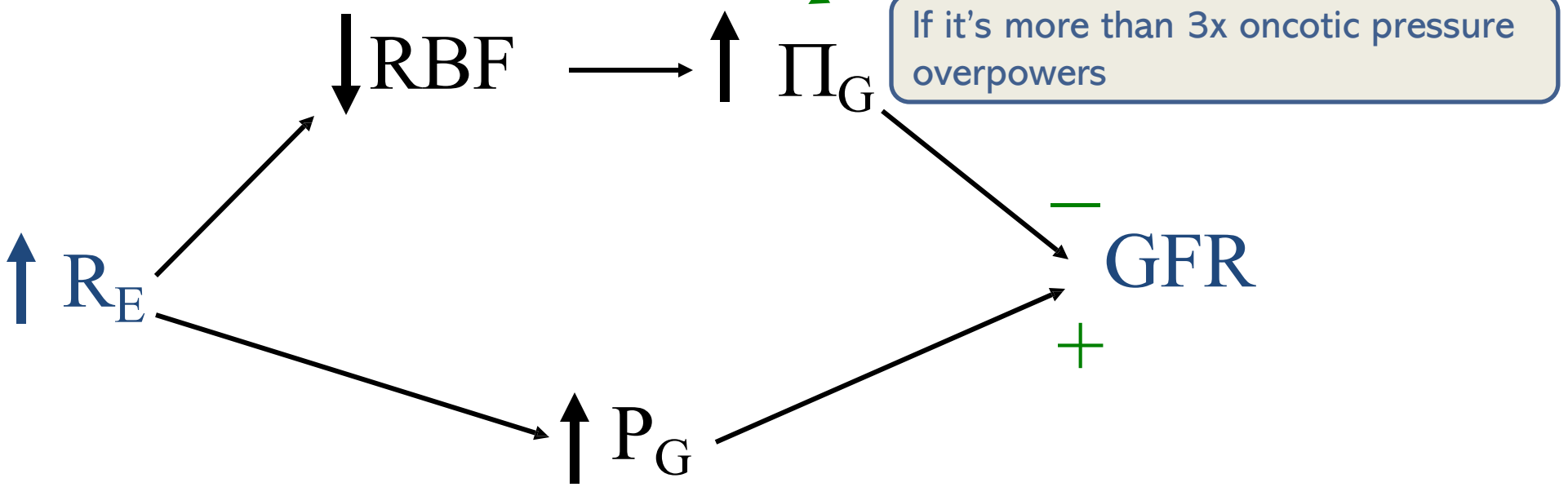
- **The first phase**: we will get a direct relationship between the resistance and GFR (from 1x the resistance to about 3x the resistance), meaning that when the resistance increases -> the GFR increases. This is because hydrostatic pressure will build up inside the glomerulus, causing more filtration.
- **The second phase**: (more than 3x the resistance), we will start seeing a decline in GFR, this is because at this level, filtration is so significant that the proteins inside the glomerulus will make a powerful **oncotic pressure** overpowering the hydrostatic pressure. Also, FF will increase significantly because RBF decreased significantly.



Why is GFR has Biphasic Curve when $R_{efferent}$ increases?

$\pi_G$ determined by : FF = GFR / RPF



# Summary of Determinants of GFR

This slide is important

- Π = Oncotic pressure
- A = Arterial
- G = glomerular
- $R_A$ = Afferent resistance
- $R_E$ = Efferent resistance

↑GFR If → ↑ $K_f$

↑GFR If → ↓ $P_B$ (Bowman's capsule pressure)

↑GFR If → ↓ $\Pi_G$

↑$\Pi_G$ If → ↑$\Pi_A$ → ↓GFR

↑$\Pi_G$ If → ↑FF → ↓GFR

↑GFR If → ↑ $P_G$

↑$P_G$ If → ↓ $R_A$ → ↑ GFR

↑$P_G$ If → ↑ $R_E$ → ↑ GFR

(as long as ↑ $R_E$ < 3-4 x normal)

# Determinants of Renal Blood Flow (RBF)

- The dr read the whole slide

$$RBF = \Delta P / R$$

$\Delta P$ = difference between renal artery pressure and renal vein pressure

R = total renal vascular resistance

= Ra + Re + Rv

= sum of all resistances in kidney vasculature

# Renal blood flow

This high amount of blood flow is not because of the metabolic demand of the kidney but for the function of it.

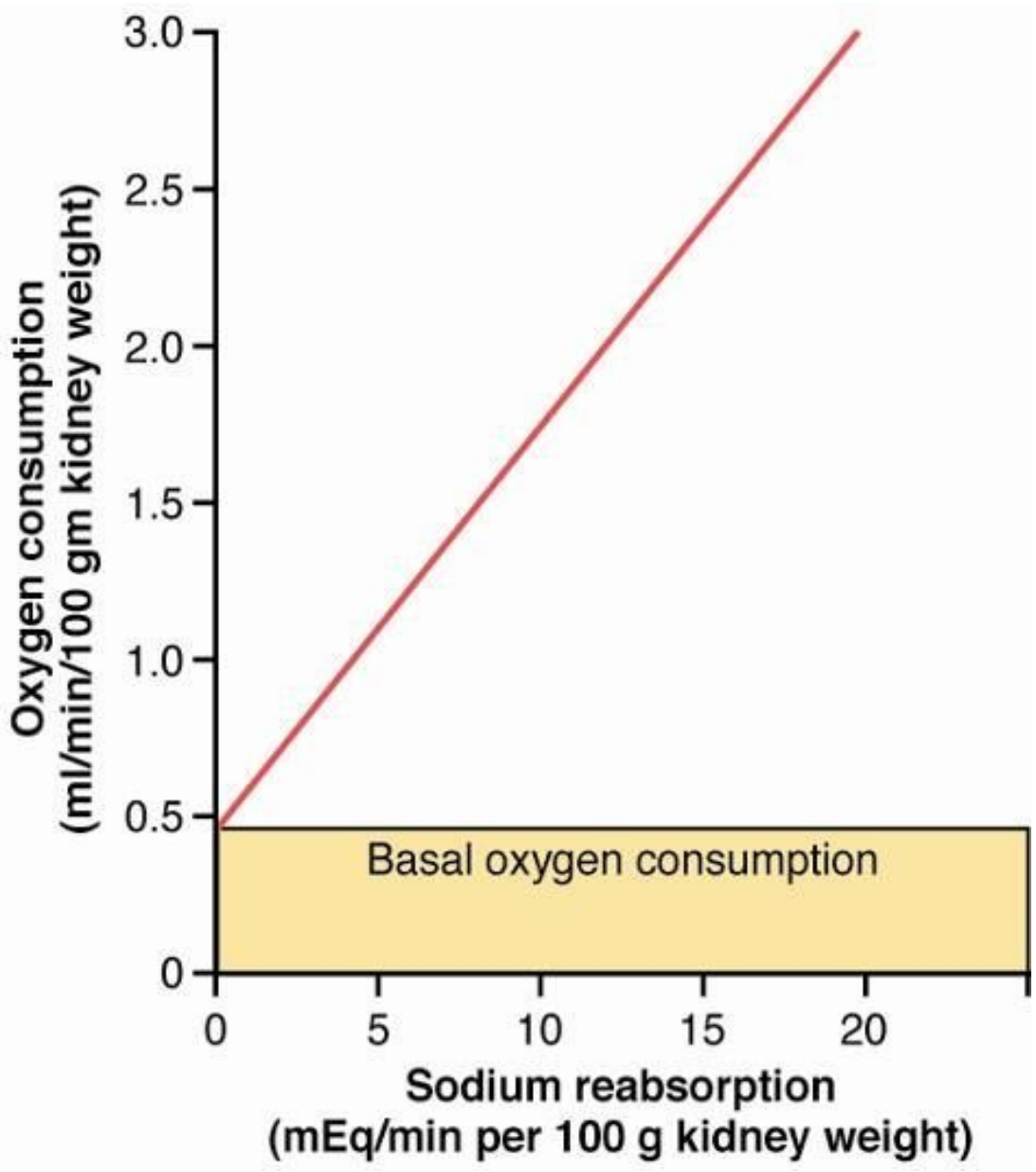
- High blood flow (~22 % of cardiac output)
- High blood flow needed for high GFR
- Oxygen and nutrients delivered to kidneys normally greatly exceeds their metabolic needs
- A large fraction of renal oxygen consumption is related to renal tubular sodium reabsorption

Because it relies on active mechanisms (using ATP)

# Renal oxygen consumption and sodium reabsorption

This is an experiment showing that oxygen consumption of the kidney is directly affected by Na+ reabsorption.

At 0 Na+ reabsorption there is still a basal oxygen consumption to maintain the vitality of the cells.



Now let's talk about control mechanisms for GFR.

# Control of GFR and renal blood flow

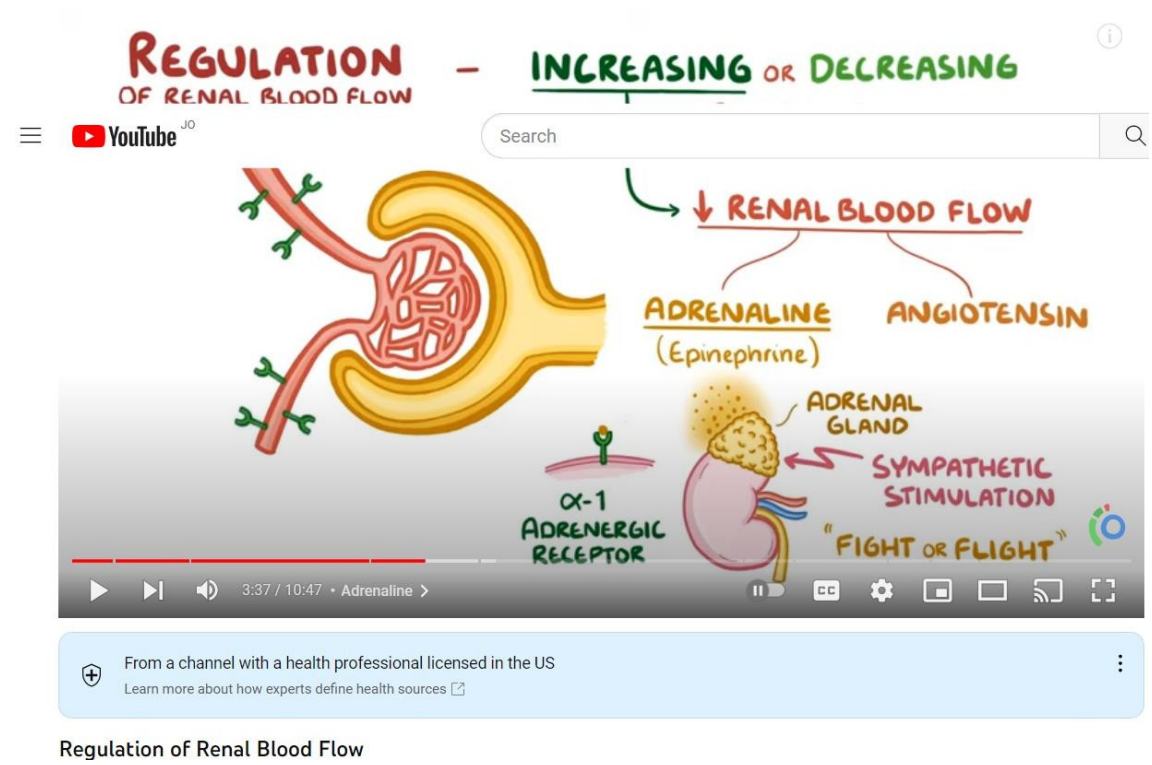
- Neurohumoral

Intrinsic control is the most important, it is limited within the kidney itself.

- Local (Intrinsic)

# Audio-visual Aid

[Regulation of Renal Blood Flow - YouTube]




Regulation of Renal Blood Flow

# Control of GFR and renal blood flow

## 1. Sympathetic Nervous System /catecholamines

$\uparrow\uparrow R_A + \uparrow R_E \longrightarrow \downarrow GFR + \downarrow\downarrow RBF$

e.g. severe hemorrhage

## 2. Angiotensin II

$\uparrow R_E \longrightarrow \longleftrightarrow GFR + \downarrow RBF$

(prevents a decrease in GFR)

e.g. low sodium diet, volume depletion

- **Sympathetic control** (neuronal) : mainly by Epinephrine, only in severe situations like severe hemorrhage for example, it increases both afferent and efferent resistances but afferent to a greater extent, causing a net decrease in GFR, but in case of mild sympathetic stimulation, afferent and efferent resistances increase equally canceling each other keeping GFR as is.

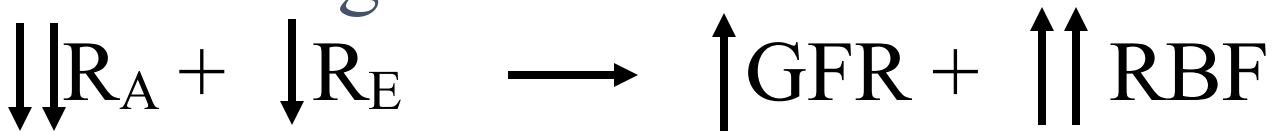
- **Angiotensin II (humoral)** : when we have a low BP (because of low Na+ in diet or volume depletion), the GFR will drop, the juxtoglomerlular apparatus has sensors for low BP and will release renin -> activating the RAAS pathway and eventually releasing Angiotensin II; this will cause the afferent and efferent glomerular arterioles resistances to increase, but efferent to a greater extent, increasing GFR. But remember, GFR was low in the first place so it will just go back to its normal level, in summary Angiotensin II prevents the decrease of GFR.

So, if the doctor asks: what is the direct effect of Angiotensin II on GFR? The answer is increase.

What is the net effect? Bringing GFR back to normal if it decreased, so don't be mislead by the symbols in the previous slide

# Control of GFR and renal blood flow

## 3. Prostaglandins




Blockade of prostaglandin synthesis → ↓ GFR

- This is usually important only when there are other disturbances that are already tending to lower GFR

- e.g. nonsteroidal antiinflammatory drugs in a
- volume depleted patient, or a patient with heart failure,
- cirrhosis, etc

3) **prostaglandins**:

❑ Hormonal local factors that are released normally via blood vessels or the kidney.

❑ The effect of prostaglandins is:

Vasodilation of afferent arteriole ➡️ decrease the resistance (Ra) ➡️ increase of renal blood flow (RPF) ➡️ increase of glomerular hydrostatic pressure (PG) ➡️ increase glomerular filtration rate (GFR).

❑ Prostaglandins work as protective procedure:

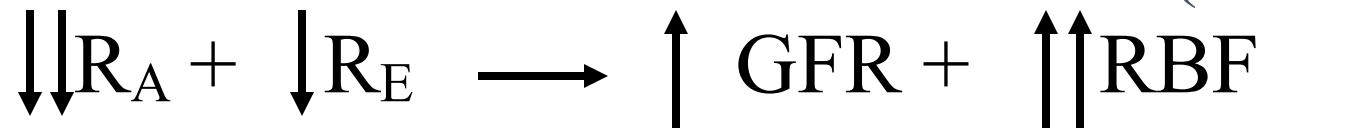
When we have impairment of GFR, the prostaglandins help the kidney to maintain normal level of GFR (prevent further decline in GFR).

❑ Clinical application:

❑ People take prostaglandins blockers such as NSAIDs, which will lead to decreased synthesis of prostaglandins so it is not indicated to give NSAIDs for a person with decreased GFR, you can give him/her paracetamol instead of it.

- Vasodilation effect on afferent Arteriole more than efferent Arteriole so the GFR will increase not decrease.

# 4. Endothelial-Derived Nitric Oxide (EDRF)




- Protects against excessive vasoconstriction
- Patients with endothelial dysfunction (e.g. atherosclerosis) may have greater risk for excessive decrease in GFR in response to stimuli such as volume depletion

- These patients have low level of EDRF so, the GFR will decrease, especially if there are other stimuli such as volume depletion or hypotension.

4) Endothelial Derived nitric oxid (EDRF) (hormone with nitric , a gas):

❑ The effect of EDRF:
Vasodilation of afferent arteriole more than efferent Arteriole ➡️ decrease the resistance (Ra) ➡️ increase of renal blood flow (RPF) ➡️ increase of glomerular hydrostatic pressure (PG) ➡️ increase glomerular filtration rate (GFR).

5) Endothelin (vasoconstriction hormone):

❑ The effect is :
Vasoconstriction of afferent Arteriole ➡️ increase the resistance of afferent Arteriole (Ra) ➡️ decrease of GFR.

# Control of GFR and renal blood flow

## 5. Endothelin

$\uparrow\uparrow R_A + \uparrow R_E \longrightarrow \downarrow GFR + \downarrow\downarrow RBF$

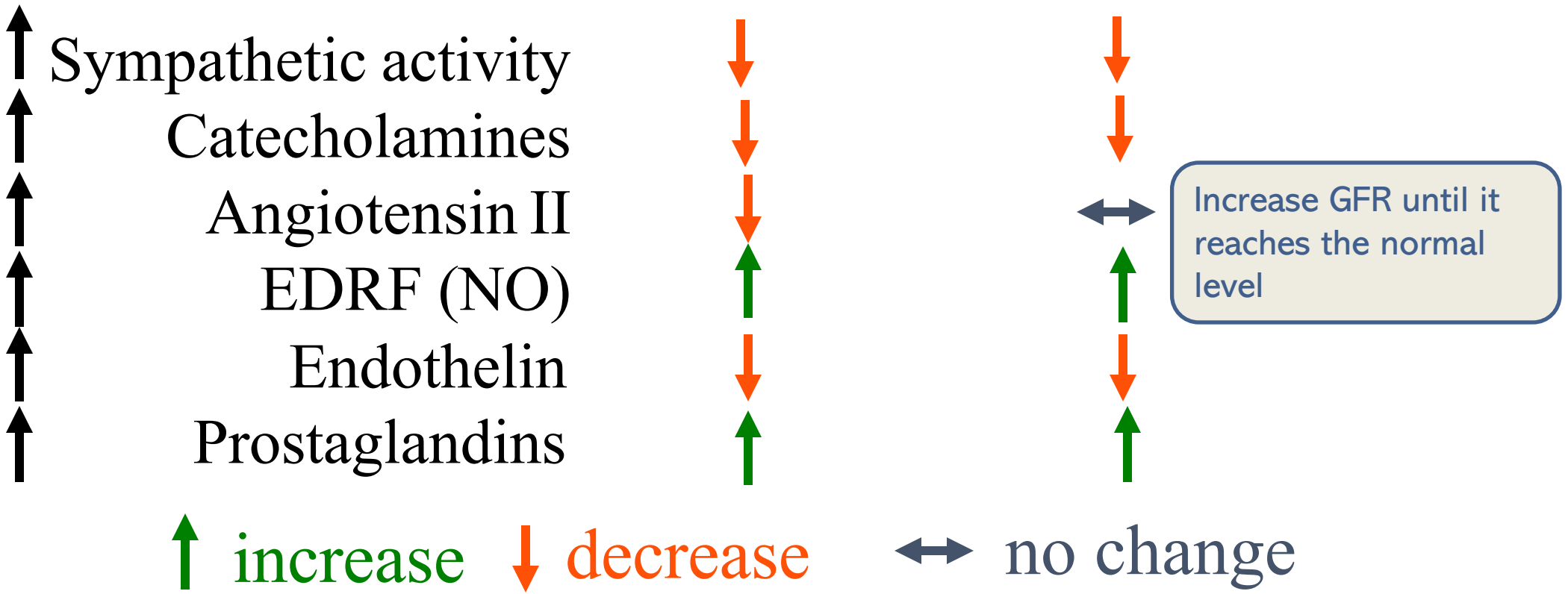
- Hepatorenal syndrome – decreased renal function in cirrhosis or liver disease?
- Acute renal failure (e.g. contrast media nephropathy)?
- Hypertensive patients with chronic renal failure?

Endothelin antagonists may be useful in these conditions

Note about the last sentence:

- You give the patient endothelin antagonists, and then discover if the endothelin is the cause of GFR decreasing or not.
- Because there are many factors other than endothelin.

# Summary of neurohumoral control of GFR and renal blood flow




- Imp explain next slid about angiotensin II

Angiotensin II effect by constriction of:

1) Efferent Arteriole more than the afferent Arteriole so, that lead to increase GFR.

2) ALL vessels of our body ➡️ increase blood pressure of the body ➡️ increase perfusion of blood in general and in the glomerulus.

# Local Control of GFR and renal blood flow

- These are more imp mechanism of regulation

## 7. Autoregulation of GFR and Renal Blood Flow

- Myogenic Mechanism
- Macula Densa Feedback (tubuloglomerular feedback)
- Angiotensin II ( contributes to GFR but not RBF autoregulation)

- Intrinsic (Local) regulation = Autoregulation = the kidney itself can regulate its GFR and Renal blood flow (RPF).
- We mention the angiotensin II again here because it is released from JGA that exist within the kidney.

# Audio-visual Aid

[Regulation of Renal Blood Flow - YouTube]


- I highly recommend watching this video before moving on to the next slides:

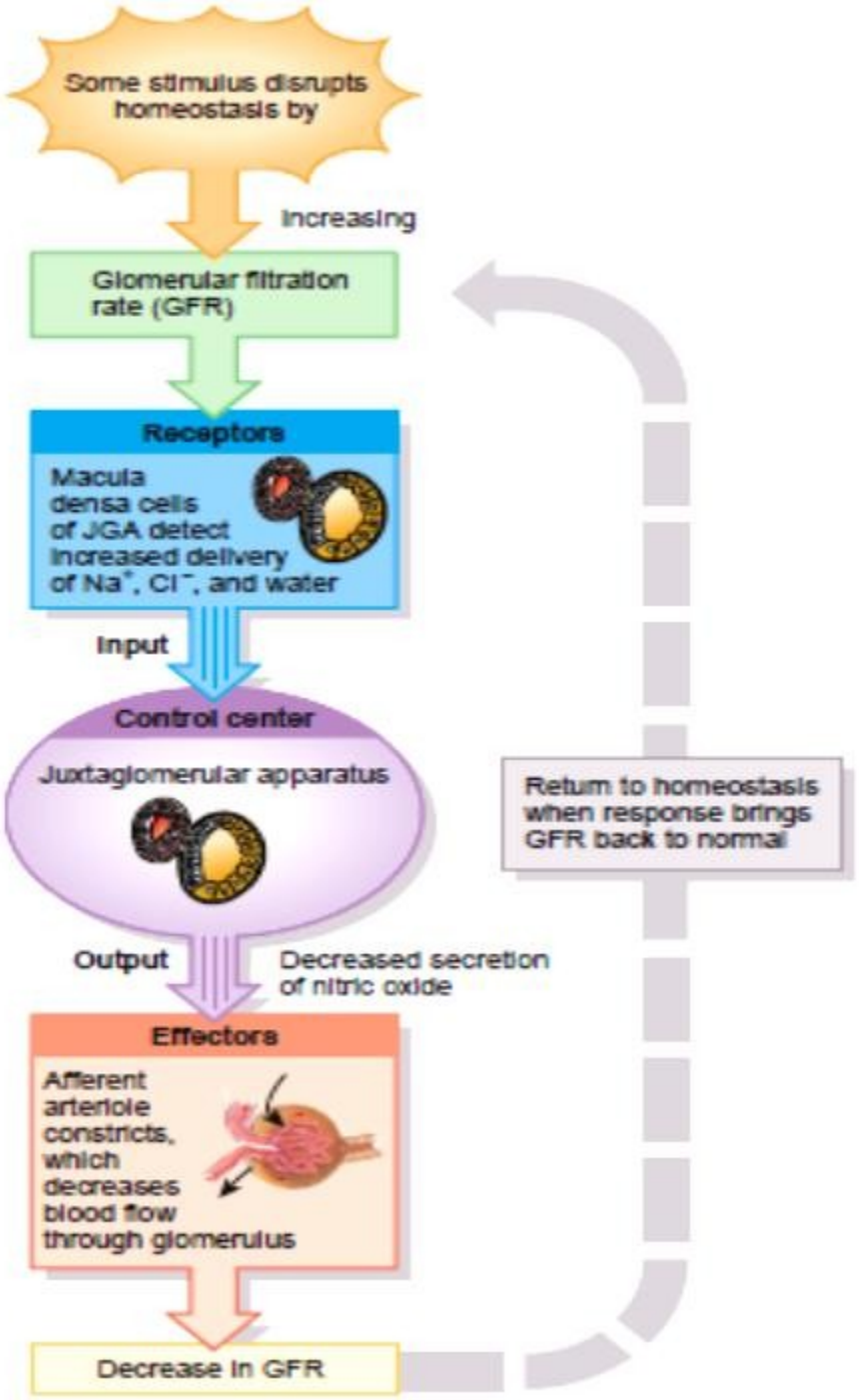
https://youtu.be/2HMPe3799QI?si=s65-QSLsLDPu9I62

- In the next slides, we rearrange the order of them for better understand and sequence of information 😁

# Renal Autoregulation of GFR

## 2. Tubuloglomerular feed back mechanism:

- Feedback loop consists of a flow rate (increased NaCl in filtrate) sensing mechanism in macula densa of juxtaglomerular apparatus (JGA)
- Increased GFR (& RBF) inhibits release of the vasodilator ; Nitric Oxide (NO)
- Ang II when blood pressure falls is released increasing systemic BP and increasing glomerular hydrostatic pressure and thus GFR, however, when blood pressure is increased renin and AngII release are inhibited



- Why is it called tubuloglomerular feedback:

Because the message come from tubule ( distal tubule) to glomerulus.
(if the name is glomerulotubular , the directions of message is the opposite).

- The process of this mechanism:

1) Macula dense of distal tubule detect the level of Na and Cl and give a feedback massage to JGCs in afferent arteriole.
2) If the level of Na and Cl is high, the macula dense will consider the cause is high filtration so the feedback massage to JGCs will be to decrease GFR !!
3) Ok, How JGCs do this decreasing?

A: by depending on many tools:

- NO synthesis: decrease the NO synthesis ➡️ decrease GFR
- Renin release: inhibit renin release ➡️ decreases GFR

- What are the factors that affect renin?

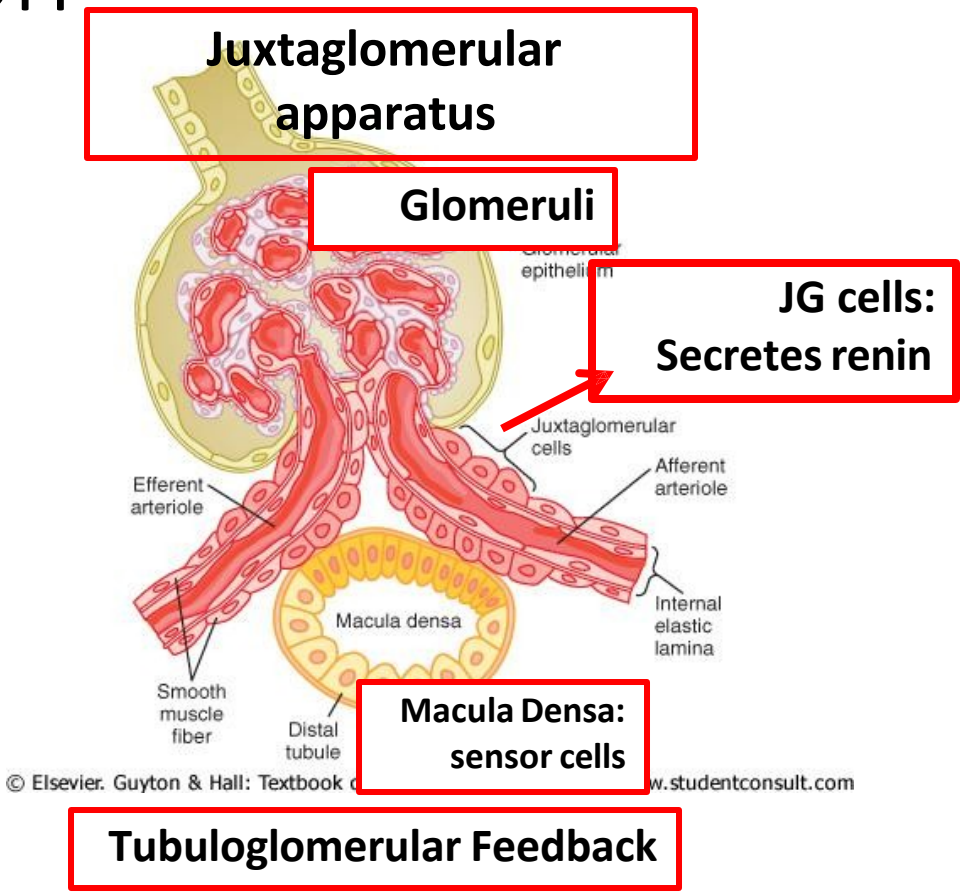
1) Perfusion pressure (BP).

2) Sympathetic nerve activity

3) NaCl delivery to macula dense of distal tubule

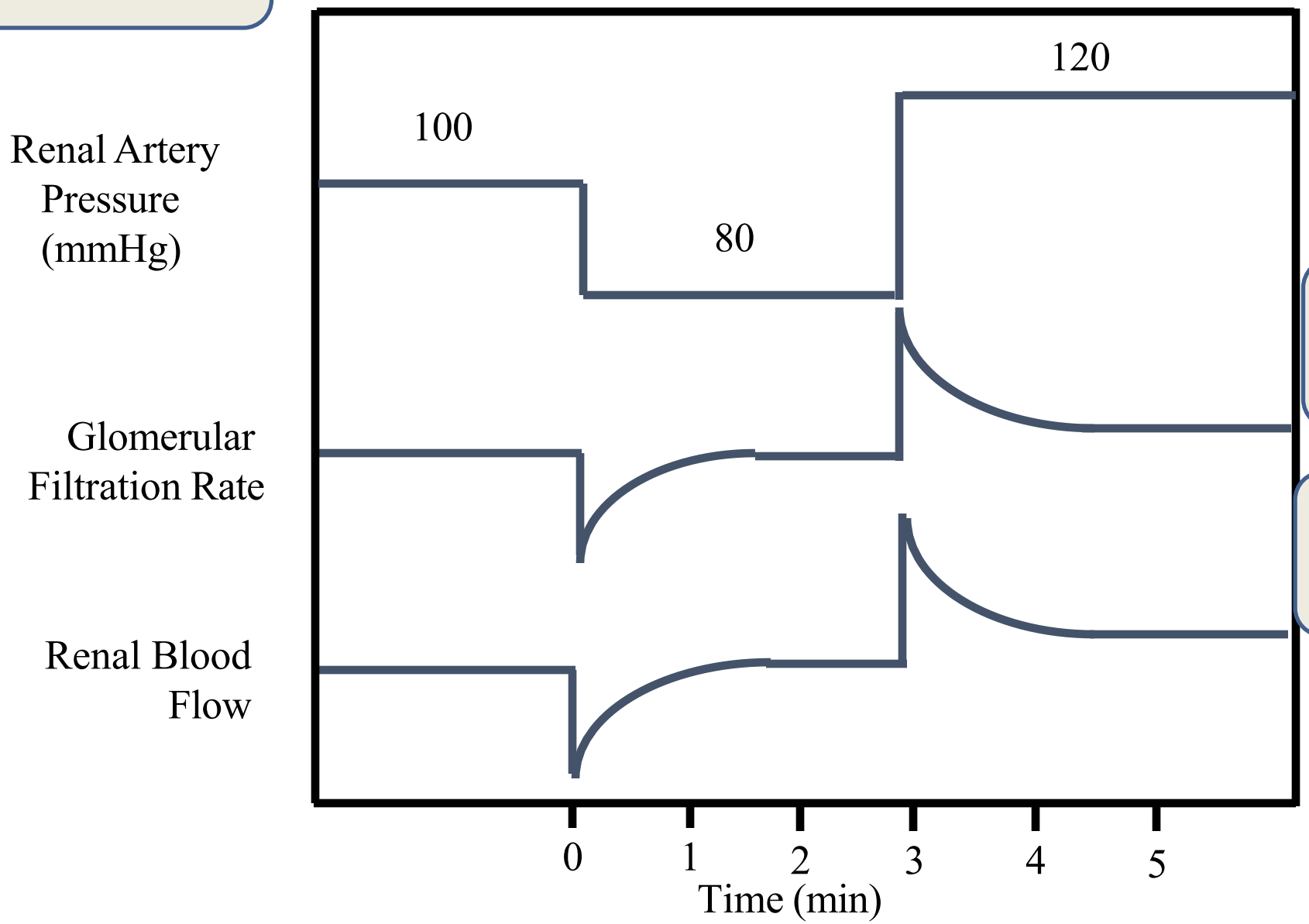
# Renin secretion regulation

1) Perfusion Pressure: low perfusion in afferent arterioles stimulates renin secretion while high perfusion inhibits renin secretion.
2) Sympathetic nerve activity: Activation of the sympathetic nerve fibers in the afferent arterioles increases renin secretion.
3) NaCl delivery to macula densa: When NaCl is decreased, Renin secretion is stimulated and vice versa. (**Tubuloglomerular Feedback)**



Very interesting diagram to understand how the autoregulation mechanism work

# Renal Autoregulation




The kidney work to maintain GFR stable = normal.

The kidney work to maintain RPF stable = normal.

❑ The normal renal artery pressure (BP) is 100 mmHg

- When it decrease to 80:

1) Sudden reduction of GFR will happen then
2) Gradually back to normal (increase) within less than 2 minutes (fast). However the BP still 80 (decreased)

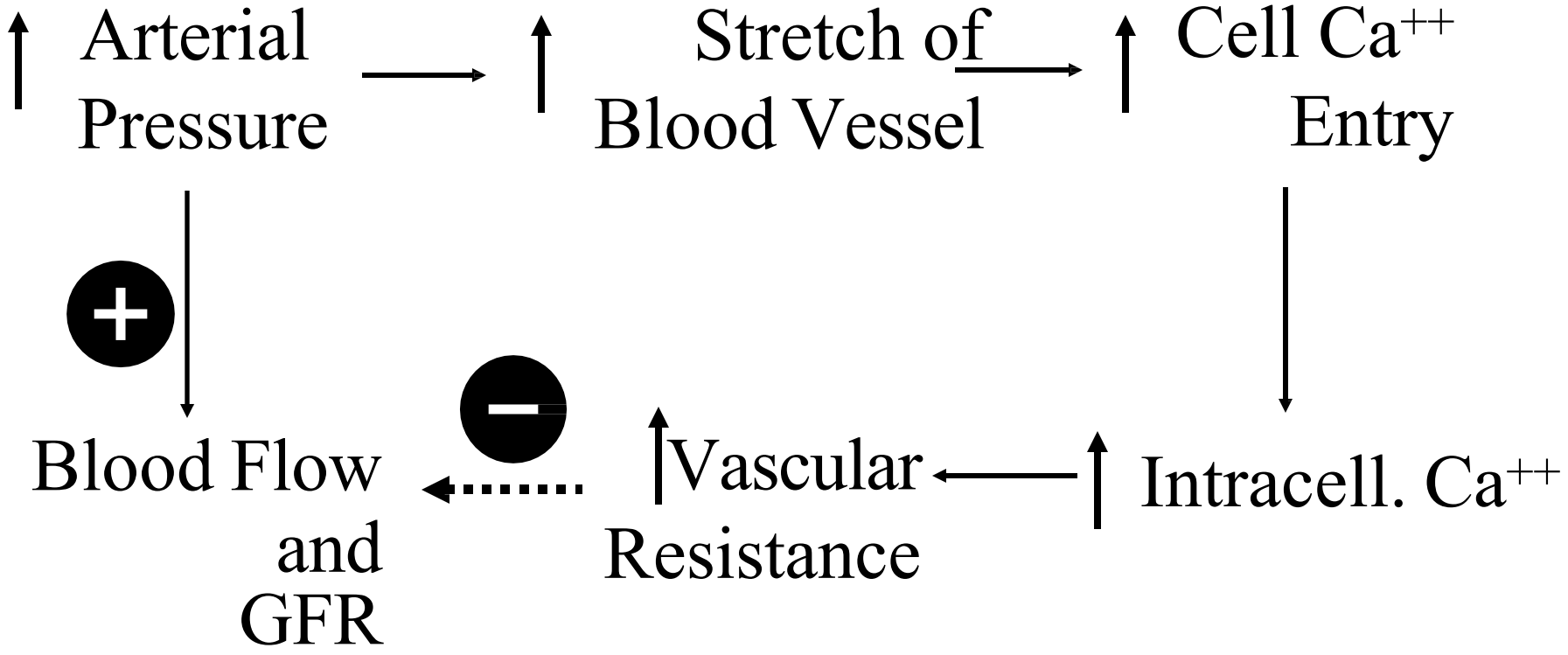
- Same thing happen to RPF.

- When it increase to 120:

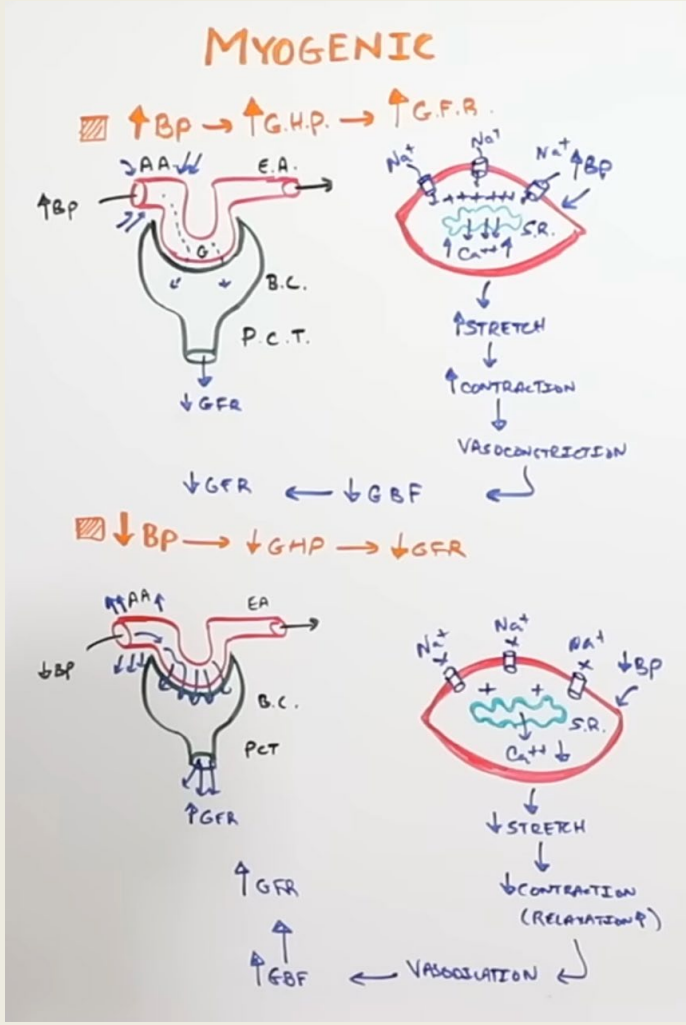
1) Sudden increase of GFR will happen then
2) Gradually back to normal (decrease) within less than 2 minutes (fast). However the BP still 120 (increased)

- Same thing happen to RPF.

# 1. Myogenic Mechanism

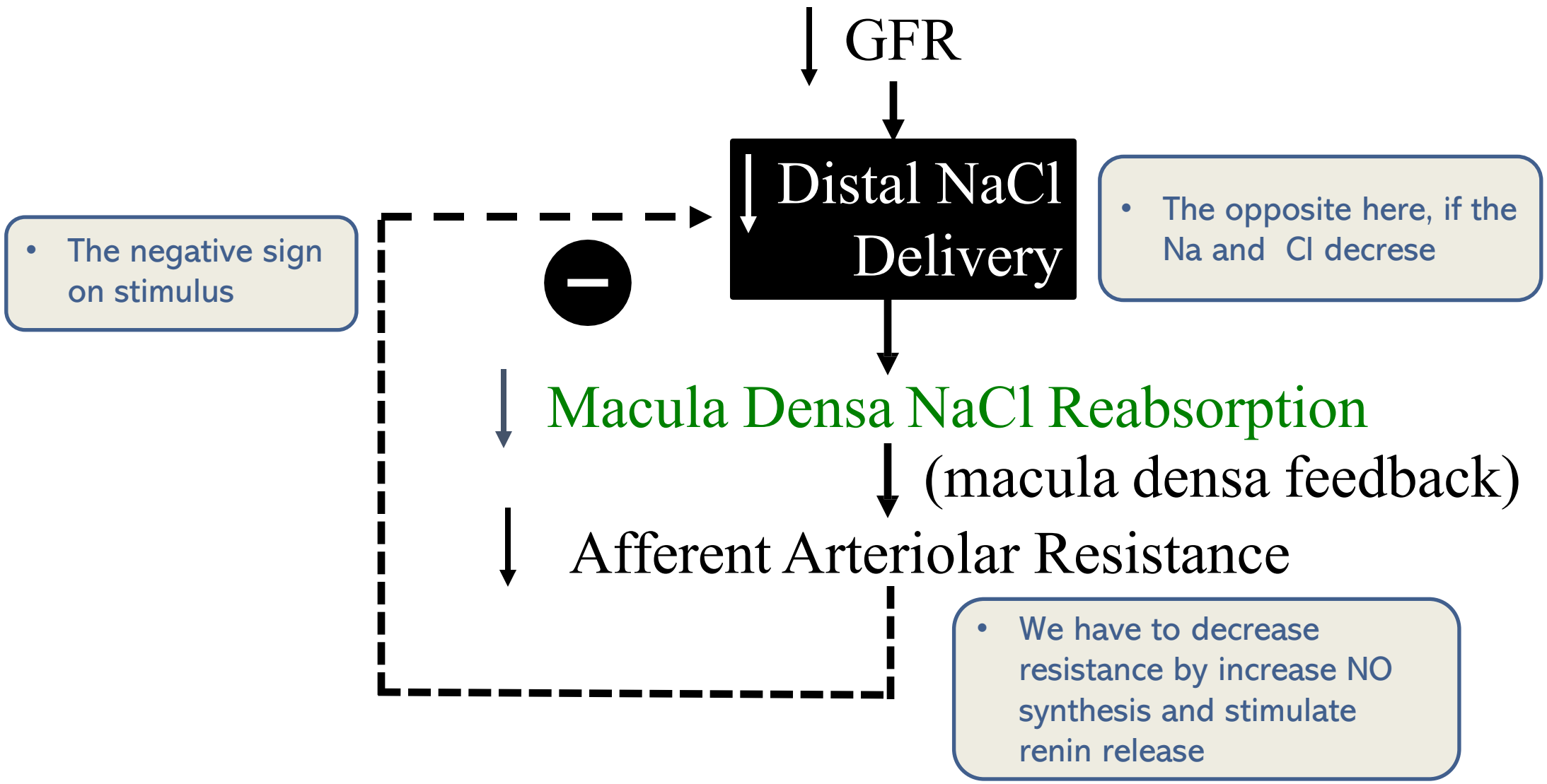


- From its name (myo), it is related to the activity of smooth muscle cells of vessels.

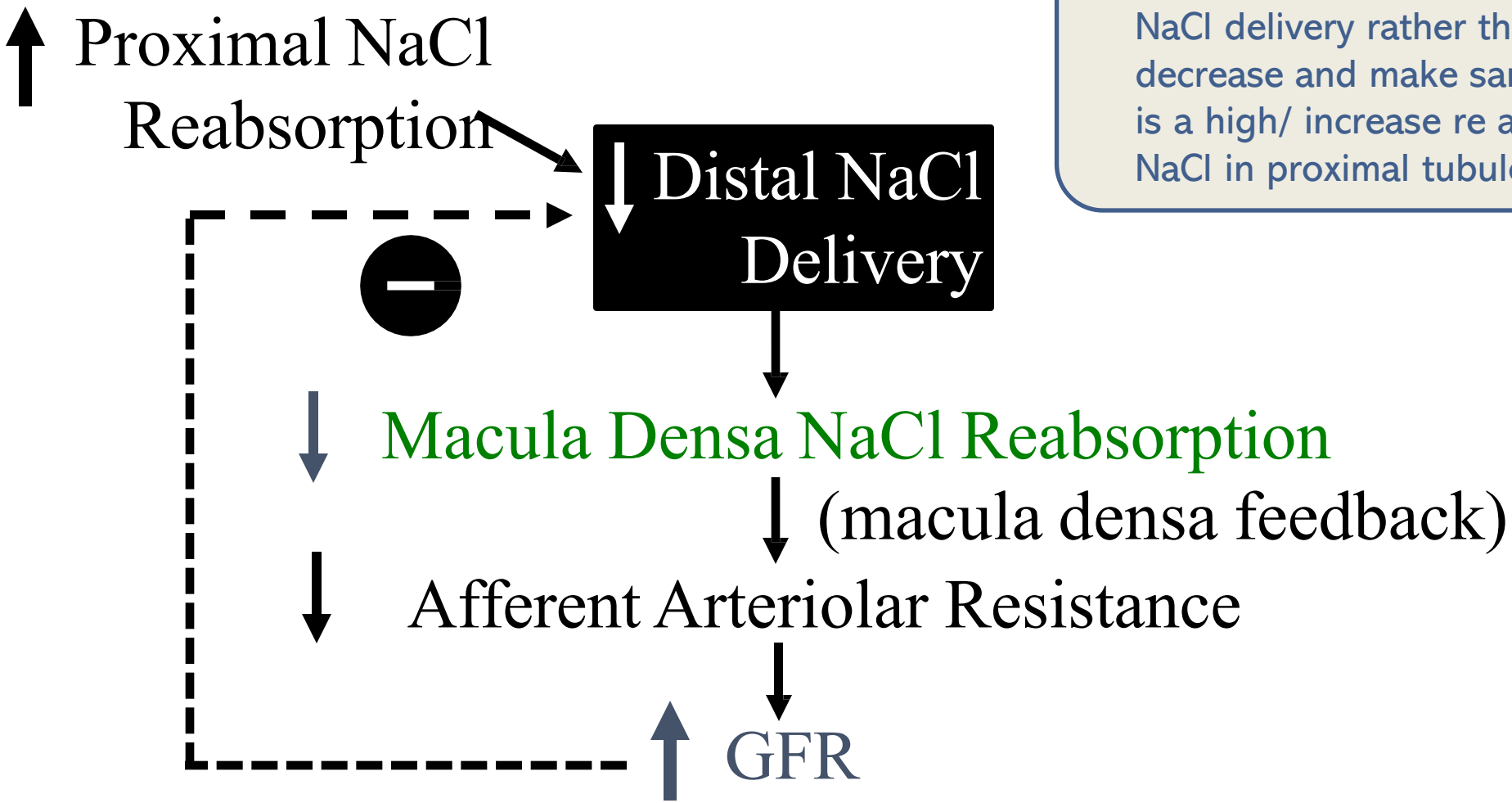



- When the vascular resistance increase, the constriction of afferent arteiole increase that lead to decrease the GFR.
- This mechanism for prevent the excessive increase of blood flow and GFR above the normal level

# Macula Densa Feedback

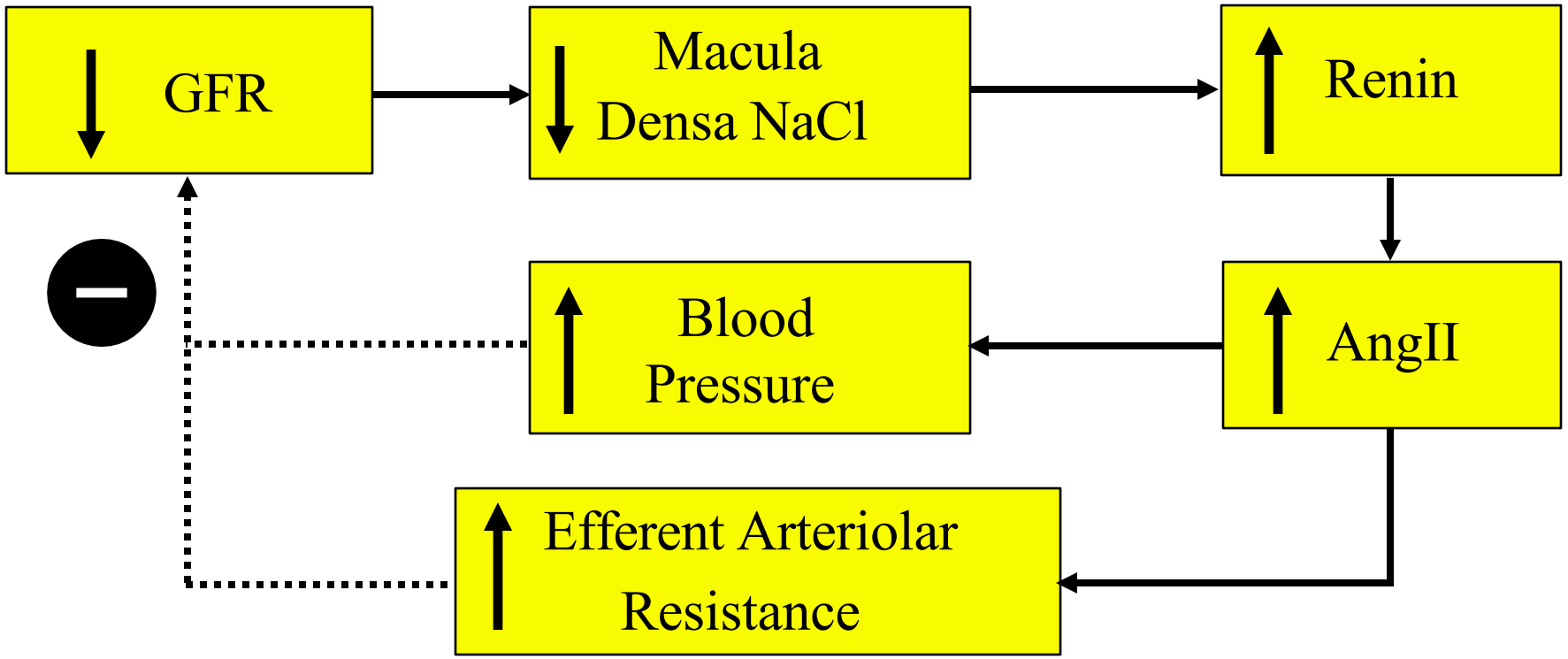


# Macula Densa Feedback

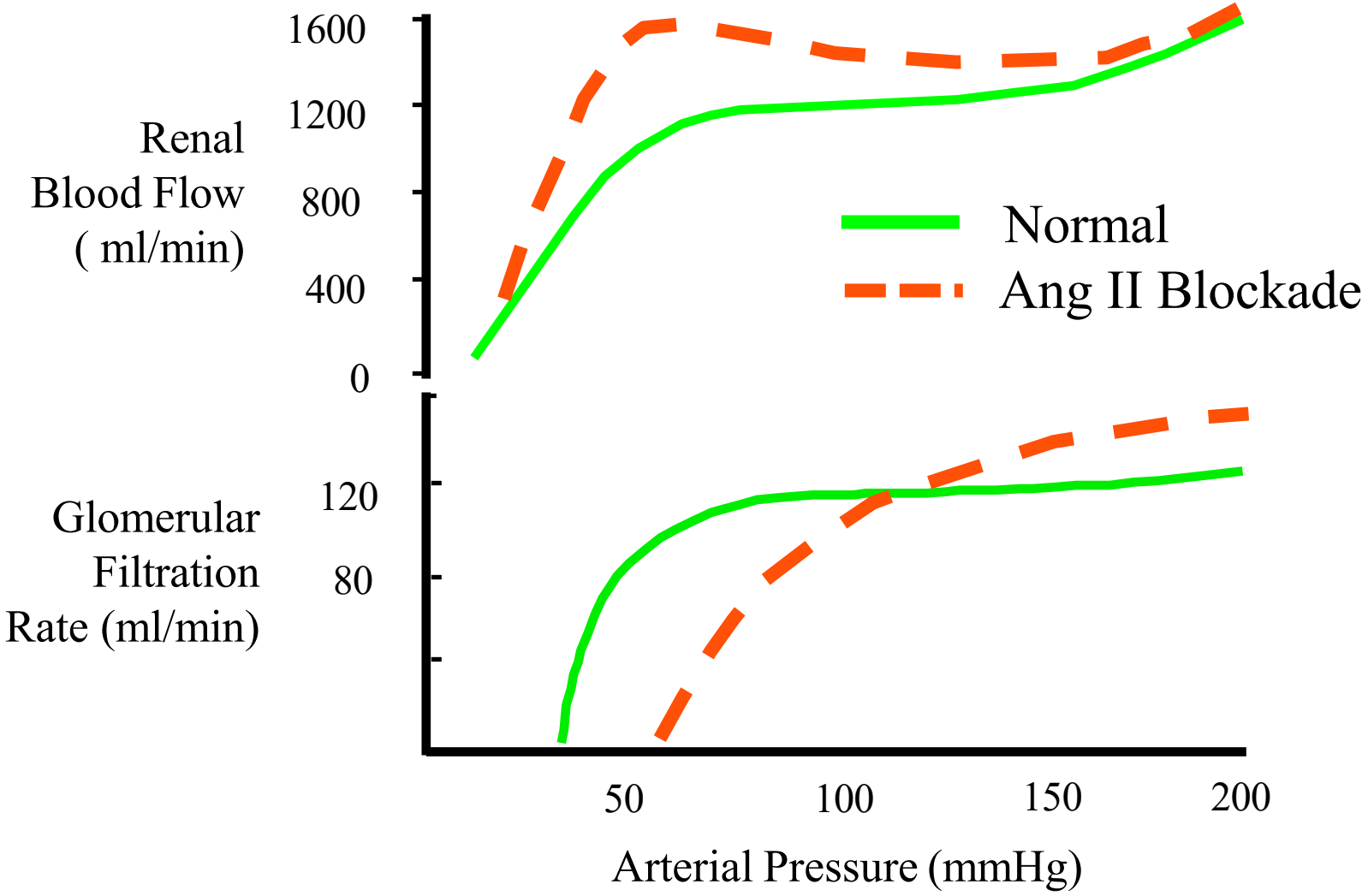



- Other cause of decreasing distal NaCl delivery rather than GFR decrease and make same feedback is a high/ increase re absorption of NaCl in proximal tubule.

# Regulation of GFR by Ang II



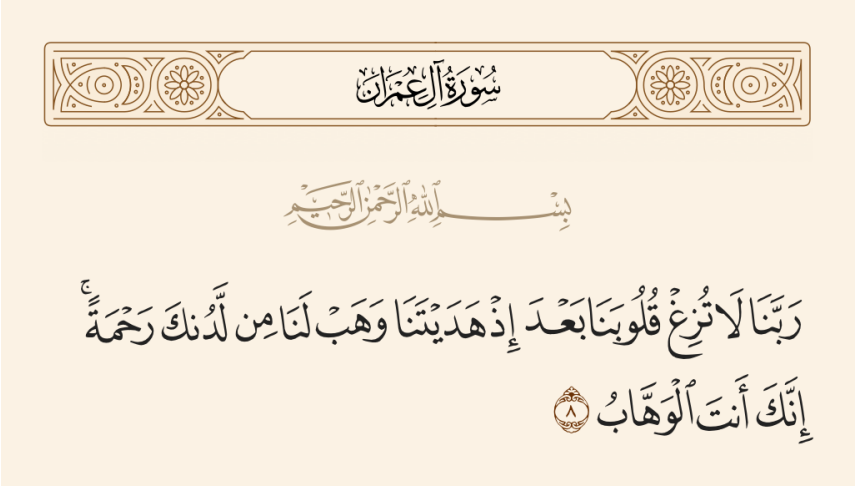
# Ang II Blockade Impairs GFR Autoregulation




- No significant effect because Ang II blockade will increase renal blood flow

impaired

- The effect appears on GFR. Ang II blockers impair the autoregulation of GFR




| VERSIONS | SLIDE # | BEFORE CORRECTION | AFTER CORRECTION |
|---|---|---|---|
| V1→ V2 | 18 | Vasodilation | Vasoconstriction |
| V2→V3 | | | |

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!