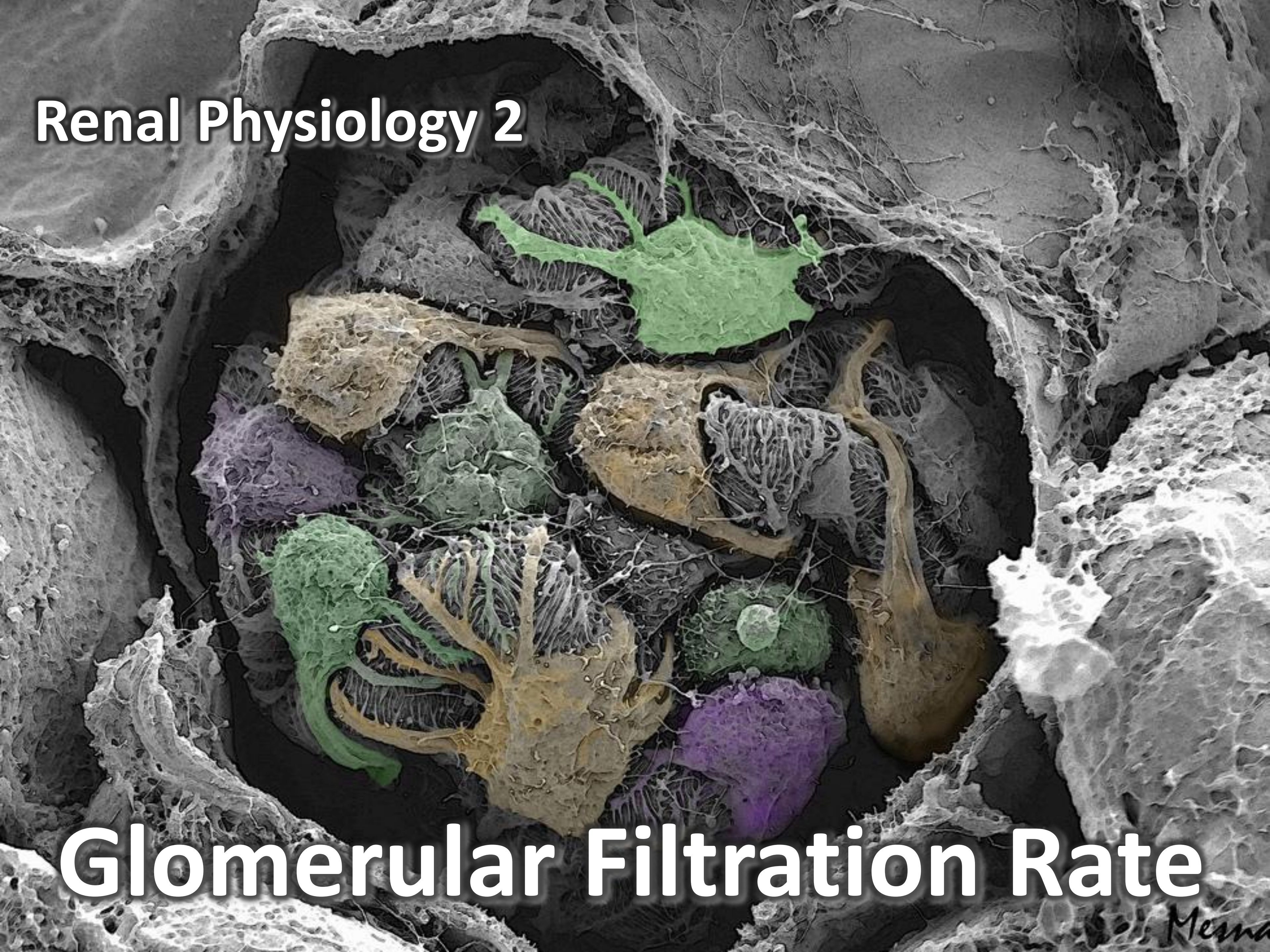

بسم الله الرحمن الرحيم

قَالُوا۟ سُبۡحَٰنَكَ لَا عِلۡمَ لَنَآ إِلَّا مَا عَلَّمۡتَنَآۖ إِنَّكَ أَنتَ ٱلۡعَلِيمُ ٱلۡحَكِيمُ ٣٢

Renal Physiology
GFR

Renal Physiology 2



Glomerular Filtration Rate

Learning Objectives:

- Describe that the **mechanism of urine formation** include three basic processes; glomerular filtration, tubular reabsorption and tubular secretion.
- Define **GFR** and quote normal value.
- Identify and describe the **factors controlling GFR** in terms of starling forces, permeability with respect to size, shape and electrical charges and ultra-filtration coefficient.
- Describe Intrinsic and extrinsic mechanism that regulate GFR.
- Describe autoregulation of GFR & tubuloglomerular feedback mechanism.

Capillary Beds of the Nephron:

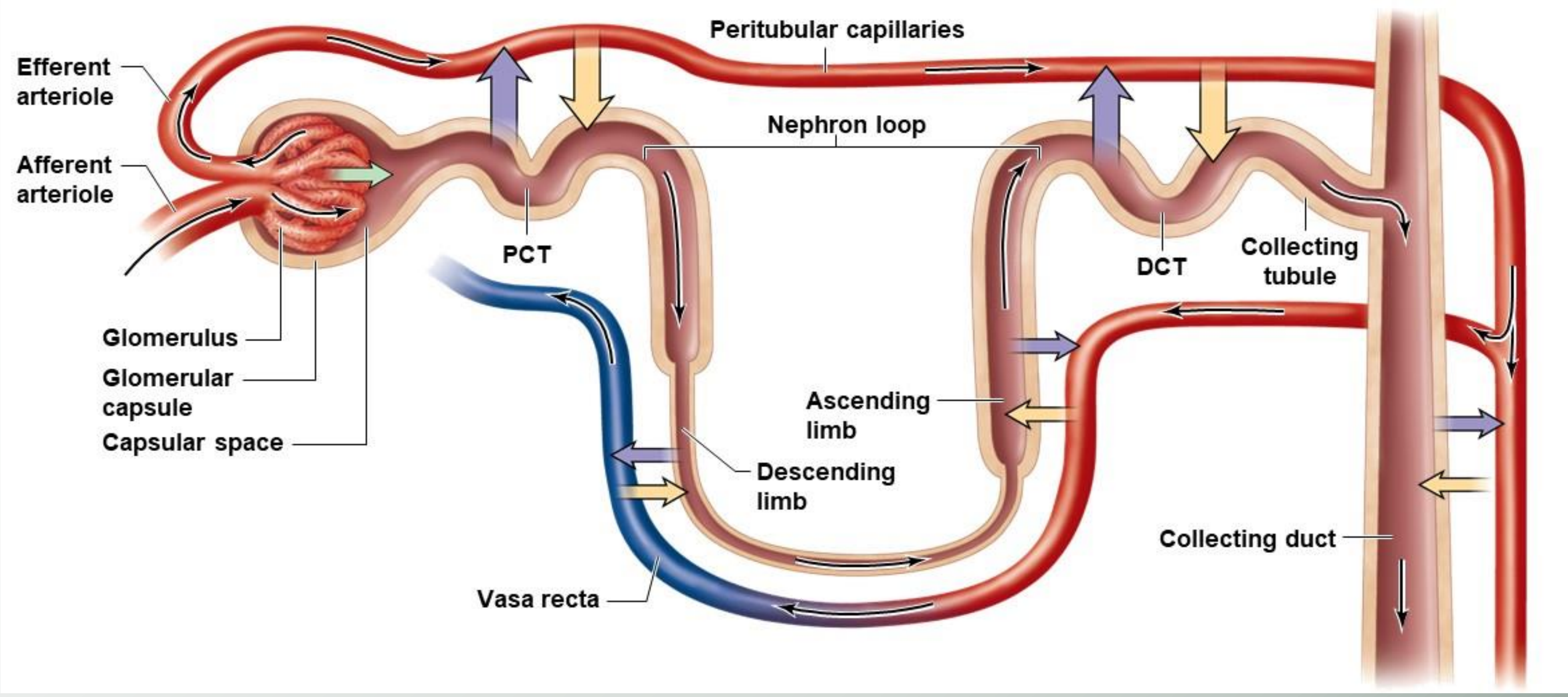
- Every **nephron** has (Glomerulus & Peritubular capillaries)
- Each **glomerulus** fed by afferent arteriole & drained by efferent arteriole.
- Blood pressure in the glomerulus is high because:
  - Arterioles are high-resistance vessels.
  - Afferent arterioles have larger diameters than efferent arterioles.
- Fluids and solutes are forced out of the blood throughout the entire length of the glomerulus

Capillary Beds & Resistance

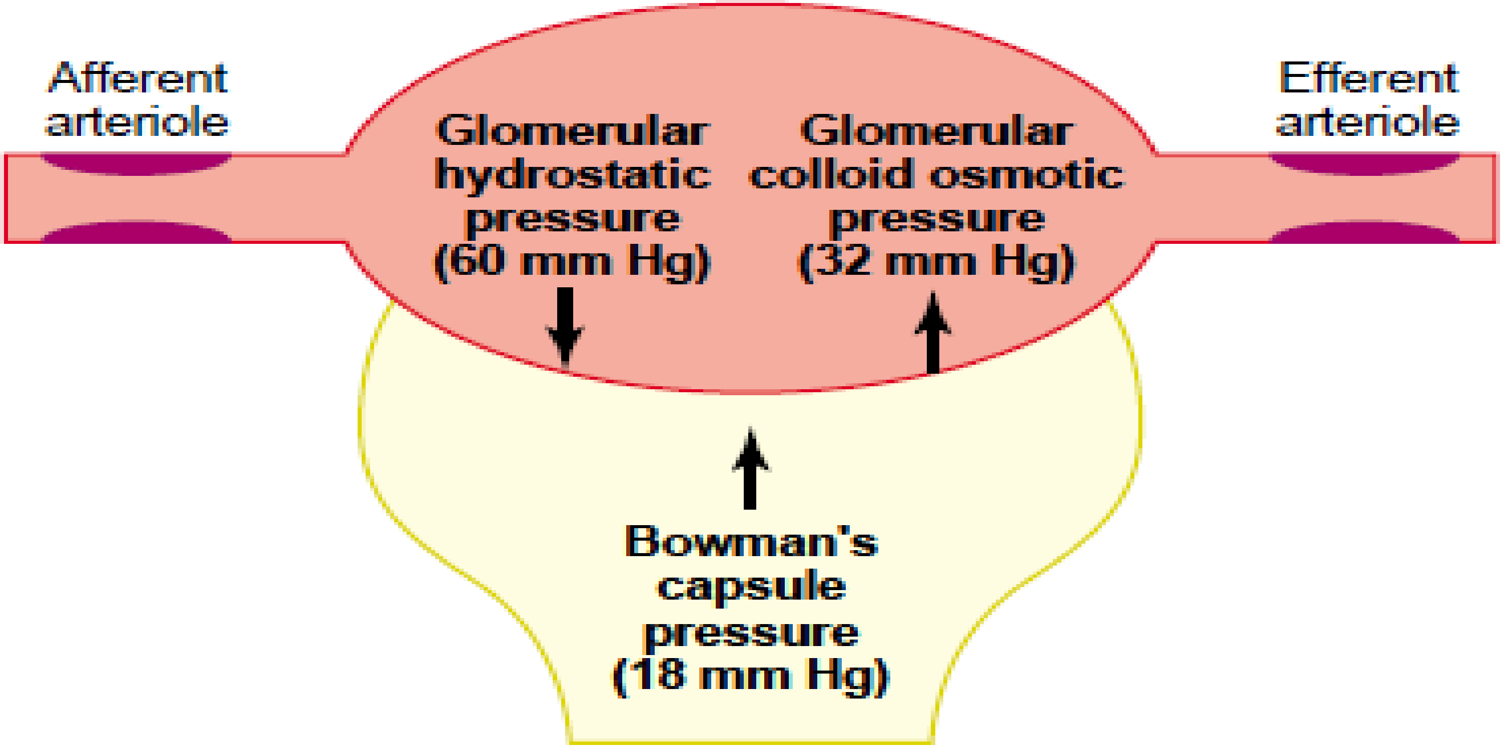
- **Peritubular beds** are low-pressure, porous capillaries adapted for absorption that:
  - Arise from efferent arterioles
  - adhere to adjacent renal tubules
  - Empty into the renal venous system
- Resistance in afferent arterioles:
  - Protects glomeruli from fluctuations in systemic blood pressure.
- Resistance in efferent arterioles:
  - Reinforces high glomerular pressure.
  - Reduces hydrostatic pressure in peritubular capillaries.

Mechanisms of Urine Formation

Glomerular filtration	Tubular reabsorption	Tubular secretion
The movement of substances from the blood within the glomerulus into the capsular space	The movement of substances from the tubular fluid back into the blood	The movement of substances from the blood into the tubular fluid



Control of GFR



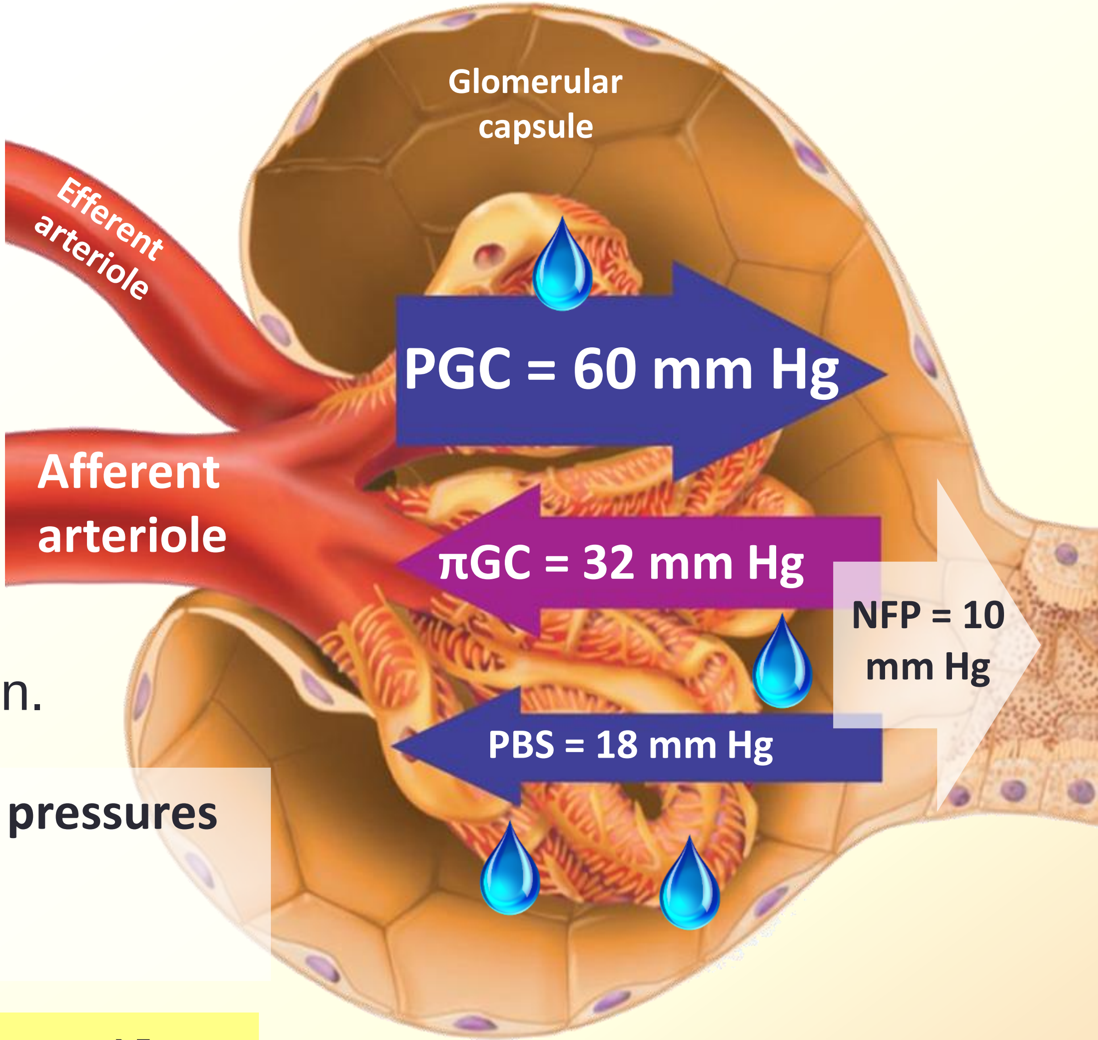
GFR = NFP X Kf (Permeability) = 125 ml/min

Determinants of GFR

<u>Filtration coefficient (K_f)</u>

Surface area available for filtration (mesangial cells)

Filtration membrane permeability



<u>Net Filtration Pressure (NFP)</u>

The cumulative pressure responsible for filtrate formation.

= OUTWARD pressures – INWARD pressures

= (PGC + πBS) – (PBS + πGC)

= (60) – (18 + 32) = 10 mm Hg

$$GFR = K_f \times [P_{GC} - (P_{BS} + \pi_{GC})]$$

Changes in GFR result from changes in glomerular blood pressure

Net Filtration Pressure (NFP)

- The pressure responsible for filtrate formation
- NFP equals the glomerular hydrostatic pressure (HP_g) minus the oncotic pressure of glomerular blood (OP_g) combined with the capsular hydrostatic pressure (HP_c)

$$NFP = HP_g - (OP_g + HP_c)$$

Or

$$NFP = P_{GC} - P_{BS} - O_{GC}$$

GFR

- Factors governing filtration rate at the capillary bed are:
  - Total surface area available for filtration.
  - Filtration membrane permeability.
  - Net filtration pressure.
- GFR is directly proportional to the NFP.

- If the GFR is **too high**:
  - Needed substances cannot be reabsorbed quickly enough and are lost in the urine.
- If the GFR is **too low**:
  - Everything is reabsorbed, including wastes that are normally disposed of.

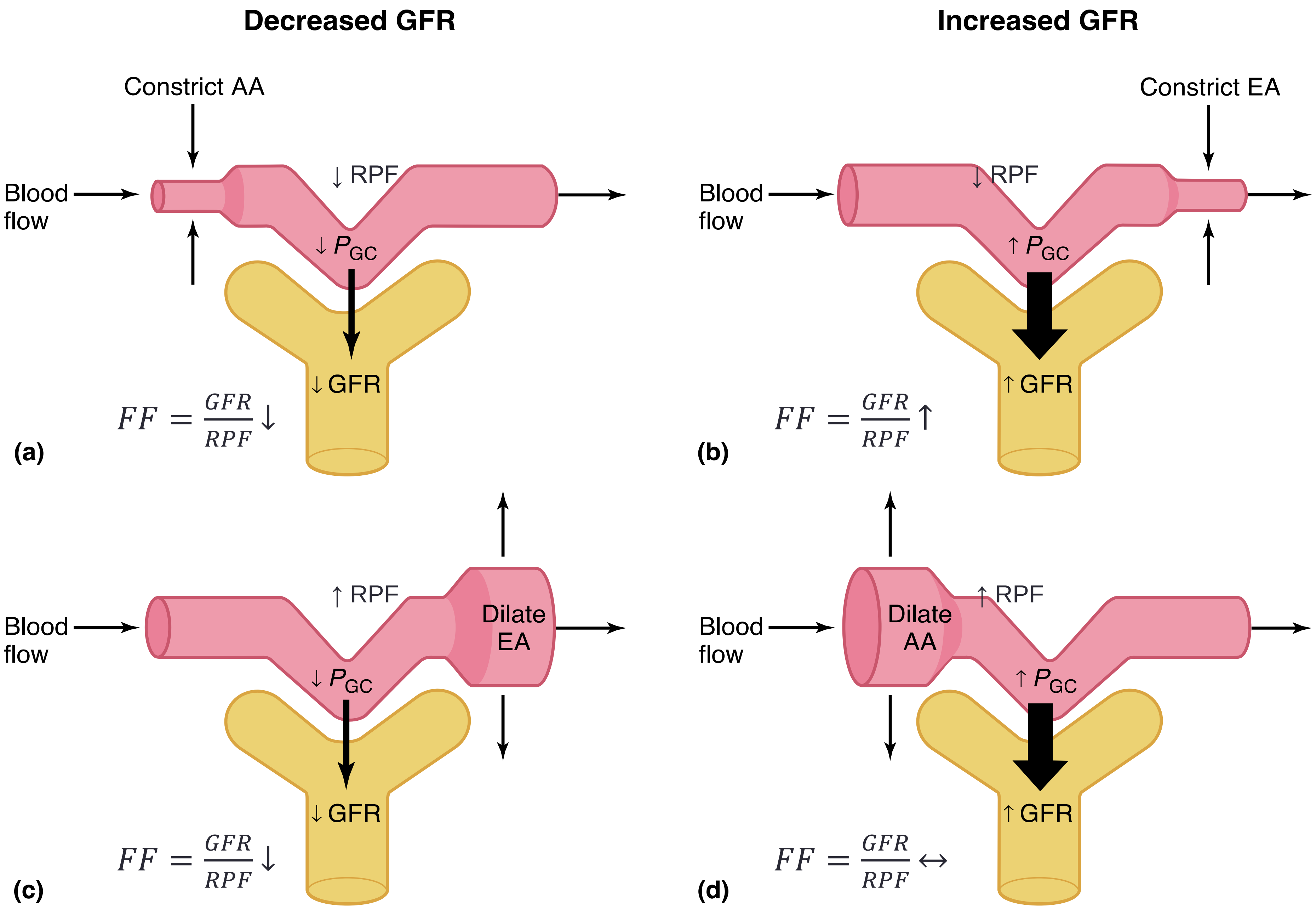
What is GFR?

The rate of production of filtrate at the glomeruli from plasma

- index of kidney function
- GFR is the sum of filtration rates of all functioning nephrons
- level depends on age, sex and body size.

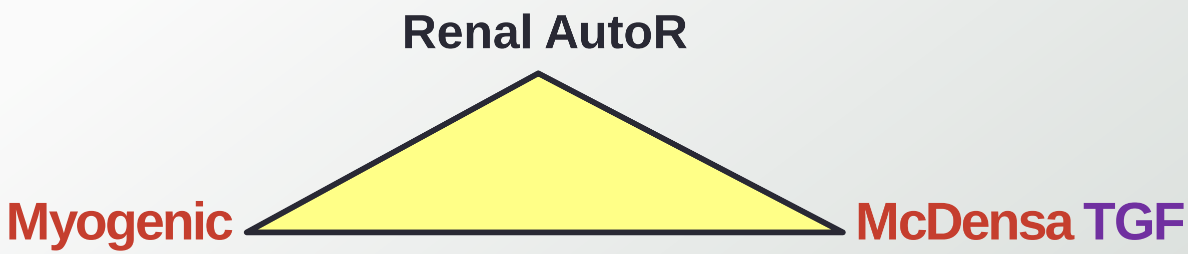
GFR (mL/min/1.73 m^2)	Period of time	Kidney damage	Comment
>90		NO	Normal
60–89		NO	Normal (elderly or infants)
60–89	≥ 3 months	YES	Early kidney disease
<60	≥ 3 months	YES	Chronic kidney disease

Constriction/dilation of afferent/efferent arterioles & GFR



Regulation of GFR & RBF

- **Intrinsic controls (renal autoregulation)**
  - Act locally - maintain GFR, **BP 80-180 mmHg**

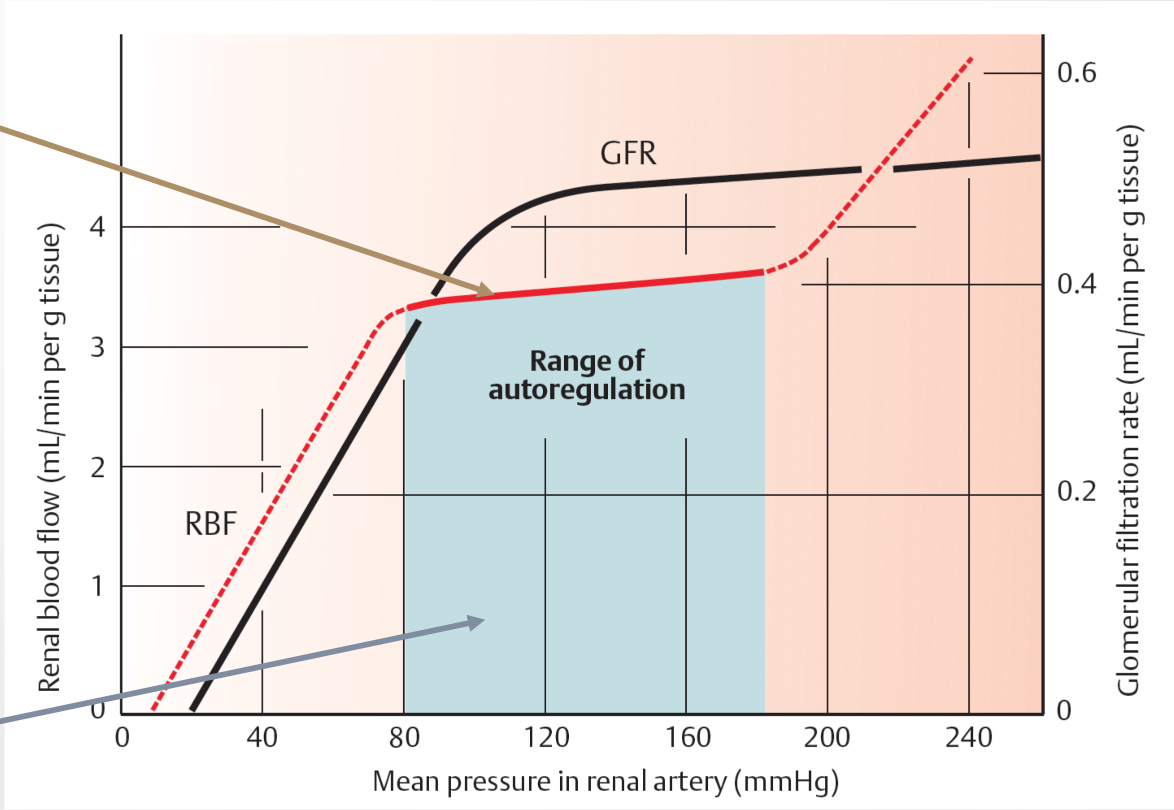


- **Extrinsic controls (Sympathetic)**
  - Neuroendocrine mechanisms - maintain BP.
  - Can negatively affect kidney function
  - Take precedence over intrinsic controls if systemic **BP < 80 or > 180 mmHg**

Intrinsic Autoregulation

RBF remains ~ constant as BP changes between **80** and **180** mmHg.

Autoregulation, is achieved by changes in resistance, mainly through the <u>a</u>fferent arterioles.



< **80 mmHg**, filtration ↓, and ceases altogether when MAP = **50 mmHg**.

- Autoregulation is <u>**independent**</u> of nerves or hormones
- occurs in denervated and in isolated perfused kidneys.

Regulation of the diameter of arterioles

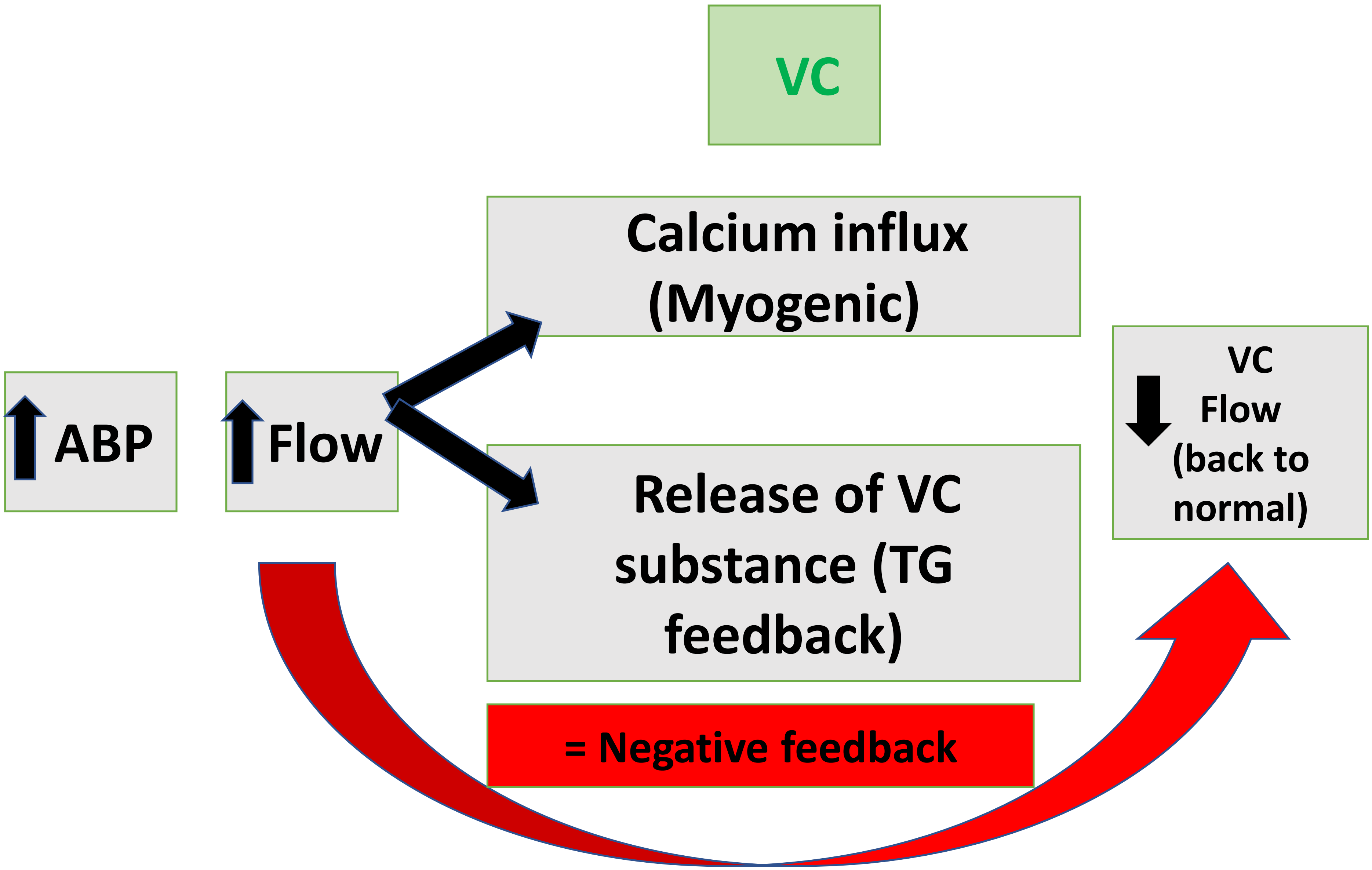
I- Local vascular regulatory mechanisms (Autoregulation).

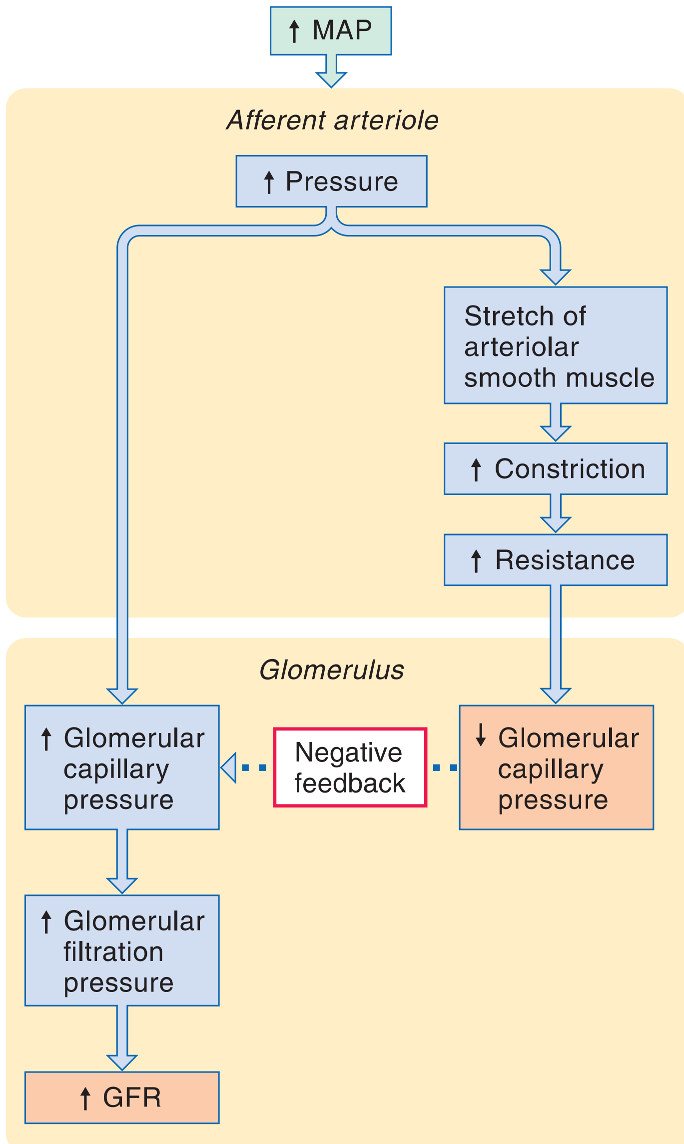
Intrinsic autoregulation of RBF

Initial change (Stimulus)	Mechanism (Physiological response)	Result
↑ ABP ↑ RBF (Back to normal)	1 - Myogenic 2 – TG Feedback	↑ ABP ↓ RBF (Back to normal)

Intrinsic autoregulation of RBF

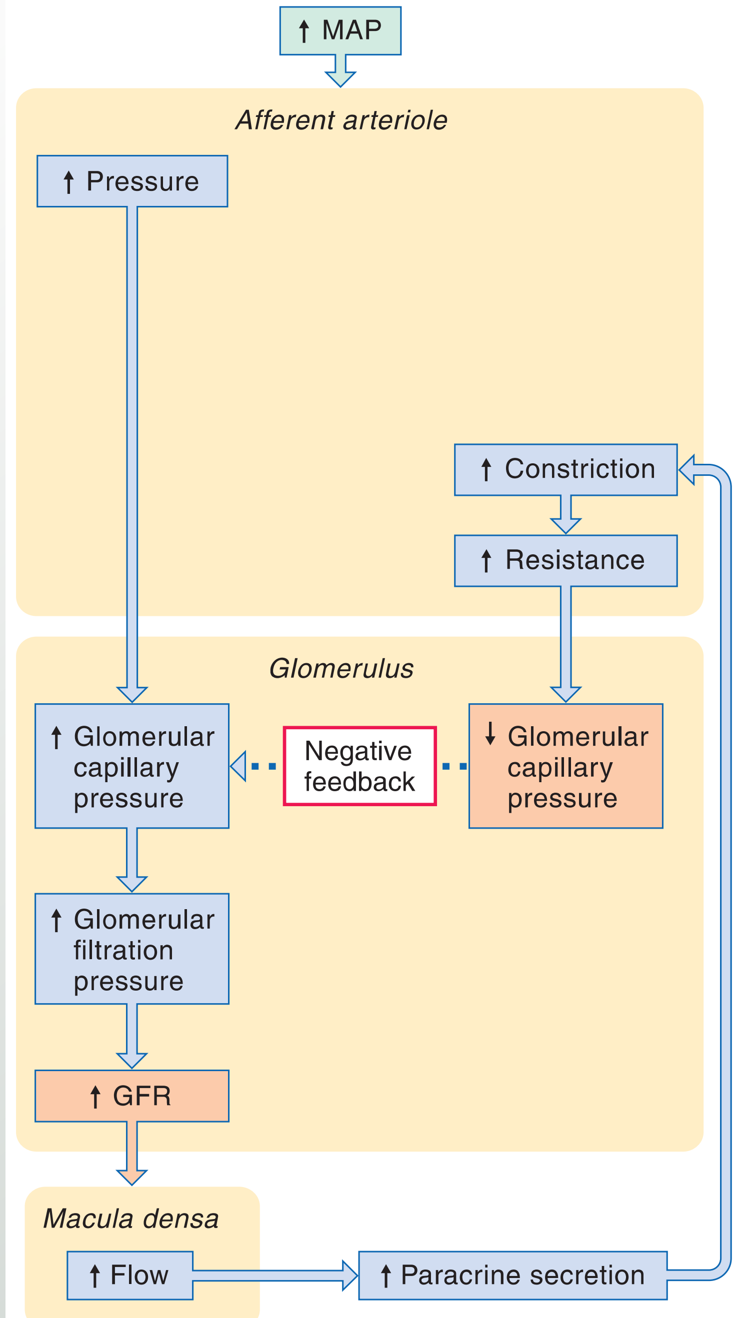
Initial change (Stimulus)	Mechanism (Physiological response)	Result
↓ ABP ↓ RBF (Back to Normal)	1 - Myogenic 2 – TG Feedback	↓ ABP ↑ RBF (Back to normal)


VC
Calcium influx (Myogenic)
ABP
Flow
Release of VC substance (TG feedback)
VC
Flow
(back to normal)
= Negative feedback



(a) Myogenic regulation

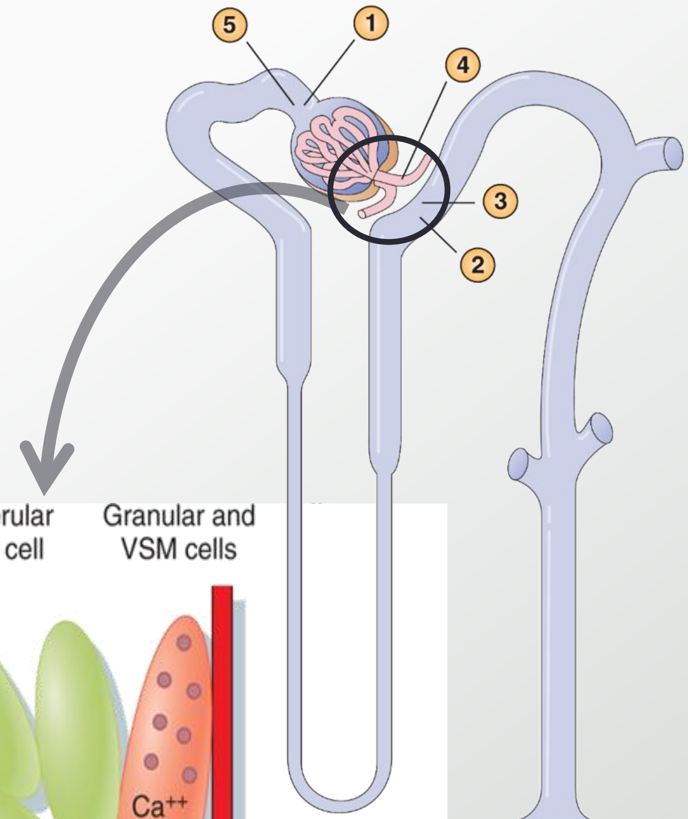
Initial stimulus
Physiological response
Result



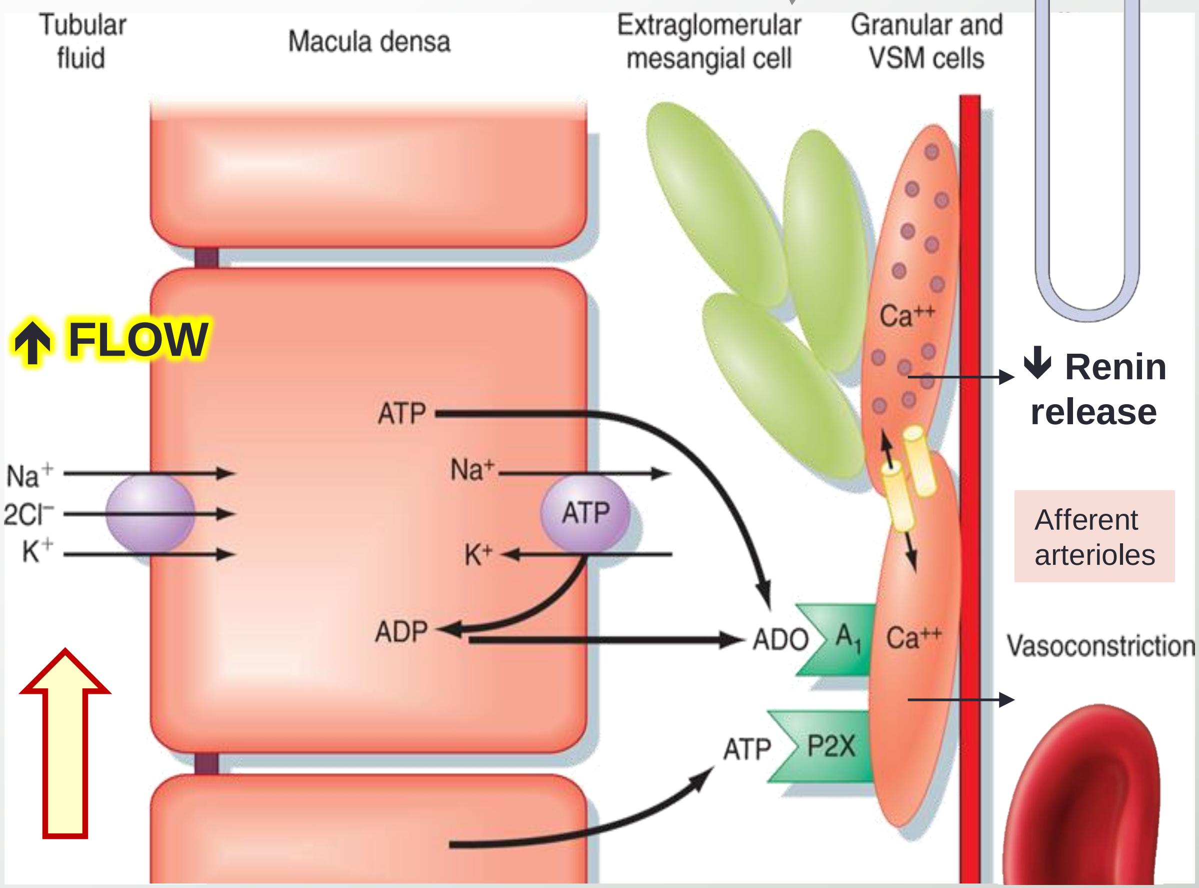
(b) Tubuloglomerular feedback

Tubulo-glomerular feedback

McDensa TGF



Step	Event
1	↑ RBF, ↑ GFR
2	↑ Delivery of Na^+ and Cl^- to juxtaglomerular apparatus (sensed by macula densa)
3	Release of vasoactive substance (e.g., adenosine) from macula densa
4	↑ Resistance of afferent arteriole
5	↓ RBF, ↓ GFR



Mediators **Adenosine** and **Renin**

[NaCl] dependent mech.

Extrinsic controls

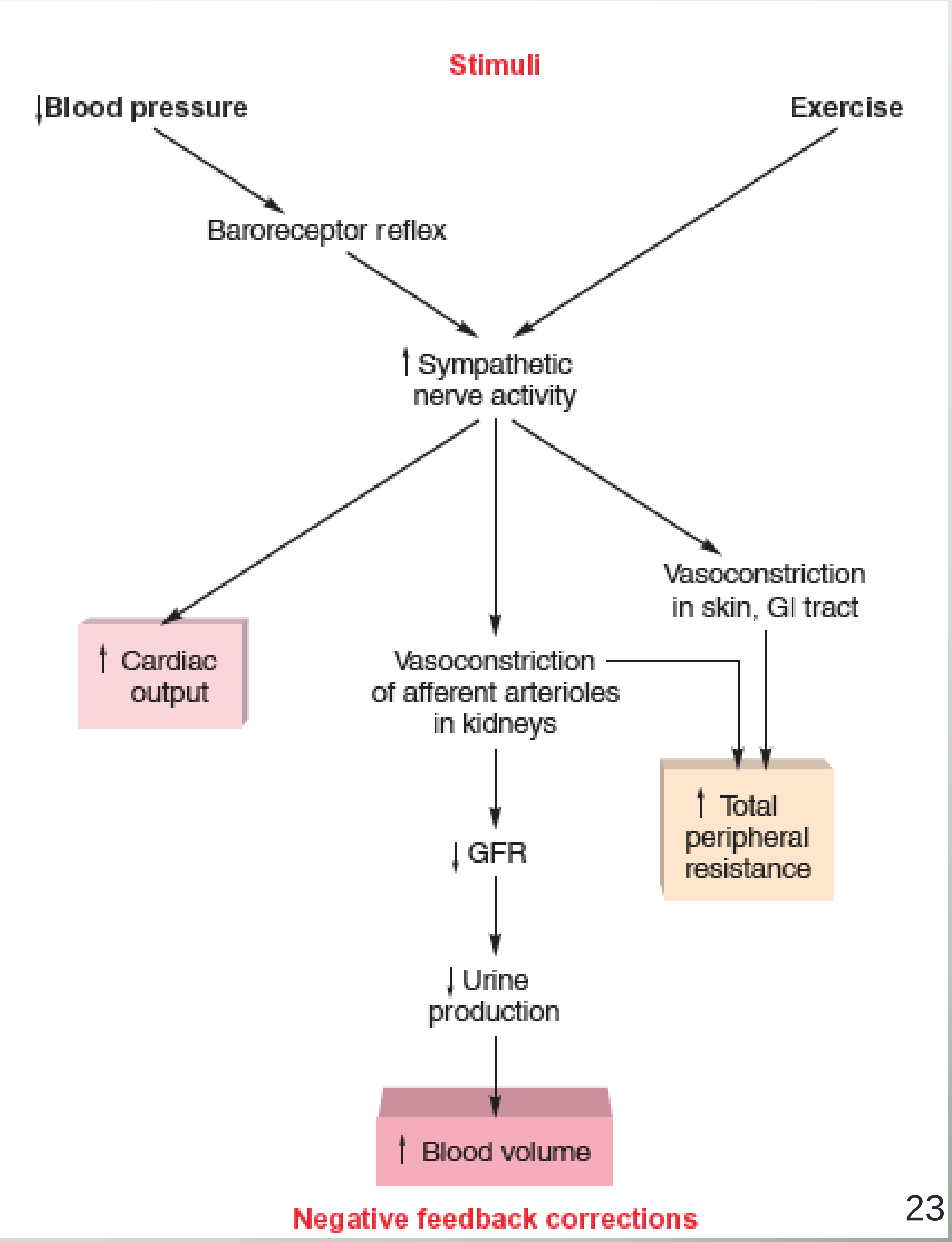
Sympathetic Regulation of GFR

- **Stimulates vasoconstriction of afferent arterioles.**

  -Preserves blood volume to muscles and heart.

Cardiovascular shock:

- ↓ glomerular capillary hydrostatic pressure.
- ↓ urine output.



Summary of neurohumoral control of GFR and RBF

<table>
<tr><th>Hormone or autacoid</th><th>Effect on GFR</th><th>Effect on RBF</th></tr>
<tr><td rowspan="2">↑ Sympathetic activity/Catecholamines
↑↑ R_A + ↑ R_E = ↓ GFR + ↓↓ RBF</td><td>↓</td><td>↓</td></tr>
<tr><td colspan="2">e.g. severe hemorrhage</td></tr>
<tr><td rowspan="2">↑ Angiotensin II
↑ R_E = ↑ GFR + ↓ RBF</td><td>↑</td><td>↓</td></tr>
<tr><td colspan="2">e.g. low sodium diet, volume depletion</td></tr>
<tr><td rowspan="2">↑ Nitric oxide
↓↓ R_A + ↓ R_E = ↑ GFR + ↑↑ RBF</td><td>↑</td><td>↑</td></tr>
<tr><td colspan="2">Protects against excessive vasoconstriction</td></tr>
<tr><td rowspan="2">↑ Endothelin
↑↑ R_A + ↑ R_E = ↓ GFR + ↓↓ RBF</td><td>↓</td><td>↓</td></tr>
<tr><td colspan="2">Antagonists are useful in acute renal failure</td></tr>
<tr><td rowspan="2">↑ Prostaglandins D,E,I
↓↓ R_A + ↓ R_E = ↑ GFR + ↑↑ RBF</td><td>↑</td><td>↑</td></tr>
<tr><td colspan="2">important when other disturbances ↓ GFR</td></tr>
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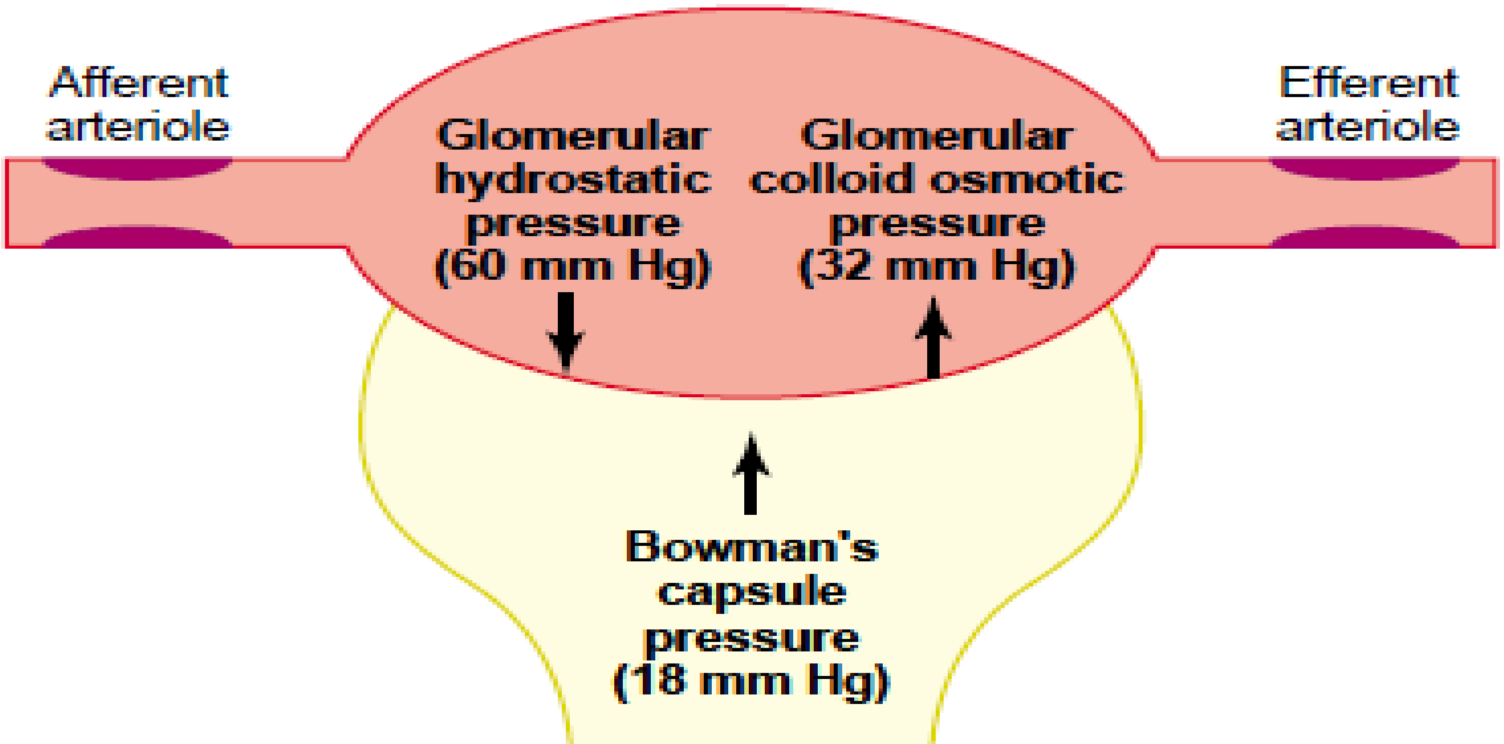
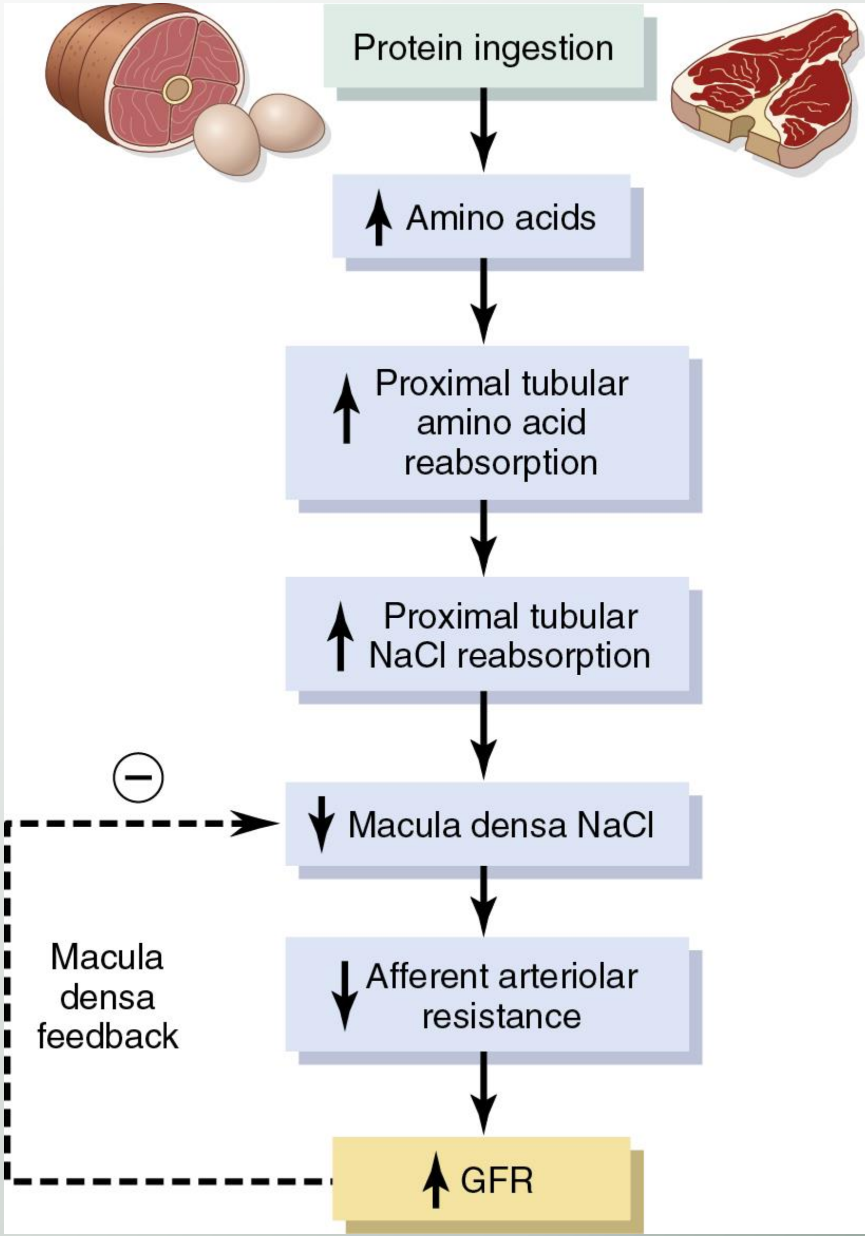
Control of GFR



Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) – Bowman's capsule pressure (18 mm Hg) – Glomerular oncotic pressure (32 mm Hg)

How does a high protein diet affect, if any, GFR?

Possible role of macula densa feedback in increasing GFR after a high protein meal



Thanks