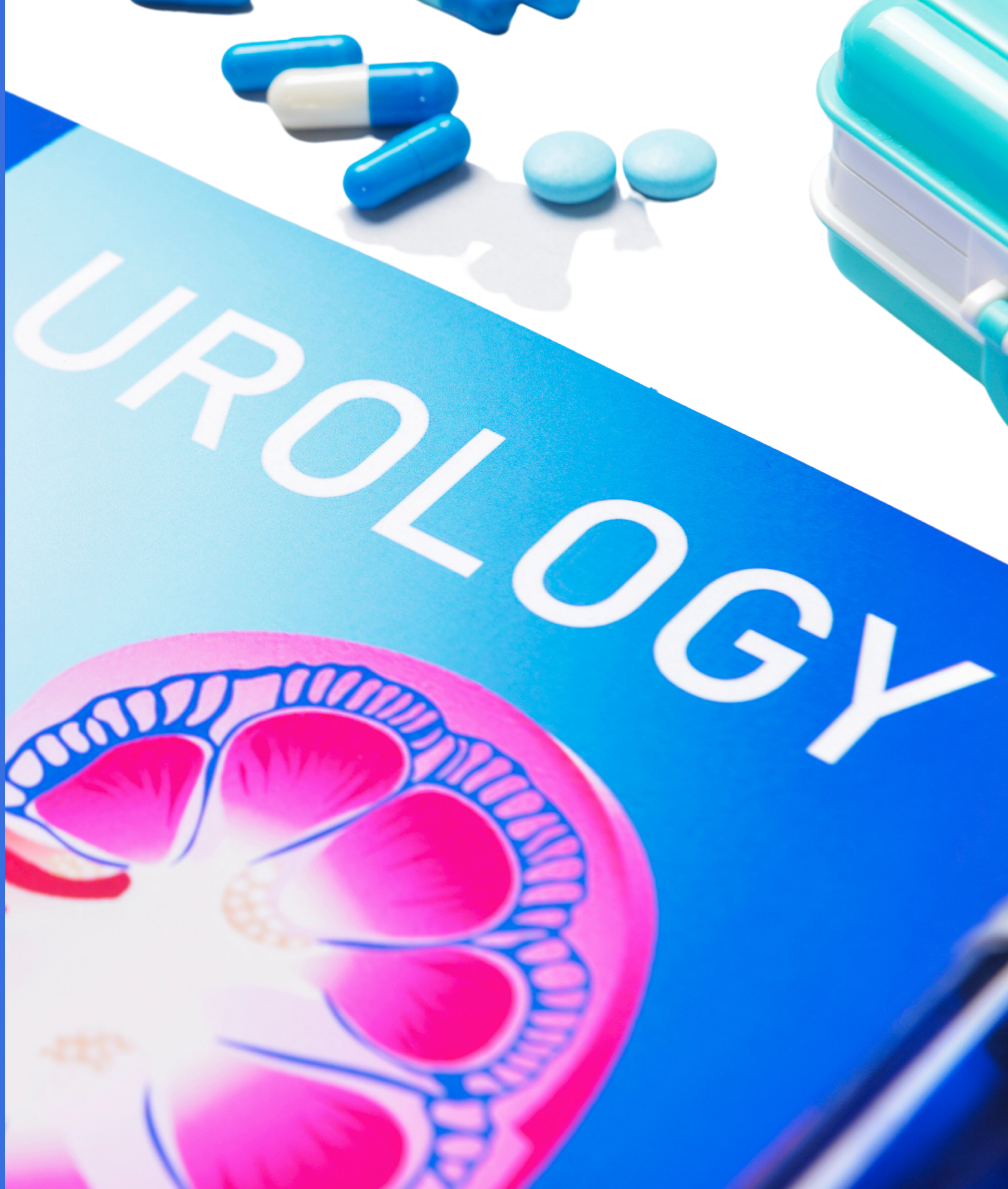
YU - Medicine Passion Academic Team

The Urogenital System



Sheet# 1 - Physiology (Part 2)

Lec. Title : Glomerular Filtration

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- **informations about the previous parts from the record:**

- Cephalosporin is an antibiotic that can cause drug interaction and (false positively) increase creatinine or even disrupt its reabsorption process. This increase is apparent not actual.

- Steroids have anabolic effects and can cause short-term vasodilation. This causes an increase in glomerular filtration rate.

- Steroids cause protein anabolism. Creatinine is a metabolite that is released due to protein breakdown. This means that steroids and starvation (muscle wasting to release ATP from aminoacids) increase creatinine levels.

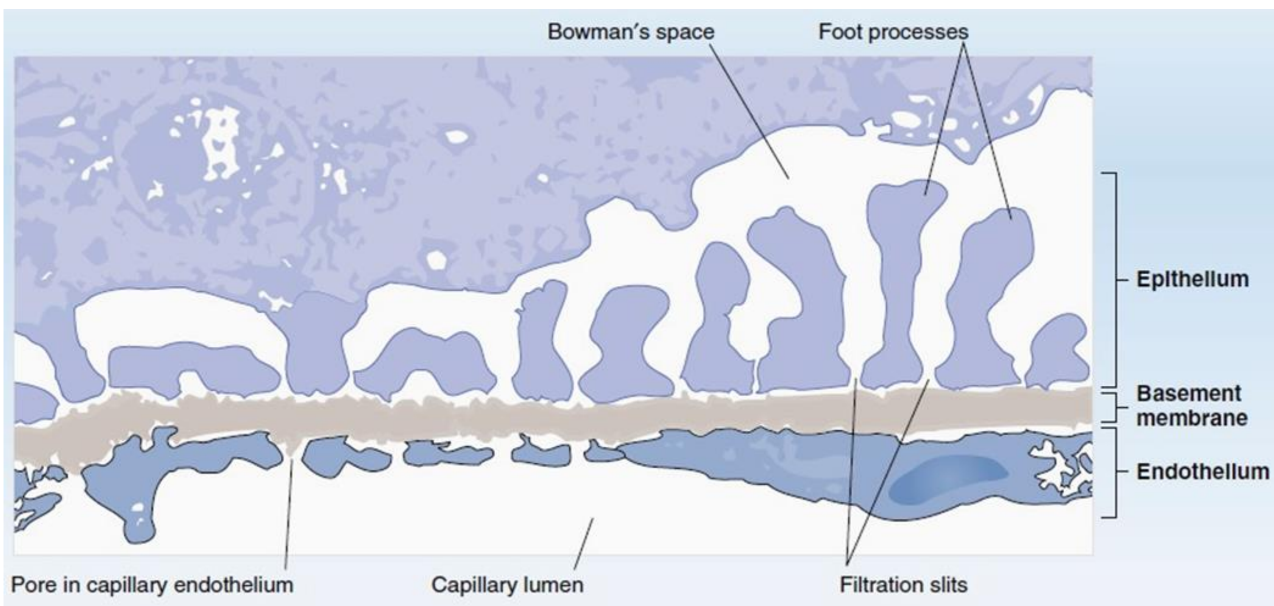
Glomerular filtration

التفريغ شامل الريكورد والكتاب (كوستانزو) بإذن الله...
دعواتكم ، كل الحُبّ...

- Glomerular filtration is the first step in the formation of urine.
- .
- As the RBF enters the glomerular capillaries, a portion of that blood is filtered into Bowman's space, the first part of the nephron. The fluid that is filtered **is similar to interstitial fluid** and is called an **ultrafiltrate** (contains water and all of the small solutes of blood, but it <u>does not contain proteins and blood cells.)</u>
- The forces responsible for glomerular filtration are similar to the forces that operate in systemic capillaries
- There are differences in the characteristics and surface area of the glomerular capillary barrier, <u>making the GFRs much higher </u>than the filtration rates across systemic capillaries.

- The **glomerular barrier** consists of

1. **The capillary endothelium**: with **large pores** → fluid, dissolved solutes, and plasma proteins all are filtered across this layer, but these **pores are not so large that blood cells can be filtered**.
2. **Basement membrane**: multilayered →does not permit filtration of plasma proteins. (the most significant barrier)
3. **Epithelium**: consists of **podocytes** (attached to the BM by foot processes)→ between processes there're relatively **small filtration slits** → barrier to filtration.



Negative Charge on the Glomerular Capillary Barrier:

- Normally, **fixed anionic glycoproteins line the filtration barrier (mainly pores & slits)** adding an **electrostatic component** to filtration.

- **Positively** charged solutes will be **attracted** to the negative charges on the barrier and be **more readily filtered**
- **negatively** charged solutes will be **repelled** from the negative charges on the barrier and be **less readily filtered**
- In normal/physiologic pH, **plasma proteins are negatively charged, so they are restricted**.
- In **glomerular disease,** the anionic charges on the barrier may be **removed**, allowing plasma proteins to be filtered ,resulting in **proteinuria (prtns. In urine)**.

Starling forces

- As in systemic capillaries, the pressures that drive fluid movement across the glomerular capillary wall are the Starling pressures, or Starling forces.
- there are **four Starling pressures**:

1. **two hydrostatic** pressures (one in capillary blood and one in interstitial fluid) and **two oncotic** pressures (one in capillary blood and one in interstitial fluid).
2. When **applying these pressures to glomerular capillaries**, there is one small modification:

The oncotic pressure of Bowman's space, which is analogous to interstitial fluid, is **considered to be zero** because filtration of protein is negligible.

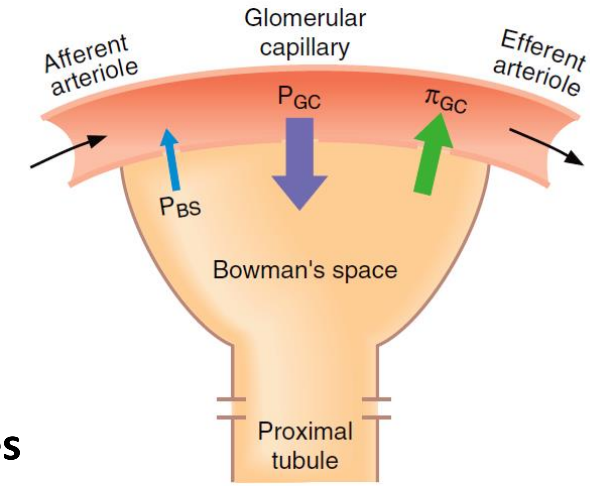


FIGURE 5.3 Starling forces across the glomerular capillaries. Heavy arrows indicate the driving forces across the glomerular capillary wall. P_{BS} = hydrostatic pressure in Bowman space; P_{GC} = hydrostatic pressure in the glomerular capillary; π_{GC} = colloidosmotic pressure in the glomerular capillary.

3. So, the forces in glomerular filtration are:

- **PGC: hydrostatic pressure in glomerular capillaries**
- **PBS, hydrostatic pressure in Bowman's space**
- **πGC, oncotic pressure in glomerular capillaries**

<u>Starling equation</u>

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

where:

- K_f = the filtration coefficient :

water permeability or hydraulic conductance of the glomerular capillary wall. Affected by 2 factors : 1. water permeability per unit of surface area 2.the total surface area…. K_f for glomerular capillaries is more than 100-fold that for systemic capillaries (both factors are higher in glomerulus)

- P_{GC} is glomerular capillary hydrostatic pressure:

It's a force **favoring** filtration. Which is **constant** along the length of the capillary <u>(45 mm Hg, relatively high</u>).

It is **increased by dilation of the afferent arteriole or constriction of the efferent arteriole (↑ blood).**

Increases in P_{GC} cause **increases** in net **ultrafiltration** pressure and **GFR**.

- P_{BS} is Bowman space hydrostatic pressure**. (10 mm Hg**)

It is a force **opposing** filtration… **increased by constriction of the ureters.**

Increases in P_{BS} cause <u>**decreases**</u> in net **ultrafiltration** pressure and **GFR**.

- π_{GC} is glomerular capillary oncotic pressure:

It's a force **opposing** filtration, **determined by [protein] in the blood**, normally **increases along the length** of the glomerular capillary because filtration of water increases, so [protein] in glomerular capillary blood increases too.

It is **increased by increases in protein concentration. Increases in π_{GC}** cause **decreases** in net **ultrafiltration** pressure and **GFR**.

- π_{BS} is Bowman space oncotic pressure:

It is usually zero, and therefore ignored.

- The driving force for glomerular filtration is the **net ultrafiltration pressure** across the glomerular capillaries (of three Starling pressures).

- **Filtration is always favored** in glomerular capillaries (fluid movement is always **out** of capillaries)… because the net ultrafiltration pressure always **favors** the movement of fluid out of the capillary.

Problem

At the afferent arteriolar end of a glomerular capillary, P_{GC} is 45 mm Hg, P_{BS} is 10 mm Hg, and π_{GC} is 27 mm Hg. What are the value and direction of the net ultrafiltration pressure?

Solution:

$$\text{Net pressure} = (P_{GC} - P_{BS}) - \pi_{GC}$$
$$\text{Net pressure} = (45 \text{ mm Hg} - 10 \text{ mm Hg}) - 27 \text{ mm Hg}$$
$$= +8 \text{ mm Hg (favoring filtration)}$$

Changes in Starling forces - effect on GFR and filtration fraction

- GFR depends on the net ultrafiltration pressure, which in turn depends on the sum of the Starling pressures (GFR changed if any one of the pressures changed).

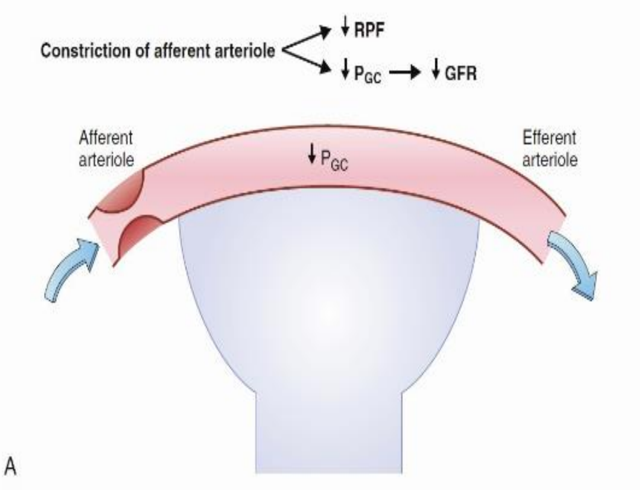
table 5.3 Effect of Changes in Starling Forces on GFR, RPF, and Fraction Filtration

	Effect on GFR	Effect on RPF	Effect on Filtration Fraction
Constriction of afferent arteriole (e.g., sympathetic)	↓ (caused by ↓ P_{GC})	↓	No change
Constriction of efferent arteriole (e.g., angiotensin II)	↑ (caused by ↑ P_{GC})	↓	↑ (↑ GFR/↓ RPF)
Increased plasma (protein)	↓ (caused by ↑ π_{GC})	No change	↓ (↓ GFR/unchanged RPF)
Ureteral stone	↓ (caused by ↑ P_{BS})	No change	↓ (↓ GFR/unchanged RPF)

GER = glomerular filtration rate; RPF = renal plasma flow.

- Figure 6.11A shows **constriction of the afferent arteriole,** in which **afferent arteriolar resistance increases**, **RPF decreases**. **GFR also decreases** because, as less blood flows into the glomerular capillary, **P$_{GC}$ decreases**, reducing net ultrafiltration pressure.

  _ Examples include the effects of the **sympathetic nervous system** and ***high* level of angiotensin II.**

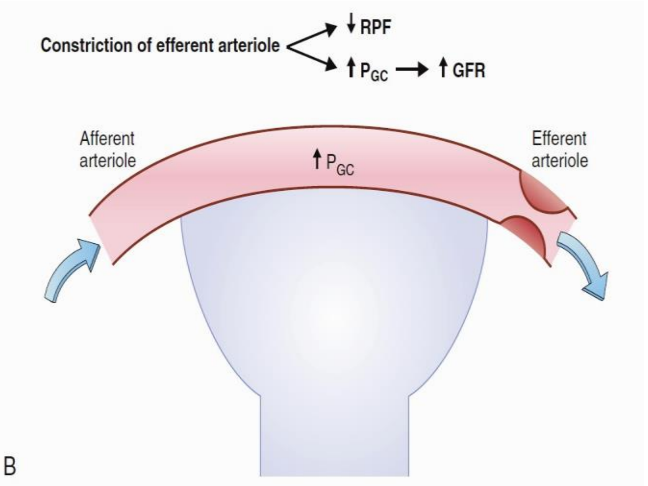


A

- Figure 6.11B shows **constriction of the efferent arteriole**

_ in which **efferent arteriolar resistance increases**. **RPF decreases**, **GFR increases**. GFR increases because blood is restricted from leaving the glomerular capillary, causing **P$_{GC}$ and net ultrafiltration pressure to increase**.

_ An example is the effect of *low* levels of **angiotensin II.**



B

Glomerular filtration rate (GFR)

- Measurement of GFR depends on the measurement of clearance of glomerular marker (we use **inulin)**

- the main characteristics of inulin:

1. freely filtered with no size or charge restriction

2. not reabsorbed or secreted by renal tubules (the amount of inulin filtered across the glomerular capillaries is exactly equal to the amount of inulin that is excreted in the urine.)

3. cannot alter the GFR

- To measure the renal blood flow, we need to measure the PAH acid clearance. This acid is fully excreted and secreted which gives us an idea about the renal blood flow.
- To measure glomerular filtration rate, we need to measure inulin clearance. We can't use PAH for GFR because it is not just excreted but secreted as well. When calculating filteration rates, you need to know just the filtered amounts of X, not absorption or secretion amounts.

Glomerular filtration rate (GFR)

$$GFR = \frac{[U]_{inulin} \times \dot{V}}{[P]_{inulin}} = C_{inulin}$$

where

GFR = Glomerular filtration rate (mL/min)

$[U]_{inulin}$ = Urine concentration of inulin (mg/mL)

$[P]_{inulin}$ = Plasma concentration of inulin (mg/mL)

$\dot{V}$ = Urine flow rate (mL/min)

C_{inulin} = Clearance of inulin (mL/min)

Other methods to estimate GFR

1. Estimates of GFR with blood urea nitrogen (BUN) and serum [creatinine].

Equation	Calculation
MDRD[12]	GFR (mL/min/1.73 m^2) = 170 x $(S_{Cr})^{-0.999}$ x $(\text{age})^{-0.176}$ x $(\text{BUN})^{-0.170}$ x $(\text{albumin})^{+0.318}$ x (0.762 if female) x (1.180 if black)
Modified (abbrev.) MDRD[13]	Estimated GFR (mL/min/1.73 m^2) = 186 x $(S_{Cr})^{-1.154}$ x $(\text{age})^{-0.203}$ x (0.742 if female) x (1.210 if African American)
Cockcroft–Gault[14]	Creatinine clearance (mL/min) = $\frac{(140 - \text{age}) \times (\text{weight})}{72 \times S_{Cr}}$ x (0.85 if female)
24-hour urine collection	Creatinine clearance (mL/min) = $\frac{U_{Cr} \times \text{volume (in mL)}}{S_{Cr} \times 1440 \text{ (number of minutes in 24 hours)}}$

Serum creatinine (S_{Cr}) in mg/dL; age in years; blood urea nitrogen (BUN) in mg/dL; weight in kg; albumin in g/dL; urine creatinine in mg/dL (U_{Cr}).
MDRD = Modification of Diet in Renal Disease Study.
GFR = Glomerular Filtration Rate.

Other methods to estimate GFR

2. Filtration fraction is the fraction of RPF that is filtered across the glomerular capillaries.

Filtration fraction = GFR / RPF

(=0.20 normally, means 20% of RPF is filtered & 80% not).

tubuloglomerular feedback

- The function of the tubuloglomerular feedback is **autoregulation**. When **renal pressure is increased**, the **renal blood flow increases** = **filteration increases** = NaCl moves through apical cell membrane to the macula densa cells = **ATP formation increases** = ATP binds to **P2X receptors** and **adenosine** binds to adenosine **A1 receptors** = triggering of Calcium release in smooth muscle cells = **contraction** = **vasoconstriction** = **increase in resistance** = **renal blood flow is fixed.**
- The **opposite is also true**.