GLomerular Filtration Rate

Renal Block
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
GFR is controlled by adjusting Glomerular blood pressure through 3 mechanisms:

**Autoregulation (intrinsic)**
- Myogenic mechanism (promote changing in blood pressure by stretching receptors)
  - Increase blood pressure: Afferent arteriole vasoconstriction and Efferent arteriole vasodilation
  - Decrease blood pressure: Afferent arteriole vasodilation and moderate Efferent arteriole vasoconstriction
  - Decrease glomerular hydrostatic pressure
  - Decrease GFR

**Tubuloglomerular feedback mechanism**
- (promote changing in sodium chloride concentration in Distal tubules)
  - Decrease resistance to blood flow in the afferent arterioles → increase glomerular hydrostatic pressure and helps return GFR toward normal
  - Increase renin release from the juxtaglomerular cells of the afferent and efferent arterioles → increase angiotensin II → constrict efferent arteriole and helps return GFR toward normal

**Hormonal Regulation**
- decrease resistance to blood flow in the afferent arterioles → increase glomerular hydrostatic pressure and helps return GFR toward normal

**Sympathetic control (extrinsic)**
- At rest: has no effect
- In severe condition (such as severe hemorrhage): constriction of afferent arteriole by releasing of vasoconstrictor mediators

**Decrease GFR**
Glomerular filtration rate (GFR): is the volume of plasma filtrate produced by both kidneys per minute.

- The average per minute is: 125 ml/min (20% of renal plasma flow)
- The average per day is: 180 L/day (gallons)
- 99% will reabsorbed (178.5 L/day) from filtrate and only 1% will excreted (1.5 – 2 L/day)

So, most filtered water must be reabsorbed or death would ensue from water lost through urination.

- These values varies with: kidney size, lean body weight and number of functional nephrons
- The relation between GFR an Net Filtration Pressure:
  - \( \uparrow \) NFP → \( \uparrow \) GFR
  - \( \downarrow \) NFP → \( \downarrow \) GFR
- Normally changes in GFR is a result from change of blood pressure.

If GFR is too high:
Fluid flows through tubules too rapidly to be absorbed (will not absorbed very well). It will lead to:
1- Urine output rises
2- Creates threat of dehydration and electrolyte depletion

If GFR is too low:
Fluid flows sluggishly through tubules. It will lead to:
1- Tubules reabsorb wastes that should be eliminated
2- Azotemia develops (high levels of nitrogen-containing substances in the blood).
Take a quick look to this picture.
Glomerular Filtration Depend on:

1- Pressure gradient across the filtration barrier:
   A. glomerular hydrostatic pressure \( (= 60 \text{ mmHg}) \). It promotes filtration.
   B. hydrostatic pressure in Bowman’s capsule \( (= 18 \text{ mmHg}) \). It opposes filtration.
   C. colloid osmotic pressure of glomerular plasma proteins \( (= 32 \text{ mmHg}) \). It opposes filtration.
   So, Net Filtration Pressure (NFP) = 60-18-32 = 10 mmHg.

2- Blood circulation throughout the kidneys
   - Renal blood flow through kidney is 20% of cardiac output \( (1200 \text{ ml/min}) \)
   - Renal plasma flow through kidney is about \( (650 \text{ ml/min}) \)
   So, GFR is about 16-20% of renal plasma flow \( (650 \times 0.19 = 125 \text{ ml/min or 180 L/day}) \)

3- Permeability of the filtration barrier (through 3 layers):
   A. The endothelium of capillary
   B. Filtration slits of epithelial lining of bowman capsule (Podocytes)
   C. Basement membrane (high negatively charge due to presence of proteoglycans)

4- Filtration membrane surface area

Any change in these factors will lead to change in GFR
Factors affecting on starling forces

A. **glomerular hydrostatic pressure** (= 60 mmHg). It promotes filtration.
   - **Increased by:** (increase GFR)
     1. Increase Arterial blood pressure (slightly affect due to autoregulation)
     2. Afferent arteriole vasodilation
     3. Moderate efferent arteriole vasoconstriction
   - **Decreased By:** (decrease GFR)
     1. Afferent arteriole vasoconstriction
     2. Efferent arteriole vasodilation

A. **hydrostatic pressure in Bowman’s capsule** (= 18 mmHg). It opposes filtration.
   - **Increased by:** (decrease GFR)
     1. Urinary obstruction (such as: Kidney stones)
     2. Kidney edema
   - **Decreased By:** (increase GFR)
     1. Afferent arteriole vasoconstriction
     2. Efferent arteriole vasodilation

A. **colloid osmotic pressure of glomerular plasma proteins** (= 32 mmHg). It opposes filtration.
   - **Increased by:** (decrease GFR)
     1. Dehydration
     2. Decrease renal blood flow
     3. Severe efferent vasoconstriction
   - **Decreased by:** (increase GFR)
     1. Hypoproteinemias
     2. Increase renal blood flow

(1) Severe efferent vasoconstriction which is a pathological condition will decrease GFR due to increase in **colloid osmotic pressure of glomerular plasma proteins**
Autoregulation of GFR and Renal Blood Flow

It is the relative constancy of GFR and renal blood flow in response to changes in blood pressure range from 75 to 160 mmHg.

The major function of autoregulation in the kidney is to maintain a relatively constant GFR and the delivery of oxygen and nutrients at a normal level and to remove the waste products of metabolism, despite changes in the arterial pressure.

A decrease in arterial blood pressure as low as 75 mmHg, or an increase as high as 160 mmHg causes a change in GFR less than 10 percent. However, autoregulation is not perfect but it prevents potentially great changes in GFR, with changes in blood pressure, therefore, kidney continue to excrete waste.
**Autoregulation of GFR and Renal Blood Flow**

*(Myogenic mechanism)*

- The ability of individual blood vessels to resist stretching during increased arterial pressure.
  - When blood pressure is increased. The constriction prevents excess increase in renal blood flow and GFR when blood pressure rises.
  - When blood pressure decreases the myogenic mechanism reduces vascular resistance and the vessel dilates.

↑ Blood Pressure → constrict afferent arteriole, & dilate efferent

↓ Blood Pressure → dilate afferent arteriole, & constrict efferent

*(Tubuloglomerular feedback mechanism)*

* The decreased in sodium chloride concentration initiates a signal from the macula densa that has two effects:
  1. **decrease** resistance to blood flow in the afferent arterioles → **increase** glomerular hydrostatic pressure and helps return GFR toward normal
  2. **increase** renin release from the juxtaglomerular cells of the afferent and efferent arterioles → **increase** angiotensin II → **constrict** efferent arteriole and helps return GFR toward normal

**Medical Tip**

- The administration of drugs (ACEI) or (ARBs) causes greater reductions in GFR than when the renal arterial pressure falls.
  * complication of using these drugs to treat patients who have hypertension because of renal artery stenosis (partial blockage of the renal artery) is a severe decrease in GFR that can, in some cases, cause acute renal failure
Importance of GFR Autoregulation in Preventing Extreme Changes in Renal Excretion (Additional Reading from guyton)

In the absence of autoregulation, a relatively small increase in blood pressure (from 100 to 125 mm Hg) would cause a similar 25 percent increase in GFR (from about 180 to 225 L/day). If tubular reabsorption remained constant at 178.5 L/day, this would increase the urine flow to 46.5 L/day (the difference between GFR and tubular reabsorption)—a total increase in urine of more than 30-fold. Because the total plasma volume is only about 3 liters, such a change would quickly deplete the blood volume.

In reality, changes in arterial pressure usually exert much less of an effect on urine volume for two reasons:
1. renal autoregulation prevents large changes in GFR that would otherwise occur
2. there are additional adaptive mechanisms in the renal tubules that cause them to increase their reabsorption rate when GFR rises, a phenomenon referred to as glomerulotubular balance
Several hormones and autacoids can influence GFR and renal blood flow.

### Hormone or Autacoid | Effect on GFR
--- | ---
Norepinephrine | ↓
Epinephrine | ↓
Endothelin | ↓
Angiotensin II | ↔ (prevents ↓)
Endothelial-derived nitric oxide | ↑
Prostaglandins | ↑

### Effects of Angiotensin II

1. **afferent arterioles**, appear to be relatively protected from angiotensin II due to release of vasodilators, especially nitric oxide and prostaglandins, which counteract the vasoconstrictor effects of angiotensin II.

2. **efferent arterioles** are highly sensitive to angiotensin II. Because angiotensin II constricts efferent arterioles in most physiologic conditions, increased angiotensin II levels raise glomerular hydrostatic pressure while reducing renal blood flow.
Sympathetic Control of GFR (Extrinsic)

AT REST

- Renal blood vessels are maximally dilated.
- Autoregulation mechanisms take place
- No sympathetic activation.

UNDER STRESS

- Norepinephrine is released by the sympathetic nervous system.
- Epinephrine is released by the adrenal medulla
- Afferent arterioles constrict and filtration is inhibited
- During fight or flight blood is shunted away from kidneys

The sympathetic nervous system also stimulates the renin-angiotensin mechanism. This induces vasoconstriction of efferent arteriole.
# Summary of all factors affect GFR

<table>
<thead>
<tr>
<th>Physical Determinants*</th>
<th>Physiologic/Pathophysiologic Causes</th>
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<tbody>
<tr>
<td>↓$K_f$ → ↓ GFR</td>
<td>Renal disease, diabetes mellitus, hypertension</td>
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<td>↑$P_B$ → ↓ GFR</td>
<td>Urinary tract obstruction (e.g., kidney stones)</td>
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<tr>
<td>↑$\pi_G$ → ↓ GFR</td>
<td>↓ Renal blood flow, increased plasma proteins</td>
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<td>↓$P_G$ → ↓ GFR</td>
<td></td>
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<tr>
<td>↓$AP$ → ↓$P_G$</td>
<td>↓ Arterial pressure (has only small effect due to autoregulation)</td>
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<tr>
<td>↓$RE$ → ↓$P_G$</td>
<td>↓ Angiotensin II (drugs that block angiotensin II formation)</td>
</tr>
<tr>
<td>↑$RA$ → ↓$P_G$</td>
<td>↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)</td>
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*Opposite changes in the determinants usually increase GFR.

$K_f$, glomerular filtration coefficient; $P_B$, Bowman's capsule hydrostatic pressure; $\pi_G$, glomerular capillary colloid osmotic pressure; $P_G$, glomerular capillary hydrostatic pressure; $AP$, systemic arterial pressure; $RE$, efferent arteriolar resistance; $RA$, afferent arteriolar resistance.

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1- How much volume filtered per day?
A- 125 ml/min  
B- 180 L/day  
C- 200 L/day  
D- 125 L/day

2- When the Glomerular Filtration Rate increase the net filtration pressure is?
A- Decrease  
B- Increase  
C- Inverse proportional  
D- Constant

3- If GFR is low the body will react by:
A- Increase fluid flow through tubules  
B- Rise in urine output  
C- Fluid flows sluggishly through tubules  
D- Dehydration

4- GFR controlled by adjusting glomerular blood pressure through:
A- renin and angiotensin  
B- parasympathetic control  
C- Estrogen  
D- Testosterone

5- Which of the following is true of autoregulation in GFR:
A- It has a wide regulation by prevents potentially great changes in GFR  
B- Increase in resistance of the afferent arterioles only  
C- It is extrinsic regulation of kidney  
D- Works when changes in blood pressure range from 75 to 160 mmHg.

6- Constrict afferent arteriole and dilate efferent arteriole that are sign of:
A- Increase in blood pressure  
B- Decrease in blood pressure

7- If an increase in ABP, which one of these mechanism will occur?
A- a decrease in resistance of the afferent arterioles  
B- Secrete angiotensin II  
C- decrease in renin release  
D- constrict efferent arteriole

8- During myogenic mechanism, it will activate if there is changing in:
A- Vascular resistance  
B- Oncotic pressure  
C- Blood pressure  
D- A & C

Ans: 1-B, 2-B, 3-C, 4-A, 5-D, 6-A, 7-C, 8-D,