Glomerular Filtration
Chapter 26

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For each substrate in the plasma a particular combination of filtration, reabsorption, and secretion occurs.

- Rate at which substances are excreted depends on the relative rates of
  - Glomerular Filtration
  - Tubular Reabsorption
  - Tubular Secretion
Different Substances: Filtration, Reabsorption & Secretion

Excreted in large amounts in the urine - urea, creatinine, uric acid, and urates because they are poorly reabsorbed

Excreted in small amounts in the urine - electrolytes like sodium ions, chloride ions, and bicarbonate ions because they are highly reabsorbed

Amino acids and glucose do not appear in urine because they are completely reabsorbed from the tubules

*Each process is regulated according to the needs of the body
*The rate of filtration and reabsorption are extremely large relative to the rates of excretion
Advantages of high GFR (Glomerular Filtration Rate)

➢ Kidneys can rapidly move waste products from the body that depend mainly on glomerular filtration for excretion

  – Ex: Metabolic waste products such as urea, creatinine, uric acid, and urates.

➢ Body fluids to be filtered and processed by the kidneys many times a day

  ◇ Entire plasma volume ~3L

  ◇ GFR ~180L/day

  – This means that the entire plasma can be filtered and processed ~60 times each day

➢ Kidneys have precise and rapid control of the volume and composition of body fluids.
Glomerular Filtration
Composition of Glomerular Filtrate

Urine formation begins with filtration of large amounts of fluid through the glomerular capillaries into the Bowman’s capsule.

Glomerular capillaries are impermeable to proteins, so the filtered fluid (glomerular filtrate) is essentially protein free and devoid of cellular elements, including red blood cells.

Calcium and fatty acids are not filtered freely because they are partially bound to the plasma proteins.
GFR is ~20% of the Renal Blood Flow

GFR is determined by:

1. Balance of hydrostatic and colloid osmotic forces acting across the capillary membrane.

2. Capillary filtration coefficient ($K_f$), the product of permeability and filtering surface area of the capillaries.

--Glomerular capillaries have a much higher rate of filtration than most capillaries because of a high glomerular hydrostatic pressure and a large $K_f$.

➢ GFR ~125 ml/min or ~180L/day

➢ ~20% of plasma flowing through the kidney is filtered through the glomerular capillaries.

- Filtration Fraction=GFR/Renal Plasma Flow
Glomerular Capillary Membrane

Three major layers…

1. The endothelium of the capillary
   - Fenestrae (small holes)

1. A basement membrane
   - Collagen and proteoglycan fibrillae that have large spaces which large amounts of water and small solutes can filter

1. An epithelial cells (podocytes) surrounding the outer surface of the capillary basement membrane
   - Slit pores separate the podocytes which the glomerular filtrate moves through

All layers of the glomerular capillary wall provide a barrier to filtration of plasma proteins
Podocytes

“Feet” attach to endothelium

Spaces between form “slit pores”

Passage of filtrate to capsular space
Anatomy of the Filtration Apparatus

Blood supply through afferent & efferent arterioles
- Maintain & regulate pressure
- Efferent arteriole
  Smaller diameter
  $\uparrow$ resistance

Filtration membrane
- Fenestrated capillary epithelium
  Passage of fluids & small solutes

➢ Figure 26-11
Filterability of Solutes

- Glomerular capillary membranes are thicker than most, but they’re also much more porous and therefore filters fluid at a high rate.

- The glomerular filtration is selective in determining which molecules will filter based on
  - Size
  - Electrical charge

  - View Table 26-1
# Substance Filterability Based on Molecular Weight

<table>
<thead>
<tr>
<th>Substance</th>
<th>Molecular Weight</th>
<th>Filterability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>18</td>
<td>1.00</td>
</tr>
<tr>
<td>Sodium</td>
<td>23</td>
<td>1.00</td>
</tr>
<tr>
<td>Glucose</td>
<td>180</td>
<td>1.00</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>17,000</td>
<td>0.75</td>
</tr>
<tr>
<td>Albumin</td>
<td>69,000</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Table 26-1.

➢ Filterability 1.00 = Substance is filtered as freely as water.
➢ Filterability 0.75 = Substance is filtered only 75% as rapidly as water

The heavier a substance the slower it will filter. *Filterability of solutes is inversely related to their size.*
Molecules Not Easily Filtered

Negatively charged large ions are filtered less easily than positively charged molecules of equal molecular size

Charge of molecule
- Proteoglycans (- charged) on surfaces of...
  - Plasma membranes of capillaries
  - Plasma membranes of Podocytes
  - Within basement membrane
Determinants of the GFR

1. Net filtration pressure = The sum of the hydrostatic and colloid osmotic forces across the glomerular membrane

   ➢ Glomerular hydrostatic pressure, \( P_G \)

   ➢ Bowman’s capsule hydrostatic pressure, \( P_B \)

   ➢ Glomerular capillary colloid osmotic pressure, \( \pi_G \)

   ➢ Bowman’s capsule colloid osmotic pressure, \( \pi_B \)

2. \( K_f \): the glomerular filtration coefficient

   \[
   GFR = K_f \times \text{Net Filtration Pressure}
   \]

   \[
   GFR = K_f \times (P_G - P_B - \pi_G + \pi_B)
   \]
Glomerular Filtration Rate (GFR)

➢ Forces favoring filtration
  - $P_G \sim 60$ mmHg
  - $\pi_B \sim 0$ mmHg

➢ Forces opposing filtration
  - $P_B \sim 18$ mmHg
  - $\pi_G \sim 32$ mmHg

➢ Normal NFP $\sim 10$ mmHg
Glomerular Capillary Filtration Coefficient $\uparrow$ GFR

$K_f = \text{glomerular capillary filtration coefficient}$
- Reflects conductivity and capillary surface area

\[ K_f = \frac{GFR}{\text{Net Filtration Pressure}} \]

GCF Coefficient is directly proportional to GFR

- Increased $K_f$ increases GFR
- Decreased $K_f$ decreased GFR
Bowman’s Capsule Hydrostatic Pressure ↓ GFR

Normal hydrostatic pressure in Bowman’s capsule ($P_B$) ~18mmHg

➢ $\uparrow P_B = \downarrow GFR$

➢ $\downarrow P_B = \uparrow GFR$

Changes in $P_B$ don’t serve as a primary means for regulating GFR

$-P_B$ can drastically change with obstruction of the urinary tract

Ex: Precipitation of calcium/uric acid → “stones” that block the urinary tract and outflow of secretions → raise Bowman’s capsule pressure → reduces GFR

Can eventually cause *hydronephrosis* and can damage/destroy the kidney unless the obstruction is relieved.
The average colloid osmotic pressure of the glomerular capillary plasma protein is between 28 mmHg and 36 mmHg.

Two factors influencing glomerular capillary osmotic pressure...

1. The arterial plasma colloid osmotic pressure
2. The fraction of plasma filtered by the glomerular capillaries (filtration fraction)

*Increasing the filtration fraction also concentrates the plasma proteins and increases the glomerular colloid osmotic pressure which decreases GFR

*A greater rate of blood flow into the glomerulus tends to increase GFR and a lower rate of blood flow into the glomerulus tends to decrease GFR
Glomerular Capillary Hydrostatic Pressure $\uparrow$ GFR

Changes in $P_G$ serve as the primary means for physiologic regulation of GFR.

- $\uparrow P_G = \uparrow GFR$
- $\downarrow P_G = \downarrow GFR$

1. Arterial pressure
   - $\uparrow$ arterial pressure tends to $\uparrow P_G$ and, as a result, $\uparrow GFR$

2. Afferent arteriolar resistance
   - $\uparrow$ resistance of afferent arterioles $\downarrow P_G$ and $\downarrow GFR$
   - $\uparrow$ dilation of afferent arterioles $\uparrow P_G$ and $\uparrow GFR$

3. Efferent arteriolar resistance
   - $\uparrow$ constriction of efferent arterioles $\uparrow$ resistance to outflow from glomerular capillaries $\rightarrow \uparrow P_G$ and slight $\uparrow GFR$ if renal blood flow is not reduced much
   - $\uparrow$ if constriction is severe this can cause $\downarrow GFR$
Efferent arteriolar resistance

- at moderate levels of constriction there are slight GFR increases
- severe constriction results in GFR decrease

Afferent arteriolar resistance

- Constriction of afferent arterioles reduce GFR
Renal Blood Flow
Renal Blood Flow

*Blood flow supplies the kidneys with nutrients and removes waste products*

The purpose of additional flow is to supply enough plasma for the high rates of the glomerular filtration that are necessary for precise regulation of body fluid volumes and solute concentrations.

The mechanisms that regulate renal blood flow are closely linked to the control of GFR and the excretory functions of the kidneys.
Renal Blood Flow & Oxygen Consumption

- Kidneys normally consume oxygen at 2X the rate of the brain but have ~7X the blood flow of the brain.
  - Oxygen delivered to the kidneys far exceeds their metabolic needs

- Oxygen consumption by the kidneys is related to the high rate of active sodium reabsorbed by the renal tubes.
  - If renal blood flow and GFR are reduced and less sodium is filtered, less sodium is reabsorbed and less oxygen is consumed.

- Renal oxygen consumption varies in proportion to renal tubular sodium reabsorption, which is closely related to GFR and rate of sodium filtered.

- If glomerular filtration ceases completely then renal sodium reabsorption also ceases and oxygen consumption decreases to ~one-fourth normal
Determinants of Renal Blood Flow

Renal blood flow is determined by…

$$\frac{(\text{Renal Artery Pressure} - \text{Renal Vein Pressure})}{\text{Total Renal Vascular Resistance}}$$

Renal vascular resistance resides in three segments…

1. Interlobular arteries
2. Afferent arterioles
3. Efferent arterioles

An increase in the resistance of any of the vascular segments of the kidneys tends to reduce the renal blood flow, whereas a decrease in vascular resistance increases renal blood flow if renal arteries and veins remain constant.
Blood flow differs in different parts of the kidney

- The outer part of the kidney (renal cortex) receives most of the blood flow.

- Blood flow in the renal medulla account for 1-2% of total renal blood flow.

  ➢ This blood is supplied by a specialized portion of the peritubular capillary system called the *vasa recta*.

  - These vessels descend into the medulla || to the loops of Henle & loop back around to return to the cortex before emptying into the venous system.
Physiological Control of GFR and Renal Blood Flow

*Sympathetic Nervous System Activation Decreases GFR*

All the blood vessels of the kidneys are richly innervated by sympathetic nerve fibers.

Strong activation of the renal sympathetic nerves can constrict the renal arterioles and decrease in renal blood flow and GFR.

Mild or moderate sympathetic stimulation has little influence on renal blood flow or GFR.

The renal sympathetic nerves seem to be the most important in reducing GFR during severe, acute disturbances lasting for a few minutes to a few hours.
Hormonal Response

- Vasoconstrictors cause reductions in GFR and renal blood flow.

- **Norepinephrine & Epinephrine**
  - Have little influence except under extreme conditions (severe hemorrhage)

- **Endothelin**
  - Peptide that can be released by damaged vascular endothelial cells of the kidneys (and other tissues)
  - Role isn’t completely understood; may contribute to hemostasis (minimizing blood loss)

- **Angiotensin II**
  - Powerful renal vasoconstrictor
  - Preferentially constricts efferent arterioles in most physiological conditions
  - Increased angiotensin levels that occur from low-sodium diet or volume depletion help maintain GFR and normal excretion of metabolic waste products
● Endothelial-derived nitric oxide
  ➢ An autacoid that ↓ renal vascular resistance and is released by the vascular endothelium throughout the body.
  ➢ Basal level important for maintaining vasodilation of the kidneys
  ➢ Increase GFR

● Prostaglandins
  ➢ PGE$_2$ and PGI$_2$
  ➢ Cause vasodilation and increased blood flow and GFR
  ➢ Not as important; may help prevent excessive reductions in GFR and renal blood flow.

<table>
<thead>
<tr>
<th>Hormone or Autacoid</th>
<th>Effect on GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norepinephrine</td>
<td>↓</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>↓</td>
</tr>
<tr>
<td>Endothelin</td>
<td>↓</td>
</tr>
<tr>
<td>Angiotensin II</td>
<td>↔ (prevents ↓)</td>
</tr>
<tr>
<td>Endothelial-derived nitric oxide</td>
<td>↑</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>↑</td>
</tr>
</tbody>
</table>

Table 26-2: Hormones and autacoids that influence glomerular filtration rate (GFR).
Autoregulation of GFR and Renal Blood Flow

*Autoregulation occurs in the kidneys to maintain a relatively constant GFR and to allow precise control of renal excretion of water and solutes*

Renal blood flow is autoregulated in parallel with GFR, but GFR is more efficiently autoregulated under certain conditions

For example…
A decrease in arterial pressure as low as 75 mmHg or and increase as high as 160 mmHg usually changes GFR less than 10 percent
Importance of GFR Autoregulation

Autoregulation prevents potentially large changes in GFR and renal excretion of water and solutes that would otherwise occur with changes in blood pressure.

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. *Glomerulotubular Balance*: Additional adaptive mechanisms in the renal tubules that cause them to increase their reabsorption rate when GFR rises.
Tubular Feedback and Autoregulation of GFR

- Feedback mechanism that links changes in sodium chloride concentration at the macula densa with the control of renal arteriolar resistance to perform autoregulation.

  ➢ Helps ensure relatively constant NaCl delivery to the distal tubule

  ➢ In many circumstances, this feedback autoregulates renal blood flow and GFR in parallel.

2 components act together to control GFR

1. An afferent arteriolar feedback mechanism

2. An efferent arteriolar feedback mechanism

Both depend on the juxtaglomerular complex. ➢Fig 26-17
• Juxtaglomerular complex

➢ Specialized tubular arrangement

- Macula densa
  ◇ Initial portion of distal tubule
  ◇ Specialized epithelial cells
  ◇ Close contact with afferent/efferent arterioles
  ◇ Contain Golgi apparatus (secretory organelles)
    ◦ suggests that these cells may be secreting a substance toward the arterioles.

- Juxtaglomerular cells
Macula Densa

Sense changes in volume via changes in Na\(^+\) & Cl\(^-\) concentrations

- Decreased flow through Loop of Henle
- Slower flow
- Increased ion reabsorption
- Decreased ion concentration in filtrate

Response to \(^-\)Na\(^+\) & Cl\(^-\)

- Vasodilate afferent arterioles
- Stimulate renin release from JG cells
- Vasoconstriction of efferent arterioles

Results in glomerular hydrostatic pressure
Tubuloglomerular Feedback Overview

- Figure 26-19
Myogenic Autoregulation of Renal Blood Flow and GFR

- Myogenic Mechanism
  - Ability of individual blood vessels to resist stretching during increased arterial pressure.
  - Response to ↑ wall tension or wall stretch by contraction of vascular smooth muscle.

- The myogenic mechanism probably operates most arterioles throughout the body, its importance in renal blood flow and GFR autoregulation has been questioned.

- This mechanism may be more important in protecting the kidney from hypertension-induced injury.