Renal System

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Declaration

• The content and the figures of this seminar were directly adopted from the textbook “Human Anatomy and Physiology / Ninth edition/ Eliane N. Marieb 2013”
Internal Gross Anatomy

- Renal cortex
- Renal medulla
- Major calyx
- Papilla of pyramid
- Renal pelvis
- Minor calyx
- Ureter
- Renal pyramid in renal medulla
- Renal column
- Fibrous capsule
Nephrons are the structural and functional units of the kidneys.

Each nephron consists of a glomerulus (a high-pressure capillary bed), a glomerular capsule, and a renal tubule that is continuous with the capsule.
Nephrons

Subdivisions of the renal tubule (from the glomerular capsule) are:

- the proximal convoluted tubule
- Nephron loop (loop of Henle)
- Distal convoluted tubule.

- A second capillary bed, the low-pressure peritubular capillary bed, is closely associated with the renal tubule of each nephron.
Nephron

Diuretics
1. Acetazolamide
2. Osmotic agents (mannitol)
3. Loop agents (e.g., furosemide)
4. Thiazides
5. Aldosterone antagonists
6. ADH antagonists
Composition of the filtrate:

- Glucose
- Sodium bicarbonate
- Amino acids
- Organic solutes and metabolites
- Electrolytes such as: $\text{Na}^+$, $\text{K}^+$, $\text{Cl}^-$ and $\text{Ca}^{2+}$
- Water

Water is curried passively to regulate osmotic equilibrium.
Proximal convoluted tubule (PCT)

- Located in the cortex of the kidney
- Reabsorbs:
  - All the glucose
  - Bicarbonate (HCO$_3^-$)
  - Amino acids
  - Metabolites
  - $\frac{2}{3}$ of Na$^+$
  - Cl$^-$
  - Water follows passively to maintain osmolar equality
Proximal convoluted tubule (PCT)

- The entire renal tubule is involved in reabsorption to some degree, but the PCT cells are by far the most active "reabsorbers"
- PCT reabsorbs all of the glucose and amino acids in the filtrate
- It reabsorbs 65% of the Na+
- Nearly all of the uric acid and about half of the urea are reabsorbed in the proximal tubule, but both are later secreted back into the filtrate
Nephron Loop

• Throughout the nephron loop, the permeability of the tubule epithelium changes dramatically.

• Here, for the first time, water reabsorption is not coupled to solute reabsorption.

• Water can leave the descending limb of the nephron loop but not the ascending limb, where aquaporins are scarce or absent in the tubule cell membranes.

• This plays a vital role in the kidneys’ ability to form dilute or concentrated urine.
Descending loop of Henle

- Passes into the medulla of the kidney
- Reabsorbs water form the isotonic filtrate resulting in 3-fold increase in salt concentration.
Ascending loop of Henle

- Impermeable to water

- In the thin segment of the ascending limb, Na\(^+\) moves passively down the concentration gradient created by water reabsorption.

- In the thick ascending limb, a Na\(^+\)-K\(^+\)-2Cl\(^-\) symporter is the main means of Na\(^+\) entry at the apical surface.
A Na\(^+\)-K\(^+\) ATPase operates at the basolateral membrane to create the ionic gradient that drives the symporter.

The thick ascending limb also has Na\(^+\)-H\(^+\) antiporters.

In addition, some 50% of Na\(^+\) passes via the paracellular route in this region.
Both Ca$^{2+}$ and Mg$^{2+}$ enter the interstitial fluid via the paracellular pathway.

• It is a diluting region of the nephron

• 25-30% of the tubular NaCl is reabsorbed there (site of action of loop diuretics)
Distal Convoluted Tubule and Collecting Duct

• Reabsorption in the PCT and nephron loop does not vary with the body’s needs.

• Reabsorption in the DCT and collecting duct is fine-tuned by hormones: Antidiuretic hormone (ADH), Aldosterone, Atrial natriuretic peptide (ANP), Parathyroid hormone (PTH)

• Most of the filtered water and solutes have been reabsorbed by the time the DCT is reached

• Only a small amount of the filtered load is subject to this fine tuning (e.g., about 10% of the originally filtered NaCl and 25% of the water).
Collecting tubule and duct

- Na+ enters the cell via Na⁺ channels (inhibited by Amiloride and Triametrene).

- Once inside the cells, Na⁺ is transported to the blood via Na⁺/K⁺ ATPase pump.

- Aldosterone increases the synthesis of Na⁺ channels and Na⁺/K⁺ ATPase pump.

- Antidiuretic hormone (ADH; vasopressin) promotes the reabsorption of water from there.
Antidiuretic hormone (ADH)

- ADH makes the principal cells of the collecting ducts more permeable to water by causing **aquaporins** to be inserted into their apical membranes.

- The amount of ADH determines the number of aquaporins, and thus the amount of water that is reabsorbed there.

- When the body is overhydrated, extracellular fluid osmolality decreases, decreasing ADH secretion by the posterior pituitary and making the collecting ducts relatively impermeable to water.
Aldosterone

- Aldosterone fine-tunes reabsorption of the remaining Na+.

- Decreased blood volume or blood pressure, or high extracellular K+ concentration (hyperkalemia), can cause the adrenal cortex to release aldosterone to the blood.

- Except for hyperkalemia (which directly stimulates the adrenal cortex to secrete aldosterone), these conditions promote the renin-angiotensin-aldosterone mechanism
Aldosterone

- Aldosterone targets the principal cells of the collecting ducts and cells of the distal portion of the DCT (prodding them to synthesize and retain more apical Na+ and K+ channels, and more basolateral Na+/K+ ATPases).

- As a result, little or no Na+ leaves the body in urine.

- In the absence of aldosterone, these segments reabsorb much less Na+ and about 2% of Na+ filtered daily can be lost—an amount incompatible with life.
Aldosterone

- Physiologically, aldosterone’s role is to increase blood volume, and therefore blood pressure, by enhancing Na+ reabsorption.

- In general, water follows Na+ if aquaporins are present.

- Aldosterone also reduces blood K+ concentrations because aldosterone-induced reabsorption of Na+ is coupled to K+ secretion in the principal cells of the collecting duct.

- That is, as Na+ enters the cell, K+ moves into the lumen.
Parathyroid hormone (PTH)

- Acting primarily at the DCT, PTH increases the reabsorption of Ca$^{2+}$
Tubular Secretion

- Adds substances to the filtrate (from the blood or tubule cells).

- It is an active process that is important in eliminating drugs, certain wastes, and excess ions and in maintaining the acid-base balance of the blood.
Clinical Evaluation of Kidney Function
Renal Clearance

- Renal clearance refers to the volume of plasma from which the kidneys clear (completely remove) a particular substance in a given time, usually 1 minute.

- Renal clearance tests are done to determine the GFR, which allows us to detect glomerular damage and follow the progress of renal disease.

- The renal clearance rate (C) of any substance, in ml/min, is calculated from the equation

\[ C = \frac{U \times V}{P} \]

- \(U\) = concentration of the substance in urine (mg/ml)
- \(V\) = flow rate of urine formation (ml/min)
- \(P\) = concentration of the substance in plasma (mg/ml)
Because it is freely filtered and neither reabsorbed nor secreted by the kidneys, **Inulin** is the standard used to determine the GFR.

Inulin is a plant polysaccharide that has a renal clearance value equal to the GFR.

When inulin is infused such that its plasma concentration is 1 mg/ml ($P = 1 \text{ mg/ml}$), then generally $U = 125 \text{ mg/ml}$, and $V = 1 \text{ ml/min}$.

Therefore, its renal clearance is $C = (125 \times 1)/1 = 125 \text{ ml/min}$,

Meaning that in 1 minute the kidneys have cleared all the inulin present in 125 ml of plasma.
What does clearance values tell us?

• If the measured $C < C$ of inulin means that the substance is reabsorbed.

• E.g., urea has a $C$ of 70 ml/min, meaning that of the 125 ml of glomerular filtrate formed each minute, approximately 70 ml is completely cleared of urea, while the urea in the remaining 55 ml is recovered and returned to the plasma.

• If the $C$ is zero (such as for glucose in healthy individuals), reabsorption is complete or the substance is not filtered.
What does clearance values tell us?

- If the C is equal to that of inulin, there is no net reabsorption or secretion.

- If the C is greater than that of inulin, the tubule cells are secreting the substance into the filtrate.

  - This is the case with most drug metabolites.

  - Knowing a drug’s renal clearance value is essential because if it is high, the drug dosage must also be high and administered frequently to maintain a therapeutic level.
Creatinine

- Creatinine, which has a C of 140 ml/min, is freely filtered but also secreted in small amounts.

- It is often used nevertheless to give a “quick and dirty” estimate of GFR because it does not need to be intravenously infused into the patient as does inulin
Urine: Physical Characteristics

Color and Transparency:
• Freshly voided urine is clear and pale to deep yellow.

• Its yellow color is due to urochrome, a pigment that results when the body destroys hemoglobin.

• The more concentrated the urine, the deeper the color.

• An abnormal color (such as pink, brown, or a smoky tinge) may result from eating certain foods (beets, rhubarb) or from the presence of bile pigments or blood in the urine.

• Some commonly prescribed drugs and vitamin supplements alter the color of urine.

• Cloudy urine may indicate a urinary tract infection.
Urine: Physical Characteristics

Odor:

• Fresh urine is slightly aromatic, but if allowed to stand, it develops an ammonia odor as bacteria metabolize its urea solutes.

• Some drugs and vegetables alter the usual odor of urine, as do some diseases.

• For example, in uncontrolled diabetes mellitus the urine smells fruity because of its acetone content.
Urine: Physical Characteristics

pH:

• pH Urine is usually slightly acidic (around pH 6), but changes in body metabolism or diet may cause the pH to vary from about 4.5 to 8.0.

• A predominantly acidic diet that contains large amounts of protein and whole wheat products produces acidic urine.

• A vegetarian (alkaline) diet, prolonged vomiting, and bacterial infection of the urinary tract all cause the urine to become alkaline.
Urine: Physical Characteristics

Specific Gravity:

• The ratio of the mass of a substance to the mass of an equal volume of distilled water.

• Because urine is water plus solutes, a given volume has a greater mass than the same volume of distilled water.

• The specific gravity of distilled water is 1.0 and that of urine ranges from 1.001 to 1.035, depending on its solute concentration.
Urine content

• **Water**: accounts for about 95% of urine volume; the remaining 5% consists of solutes.

• **Urea**: The largest component of urine by weight. It is derived from the normal breakdown of amino acids.

• **Uric acid** (an end product of nucleic acid metabolism)

• **Creatinine** (a metabolite of creatine phosphate, which is found in large amounts in skeletal muscle tissue where it stores energy to regenerate ATP).
Urine content

- Normal solute constituents of urine, in order of decreasing concentration, are urea, Na+, K+, PO$_4^{3-}$, SO$_4^{2-}$, creatinine, and uric acid.

- Much smaller but highly variable amounts of Ca$^{2+}$, Mg$^{2+}$, and HCO$_3$.

- Unusually high concentrations of any solute, or the presence of abnormal substances such as blood proteins, WBCs (pus), or bile pigments, may indicate pathology.
# Urine content

## Table 25.2 Abnormal Urinary Constituents

<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>NAME OF CONDITION</th>
<th>POSSIBLE CAUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>Glycosuria</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Proteins</td>
<td>Proteinuria, albuminuria</td>
<td>Nonpathological: excessive physical exertion, pregnancy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pathological (over 150 mg/day): heart failure, severe hypertension, glomerulonephritis, often initial sign of asymptomatic renal disease</td>
</tr>
<tr>
<td>Ketone bodies</td>
<td>Ketonuria</td>
<td>Excessive formation and accumulation of ketone bodies, as in starvation and untreated diabetes mellitus</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Hemoglobinuria</td>
<td>Various: transfusion reaction, hemolytic anemia, severe burns, etc.</td>
</tr>
<tr>
<td>Bile pigments</td>
<td>Bilirubinuria</td>
<td>Liver disease (hepatitis, cirrhosis) or obstruction of bile ducts from liver or gallbladder</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>Hematuria</td>
<td>Bleeding urinary tract (due to trauma, kidney stones, infection, or cancer)</td>
</tr>
<tr>
<td>Leukocytes (pus)</td>
<td>Pyuria</td>
<td>Urinary tract infection</td>
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**Intrinsic mechanisms** directly regulate GFR despite moderate changes in blood pressure (between 80 and 180 mm Hg mean arterial pressure).

**Extrinsic mechanisms** indirectly regulate GFR by maintaining systemic blood pressure, which drives filtration in the kidneys.

**Myogenic mechanism of autoregulation**
- Decrease in blood pressure in afferent arterioles; decrease in GFR
- Stretch of smooth muscle in walls of afferent arterioles
- Vasodilation of afferent arterioles

**Tubuloglomerular mechanism of autoregulation**
- Decrease in filtrate flow and decrease in NaCl in ascending limb of nephron loop
- Release of vasoactive chemicals inhibited
- Vasodilation of afferent arterioles
- Increase in GFR

**Hormonal (renin-angiotensin-aldosterone) mechanism**
- Granular cells of juxtaglomerular complex of kidney
- Release
- Catalyzes cascade resulting in formation of Angiotensin II
- Increase in aldosterone secretion by adrenal cortex
- Vasoconstriction of systemic arterioles; increase in peripheral resistance
- Increase in Na⁺ reabsorption by kidney tubules; water follows
- Increase in blood volume
- Increase in systemic blood pressure

**Neural controls**
- Inhibits baroreceptors in blood vessels of systemic circulation
- Sympathetic nervous system