RENAL ANATOMY AND PHYSIOLOGY
Dr. Robin Paudel

1. Regulation of blood ionic composition
2. Maintenance of blood osmolarity
3. Regulation of blood volume
4. Regulation of blood pressure
5. Regulation of blood pH

MAJOR FUNCTIONS OF THE KIDNEYS AND THE URINARY SYSTEM

8. Excretion of wastes and foreign substances

NEPHRON - THE FUNCTIONAL UNIT OF THE KIDNEYS

- Cortical Nephrons: 80 to 85% of nephrons. Have short Loops of Henle that lay mainly in the cortex.
- Juxtamedullary Nephrons: 15 to 20% of nephrons. Have long Loops of Henle that extend into the deepest regions of the medulla. Produce the most concentrated urine.

- 7/8 of all nephrons are cortical nephrons
- 1/8 of all nephrons are juxtamedullary nephrons
- Nephron structures in the medulla consist of the long loops of Henle and the terminal regions of the collecting ducts.
- All other structures, including the first section of the collecting ducts, are in the cortex.
THE ANATOMY OF A NEPHRON

0 Subdivision of a Nephron:
1. Renal Corpuscle
2. Proximal Convoluted tubule
3. Descending limb of Loop of Henle
4. Ascending limb of Loop of Henle
5. Distal Convoluted tubule
6. Collecting duct
7. Papillary duct

URINE DRAINAGE THROUGH THE KIDNEY AND BODY

0 From papillary duct
0 Minor Calyx
0 Major Calyx
0 Ureter
0 Urinary Bladder
0 Urethra: prostatic membranous penis

BLOOD FLOW THROUGH THE KIDNEY

BASIC FUNCTIONS OF A NEPHRON

THE GLOMERULAR FILTRATION MEMBRANE
Filtration Pressures and Glomerular Filtration Rate

- Filtration Pressure is the force that drives the fluid and its dissolved substances through the glomerular filter.

Net Filtration pressure NPF (or Net Hydrostatic Pressure NHP) is the difference between three pressures:
1. Glomerular (blood) hydrostatic pressure GHP or GBHP
2. Capsular Hydrostatic Pressure (CHP)
3. (Blood) Colloid Osmotic Pressure (BCOP)

The relationship can be expressed by:
\[ NPF = GBHP - (CHP + BCOP) \]

Glomerular Filtration Rate: amount of filtrate the kidneys produce each minute. (about 125 ml per minute)

Factors Affecting Filtration Rate in the Kidney

Regulation of Glomerular Filtration Rate

**NEURAL REGULATION**

<table>
<thead>
<tr>
<th>Regulation</th>
<th>Major Stimulus</th>
<th>Mechanism</th>
<th>Effect on GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sympathetic Nerves</td>
<td>Acute fall in systemic blood pressure.</td>
<td>Constriction of afferent</td>
<td>Decrease GFR and filtrate volume to maintain blood volume</td>
</tr>
<tr>
<td>(Autonomic)</td>
<td>Release of norepinephrine</td>
<td>efferent arterioles</td>
<td></td>
</tr>
</tbody>
</table>

**HORMONAL REGULATION** (see page 1014-1015)

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<tr>
<td>Angiotensin II</td>
<td>Decreased blood volume or decreased blood pressure</td>
<td>Constriction of both afferent and efferent arterioles</td>
<td>Decreases GFR</td>
</tr>
<tr>
<td>Atrial natriuretic peptide</td>
<td>Stretching of the arterial walls due to increased blood volume</td>
<td>Relaxation of the mesangial cells increasing filtration surface</td>
<td>Increases GFR</td>
</tr>
<tr>
<td>Antidiuretic hormone ADH</td>
<td>Increased Angiotensin II or decreased vol./ osmolality of extracellular fluid</td>
<td>Stimulate insertion of aquaporin-2 (water channels) in apical membrane or principal cells</td>
<td>Increases blood volume to return GFR to normal</td>
</tr>
<tr>
<td>Aldosterone</td>
<td>Secreted from adrenal cortex because of increased Angiotensin II levels</td>
<td>Increases reabsorption of Na+ and water by principal cells of the DCT collecting duct</td>
<td>Increases blood volume to return GFR to normal</td>
</tr>
</tbody>
</table>
**Angiotensin II Pathway**

1. Renin is released to the blood by JGA cells due to decreased renal blood flow or perfusion.
2. Renin converts a plasma protein (angiotensinogen) into angiotensin I.
3. Angiotensin-Converting Enzyme (ACE) in the lungs converts Angiotensin I into Angiotensin II.

**Renin – Angiotensin – Aldosterone System**

\[ \text{Renin} \rightarrow \text{Angiotensin I} \rightarrow \text{Angiotensin II} \rightarrow \text{Aldosterone} \]

**Urine Concentration via Countercurrent Multiplication**

- Thin descending limb of Henle is permeable to water but not solutes.
- Thick ascending limb of Henle is impermeable to water and solutes. Contains active transport mechanisms for sodium and chloride.

- Sodium and Chloride are reabsorbed by thick ascending limb into the peritubular fluid.
- These ions elevate the medullary osmotic pressure.
- This increases osmotic flow of water out of the thin descending limb.
- Increased osmotic potential of tubular filtrate increases active transport in the TAL.
**Roles of the Different Nephron Regions in Urine Formation**

**Proximal Convoluted Tubule**
- **Reabsorption:**
  - 60%-70% of water (108 to 116 L/D)
  - 100% of glucose and other sugars, amino acids, and some vitamins
  - 60%-70% sodium and chloride, along with calcium, magnesium, phosphate, and bicarbonate
- **Secretion:**
  - Hydrogen ions, ammonium ions, creatinine, drugs, toxins

**Loop of Henle**
- **Reabsorption:**
  - Descending limb: 25% of the water (obligatory water reabsorption)
  - Thick Ascending limb: 20-25% of the sodium and chloride to help maintain the countercurrent system

**Distal Convoluted Tubule**
- **Reabsorption:**
  - Up to 5% of water under ADH control (principle cells)
  - Variable amounts of sodium and chloride under Aldosterone control (principle cells)
  - Variable amounts of Calcium
- **Secretion:**
  - Hydrogen ions, ammonium ions, creatinine, drugs, toxins

**Collecting Duct**
- **Reabsorption:**
  - Variable amounts of water under ADH control (principle cells)
  - Variable amounts of sodium and chloride under Aldosterone control (principle cells)
  - Variable amounts of bicarbonate (intercalated cells)
- **Secretion:**
  - Potassium and hydrogen ions

**Summary of the Roles of the Different Nephron Regions in Urine Formation**
**NEPHRON HEMODYNAMICS**

- **Series Hemodynamics and Parallel Hemodynamics**
  - The individual nephrons that make up both kidneys are connected in parallel.
  - However, the flow through a single nephron represents two arterioles and two capillary beds connected in series.

**HEMODYNAMICS OF A SINGLE NEPHRON**

- Connected in series are the high-pressure filtering capillaries of the glomerulus and the low-pressure reabsorbing peritubular capillaries.

**ATERIALS FILTERED**

- **Freely Filtered**
  - Major electrolytes
  - Sodium
  - Chloride
  - Potassium
  - Bicarbonate
  - Metabolic waste products
  - Urea
  - Creatinine
  - Metabolites
    - Glucose
    - Amino acids
    - Organic acids (ketone bodies)
  - Nonnatural substance
    - Inulin
    - PAM (p-aminohippuric acid)
  - Lower-weight proteins and peptides
    - Insulin
    - Myoglobin

- **Not Freely Filtered**
  - Albumin and other plasma proteins
  - Lipid-soluble substances transported in the plasma attached to proteins
  - Lipid-soluble bilirubin
  - T4 (thyroxine)
  - Other lipid-soluble hormones
Negative Charge on the Filtering Membrane
- There is a negative charge on the filtering membrane that inhibits the filtering of protein anions. If this negative charge is not present, significant protein filtration takes place. This simply points out that the glomerular capillaries are very permeable.

Fluid Entering Bowman's Capsule
- The fluid entering Bowman's capsule is an ultrafiltrate of plasma, that is, the filtrate has the same concentration of dissolved substances as plasma, except proteins.
- The osmolarity of the filtrate is 300 mOsm/L. The criteria for effective osmolarity are the same as those previously stated for extracellular fluid.
- If a substance is freely filtered by the kidney, the ratio of the filtrate concentration/plasma concentration = 1.0. This means the concentrations in Bowman's capsule and the plasma will be the same.

Factors Affecting GFR and Filtration Fraction (FF)
- FF = fraction of the material that enters the kidney that is filtered
  - For a freely filtered substance, it is 20%
  - GFR/RPF = 120/600 = 0.2 = 20%

Determinants of GFR
- Except for an unusual situation when plasma protein concentration changes dramatically or renal obstruction develops, the main factor determining GFR is glomerular capillary pressure.
- An increase in capillary pressure increases GFR, and a decrease in capillary pressure decreases GFR.
- Flow does have a small effect on GFR; an increase in flow will independently increase GFR.
- Factors affecting FF
  - In many circumstances, the main factor affecting FF is renal plasma flow. The longer the fluid remains in the glomerular capillaries, the greater the percentage of the fluid that tends to be filtered.
  - Therefore, as flow decreases, FF will always have a tendency to increase.

Filtered Load
- Filtered load is the rate at which a substance filters into Bowman's capsule.
  - Units are an amount per unit time, e.g., mg/min.
  - Filtered load = GFR \times P_x
    - GFR = glomerular filtration rate
      - units = volume/time, e.g., ml/min, L/day
    - P_x = concentration of the substance in the plasma
      - units = amount/volume, e.g., mg/ml

Tubular Reabsorption
- Active Mechanisms
  - There are two types of active reabsorption based on system dynamics: Tm and gradient-time.

Transport Maximum (TM) Systems
- For example, proximal tubular reabsorption of glucose.
- General Characteristics of TM Systems
  - Carriers are easily saturated.
  - Carriers have a high affinity for the substrate.
  - Low back leak.
  - Back leak refers to the back diffusion of the substance into the tubule after it is reabsorbed into the interstitium. Minimal back leak of glucose occurs because the proximal tubule is not permeable to glucose.
  - The entire filtered load is reabsorbed until the carriers are saturated; then the excess is excreted.
Substances Reabsorbed by Tm System
- Almost all natural organic and some inorganic substances that are reabsorbed by the nephron are reabsorbed by a Tm system.
- These substances include:
  - Glucose
  - Amino acids
  - Small peptides and proteins
  - Ketone bodies
  - Calcium
  - Phosphate.
- An exception with respect to natural organic substances is urea. Urea is freely filtered and partially reabsorbed, mainly by passive mechanisms.

Gradient-Time System
- For example, the proximal tubular reabsorption of sodium
- General Characteristics
  - Carriers appear to be never saturated.
  - Carriers have a low affinity for the substrate.
  - High back leak.
- High back leak means that some of the sodium that is actively reabsorbed back diffuses into the proximal tubule. The proximal tubule has leaky tight junctions to sodium and also to a few other substances, such as potassium, chloride, and water.

Approximately a constant percentage of the filtered sodium is reabsorbed in the proximal tubule.
- Under normal conditions it is close to 66%, which means about two-thirds of the filtered sodium is reabsorbed in the proximal tubule.
- Also, the active reabsorption of sodium by the proximal tubule is the main metabolic process going on in the kidney. Thus, oxygen consumption of the kidney is directly proportional to sodium reabsorption and GFR.

Tubular Secretion
- Transport Maximum System
  - p-Amino hippuric Acid(PAH) Secretion
    - PAH secretion from the peritubular capillaries into the proximal tubule is an example of a transport maximum system. It has the general characteristics discussed for the reabsorption of glucose except for the direction of transport.
    - At low plasma levels, 20% of the PAH entering the kidney is filtered, and 80% is actively secreted.

Net Reabsorption
- Filtration > Excretion

Net Secretion
- Filtration < Excretion
CLEARANCE
- Definition: theoretical volume of plasma from which a substance is removed over a period of time.
- Give some examples!!
  - Clearance of substance x = excretion rate/ plasma conc.
  - Excretion rate= urine concentration * urine flow rate
- CLEARANCE OF INULIN AS AN INDEX OF GFR AND RENAL FUNCTION
  - The concentration of inulin in the nephron tubule is an index of water reabsorption.
  - The segment of the nephron with the highest concentration of inulin is the terminal collecting duct.
  - The segment of the nephron with the lowest concentration of inulin is Bowman’s capsule.

RENAL PLASMA FLOW (RPF)
- The clearance of PAH is generally regarded as the standard estimate of the RPF.
- Renal Blood Flow:
  - Renal Plasma Flow/ (1 – hematocrit)
- Concept of Free water Clearance

LOOP OF HENLE

DISTAL TUBULE AND COLLECTING DUCTS