Biochemistry of kidney tissue:

- Biochemical functions
- Metabolism
- The investigation of the urine from healthy and diseased person

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The kidney is involved in:

- the maintenance of acid-base balance and of osmotic pressure of fluid media of human organism
- the regulation of water and salt balance
- the removal of terminal products of metabolic processes
- the blood pressure control
- the stimulation of erythropoiesis
Fig. 1 Diagrammatic representation of a nephron.
Processes associated with nephron function:

1. Ultrafiltration of blood at the glomerulus
2. Tubular reabsorption
3. Tubular secretion

Primary urine (~170L/day)

Tubular reabsorption

Tubular secretion

Final urine (~2L/day)
Proximal Renal Tubule Endothelial cell
Metabolic pathways in renal tubule cells:

- Aerobic oxidation of monosacharides
- Gluconeogenesis
- Hexose Monophosphate Shunt
- Replication; Transcription; Translation
- Fatty acids oxidation
- Ketone bodies utilization
- Transport systems function in cellular membrane (reabsorption)
- Antioxidant enzyme systems function
Proximal part of nephron

- Passive reabsorption of water, because

Interstitial osmolality:

Primary urine osmolality

= 1400:290
Reabsorption of Bicarbonate by Renal Tubular Cells

- $\text{Na}^+$
- $\text{HCO}_3^-$
- $\text{Na}^+$
- $\text{HCO}_3^- + H^+$
- $\text{H}_2\text{CO}_3$
- Carbonic anhydrase
- $\text{H}_2\text{O} + \text{CO}_2$
- $\text{H}^+ + \text{HCO}_3^-$
- $\text{H}_2\text{CO}_3$
- $\text{CO}_2 + \text{H}_2\text{O}$

Blood | Renal Tubular Cell | Tubular Lumen
Phosphate Buffering in the Renal Tubule

\[ \text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3 \rightarrow \text{HCO}_3^- + \text{H}^+ \]

\[ \text{H}^+ + \text{HPO}_4^{2-} \rightarrow \text{H}_2\text{PO}_4^- \]

\[ \text{Na}^+ \leftarrow \text{ATPase} \rightarrow \text{K}^+ \]

Blood \hspace{1cm} Renal Tubular Cell \hspace{1cm} Tubular Lumen
Ammonia Buffering in the Renal Tubule

- Glutamine
  - Glutaminase
  - Glutamate + NH₃
  - Glutamate
    - ATPase
    - Na⁺ (Blood)
    - K⁺ (Blood)

- NH₃
  - NH₄⁺ (Tubular Lumen)
  - Na⁺ (Blood)
  - K⁺ (Blood)

- H⁺
  - H⁺ + NH₃
  - NH₄⁺ (Tubular Lumen)
  - Na⁺ (Blood)

Blood
Renal Tubular Cell
Tubular Lumen
The function of kidney in maintenance of acid-base balance in organism

Glutamine $\xrightarrow{\text{H}_2\text{O}}$ Glutamic acid + NH$_3$

Glutaminase

Glutamate $\xrightarrow{\text{NAD}^+} \text{NADH}+\text{H}^+$

Glutamate dehydrogenase

Alpha-ketoglutarate + NH$_3$

H$^+$ + NH$_3$ $\rightarrow$ NH$_4^+$
Impaired H+ excretion

Increased H+ production or ingestion

Loss of HCO₃⁻

Loss of H+ in vomit

Alkali ingestion

Potassium deficiency

Acidosis stimulates NH₄⁺ production

Alkalosis stimulates urea production
The role of kidney in hormonal regulation
A control of water reabsorption in renal tubules

Blood plasma

\[
\text{H}_2\text{O} \quad \text{ANP} \quad \text{Aldosterone} \quad 3\text{Na}^+ \quad 2\text{K}^+ \quad 2 \text{Cl}^{-}
\]

In proximal part and Henle's loop

\[
\text{Vasopressin (adiuretin)} \quad \text{Water follows osmotic gradient}
\]

In distal part

\[
2 - \text{Na}^+, \text{K}^+ - \text{ATPase}
\]

Urine
A control of calcium and phosphate ions reabsorption in renal tubules.
The clearance is in use to estimate glomerular filtration rate (GFR). It is the ratio of urine concentration of a given substance to blood serum concentration of one per minute diuresis.

\[ C_{Cr} = \frac{U_{Cr} \times V}{S_{Cr}} \text{ ml/min} \]

- \( U_{Cr} \) - concentration of Creatinine (or Inulin) in the urine;
- \( S_{Cr} \) - concentration of Creatinine (or Inulin) in the blood serum;
- \( V \) - minute diuresis.
The calculation of clearance ($C$), using average values for:

<table>
<thead>
<tr>
<th></th>
<th>Inulin</th>
<th>Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>$S_{In}$</td>
<td>$1 \text{ mg/mL}$</td>
<td>$S_{Cr}=0.01 \text{ mg/ml}$</td>
</tr>
<tr>
<td>$U_{In}$</td>
<td>$150 \text{ mg/mL}$</td>
<td>$U_{Cr}=1.25 \text{ mg/mL}$</td>
</tr>
<tr>
<td>$C_{In}$</td>
<td>$150 \text{ ml/min}$</td>
<td>$C_{Cr}=125 \text{ mL/min}$</td>
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Cystatin C

It is a low molecular weight protein (13.36 KD) and produced by all nucleated cells in a stable production rate. Cystatin C is freely filtered by the glomerulus and metabolized after tubular reabsorption.

• The normal level of cystatin C in blood plasma at the age of 14 to 50 years is 0,63-1,33 mg / L, at the age of over 50 years - 0,74-1,55 mg / L.

• The level of protein in the blood does not depend on body weight and growth, on muscle mass and sex. An increase in the level of cystatin C is an unfavorable sign, indicating a violation of the filtration function of kidneys.
Main indexes of urine for diagnostics of kidney function

- Urea
- Creatinine
- Sodium and Potassium
- Proteins
The fractional excretion of filtered sodium, approximated by:

\[
FE_{Na} = \frac{(\text{Urine Sodium}) \times (\text{Serum Creatinine})}{(\text{Serum Sodium}) \times (\text{Urine Creatinine})}
\]

- Values less than 1% indicate pre-renal azotemia;
- Values over 2% indicate acute tubular necrosis.
The real concentration of urea is $\text{BUN} \times (60/28)$, or $\text{BUN} \times 2.14$. 8-25 mg/dL (2.9-8.9 mmol/L)

[Blood Urea Nitrogen]$_{\text{plasma}}$ ↑↑ - AZOTEMIA:

**RENAL**: acute tubular necrosis, chronic interstitial nephritis, some glomerulonephritis

**PRE-RENAL**: glomerulonephritis is likely also to be "pre-renal" if mild, since it comprises renal blood flow more than tubular function

**POST-RENAL**: results from obstruction of urinary flow: prostate trouble, stones, surgical mishaps, tumors
### Suppressed function of renal tubules under the normal function of glomerulus (Clearance is normal)

**In the blood plasma:**
- Urea~ N
- Creatinine~ N
- $[\text{HCO}_3^-]$ ↓
- $[\text{K}^+]$ ↓
- $[\text{Phosphates}]$ ↓
- $[\text{Urates}]$ ↓
- pH ↓

**In the urine:**
- Urea<<N
- May be not changed
- $[\text{HCO}_3^-]$ ↑ or N
- $[\text{Na}^+]$ ↑
- Diuresis ↑, osmolality↓
- $[\text{Urates}]$ ↑ or N
- $[\text{H}^+]$ ↓, pH↑
Neutrophil gelatinase-associated lipocalin (NGAL) in human urine and blood

- The amount of NGAL in blood or urine is measured using a particle-enhanced turbidimetry laboratory technique.
- An accumulation of NGAL in blood plasma, and urine could indicate acute kidney injury.
- Increased concentrations of NGAL can present earlier (in 24-48 hours) than other biomarkers used to detect acute kidney injury. Low (normal) levels for NGAL have been considered to be 20 ng/mL, and high levels 1200 ng/mL (at kidney injury).
Proteins used for estimation of kidney function

• Glycine amidinotransferase (serum)
• N-acetyl-beta-D-glucosaminidase (serum, urine)
• Adenosine Deaminase Binding Protein (urine)
• Urinary alkaline phosphatase
• Alanine aminopeptidase isozyme 3 (serum)
• Lactate dehydrogenase isozymes (serum):
  • LDH1 and LDH2 isozymes (renal cortex)
  • LDH4 and LDH5 isozymes (renal medulla)
• Beta-2-microglobulin
The physicochemical properties of the urine of humans

1. Diuresis (D, urine output):
   men – 1500 ml/day; women – 1200 ml/day

   Polyuria  Oligouria  Anuria
   D> 3000 ml/day  D<1200 ml/day  D~0

2. The pH of urine
   Normal average value: 5.3-6.5
   For vegetarians: >6.5
   After animal food intake: ~5.0
   The higher the pH of urine the lower the acidity of urine.
   pH < 4.5 at ketoacidosis, aminoaciduria states.
   pH > 7.0 at chronic cystitis and pyelitis.
3. The specific gravity of the urine

The normal value: 1.012 – 1.020 g/ml

In patients with:

1) **diabetes insipidus** - about 1.001-1.004 g/ml

2) **diabetes mellitus** - higher than 1.02 g/ml

4. The color of the urine

The urine of healthy humans is transparent, straw-yellow or amber liquid.

But at some pathological states may be:

- dark;
- dark brown (like beer);
- green or blue;
- black;
- with red shade;
- muddy (sediment is present).
5. Special odor of the urine

The urine odor is associated usually with the presence of ammonia salts and urea in it.

But at pathological states:

- Maple syrup urine disease (like maple syrup odor);
- Phenylketonuria (like mouse odor);
- Intensive putrefaction of proteins in the intestine; at the appearance of excretes from vagina of diseased women at pathologies such syphilis or gonorrhea (the smell of rotten meat);
- Glucosuria state at diabetes mellitus (special fruity odor)
The pathological components of the urine

- **Proteins** in the urine (higher than 150 mg/daily) → Proteinuria may be in association with:
  1) hemoglobinuria; 2) hematuria

- **Ketone bodies** in the urine → Ketonuria state

- **Glucose** in the urine → Glucosuria state

- **Bile pigments**: urobilin and conjugated bilirubin

- **Creatine** → Creatinuria state
Thanks for your attention!