RENAL PHYSIOLOGY,
HOMEOSTASIS OF FLUID COMPARTMENTS (2)

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TUBULAR FUNCTIONS
(Learning objectives 54-57)
**Tubular Transport**

About 99% of filtrated water and more than 90% of the filtrated substances will be resorbed. Additionally some substances will be secreted.
Epithelial transport (Learning objective 54)

**STRUCTURAL POLARITY**

- **non-polar cells**
- **polar cells**

epithelial cells
1. adhere tightly together
2. separate compartments

- tubules (kidney),
- sacs (gallbladder),
- canaliculi (liver).

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<table>
<thead>
<tr>
<th>Substanz</th>
<th>Resorption bzw. Sekretion in Anschnitt</th>
<th>D7+SR</th>
<th>Urin</th>
<th>beteiligte Transportmechanismen</th>
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<tbody>
<tr>
<td>Wasser</td>
<td>60</td>
<td>20</td>
<td>19</td>
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<tr>
<td>Kreatinin</td>
<td>0</td>
<td>0</td>
<td>100</td>
<td>osmotischem Gradient folgend (Diffusion)</td>
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<tr>
<td>Natrium</td>
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<td>30</td>
<td>10</td>
<td>kein nennenswerten Transport</td>
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<td>Chloride</td>
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<td>35</td>
<td>9</td>
<td>Diffusion, sobald drg, aktiv</td>
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<td>90</td>
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<td>10</td>
<td>aktiv, Diffusion, sobald drg</td>
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<tr>
<td>HCO₃⁻</td>
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<td>10</td>
<td>aktiv, Diffusion, sobald drg</td>
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<td>Kalzium</td>
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<td>20</td>
<td>9</td>
<td>aktiv, Diffusion</td>
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<td>Phosphat</td>
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<td>0</td>
<td>aktiv, Diffusion</td>
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<tr>
<td>Glukose</td>
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<td>1</td>
<td>0</td>
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<tr>
<td>Glycin, Hystidin</td>
<td>99</td>
<td>6</td>
<td>0</td>
<td>aktiv, Diffusion</td>
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<td>Other amino acids</td>
<td>50</td>
<td>-60</td>
<td>60</td>
<td>aktiv, Diffusion</td>
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<tr>
<td>Urea</td>
<td>60</td>
<td>30</td>
<td>0</td>
<td>aktiv, Diffusion</td>
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<tr>
<td>Oxalate</td>
<td>-30</td>
<td>-10</td>
<td>10</td>
<td>aktiv, Diffusion</td>
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</tbody>
</table>
FUNCTIONAL POLARITY

*Epithelia can transport solutes and water in two directions:*

**Absorption** is the transport from some lumenal compartment back into blood. The fluid transported is either isotonic, or hypertonic to plasma.

**Secretion** is transport from blood into a given lumenal compartment. The fluid can be either isotonic or hypotonic.
Highly Water Permeable Epithelia:
(e.g. proximal tubule)
Iso-osmotic Absorption.
Epithelia that transport large amounts of solute and water have long and highly enfolded lateral intercellular spaces. The apical surface area is usually enhanced by long and numerous microvilli called the brush border. It reduces the amount of fluid in one compartment and add fluid to another compartment without changing the ionic composition of either compartment.

Water Impermeable Epithelia.
These epithelia have low water permeability of their apical surfaces. They transport a solution that is strongly hypertonic.
Hyper-osmotic Absorption
In these epithelia salts are absorbed but not water. The net effect is that salt is removed from the luminal compartment into the interstitial fluid without changing the amount of fluid in each compartment. Examples of this kind of epithelium are the thick ascending limb of the loop of Henle and the distal nephron.
*In some epithelia water permeability is regulated.*
Transepithelial transport (Polarized cell)

Transepithelial transport

Reabsorbed = Filtered = Excreted
Transcellular and paracellular ways of transepithelial transport

Transepithelial transport can be found in kidney, gastrointestinal tract, exocrine glands, choroid plexus.

“Solvent drag” mechanism
Direction of transport

Uniport

Cotransporter (symport)

Exchanger (antiport)

Passive transport

\[ \frac{dm}{dt} = -D \frac{A}{d} (c_1 - c_2) = -D \frac{A}{d} \Delta c_i \]
Facilitated diffusion

Primary active transport (ion pumps)

Na\(^+\)-K\(^+\) pump (Na\(^+\)-K\(^+\)ATPase)
Ca\(^{2+}\) pump (Ca\(^{2+}\) ATPase)
H\(^+\)-K\(^+\) pump (H\(^+\)-K\(^+\) ATPase)
H\(^+\) pump (H\(^+\) ATPase)
Secondary and tertiary active transport

Characterization of tubular functions
(Learning objective 55)

**Clearance-principle**

*Clearance* is the amount of plasma that is cleared of a substance during one minute (or one sec).

It is a virtual plasma volume characteristic to a substance in question.

\[
C = \frac{U \times V}{P}
\]
**Significance of Clearance:**

Characterization of kidney function.
Estimation of characteristic parameters of the kidney.
Characterization of the fate of particular substances in the kidney.

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

For example:
The creatininconcentration in the plasma is (P) 0.1 mmol/l, in the urin (U) 5 mmol/l, minutediuresis (Vu) 2 ml/min. \[ C = GFR = \frac{U \times V_u}{P} = 100 \text{ ml/min}. \]

\[ C = 0 - 600 \text{ ml/min} \]

0<C<GFR filtrated and partially reabsorbed
GFR<C<RPF filtrated and partially secreted

**Clearance**
Paraaminohippuricacid clearance (PAH)

PAH filtrated free and will be totally secreted in the tubulussystem. The whole amount will be extracted by the kidney. Thus the PAH-Clearance equal to the renal plasma flow (RPF). PAH-Clearance is 600 ml/min, thus the RPF is also **660 ml/min**.

In the knowledge of RPF and the hematokrit we could calculate the renal blood flow (RBF)

\[ \text{RBF} = \text{RPF} / (1 - \text{Hematokrit}) \]

Thus the **RBF** is about **1320 ml/min**.

Osmotic Clearance

The amount of plasma that will be cleaned by the kidney of the osmotic active substances in a minute.

\[ C_{\text{osm}} = V_u \times U_{\text{osm}} / P_{\text{osm}} \]

Free water-Clearance

After the subtraction of the osmotic clearance from the whole amount of urine we get the free water-clearence

\[ C_{\text{H2O}} = V_u (1 - U_{\text{osm}} / P_{\text{osm}}) \]

Osmotic diuresis
<table>
<thead>
<tr>
<th>Glomerular filtrate</th>
<th>Urine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume 180 l/day</td>
<td>1.5 l/day</td>
</tr>
<tr>
<td>Glucose 16 g/day</td>
<td>Ø</td>
</tr>
<tr>
<td>Protein 20 g/day</td>
<td>Ø</td>
</tr>
<tr>
<td>Sodium 700 g/day</td>
<td>5-15 g/day</td>
</tr>
<tr>
<td>Cells Ø</td>
<td>Ø</td>
</tr>
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</table>

**PROXIMAL TUBULE**

(Learning objective 56-57)

**Histology**

- cuboid cells, microvilli
- (brush-border), interdigitation,
- many mitochondria

The epithelium of the proximal tubule is maximally permeable to water.

Water reabsorption: transcellular and paracellular route
Reabsorption in the proximal tubule

1. 70% of Na\(^+\) and water in the glomerular filtrate
2. All filtrated glucose and amino acid
3. All filtrated protein
4. Filtrated K\(^+\) in the 1\(^{st}\) and 2\(^{nd}\) segments
5. Ca\(^{++}\), Mg\(^{++}\) and phosphate ions.
6. lactate, citrate, other components of the Krebs cycle.
7. Water soluble vitamins
8. Uric acid
9. Urea
Secretion in the proximal tubule

Organic acids and bases

K⁺ in the 3rd segment.

H⁺ ion.
Carrier mechanisms

1. Na⁺/solute symport,
2. Na⁺/H⁺ exchange (HCO₃⁻),
3. Cl⁻ driven Na⁺ transport

ad 1. Na⁺/solute symport

Site: 1. segment.

The entry of Na⁺ in the cell is a carrier-mediated process and is driven by an electrochemical gradient. Cl⁻ follows the movement of Na⁺ because of the electrochemical gradient and water enters because of the osmotic gradient.

We assume that “leaky tight junctions” are in the proximal tubules.
ad 2. Na⁺/H⁺ antiport mechanism

The Na⁺/K⁺ ATP driven Na⁺ ion is accompanied by the secretion of a H⁺ ion.

There is Cl⁻ and HCO₃⁻ reabsorption, too.

HCO₃⁻ is provided by the carbonic acid.

Cl⁻ is reabsorbed if the H⁺ in the antiport mechanism originates from formic acid. The formic acid is produced in the metabolism and dissociates to H⁺ and formiat anion in the proximal tubular cells.

\[ \text{HCOOH} \Leftrightarrow \text{H}^+ + \text{HCOO}^- \]

The H⁺ ion is secreted, the formiat is exchanged for one tubular Cl⁻ that diffuses into the peritubular space.
Na/H antiport system

PROXIMAL TUBULE

TUBULAR LUMEN

PERITUBULAR SPACE

HCO₃⁻ \rightarrow \text{Na}^+ \rightarrow \text{H}^+ \rightarrow \text{H}⁺, \text{CO}_2 \rightarrow \text{HCO}_3⁻ \rightarrow \text{Na}⁺

\text{HCO}_3⁻ \rightarrow \text{Na}⁺ \rightarrow \text{H}⁺, \text{CO}_2 \rightarrow \text{HCO}_3⁻ \rightarrow \text{Na}⁺

("reasorbed" HCO₃⁻)

PASSIVE MOVEMENT

Cl⁻ resorption in proximal tubule

pH = 6.5

Cl⁻, H⁺

HCOOH

pH = 7.2

HCOO⁻, Cl⁻

NHE3, Na⁺, K⁺

Cl⁻ channel

paracellular

Cl⁻

\text{K}⁺
ad 3. A Cl⁻ driven Na⁺ transport

While HCO₃⁻ and Cl⁻ concentrations in the glomerular filtrate equals that of the plasma, mechanism 1 and 2 reduce HCO₃⁻ concentration in a larger extent than Cl⁻ concentration. This yields a Cl⁻ concentration gradient in the 2. and 3. segments. Because of this gradient, Cl⁻ diffuses into the peritubular space. This leads to a transepithelial potential difference (lumen positive). The positive charge of the lumen causes a passive transport of Na⁺ towards the peritubular fluid.
Water reabsorption (passive)

transcellular,
paracellular,
"solvent drag" mechanism.

Glucose-type reabsorption

Glucose
Filtrates entirely in the glomerulus,
Reabsorbed entirely in the proximal tubulus
carrier mediated transport.

$T_m\text{glucose}$
Glucosuria (pathological conditions) :

*diabetes mellitus, renal glucosuria*
A glucose-type reabsorption occurs:
phosphates (hormone sensitive reabsorption),
amino acids, small peptides,
citrate
uric acid (gout).
water soluble vitamins
Reabsorption of amino acids

Reabsorption of phosphate

Klinke, Pape, Silbernagl: Physiologie, 5. Auflage 2005