Lecture-3
water, sodium and potassium homeostasis

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Water & sodium balance

- Internal and external balance
- Internal balance is the distribution between different body compartment
- External balance match input and output

Total body water (TBW) /70 kg adult

- \(42\text{ liter} = 60\%\) of body mass
- distributed in two compartments
  - \(2/3 (66\%) = 28\text{L}\) in the intracellular fluid compartment (ICF)
  - \(1/3 (33\%) = 14\text{L}\) in the extracellular fluid compartment (ECF)

Total body water (TBW) - distributed in two compartments. (conti)

- ECF
  - \(75\% (11\text{L})\) of ECF is interstitial fluid (ISF)
  - \(25\% (3\text{L})\) of ECF is intravascular (IVF) (plasma)
  - CSF is about 150 ml
Water is passively transported in the body, freely permeable through cell membranes (ICF and ECF).

Sodium is the major extracellular cation (95%)

- Total body sodium /70 kg adult 4200 mmol
  - 50% in ECF
  - 40% in bones
  - 10% ICF

The capillary endothelial is freely permeable to sodium

$[\text{Na}^+]$ of the ISF is equal to that of plasma

The capillary endothelial is only slightly permeable to plasma proteins

$[\text{protein}]$ of the ISF is $<<$ that of plasma
The capillary endothelial is only slightly permeable to plasma proteins. [protein] of the ISF is << that of plasma.

**Movement of Body Fluids**

- Water distribution between compartments is determined by:
  1. Osmolality - controls water distribution between ICF and ECF
  2. Colloid osmotic pressure - controls water distribution between IVF and ISF

**Osmolality**

- Osmolality is the number of dissolved particles (molecules and ions) per kg of solution
- Affect movement of water across cell membrane

**Diffusion** = net movement of particles (solute) down concentration gradient to establish equilibrium between two sides of membrane

**Osmosis** = diffusion of water from high concentration to low concentration
How can we calculate osmolality?

- Osm is equal to the sum of all molecules and ions cross cell membrane/unit wt

- The major contributor to ECF osmolality is Na, and other such as glc, urea and K:

  \[ \text{Osm} = 2[Na^+] + 2[K^+] + [\text{glc}] + [\text{urea}] \]

  \[ = 2 \times 135 + 2 \times 4 + 5 + 5 \]

  \[ = 282-295 \text{ mmol/kg} \]

Osmal gap

- plasma protein or lipids

Tonicity

- # of solute particles in solution which can effect osmotic pressure (e.g. Na+),

- which means solutes which are not freely permeable though cell membrane, causes movement of water into and out of the cells

- Tonicity is not the same as Osmolality but often used interchangeably

- substances such as alcohol and urea does not contributes to tonicity since they are readily diffusible down concentration gradient and reach equilibrium

- Hypertonic -- high amount of solute

- Hypotonic = dilute

Colloid osmotic pressure exerted by plasma proteins across cell membrane
at arterial end of capillary, $CHP > COP$, so fluid moves out of the capillary.

at venous end of capillary, $COP > CHP$, so fluid moves from around cells; containing wastes and CO2 moves into capillary.

Regulation of external water balance:

- Water intake is variable, and largely depends on social habits.

- **Water intake = water output**

Average daily water output and intake:

- Minimum daily intake need for maintenance of water balance is **1100ml**

<table>
<thead>
<tr>
<th>Obligatory losses</th>
<th>Sources</th>
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<tbody>
<tr>
<td>Skin 500</td>
<td>-diet and drunk 1100</td>
</tr>
<tr>
<td>Lungs 400</td>
<td>-oxidative</td>
</tr>
<tr>
<td>Gut 100</td>
<td>metabolism 400</td>
</tr>
<tr>
<td>Kidneys 500</td>
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</tbody>
</table>

**1500 ml**
Water intake is controlled by Sensation of thirst and output by anti-diuretic hormone (ADH)

Regulation of external water balance-cont

- Change body water change Osmolality (282-295)

- Loss of water from ECF increases Osmolality. This will cause
  - Movement of water from ICF → ECF
  - Stimulates hypothalamus thirst center which promotes the desire of drink
  - Stimulates ADH secretion

 Regulators of Vasopressin release

1. Osmotic control
   hypothalamic Osmoreceptor sensitive for small changes in osmolality as small as 1%
Regulators of Vasopressin release conti.

- Above a 282 mosmol/l the concentration of ADH increases.
- Below 282 mosmol/l ADH is undetectable in plasma.

2. Baroreceptor
Decreased blood volume/pressure stimulates the release of ADH.

Baroreceptor is less sensitive than the osmoreceptors; detect a 8–10% change in volume or pressure.

Factors affecting ADH secretion

<table>
<thead>
<tr>
<th>Stimulated by:</th>
<th>Inhibited by:</th>
</tr>
</thead>
<tbody>
<tr>
<td>High osmolality</td>
<td>Low ECF</td>
</tr>
<tr>
<td>Low blood volume</td>
<td>Osmolality</td>
</tr>
<tr>
<td>Low blood pressure</td>
<td>Hi blood volume</td>
</tr>
<tr>
<td>Angiotensin II</td>
<td>Hi blood pressure</td>
</tr>
<tr>
<td>and volume receptor</td>
<td>Alcohol</td>
</tr>
<tr>
<td>stress including pain</td>
<td></td>
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</table>

Regulation of external sodium balance

Na input = Na output

- There is an obligatory loss for Na (10mmol/day)
  kidneys, (skin and GIT to less extent)
Sodium distribution (contd)

- There are massive internal turnover of Na:
  - GIT = 10mmole/day
  - kidney = 25000mmol/day

- In disease, GIT can be a major loss of Na+

Sodium and ECF volume

Serum normal range = 135-150 mmol/L

- Na is most important ion in regulating water balance

- [Na+] affects ECF osmolarity

- [Na+] affects blood pressure & ECF volume

Sodium balance is maintained by regulation of its renal excretion which affected by

1. The glomerular filtration rate (GFR)

- 70% of filtered Na+ is reabsorbed in the proximal tubules
- Less than 5% reach the distal tubules
1. Reduced GFR less Na\(^+\) is filtered and excreted and Vice versa

2. Renin Angiotensin system (II)

3. Atrial natriuretic peptide (ANP)
   - Works at kidney
Atrial natriuretic peptide (ANP)

- ANP is a 28 AA polypeptide secreted by right atrium in response to volume expansion, which causes stretching of the myocardium.

- ANP lowers blood volume and pressure—antagonize RAS.

- Two other structurally similar peptide has been identified (BNP) and (CNP).

Water Homeostasis
Two types of disorders:

- **Water depletion:**
  - Usually accompanied Na$^+$ depletion
    - Is due to decreased intake or increased loss --> Hyperosmolality

- **Water excess:**
  - Increased intake or decreased loss --> Hypoosmolality

Water and Na$^+$ depletion

- Losses are > than intake.

- Pure water depletion is less common (may occur in DI and from lung).

- Na$^+$ can’t excreted with out water.
**Water depletion (hypovolemia)**

**Clinical feature**
Fluid lost from blood vessels, leads to decreased ECF volume

**Signs**
- Decr’d urine output
- Weight loss (through fluid weight)
- Can leads to hypovolemic shock

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**Symptoms of hypovolemia**
- Thirst, dryness of the mouth
- Decr’d blood pressure
- Increased heart rate

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**Causes of water depletion**

**Decreased intake**
Infancy, old age, unconsciousness, dysphagia

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**Increased loss**
- From kidney
  - Diabetes insipidus
  - Increased osmotic load (DM)
  - Osmotic diuretics
- From skin
- From lungs
- From gut
  - Diarrhea – in infant
Which one is more dangerous, the losses of pure water of isotonic fluid?

Water excess (hypervolemia)
- Usually occur due to impaired water excretion
- Healthy Kidney can excrete 20ml/min
- Causes cerebral over-hydration
- Hyponatraemia is invariable present

Water excess (hypervolemia) conti
- Clinical feature
  - With incr’ed ECF volume
  - Weight gain (fluid weight)
  - Diluted urine
  - Increased blood pressure
  - Can also edema
  - Confusion and headache

Causes of water excess
- Increased intake
  - Compulsive water drinking
  - Excessive IV fluids
Causes of water excess

- Decreased excretion
  - Renal failure
  - Inappropriate or ectopic secretion of vasopressin (SIADH)
  - Some drugs (e.g. cortisol)

SIADH

= syndrome of inappropriate ADH secretion
- Prevents urinary excretion of water
- Results in a state of water excess:
  - Low plasma osmolality; low plasma Na+
  - High urine osmolality
  - No edema
  - Normal renal and adrenal function

Major Causes of SIADH

- Tumor - ectopic production of ADH
  - Carcinoma of the lung
  - Prostate & pancreas
- Inappropriate secretion
  - Pulmonary diseases
  - Pneumonia
  - Tuberculosis

Major Causes of SIADH- conti

- Pain e.g. postoperative
- Drugs - enhanced release of ADH or response to ADH. Cyclophosphamide, carbamazepine, Prozac, narcotics
Sodium excess

- Too much Na\(^+\) or too little water
- Can be due to increased intake or decreased excretion

Characteristics of excess sodium:

- Increases osmolality
  - movement of water from ICF to ECF
  - Cells dehydrate
  - Overall increased ECF volume (at expense of the cell volume)

Causes of sodium excess

**Increase intake**
- Administration of hypertonic IV solution

**Renal retention**
- decreased GFR
- Acute and chronic renal failure

Causes of sodium excess contd.

**primary mineral corticoid excess**
- Cushing syndrome
- Conn’s syndrome

**Secondary mineralcorticoids excess**
- CHF
- Nephrotic syndrome
- Sever liver disease i.e. cirrhosis
Causes of sodium excess conti.

Loss of excess of water
- skin
- Lung
- renal

Sodium excess and edema

**Causes of edema**
- Accumulation of isotonic fluid in interstitial space (increased ISF)
- Decreased colloid oncotic pressure - hypoproteinemia

Clinical feature
- Peripheral edema
- Lethargy
- Neurological dysfunction (dehydration of brain cells)
- Hypertension
- Weight gain

Sodium depletion

- Na+ can be lost from the body in either isotonic or hypotonic fluids.
- In each case there will be a decrease in ECF volume
The normal responses to hypovolemia are:
- Increases aldosterone secretion
- Low urine volume due to decreased GFR
- Increase ADH in case of severe hypovolemia

**Causes of sodium depletion**

**Excess loss**
- From kidney
  - Diuretic phase of acute renal failure
  - Diuretic therapy
  - Osmotic diuresis
  - Mineralcortical deficiency - Addison disease

**From gut**
- Vomiting
- Diarrhea

**From skin**
- Excessive sweating, burns

**Inadequate intake** - Rare

**Clinical features results from decreased ECF**

**Symptoms**
- Weakness, apathy, postal dizziness
- Sign
- Weight loss, tachycardia
- Hypotension
### Clinical and laboratory findings in sodium and water depletion

<table>
<thead>
<tr>
<th></th>
<th>Na depletion</th>
<th>H2O depletion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma Na</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>PCV</td>
<td>↑↑↑</td>
<td>N or S ↑</td>
</tr>
<tr>
<td>ECF volume</td>
<td>↓↓↓</td>
<td>N</td>
</tr>
<tr>
<td>Plasma urea</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Urine Conc.</td>
<td>↑</td>
<td>↑↑↑</td>
</tr>
</tbody>
</table>

#### Hypo and hypernatremia

- Hypo and hypernatremia define as 5mmole above are lower the healthy controls
- Hyponatremia frequently found in hospitalized patients due to **sick cell syndrome**

### Causes of Hyponatremia

**↑ Water and/or ↓ Sodium**

- Excess of water (dilutional)
- SADH
- Sick cell syndrome
- CHF

### Causes of Hyponatremia-conti

**↑ Water and/or ↓ Sodium**

- Loss of Na$^+$ from GIT  
  - vomiting diarrhea  
    (urine Na$^+$ < 20mmol/l)
- Loss of Na$^+$ from kidney  
  - Addison disease  
    (urine Na$^+$ > 20mmol/l)
Hypernatremia

- Sodium and/or Water

Hypernatremia is much less common than hyponatremia
- Loss of water > Na+
  - GIT - diarrhea,
  - Renal osmotic diuresis,
  - fever

Hypernatremia

- Sodium and/or Water

- Increased body Na+
  - steroid excess

Potassium balance

- Potassium is the major intracellular cation
- 2% in the ECF
- Gradient maintained by Na/K pump

Potassium – cont’d

- Serum K+ level maintained within a narrow limit
- Decreased K+
  - Increases cardiac muscle excitability—arrhythmia
  - Muscle weakness
  - Cardiac arrest occurs in both high and low K+
• External K⁺ balance controlled by kidney and to less extent by GIT.

99% of filtered K⁺ reabsorbed in the proximal tubules. obligatory losses is 10-20mmol/day

Factors effecting K⁺ excretion

1. amount of Na⁺ available for absorption
2. The relative availability of H⁺ and K⁺ ions in the distal cell

Factors effecting K⁺ excretion

3. aldosterone directly and indirectly stimulated K⁺ excretion

Internal distribution

Factors effecting K⁺ shifting from ICF to ECF

- insulin deficiency
- acidosis
- hyperosmolality
- cell death
Factors effecting K\(^+\) movement into cells

- after insulin therapy
- alkalosis

Hypokalemia

Serum K\(+\) < 3.5 mmol/L

- decreased K intake (rare)

- Tran-cellular K\(+\) shift
  - alkalosis
  - insulin therapy

Hypokalemia conti.

**renal**

Osmotic diuresis
diuretics
  - thiazides decreased Cl\(^-\) absorption
  - loop diuretics increase tubular flow, thus Na delivery to the distal

Mineralcorticoid excess
  - primary and secondary
cabenofoxalone, liquorice

RTA

Hypokalemia conti.

**GIT**

diarrhea
vomiting (K\(^+\) loss, alkalosis,↑RAS)
**Hyperkalemia**

Serum $K^+$ $> 6.5$ mmol/L

**Remember**: About 98% $K^+$ is intracellular leaving only 2% extracellular. Hence, a $K^+$ shift from the ICF to the ECF of only 2% can double the plasma [$K^+$].

Serum $K^+$ $> 6.5$ mmol/L required urgent treatm.

**Potassium Imbalances – Hyperkalemia**

- **Spurious or artifact**
  - hemolysis

- **Trans-cellular $K^+$ movement**
  - tissue damage
  - systemic acidosis
  - insulin deficiency

**Potassium Imbalances – Hyperkalemia conti.**

- **Decreased $K^+$ excretion**
  - acute renal failure
  - chronic renal failure (late)
  - $K^+$ sparing diuretics ACE inhibitors

- **Addison’s disease**

**Hyperkalemia conti.**

- Clinical feature
  - Muscle weakness, paralysis
  - Change in ECG pattern
Metabolic responses to trauma