Urine Osmolality and Electrolytes

Why do we do it?
What does it mean?
and What can go wrong?

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Outline

• Definitions
• Osmometry
• Applications
  – Polyuria
  – Hyponatraemia
  – Renal Failure
Definition

- **Concentration**
  - Number of moles per L of solution

- **Osmolarity**
  - Number of osmoles per L of solution

- **Osmolality**
  - Number of osmoles per kg solvent

- **Tonicity**
  - Non-penetrating osmoles

- **Plasma osmolarity** is 1-2% less than osmolality
Colligative properties

• Parameters proportional to # osmoles:
  – Depressing freezing point
  – Elevating boiling point
  – Increasing osmotic pressure
  – Lowering vapour pressure
## Osmolality Measurement

<table>
<thead>
<tr>
<th>FP↓</th>
<th>ΔT ≈ -1.86 C°/osm</th>
<th>Simple, common</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP↑</td>
<td>ΔT ≈ +0.52 C°/osm</td>
<td>Organic compounds unstable.</td>
</tr>
<tr>
<td>VP↓</td>
<td>ΔP ≈ -0.3 mmHg/osm</td>
<td>Volatile chemicals invalidate</td>
</tr>
<tr>
<td>OP↑</td>
<td>ΔΠ ≈ 17000 mmHg/osm</td>
<td>Technically hard</td>
</tr>
</tbody>
</table>
Why “≈” in those equations?

![Graph showing cryoscopic constant vs. molal concentration for sucrose, citric acid, and glycerin. The graph illustrates the deviation from ideality as concentration increases.](image-url)

Cryoscopic constant

Molal concentration (osm/kg)

Physical Pharmacy 1983 p. 159
Freezing point osmometry

- Super-cooled liquid
- Ice-liquid slurry
- Solid

Temperature (Temp)
- $0^\circ C$
- $T_{FP}$
- $-5.6^\circ C$

Time

Percussion
Freezing Point Analytical Interferents

• High viscosity
• Particles
Specimen
Dew Point

- equilibrium
- Cooling
- condensation
- No net condensation
- Return to equilibrium

Temp

$T_{equilib.}$

$T_{DP}$

Time
Methods

• Freezing point depression
  – Almost exclusive method now
  – Large coefficient so good CV’s
  – Simple, robust instruments

• Dew Point
  – Invalid for volatiles
Alternative Test

→ Refractometry correlates with osmolality
→ weaker correlation with dipstick SG and osmolality
Limitation: glucose and protein lessen relationship

Arch. Dis. Child 85: 155
Specimen

• No special preparation
  – Usually need serum/plasma results

• Random urine
  – Acute conditions/decisions
  – Simple to collect
  – Creatinine improves interpretation

• Timed urine
  – More reliable (Na excretion is variable)
Normal values

• No normal values for urine electrolytes & osmolality

• Range of physiologically expected results
  – U.osm 50-1200 mosm/kg
  – Range narrows as one ages

• “Expected” values depend on clinical picture
Urine Osmolality

• Typical values
  – 500-800 mosm/kg (24 hour)
  – 300-900 mosm/kg (random)
  – After 12 hours fasting >850 mosm/kg
  – A.m. specimen ≈3 times serum osmolality
Urine Osmolality

- **Increased**
  - Dehydration
  - SIADH
  - Adrenal insufficiency
  - Glycosuria
  - Hypernatraemia
  - High protein diet

- **Decreased**
  - Diabetes insipidus
  - Excess fluid intake
  - Renal insufficiency
  - glomerulonephritis
Urine Osmolality Cautions

- EtOH
- Extremes of protein in diet
- Diuretics
Other Specimens

• Pleural, ascitic
  – In equilibrium with serum
  – Thus, equal to serum
  – Rarely indicated
  – No special requirements for measurement
Faecal specimens

• Rare test for cause of diarrhoea
• $F_{\text{o sm}} - 2(F_{\text{Na}} + F_{\text{K}})$
  – $<50$: non-osmotic
  – $>150$: osmotic diarrhoea
    • Laxatives
    • Malabsorption (including lactose intolerance)
    • Sorbitol, mannitol, lactulose

• Limitation:
  – bacterial activity ↑’s gap
  – Only very watery specimens
Clinical Indications

- Polyuria
- Hyponatraemia
- Renal failure
- Low anion-gap metabolic acidosis
Polyuria
Case

- 65 year old
- c/o going to the w/c 4 or 5 times/night
- Constantly thirsty
- Drinks 4 or 5 L of ice cold water/day
- Urine output measured at 3.5 L/day
Normal Urine Output

- <50 mL/day: anuria
- <500 mL/day: oligouria
- >3L/day: polyuria

- Depends on individual
  - If hypernatramic or hypovolaemic
    >800 mL/d is polyuria
Water & Electrolyte Balance

- Na/K/Cl intake
- Protein intake

Water intake

- Na/K/Cl output
- Protein (urea) output

Water output

- ≈400 mosm/day
- ≈500 mosm/day

- ≈900 mosm/1.5 L
- ≈600 mosm/L
Water Balance

- Metabolism 10% 250mL
- Food 30% 750mL
- Beverages 60% 1500mL
- Faeces 4% 100 mL
- Sweat 8% 200 mL
- “Insensible” (skin + lungs) 28% 700 mL
- Urine 60% 1500 mL
Water Regulation

↑P.osm
↓saliva

Renin/angiotensin

↓BP

↓P.volume

Dry mouth

ADH (vasopressin)

↑P.osm

hypothalamus

pituitary

↓P.volume

↓saliva

↓BP
Assessing Intravascular Volume

• Clinical (sensitivity ~50%)
  – Orthostatic hypotension
  – Weak pulse
  – Cool extremeties
  – HR
  – Skin turgor
  – Mucous membranes
  – JVP

• Investigation
  – Urine Volume & Colour
  – Chest X-ray
  – Haemoconcentration
  – Creatinine, urea
  – Radioactive albumin dilution
  – BNP
Urine Concentration

\[
\begin{align*}
H_2O & \quad 300 \\
Na/Cl & \quad 600 \\
H_2O & \quad 400 \\
H_2O & \quad 1200
\end{align*}
\]

\[
\begin{align*}
H_2O & \quad 100 \\
Na/Cl & \quad 400 \\
H_2O & \quad 600 \\
H_2O & \quad 1200
\end{align*}
\]

\[
\begin{align*}
H_2O & \quad 400 \\
H_2O, & \quad 600 \\
urea & \quad 700
\end{align*}
\]
Polyuria Assessment

Polyuria

osmolality

flow

Osmole excretion
Polyuria

• <150 mosm/kg
  – Water diuresis
    • Diabetes Insipidus (P.Na high/normal)
    • Polydipsia (P.Na low/normal)

• >300 mosm/kg
  – Solute diuresis
Polyuria

- U.Osm
  - <150: "water" diuresis
  - >300: "osmole" diuresis

  - DI Polydipsia
    - "osmotic" diuresis
      - glucose
        - high DM Renal glucosuria
        - low Excess protein Excess catabolism Mannitol

  - Lytes 2(Na+K)
    - << U.osm
      - Diuretics Na/Cl load Renal disease Bicarbonaturia ketoacidosis
    - ≈ U.osm
      - Salt + water diuresis
Water Deprivation Test

- Preparation: Patient drinks until 6:00 am morning of test
- Weight, P.osm, P.Na, U.osm, U.Na
- Nothing to eat/drink during test
- Urine hourly
- Stop test if U.osm > 500, P.Na >145, weight loss >10%.
- +/- DDAVP
Water Deprivation Test

- Normal
- Psychogenic polydipsia
- Central DI
- Nephrogenic DI

U.osm vs time

Give ADH (DDAVP)
ADH & plasma osmolality

- P.ADH (pg/mL)
- P.osmolality (mOsm/kg)

- SIADH
- Normal & Psychogenic polydipsia
- Central Diabetes Insipidus
- Nephrogenic Diabetes Insipidus
Hyponatraemia
Renal Handling

• Average 70 kg male filters approximately 1.2 kg of salt per day!
• Vast majority must be reabsorbed
Urine Sodium

Freely filtered

70-80%

5-10% Na/K/H

20-25% Na/K/2Cl
Dysnatraemia

Amount of salt

\[
\text{mmol} \quad \text{L}
\]

Amount of water
Case

- 6 month old with astrocytoma on vincristine
- P.Na 126 L 135-145 mmol/L
- P.Osm 255 L 280-300 mosm/kg
- U.Na 32
- Cerebral salt wasting vs SIADH
Hyponatraemia

Serum osmolality

>300

- Glucose
- Manitol

<280

- Hyperlipid
- Hyperprotein

Dilutional

- Hypervolaemic
- Euvolaemic
- Hypovolaemic

- CHF Renal failure cirrhosis
- SIADH Hypocortisol Hypothyroid Psychogenic polydipsia
- Renal loss GI loss Haemorrhage Skin loss
Case...

• SIADH:
  – Kidneys act to preserve perfusion
  – SIADH = excess of water, hence intravascular volume, in face of low Na.
  – Kidney response is to lose Na

• Cerebral Salt Wasting
  – Inappropriate Na excretion →
    ↑urine volume →
    ↓intravascular volume
SIADH

• Laboratory Features
  – ↓S.Na
  – ↓P.osm
  – ↑U.osm (typ. >50 mosm/L)
  – U.Na >20 mmol/L
  – Normal renal, thyroid & adrenals
  – Euvolaemic
SIADH Causes

• Tumour
  – Small cell, bronchogenic CA, pancreatic, Hodgkin’s

• Pulmonary
  – Pneumonia, lung abscess, TB

• Medications
  – NSAID, barbiturates, carbamazepine, TCA, oxytocin

• CNS
  – Brain tumour, encephalitis, SAH, AIP, trauma

• AIDS

• Ventilation

• Post-operative
SIADH Treatment

• Water restriction (~1 L/day)
• Salt
• Weigh daily
• Loop diuretic
• Urea (rarely used)
Cautions

• No renal or adrenal problems
• No bicarbonaturia
  – Obligate excretion of Na
  – E.g. recent vomiting
• No carbonic anhydrase inhibitors
• No acid/base disturbance
• No diuretics
Hyponatraemia

• Reset osmostat
  – Test: water load to further drop S.Na
  – Rarely performed test
  – Only done in patients with mild hyponatraemia
  – SIADH $\rightarrow$ urine remains concentrated
  – Reset osmostat $\rightarrow$ urine becomes dilute

• Importance: treatment different
Treatment cautions

- Dangerous to correct too correctly
- Central pontine myelinolysis
- $\uparrow$ Na by 1-2 mmol/L/h, maximum of 8 mmol/L/day
Hypernatraemia

• Very rarely *need* urine studies
  – Can be used as an adjunct study
Urine Potassium

• Less predictable due to many influences
  – Potassium intake variable
  – Na effects via aldosterone
  – Hydration

• Range 10-400 mmol/d

• Transtubular potassium gradient
  – Can be calculated
  – Clinically doesn’t add much information
  – Rarely used now
Renal Failure
Renal Failure Classifications

• Duration
  – Acute renal failure
  – Chronic renal failure

• Location
  – Pre-renal
  – Renal
  – Post-renal
Renal Failure

- Pre-renal
  - Dehydration
  - CHF
  - Arterial supply

- Renal
  - Glomeruli
  - Renal tubules
  - Interstitium

- Post-renal
  - Stone
  - Tumour
  - Prostate
Fractional Excretion

- Corrects for urine concentration
- \( \text{FENa} = \frac{\text{U.Na} \times \text{P.Cr}}{\text{U.Cr} \times \text{P.Na}} \)
- N.B. match units
  - Plasma creatinine in \( \mu \text{mol/L} \)
  - Urine creatinine in mmol/L
- FeNa <1% pre-renal
- FeNa >1% renal
Case #1

- 50 y.o. goes to the ER with history of vomiting and diarrhoea. Looks dehydrated

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
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<tbody>
<tr>
<td>Plasma.Na</td>
<td>140</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Plasma.Cre</td>
<td>150 Δ</td>
<td>umol/L</td>
</tr>
<tr>
<td>U.Na</td>
<td>25</td>
<td>mmol/L</td>
</tr>
<tr>
<td>U.Cre</td>
<td>1</td>
<td>mmol/L</td>
</tr>
<tr>
<td>FENa</td>
<td>2.7%</td>
<td></td>
</tr>
<tr>
<td>U.osm</td>
<td>320</td>
<td>mosm/kg</td>
</tr>
</tbody>
</table>
Case #2

- 50 y.o. goes to the ER with history of vomiting and diarrhoea. Looks dehydrated

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<tr>
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<td>25</td>
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</tr>
<tr>
<td>U.Cre</td>
<td>10</td>
<td>mmol/L</td>
</tr>
<tr>
<td>FENa</td>
<td>0.27%</td>
<td></td>
</tr>
<tr>
<td>U.osm</td>
<td>600</td>
<td>mosm/kg</td>
</tr>
</tbody>
</table>
Interpretation

- FENa <1% -- pre-renal
- FENa >3% -- acute kidney injury
- U.Osm >500 – pre-renal
- U.Osm <350 – acute kidney injury

- No gold-standard test
- Acute kidney injury can develop from pre-renal failure
Caution

• Loop diuretics increase FENa
  – Cannot interpret while on diuretics
• Severe protein malnutrition/starvation or wash-out of kidney
RTA
Metabolic Acidosis

• Increased anion gap
  – Relatively straight-forward
  – “MUDPILES”

• Normal anion gap
  – Factitious
    • Hypoalbuminaemia
    • Unusual cations (e.g. monoclonal band)
  – HCl or NH$_4$Cl loading
  – HCO$_3$ loss
    • GI (diarrhoea, illeus)
    • Renal (proximal RTA, carbonic anhydrase inhibitor)
  – Failure to generate “new” bicarbonate (distal RTA)
  – Gain of an acid with excretion of conjugate base
Acid production

• Typical North American diet produces 1 mmol H⁺/kg body weight/day
• Mainly from protein oxidation
• Buffering acid load consumes equivalent amount of bicarbonate.
• S.pH ~7.4, U.pH ~6.0
Renal Acid-Base: Recovery

Blood

Renal Tubular Cell

Urine

NaHCO$_3$

HCO$_3^-$ + H$^+$

Na$^+$

H$^+$

CO$_2$

Na$^+$ HCO$_3^-$

H$_2$CO$_3$

CO$_2$ + H$_2$O
Renal Acid-Base: Loss of H⁺

Blood

Renal Tubular Cell

CO₂ + H₂O

HCO₃⁻ + H⁺

Na⁺

glutamine

NH₃

glutamate

α-KG

H⁺

Na⁺

NH₃

Urine

Na₂HPO₄

NaHPO₄

NH₄⁺
Ammonia

- Theoretically can be measured; however, technically very difficult in urine
- Essentially research-only method
- Calculating
Electroneutrality

\[\begin{align*}
+ \text{Na}^+ & \quad + \text{Cl}^- \\
+ \text{K}^+ & \quad + \text{HCO}_3^- \\
+ 2\text{Ca}^{++} & \quad + \text{H}_2\text{PO}_4^- \\
+ 2\text{Mg}^{++} & \quad + 2\text{HPO}_4^{=} \\
+ \text{NH}_4^+ & \quad + 2\text{SO}_4^{=} \\
& \quad + \text{organic anions}
\end{align*}\]
Electroneutrality

\[ \text{Na}^+ + \text{K}^+ + \text{NH}_4^+ = \text{Cl}^- + 80 \]

\[ \text{NH}_4^+ \alpha \text{Na}^+ + \text{K}^+ - \text{Cl}^- \]
Cautions of net charge

- Unmeasured anions → underestimate NH₄
  - Ketonuria
  - DKA
  - Drugs (penicillin, salicylates)
Non-Anion gap Metabolic Acidosis

**Na+K-Cl**

- **Negative** (high NH$_4^+$)
  - GI bicarb loss
  - Acetazolamide
  - NH$_4$Cl, HCl

- **Positive** (low NH$_4^+$)
  - Urine pH
    - $<5.3$ (NH$_3$ defect)
    - $\approx 6.0$ (reduced H$^+$ secretion)
      - Low GFR
      - Hyperkalaemia
      - Interstitial dz
      - Defect distal H+ secretion (low S.K)
      - Voltage defect (high S.K)
      - Amphotericin B
Conclusions
Urine Osmolality & Lytes Utility

- Rarely needed, but critical test
  - Polyuria
  - Hypernatramia
  - Supportive role
    - Pre-renal vs renal oliguria
    - Integrity of the medullary interstitium
Summary

• No “normal” ranges – interpret in clinical context

• Cautions:
  – No diuretics
  – No adrenal or thyroid disease
  – Relatively normal diet