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Fluid & Electrolyte Disorders

Dr Nicola Barlow
Clinical Biochemistry Department, City Hospital

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Overview

- Introduction
- Fluid and electrolyte homeostasis
- Electrolyte disturbances
- Analytical parameters
- Methods
- Artefactual results
- Cases

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Introduction

- Fluid & electrolytes are fundamental biochemical systems
- Tightly controlled homeostatic mechanisms
- Simple and cheap analytical processes
- Underlying physiology complex

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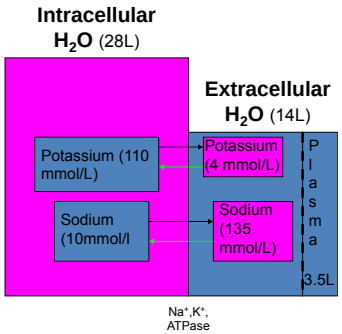
Water distribution



Total adult water content – **42L**

- 60% body weight (men)
- 55% body weight (women)

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Water balance

Water IN
- Metabolism 400mL
- Diet 1100mL

Water OUT (obligatory)
- Skin 500ml
- Lungs 400ml
- Gut 100ml
- Kidney 500 ml

Total in 1500mL = Total out 1500mL

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Control of water balance

- Thirst
- Fluid shifts between ICF and ECF
- Anti Diuretic Hormone (ADH) or vasopressin

In response to changes in:

ECF Osmolarity

(sensed by osmoreceptors)

Osmolarity – measure of solute concentration (no. of moles of solute per unit volume of solution (Osm/L))

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Action of ADH

- Released from posterior pituitary
- Acts on renal collecting ducts to allow re-absorption of water
- Primary aim is to keep ECF osmolarity constant
- BUT volume depletion – ECF volume maintained at expense of osmolarity

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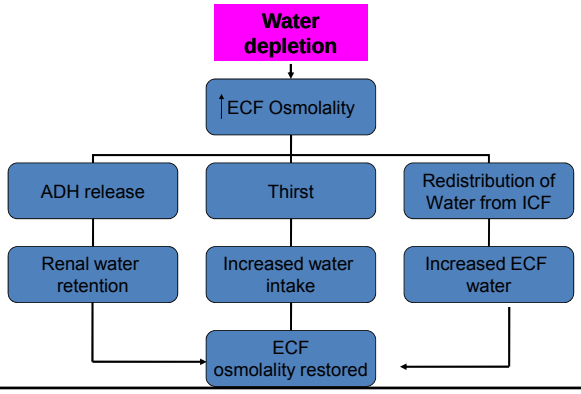
Water homeostasis



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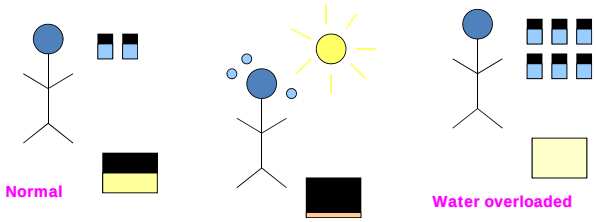
Water homeostasis



Normal

Serum osmo = 290mosm/L

Urine osmo = 100-600mosm/L

Dehydrated

Serum osmo >290mosm/L

Urine osmo >600mosm/L

Water overloaded

Serum osmo <290mosm/L

Urine osmo <100mosm/L

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Sodium balance

Sodium IN

- Diet 100-200 mmol

Sodium OUT

(Obligatory losses)

- Gut/skin 10 mmol

(Loss dependent on intake)

- Kidney 90–190mmol

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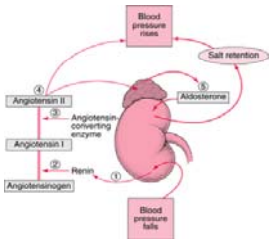
Control of sodium balance

- Renin – angiotensin – aldosterone system



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Aldosterone

- Produced by adrenal
- Acts on renal distal tubule to increase re-absorption of sodium (in exchange for K^+ / H^+)

In response to changes in:

ECF Volume

(sensed by baroreceptors)

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Sodium content *vs* concentration

- ECF Na content determines ECF volume
- ↑ Na content leads to hypervolaemia
- ↓ Na content leads to hypovolaemia

- [Na+] reflects water balance NOT sodium balance (in most cases)
- ↑ [Na+] = water depletion (dehydration)
- ↓ [Na+] = water overload
  - Na content may be normal, low or high

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Electrolyte Disturbances

Hypernatraemia

- Inadequate fluid intake
- Diabetes insipidus
  - Pituitary - ADH deficiency
  - Nephrogenic ADH resistance

Hyponatraemia

- Excessive fluid intake / administration
- Impaired water excretion (↑ADH)
  - Physiological - response to hypovolaemia
  - Pathological - SIADH (Syndrome of Inappropriate ADH Secretion)

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Hyponatraemia

- Sodium deplete (hypovolaemic) (2° ↑ADH and H_2O overload)
  - Mineralcorticoid deficiency, e.g., adrenal insufficiency
  - Diarrhoea / vomiting
  - Diuretics
  - Na-losing nephropathy
- Sodium overload (hypervolaemic) (2° ↑ADH and H_2O overload)
  - Cirrhosis
  - Renal failure
  - Heart failure
  - Nephrotic syndrome
- Normal sodium balance (normovolaemic)
  - Cortisol deficiency, hypothyroidism, renal failure
  - SIADH – drugs, tumours, chest infections, CNS (excessive ADH secretion)

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Potassium balance

Potassium IN

- Diet 60-200 mmol

Potassium OUT

(Obligatory losses)

- Faeces 5-10 mmol
- Skin 5-10 mmol

(Loss dependent on intake)

- kidney 40-190 mmol

Kidney – main regulator of total body potassium

Aldosterone allows excretion of K^+ in exchange for Na^+

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Potassium distribution

- Intra-cellular cation
- Plasma [K^+] poor indicator of total body K^+
- Potassium moves in and out of cells due to:
  - Hormonal control, e.g., insulin
  - Reciprocal movement of H^+

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Electrolyte Disturbances

Hypokalaemia

- Low intake – oral (rare), parenteral
- K^+ into cells
  - Insulin, theophylline, catecholamines
  - Alkalosis
- Increased losses
  - Gut – diarrhoea, laxative abuse, vomiting
  - Kidneys – Mineralocorticoid excess, renal tubular defects

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Electrolyte Disturbances

Hyperkalaemia

- Increased intake (+ impaired excretion)
- Out of cells
  - Insulin deficiency
  - Acidosis
  - Cell breakdown – rhabdomyolysis, tumour lysis
- Impaired excretion
  - Renal failure
  - Mineralocorticoid deficiency
  - Drugs - ACEi, K^+ sparing diuretics
  - Acidosis

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Analytical parameters

- Serum / plasma
  - Na
  - K
  - Osmolarity (osmolar gap)
- Urine
  - Na
  - K
  - Osmolarity

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Osmolarity

- Osmolarity (osm/L) vs osmolality (osm/Kg)
  - Osmolality is measured (NOT temperature dependent)
  - If concentration of solutes is low: osmolality ≅ osmolarity
- Calculated osmo =2[Na^+]+[K^+]+[urea]+[gluc]
- Osmolar gap = Measured osmo – calculated osmo
  - Normal range 10 – 15 mmol / L
  - Increased osmolar gap due to e.g., ethanol, methanol, ethylene glycol

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Indications for measurement (1)

- Serum Na / K
  - Renal function
  - Fluid status
  - Adrenal function
  - Pituitary function
  - Drug side effects
  - Acute illness (e.g., DKA, severe V&D)
  - Nutritional status (e.g., TPN)
- Urine Na / K
  - Investigation of hyponatraemia / hypokalaemia
  - TPN

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Indications for measurement (2)

- Serum Osmo
  - Verification of true hyponatraemia
  - Investigation of diabetes insipidus*
  - ?Poisoning / alcohol
- Urine Osmo
  - Investigation of hyponatraemia
  - Investigation of diabetes insipidus*

*May be as part of water deprivation test

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Water Deprivation Test (1)

- Investigation of Diabetes Insipidus (DI)
- Principle: Deprive patient of fluids to allow serum osmo to rise and see whether urine concentrates (i.e., urine osmo increases).
- Protocol:
  - Patient usually fasted overnight. May or may not be allowed fluids overnight.
  - Serum and urine osmo measurements performed approx every hour (and patient's weight and urine volume recorded)

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Water Deprivation Test (2)

- End points: serum osmo > 300 mosm/L or >5 % loss of body weight
  - Urine osmo > 600 mosm/L DI excluded
  - Urine osmo < 200 mosm/L DI diagnosed
  - Urine osmo 200-600 equivocal
- If DI diagnosed, synthetic ADH (DDAVP) given nasally.
  - Urine osmo > 600 mosm/L pituitary DI
  - Urine osmo < 200 mosm/L nephrogenic DI

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Methods

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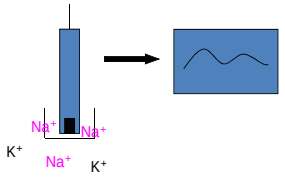
Ion selective electrodes



- Ion selective membrane
  - Na^+ (glass), K^+ (valinomycin)
- Ions interact with electrode to create potential difference
- Produces a current, which is proportional to $[Na^+]$

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Direct vs indirect ISE

- Direct ISE (e.g., Li analyser)
  - Measures activity of Na^+ in neat sample
  - Unaffected by electrolyte exclusion effect
  - Unsuitable for urine analysis
- Indirect ISE (e.g., Roche Modular)
  - Measures activity of sample diluted in high ionic strength buffer
  - Suitable for urine analysis
  - Unsuitable for whole blood
  - Affected by electrolyte exclusion effect

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Electrolyte exclusion effect

- Normal serum contains 93 % water
- Water content lower in lipaemic or high protein concentration samples
- Spuriously low [Na^+] in e.g., lipaemic samples when analysed using indirect ISE

Treat sample with lipoclear, then analyse using direct ISE

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Osmometry

- Freezing point depression principle
  - The freezing point of a solvent lowers when a solute is added to aqueous solutions
  - One osmole of solute per Kg of solvent depresses the freezing point by 1.85 °C

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Artefactual electrolyte results

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Artefactual hyponatraemia

- Electrolyte exclusion effect (indirect ISE)
  - Lipaemic samples or high total protein
  - Normal serum osmo
  - Measure on direct ISE
- Hyperosmolar hyponatraemia
  - Very high glucose (high serum osmo)
  - Causes fluid shifts from ICF to ECF, which dilutes [Na^+]
  - Artefactual – does not require treatment

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Artefactual hyperkalaemia

- Causes
  - Haemolysed
  - On cells (worse at 4ºC)
  - EDTA contamination
  - Very high WCC or platelets
- Integrity checks
  - Haemolysis index
  - Sample date / time
  - Calcium / Mg
  - Check FBC, repeat in LiHep if necessary

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Reference ranges

- Na 133 – 146 mmol/L
- K 3.5 – 5.3 mmol/L

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Panic ranges (1)

- Na^+ >155 mmol/L
  - Thirst, difficulty swallowing, weakness, confusion
- Na^+ <120 mmol/L
  - Weakness, postural dizziness, behavioural disturbances, confusion, headache, convulsions, coma

Rate of change of [Na^+] important

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Panic ranges (2)

- K^+ >6.5 mmol/L
  - Increased risk of sudden cardiac death
- K^+ <2.5 mmol/L
  - Weakness, constipation, depression, confusion, arrhythmias, polyuria

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Case example - 1

- 48 y female
- Partial ptosis (drooping of eyelid)
  - Na 144 mmol/L (133 – 146)
  - K +7.0 mmol/L (3.5 – 5.3)
  - Urea 4.5 mmol/L (2.5 – 7.8)
  - Creat 65 µmol/L (44 – 133)
  - eGFR 85 mL/min (>90)

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Case example - 1

- Check sample
- ?Haemolysed – NO
- Date/time – OK
- Ca/Mg added
  - Ca -1.0 mmol/L (2.2–2.6)
  - Mg -0.11 mmol/L (0.7 – 1.0)

  - EDTA contamination

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Case example - 2

- 17 y female
- 2 month hx lethargy and tiredness
- Dizzy on standing
- Pigmentation in mouth and in palmar creases
- BP 120/80 mmHg lying, fell to 90/50 mmHg when standing

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Case example - 2

- Na -128 mmol/L (133-146)
- K +5.4 mmol/L (3.5-5.3)
- Urea +8.5 mmol/L (2.5-7.8)
- Creat 55 µmol/L (44-133)
- Fasting glucose -2.5 mmol/L

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Case example - 2

- Short Synacthen test
  - 09:00 h 150 nmol/L
  - 09:30 h 160 nmol/L
  - 10:00 h 160 nmol/L

(Normal response: cortisol >550 nmol/L, with increase of >200 nmol/L)

  - ACTH 500 ng/L (<50)
  - High titre anti-adrenal antibodies

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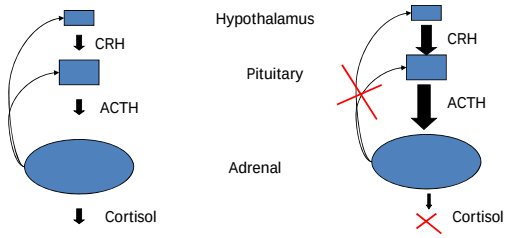
Case example - 2

- Primary adrenal insufficiency



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Case example - 2

- Addison's disease (autoimmune adrenal insufficiency)
- Led to hyponatraemia
  - Lack of aldosterone – uncontrolled Na loss from kidneys
  - Hypovolaemic - 2° increase in ADH and water retention
- Treatment: mineralocorticoid (aldosterone) and glucocorticoid (cortisol) rx

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Thanks for listening
Any questions?