Fluid Assessment and Balance
Dysnatraemia
Dyskalaemia

Tim Pianta
Nephrologist
“Can you chart some extra fluids?”

“It’s for 6B. She’s currently on a 6 hourly saline, I just need another one charted ‘til the team reviews her.”
The 4 surest ways a resident can kill a patient

• Fluids
  – Laziness, ignorance, hubris...

• Warfarin
  – Laziness, ignorance, disorganisation...

• Lie
  – Fudge, distract, obfuscate...

• Not ask for help when needed
  – Fear, ignorance, hubris...
“Can you chart some extra fluids?”

A difficult decision
It helps to know where you’re heading
Why chart intravenous therapy?

Fluids are probably the most common drug you will prescribe in the next 10 years.
Goals of fluid management (and hence iv therapy)

- **Normalise intravascular fluid volume (to allow adequate tissue perfusion)**
  - Hypovolaemia (haemorrhage, loss of extravascular fluid)
  - Vasodilatation (sepsis, anaphylaxis)
    - +/- measures to correct vasodilatation
- **Normalise total extracellular fluid volume (to optimise function or reduce symptoms)**
  - Oedema
    - Tissues: Dependent or generalised
    - Organ
      - Pulmonary
      - Bowel, (hepatic)
    - Cavities: ascites or pleural effusions
- **Normalise extracellular (incl. plasma) fluid composition**
  - Electrolyte contents: Na +, K+, (other: Mg, PO4, ...)
  - Acidity (pH)
  - (Transfusions and infusions: Hb, platelets, plasma components, albumin, etc)
- **Maintain flow in the distal renal tubules/ urinary tract**
  - Prevent precipitation drugs or metabolic toxins (e.g. Ca++, urate, myoglobin) or radiocontrast
    - There are few real reasons to “flush the kidneys”, despite perceptions
What is a fluid assessment?

- A clinical synthesis of the goals, risks, and benefits of fluid management.
- As with any clinical evaluation (relevant)
  - History
    - Presenting
    - Progress
  - Examination
    - ~ Focused cardiac examination
    - ~ Fluid balance assessment
  - Investigations
    - Some or all of
      - EUC: Na, K, HCO3, Cl, sCr (Ca, Mg, PO4)
      - CXR
- Woven through many other assessments, takes practice
  - Like “being a good doctor”
  - Often biased by setting (ED, surgery, ICU, dialysis)
  - Easy to think “everything” is “fluid”
    - Non cardiogenic pulmonary oedema
    - Pleural effusions, ascites (infection, malignancy, chylous effusions, etc.
    - Venous insufficiency, lymphoedema, non-cardiogenic pulmonary oedema, etc.
“Can you chart some extra fluids?” (1/2)

• A synthesis of goals of therapy
  – History (*incl.* information from colleagues, review of notes, *etc.*)
    • How have we got to here?
      – Clinical situation (surgery, cardiac failure, etc.)
      – Drugs (antihypertensives, antiarrhythmics, etc.)
  • Where are we going?
    – Goals of fluid management
    – Ongoing losses, etc
      » Insensible losses + Obligate renal losses
      » Excessive
        • Renal, GIT, skin, respiratory
        • Drains
    – Short term “fixes” (resuscitation) that need longer-term solutions? E.g.
      » Bolus saline
      » K+ lowering manoeuvres, etc
“Can you chart some extra fluids?” (2/2)

- **Examination and Investigation**
  - **Examination**
    - Focused cardiorespiratory examination concentrating on
      - Intravascular fluid
        - JVP
        - Sympathetic response (compensation)
          - Vital signs
          - Peripheral perfusion
          - Signs of decompensation
      - Extravascular (total extracellular) fluid
        - Oedema (or its “opposite”, see later)
        - Ascites and effusions
  - **Environment**
    - Drains, catheter, iv therapy
      - Often summarised on fluid balance chart
  - **Investigations**
    - Plasma fluid composition (esp Na, K, albumin)
    - Acid-base (HCO3, ABG, etc)
    - Surrogates of kidney function (sCr)
    - CXR

- **Balancing**
  - Time/ information poor vs inability to conduct a thorough assessment via the telephone
Fluid balance chart (daily)

### FLUID INTAKE AND OUTPUT WORKSHEET

- **Type of drain:** __________________
- **Total drainage last 24/24:** __________________
- **Total drainage from G/IV insertion:** __________________
- **Daily weight:** __________________
- **Diet/fluid restriction:** __________________

**AFFIX PATIENT IDENTIFICATION LABEL HERE**

- **U.R. NUMBER:** __________________
- **SURNAME:** __________________
- **GIVEN NAME:** __________________
- **DATE OF BIRTH:** ______/______/______
- **SEX:** ______

<table>
<thead>
<tr>
<th>DATE:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTAKE</strong></td>
<td><strong>OUTPUT</strong></td>
</tr>
<tr>
<td><strong>TIME</strong></td>
<td><strong>ORAL</strong></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2400

TOTAL

The above 2400 total row is to be used only for cases where the front sheet holds all information for that day. If not, please continue over page.

<table>
<thead>
<tr>
<th>STOCK STANDARD VOLUMES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>UHT milk (tea/coffee): 18ml</td>
<td></td>
</tr>
<tr>
<td>PC milk (cereal): 150ml</td>
<td></td>
</tr>
<tr>
<td>Semi thick drink (tetra): 165ml</td>
<td></td>
</tr>
<tr>
<td>China cup: 200ml</td>
<td></td>
</tr>
<tr>
<td>Ice cream: 100ml</td>
<td></td>
</tr>
<tr>
<td>Sous bowl: 220ml</td>
<td></td>
</tr>
<tr>
<td>Glass: 250ml</td>
<td></td>
</tr>
<tr>
<td>Jelly: 90ml</td>
<td></td>
</tr>
<tr>
<td>Thick drink (glass): 250ml</td>
<td></td>
</tr>
<tr>
<td>PC juice: 110ml</td>
<td></td>
</tr>
</tbody>
</table>
Fluid balance (summary)

- Picture
**IV fluid (orders)**

<table>
<thead>
<tr>
<th>PHARMACY USE ONLY</th>
<th>DATE</th>
<th>FLASK NO.</th>
<th>TO COMMENCE AT (HOURS)</th>
<th>NATURE OF FLUID</th>
<th>VOL. OF FLASK (ml)</th>
<th>ADDITIONS TO FLASK</th>
<th>RATE</th>
<th>MEDICAL OFFICER'S SIGNATURE</th>
<th>NURSING STAFF SIGNATURE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fluid assessment

1) Intravascular: reduced, normal ("euvolaemic"), or excess.
   - Directly amenable to IV Rx
     • albeit with usually rapid equilibration

2) Extravascular: Excess (oedema), normal, reduced (can you really tell?)
   - Correction via
     • intravascular space (ie indirect)
       - iv or oral fluids, vs
       - restriction, diuretics, dialysis
     • Paracentesis (thoracic - pleural effusion, abdominal – ascites)

*Intravascular and extravascular fluid usually “go together”*
   - Assessing one helps *guess* at the other but are they not the same
   - Clinically need to know
     • The difference in symptoms and signs
     • Common clinical scenarios when they don’t “go together”
     • The effect of treatment often “disrupts” the connection, esp. acutely
Key concepts (1)

- Total body water $\approx 0.6 \times$ weight = 42L
  - Intracellular fluid $\approx 0.4 \times$ weight = 28L
  - Extracellular fluid $\approx 0.2 \times$ weight = 14L
    - Plasma volume $\approx 3.5$L
    - Interstitial fluid $\approx 10.5$L

  - You will see slight variations on these numbers, don’t fret too much

- Ongoing fluid requirements must at least meet
  - Free water ($\approx 1 – 1.5$L)
    - Obligate renal losses $\geq 0.5 - 0.75$L daily
      - 600 – 900 mOsm/day in Western diet
      - Maximally concentrated urine $\approx 1200$ mOsm/L
      - 600/1200 = 0.5L; 900/1200 = 0.75L
    - Insensible losses (500 – 700mL)
      - Skin (500mL) + Lungs (400mL) + Faeces (200 mL)
      - Nb Oxidation of carbohydrates and fatty acids $\rightarrow$ CO2 + water (500 - 700mL)

  - Plus account for
    - Deficits
    - Increased insensible losses (fever, esp.)
    - Ongoing losses (GIT, renal, drain tubes, etc)
Intravascular volume: low

• “Low” jugular venous pressure
  – Clinical correlate of central venous pressure (CVP)
  – In turn surrogate of RA pressure $\rightarrow$ RV filling pressure $\rightarrow$ Filling responsiveness $\rightarrow$ Cardiac output $\rightarrow$ Tissue perfusion

Thus surrogates often wrong...welcome to clinical medicine!

• If low $\rightarrow$ hypoperfusion $\rightarrow$ sympathetic response to
  – increase cardiac output
    • Tachycardia (except if using beta blockers)
    • Inotropic response (usu. hard to measure)
  – Preserve central circulation
    • Vasoconstriction (mottled and cool peripheries)
    • Increased ADH (reduced urinary volume, not invariable)

• Partial failure of compensation
  – Postural tachycardia and hypotension (often not measured)
Hypovolaemia

• Features of shock represent a failure of compensation
  – Frank hypotension
    • a late sign esp. in the young and fit
    • May be relative if chronic hypertension
  – Hypothermia
  – Organ dysfunction
    • Brain, kidney, etc

• Practical points
  – There are alternative causes for all of the above so look for the “syndrome”
  – Hypovolaemic patients usually don’t turn up in exams (except intensive care)
    • They are too busy being acutely unwell
Extravascular volume: low

– Declaration: I deal *mostly* with the elderly
  - Wrinkles!
    - Affect skin turgor
  - Oral mucosa
    - Variable oral health $\rightarrow$ dry mucosa but normal volume
    - Cups of tea aplenty! $\rightarrow$ wet mucosa but hypovolaemic
  - High rates of keratoconjunctivitis sicca (dry eye syndrome)

– For *me* the following are unreliable
  - Skin turgor
    - cf temperature, mottling
    - cf paediatric patients
  - Xerostomia (dry mouth)
  - Xerophthalmia (dry eyes)

– Use these (soft) signs at your peril!
Intravascular volume: high

- Elevated CVP/ JVP
  - Most important abnormalities:
    - Elevation \textit{per se}
    - Large V waves of TR
  
- NOTE: Compensations in the well $\rightarrow$ loss of salt and water
  - Natriuresis: BNP, ANP
  - Reduced sympathetic tone
  - Reduced RAAS activity
  - \textit{ADH (mainly controlled by osmolarity)}

- Thus elevated JVP usually indicates pathologically elevated right atrial pressure
  - Elevated RV filling pressure
    - RV failure/ dysfunction
      - Primary or secondary to LV failure
  - Tricuspid regurgitation
    - Primary or secondary to elevated RV pressure (RV dysfunction, right heart failure)
    - or TS less commonly
  - Pericardial constriction (effusion or obstruction)
  - SVC obstruction
Extravascular volume: high

- Oedema
  - Peripheral
    - Dependant
      - Peripheral (ankle)
      - Sacral (if bed-bound)
  - Generalised (anasarca)
    - Hypoalbuminaemia
    - Profound vasodilatation (sepsis, SIRS)
      » Eg overloaded ICU patient after several days...

- Pulmonary
  - Tachypnoea, hypoxia (cyanosis)
  - Presence of fluid in alveolar spaces: crackles
  - Presence of interstitial fluid causing obstruction: wheeze
  - Pleural effusion: Dull percussion, Reduced breath sounds, no resonance

- Gut and hepatic congestion
  - Abdominal distention
    - often just anorexia
  - Enlarged, tender liver
    - often just LFT abnormalities
  - Ascites: full flanks to frank distention, shifting dullness
Clinical tips

– Oedema, etc is rare except
  – Abnormal cardiac, liver, renal or function
    » Usually represent acute decompensation of cardiac, liver, renal disease and the underlying cause should be sought for
      • Decompensation
      • Disease (if suggestions chronic)
  – Iatrogenic fluid excess

– (Reliable) change in weight a good guide to changes over day(s)
  • Only works if done
    – E.g. starting at admission, not D3
    – Communication

– Ankle wrinkling usually a reflection of improved oedema
A non-exhaustive list

<table>
<thead>
<tr>
<th>Intravascular (CVP)</th>
<th>Extravascular</th>
<th>Normal</th>
<th>Excessive (equilibration can be very slow despite correction of intravascular volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deplete</td>
<td>Deplete</td>
<td>GIT losses, eg diarrhea (scenario 3)</td>
<td>Acute haemorrhage</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Ivy fluid excess + normal heart &amp; renal function during correction of below</td>
</tr>
<tr>
<td>Excessive</td>
<td>Rapid bolus fluids (usually rapidly equilibrates)</td>
<td></td>
<td>decompensated heart failure (eg oedema, JVP up)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>excessive fluid in presence of above</td>
</tr>
</tbody>
</table>
Fluids available (1)

- Free (Osmol or sodium) water
  - Oral fluids (food)
  - 5% dextrose = D5W
    - glucose rapidly metabolised effectively leaving “free” water
- Crystalloids
  - Normal saline: hyperchloraemic relative to plasma
    - 0.9% = 154mM NaCl = 308 mOsmol/L
  - Balanced
    - compound sodium lactate (CSL) a.k.a Hartmann’s Solution
      - Na 131 mM, K 5 mM, Cl 112 mM, Ca 2 mM, bicarbonate lactate 28 mM
    - Proprietary balanced solutions
      - Eg Plasmalyte 148: Na 140 mM, K 5 mM, Mg 1.5 mM, Cl 98 mM, acetate 27 mM and gluconate 23 mM
- Hybrids
  - 4% dextrose + 1/5 normal saline
  - ½ Normal saline
Fluids available (2)

- **Colloids**
  - **Albumin**
    - **4% albumin**
      - human albumin 40 g + Na 140 mM, Cl 128 mM, octanoate 6.4 mM, trace Al
        » SAFE study (N Engl J Med 2004; 350:2247-2256)
        » Ongoing studies
  
  - **20% albumin**
    - Supportive therapy for abdominal paracentesis (i.e. ascitic tap)
    - Assistive management of severe, problematic hypoalbuminaemia (i.e. specialised use)

- **Synthetic colloids**
  - Succinylated gelatin (gelofusin), Hydroxyethyl starch (Volumen), etc....
    - Marred by
      » Renal toxicity (AKI, tubular toxins)
      » Serial scientific misconduct
  
- No evidence place place in contemporary management
Fluids available (3)

• Potassium additives
  – Premixed KCl
    • KCl 10 mmol in 100mL 5% dextrose
    • KCl 30 mmol in 1L NS, 5%D, or 4%D + 1/5NS
  – Additives
    • Ampoules
      – Restricted venues (ICU, pharmacy), access (subject of repeated coronial Ix), etc
        » 10 mmol in 10mL
        » K$_2$HPO$_4$
  – Mg, Ca, PO$_4$, etc: Not for today
Hyponatraemia and hypernatraemia

But first a digresssion
Water balance and sodium balance: key concepts (1)

• Sodium is the main determinant of osmolarity but ...
• Abnormalities of $[\text{Na}]_{\text{plasma}}$ are fundamentally problems of water and ADH (release or effect)
  – $\text{Osm}_{\text{plasma}} \sim 2 \times [\text{Na}]_{\text{plasma}}$
    • Plasma tonicity $= 2 \times [\text{Na}] + [\text{glucose}] + \text{other osmols (eg alcohol)}$
  – Osmolarity (more correctly *tonicity*): the main determinant of
    • ADH release
    • thirst
      – hence $[\text{Na}]_{\text{plasma}}$
  – Osmolarity is controlled via ADH $\rightarrow$ V2 receptors $\rightarrow$ aquaporins $\rightarrow$ water loss
  – Intracellular osmolarity = extracellular osmolarity

• “Free water” deficit (excess) =
  – amount of extra (osmol-free) water needed to normalise osmolarity
• Most therapeutic measures addressing salt or water affect both together ("salt-and-water")
  – Do not radically change $[\text{Na}]_{\text{plasma}}$
    • Salt gains are approximately accompanied by water because...
    • $[\text{Na}]_{\text{plasma}}$ usu. very tightly regulated by ADH unless abnormalities
  – Major clinical impact
    – Intravascular fluid: hypertension
    – Extravascular fluid: oedema
Therapies that address “salt-and-water” balance

• Decrease salt and/or water
  • Moderate fluid restriction
  • Salt restriction (especially important to control thirst)
  • Diuretics
    • Loop (frusemide, bumetanide)
    • Aldosterone antagonist (receptor: spironolactone, eplerenone)
      • amiloride
    • *nb*: Thiazides usually don’t BUT CAN AND DO cause hyponatraemia: common cause
      • Acetazolamide usu. only used in ophthalmology
  • Dialysis
    • Haemodialysis and CVVHDF
    • Peritoneal dialysis
  • Paracentesis
    • Often diagnostic as well as therapeutic

• Increase salt and water
  • Liberal oral fluid intake
  • High salt diet (provided access to water as well)
  • IV fluids
  • Mineralocorticoids (aldosterone, fludrocortisone)
    — Corticosteroids (lesser but important effect on mineralocorticoid receptors)
Hyper and hyponatraemia

- Normal [Na]_{plasma} = 140 (i.e. 135 – 145 mmol/ L)
- Clinical manifestations of hyponatremia and hypernatremia
  - Overt: mainly neurological
    - Confusion (delirium), seizures, falls, etc.
    - rapid changes in [Na]_{plasma} in (either direction) can cause permanent and severe, (incl lethal) injury.
  - Accompanied by an excess in mortality rate
    - “Black-box” non-specific effect
      - Cardiac death
      - Infection, etc.
**Hypernatraemia**

- Insufficient water for amount of sodium in ECF
  - Usually a function of water intake/loss (cf Na⁺)
  - Always indicates hypertonicity
    - Hyponatraemia *usually* indicates hypotonicity

- Inadequate free water intake
  - Incapacitated patient, “desert” scenario

- Loss of free water
  - Osmotic diuresis: glucose, (mannitol)
  - Diabetes insipidus
    » Central
    » Nephrogenic
      - Lithium
      - CKD (severe quite rare in isolation)
  - Rarely
    - (mal)administration of hypertonic saline
Management

- Acute
  - Correct access to water
  - Beware of rapid correction of chronic problems
    - Rapid fall $\rightarrow$ cerebral oedema (mainly children)
    - Rapid rise $\rightarrow$ (pontine) demyelination
      - Free water deficit readily calculable online (eTG)
      - Generally no more than 0.5mM/h

- Diagnose/treat central DI $\rightarrow$ desmopressin
  - Water deprivation in an endocrine referral unit $\rightarrow$ response to exogenous desmopressin.
    - Nephrogenic DI failure of urine osmolality to increase
    - Not if obvious precipitant e.g. head injury or pituitary surgery.
Hyponatraemia

- Factors overwhelm the usually tight osmotic control of ADH release and Na/ water handling
  - Osmols other than Na^+
  - Kidney level
  - Antidiuretic hormone
    - “Appropriate”
    - “Inappropriate”: SIADH
ADH independent

- Other (effective) osmoles instead of Na+/K+
  - Hyperglycaemia
  - Severe alcohol intoxication
- Kidney level: impaired urinary dilution
  - Thiazides:
    - +/- role of ADH if volume deplete
    - Most commonly prescribed in combination Rx
      » E.g. Coversyl plus, AvaproHCT
      » other diuretics not usually severe in isolation
  - Chronic Kidney Disease
    -Usu stage 5 and rare, impairment in concentration → nocturnal polyuria more usual
  - Polydypsia
    - Primary (psychogenic) remembering even up to 10L tolerated by kidneys with normal diluting capacity
ADH dependent

- Release of ADH “appropriate” to hypoperfusion
  - Baroreceptors hypoperfusion: true or effective arterial volume depletion
    - Carotid & aortic arch → sympathetic activity → ADH release
      - glomerular afferent arterioles → RAS
      - atria and ventricles → natriuretic peptides
  - Persistent hypovolaemia (acutely rarely hyponatraemic)
    - Cardiac failure (inadequate perfusion, “forward failure”)
    - Liver failure (vasodilatation ± hypoalbuminaemia)
    - Hypoalbuminaemia (hypovolaemia ???)

- SIADH
  - Enhanced ADH release (or effect)
    - CNS disease
    - Drugs:
      - SSRIs, carbemazepine, cyclophosphamide (elderly more susceptible to all)
      - Ecstasy, exercise induced hyponatraemia: usually with water intoxication
    - Pain (typically surgery)
    - Hypothyroidism, Addison’s disease, (Pregnancy)
  - Ectopic ADH production
    - Pulmonary: infection,
    - Malignancy (classically NSCLC)
A pragmatists approach to hyponatraemia

• Exclude hyperglycaemia, alcohol
• Drugs are the most likely, reversible cause
  • Thiazide diuretics (ACEi/ARB + HCT)
  • SSRIs/ SNRIs, Carbemazepine
  • Ecstasy (MDMA)
• Endocrinopathies are treatable, serious conditions
  • TSH (+/- T3, T4 if on treatment)
  • Pregnancy (nb mild hyponatraemia unless hyperemesis gravidarium)
  • Oxytocin (induction of labour)
  • Addison’s disease (Diagnosis has to be considered, never presented on a plate)
    » consider iatrogenic (exogenous corticosteroids)
    » Consider the role of 6AM cortisol, short synacthen tests, etc to establish diagnosis
• Other causes can usually be identified from history and examination:
  • Cardiac failure, liver disease,
  • GIT losses
  • Uncontrolled pain
  • Exercise-induced hyponatraemia
• If not consider SIADH (and underlying cause)
  • Malignancy (SCC lung, NSCLC, other)
  • CNS disease or surgery (vs cerebral salt wasting)
  • Non-malignant pulmonary disease
  • Hereditary
Management

• Identify and correct underlying problem where possible
• Options
  • Severe water restriction (e.g. 500mL)
  • SIADH should not be treated with isotonic solutions e.g. 0.9% saline
    – infused sodium will be excreted in smaller volumes of urine
    • net retention of “(electrolyte-) free water”
  • Hypertonic Na is a specialist drug that you “never” need use
    – In practical terms: suggest “only” in ICU and v.v. rarely in v.v small amounts
  • V₂R antagonists: new
    – Tolvaptan, conivaptan
    – ?role in practice
    – Probably refractory hyponatraemia in:
      » SIADH
      » Cardiac failure
Hyperkalaemia and hypokalaemia
Key concepts: potassium (1)

• Normal $[K]_{\text{plasma}} = 3.5 – 5.0 \text{ mmol/L} \ldots \text{some labs} \ 5.2$

• Hyperkalaemia
  – Muscle weakness
  – Cardiac
    • Arrhythmias
    • ECG abnormalities (interesting and alarming, but insensitive)
      – Peaked and early T waves (shortened QT)
      – P waves
        » “early”: prolonged PR interval and
        » decreasing amplitude (may disappear): atrial arrest
      – QRS widening into sine pattern

• Hypokalaemia
  – Muscle weakness (usu. K < 2.5 mmol/L)
  – Cardiac
    • Cardiac arrhythmias
      – Esp if increased susceptibility e.g. after myocardial ischaemia
    • ECG changes
      – ST depression
      – Low amplitude T waves
      – U waves
    – Hypokalaemia-induced renal dysfunction (a variety of “atypical” kidney abnormalities)
Key concepts: potassium (2)

- Most potassium is intracellular
  - \([K]_{\text{intracellular}} = 150 \text{ mM} \quad [K]_{\text{extracellular}} = 3.5 - 5.0 \quad \text{e.g. } [K]_{\text{plasma}}

- Gradient determined by
  - pH
    - \(\text{H}^+ \leftrightarrow \text{K}^+\) exchanged to maintain electroneutrality across cell membranes
  - Insulin
    - Enhanced activity of the Na-K-ATPase pump in skeletal muscle
  - B\(_2\) adrenergics
    - Enhanced activity of the Na-K-ATPase pump in skeletal muscle
    - Na-K-2Cl co-transporter

- Total body potassium not determined by above factors but
  - GIT intake and output
  - Renal losses dependent on
    - Aldosterone
    - Flow (distal salt and water delivery)
    - Normal tubular function
Hyperkalaemia (1)
Increased release from cells

- Increased release *in vitro*
  - Pseudohyperkalaemia *probably* most common
    - Traumatic collection or sample handling (simple recollection)
    - Essential thrombocytosis or CLL (Liase with lab)
- Increased release from cells *in vivo*
  - Metabolic acidosis
  - Insulin deficiency
    - Diabetic ketoacidosis
      - and hyperosmolar hyperglycaemic state
    - Beware: total body K often low due to osmotic diuresis
      - Potassium replacement usually necessary when urgent issues corrected
  - Release from pathological cells
    - Crush injury, tumour lysis, rhabdomyolysis, etc
  - Non selective beta agonists (propranolol or labetalol, rarely severe)
  - Hyperkalaemic periodic paralysis (rare, but fascinating)
Hyperkalaemia (2)
Increased total body potassium

- Kidneys
  - Reduced aldosterone release or effect
    - Reduced renin
      - NSAIDs (ibuprofen, indomethacin, esp)
      - Kidney disease (diabetes and interstitial nephritis, esp.)
    - Angiotensin converting enzyme (ACE) inhibitors & angiotensin II RBs
    - Adrenal insufficiency
      - Primary: usually with features of cortisol deficiency (Addison’s disease)
      - Congenital hypoaldosteronism
  
- Effect
  - Aldosterone receptor antagonists (spironolactone, eplerenone), amiloride

- Flow (distal salt and water delivery)
  - Usually contributes rather than primary cause
    - True hypovolaemia
    - Cardiac failure

- Abnormal tubular function
  - Acute or chronic kidney disease

- Increased intake
  - Excessive potassium substitution
    - Usually in combination with above
Hyperkalaemia (3)

• Often multifactorial
  – E.g. 73 y.o. woman with urinary tract infection
    • causing acute kidney injury with mild metabolic acidosis
      » Reduced tubular function
      » Increased release from cells
  • complicating chronic kidney disease due to diabetes
    » Reduced tubular function
    » Low renin production
      • Hyporeninaemic hypoaldosteronism (type 4 RTA)
  • on a background of heart failure treated with combination of medications including
    – Perindopril
      » Reduced angiotensin II $\rightarrow$ aldosterone
    – Spironolactone
      » Aldosterone receptor antagonist
Correction of hyperkalaemia: immediate

- Acute management: Graded response depending on severity
  - Mild: >5.5 to 5.9 mM
    - Confirm abnormality
    - Identify and correct underlying cause if possible (medications, etc.)
    - Monitor
  - Moderate: 6.0 – 6.9 mM
    - Concurrently identify ECG changes and tempo of change
  - Severe: ≥7.0 mM or > 6.5 and rapidly increasing, or ECG changes
    - ECG changes: stabilise myocardium, summon help: resusc. bay or equivalent, MET call
      - Ca gluconate: 10% 10 mL (= 1 g) IV over 2 to 3 minutes into a large vein.
      - Monitor response by ECG
    - Insulin + dextrose (regimens vary)
      - Actrapid 10 units iv stat PLUS glucose 50% 50 mL IV over 5 minutes.
      - PLUS CLOSE GLUCOSE MONITORING + EXCELLENT COMMUNICATION
        » Contraindicated if adrenal insufficiency
    - Correction of hyperglycaemia may be sufficient, but principle: INSULIN + MONITORING
      - If diabetic ketoacidosis, should be in the totality of management.
    - Correct acidosis if volume depleted
      - NaHCO₃: 150 mmol in 1L 5% dextrose over 2 - 4 h (see protocols)
      - Not if likely to \( \rightarrow \) overload
    - Salbutamol (beta-agonist) may reduce K but risks cardiac arrhythmia: contraindicated.
Correction of hyperkalaemia: *secondary*

- Acute correction of hyperkalaemia addresses potassium gradient

- Usually needs to be followed up by addressing total body K⁺
  - Diabetic ketoacidosis usually total body K low
    - Replace K if/when once \([K]_{\text{plasma}} < 5.3\)
  - Most hyperkalaemia associated with increased total body K⁺:
    - Low K diet
      - Usually requires dietician input, educational materials
    - *Cease* drugs which conserve K
      - ACEi, ARBs, spironolactone
        - If subsequently reintroduced: with extreme caution
    - Potassium wasting strategies
      - Loop diuretics, thiazides
      - ? Fludrocortisone for type 4 RTA (not my practice, commonly)
    - Cation exchange resin: Widely prescribed, marginal evidence of benefit
      - Sodium polystyrene sulfonate (Resonium A) or Calcium Resonium
    - Dialysis
      - Usually when other acute or chronic indications present

- There is debate about what is severe and at what threshold to instigate Rx
  - Acute vs chronic (although evidence for this *debatable*)
  - Rapidly rising
  - Local protocols
Hypokalaemia

- Reduced total body potassium
  - GIT: Diarrhoea
    - Other: Villous adenoma, laxative abuse, bowel prep (colonoscopy)
  - Urinary
    - Tubular function
      - Diuretics: loop diuretics, thiazides, (acetazolamide)
        » Other: Hypomagnesaemia, amphoterocin
        » Renal tubular acidosis, Bartter’s and Gitelman’s syndrome
  - Salt and water delivery
    - Diuretics (compounding above)
    - Polyuria: hyperglycaemia (incl DKA), compulsive water ingestion, diabetes insipidus
    - Esp. with DKA (B-hydroxybutarate), H+ loss (HCO₃⁻), glue sniffing (toluene)
      » Non-resorbable anions
  - Hyperaldosteronism
    - “Conn’s syndrome”
      » fully expressed (rare): hypertension, hypokalaemia, mild hyponatraemia.
      » Eg, bilateral idiopathic hyperaldosteronism, aldosterone producing adenoma (Conn’s disease), etc

- Shift of potassium into cells (often iatrogenic, temporary so beware overcorrection)
  - Alkalosis, Beta agonists (salbutamol), Insulin
Multifactorial

- 73 year old woman usually takes frusemide to control ankle swelling now has UTI complicated by severe vomiting.
  - Na 142, K 2.9, HCO$_3$- 35, sCr 110, Urea 19.6 mmol/L
  - Frusemide: loop diuretic (potassium wasting)
    - Impaired tubular function
    - Na-K-2Cl in tubular thick ascending loop
    - Increased distal flow of Na
  - Vomiting: maladaptive (at least in terms of K+ balance) correction of
    - Hypovolaemia $\rightarrow$ hyperaldosteronism
    - Loss of HCl $\rightarrow$ Alkalosis $\rightarrow$ increased distal flow of NaHCO$_3$
Summary: useful rules of thumb

- "Volume" is a function of "salt-and-water"
  - The **most common** drug **you** will prescribe in next 5 years
  - Regulated by
    - Sympathetic nervous system
    - Renin-angiotensin-aldosterone system (RAAS)
    - Renal tubuloglomerular feedback
    - Natriuretic peptides (mostly from heart)
  - Intravascular
    - most common problem is too little (hypovolaemia)
  - Extravascular
    - most commonly too much (pulmonary or peripheral oedema)

- Plasma sodium is a function of "free water"
  - Primarily regulated by ADH in response to osmolarity (tonicity)
  - Some regulation by SNS when hypoperfusion overrides tight regulation
  - Beware rapid correction: permanent brain damage
Summary: useful rules of thumb

• High or low potassium mainly affects muscles
  • Cardiac: potentially fatal arrhythmias
  • Skeletal: weakness

• In hyperkalaemia:
  • Urgent efforts usu drive K+ to intracellular reservoirs
    – Secondary efforts should address total body K+

• In hypokalaemia
  • K replacement is often reflexive
    – A little physiology and thought can go a long way
The end
Sodium balance: “trivia”

– Sodium reservoir
  – Sodium bound in polyanionic proteoglycans
    » Skin, bone, cartilage