Metabolic/Electrolyte Management in Children

Ensure all abnormal results are immediately repeated to eliminate an operator/lab error before correction.

These guidelines cover:
A. Hyponatremia
B. Hypokalaemia
C. Hypomagnesaemia
D. Hypocalcaemia
E. Hypophosphatemia
F. Hypoalbuinemia
G. Hyperkalaemia
H. Hypercalcaemia

Guide to overview of sodium abnormalities:

<table>
<thead>
<tr>
<th></th>
<th>Na</th>
<th>Urea</th>
<th>U Na</th>
<th>Serum Osmo</th>
<th>Urine Osmo</th>
<th>Urine SG</th>
<th>Urine output</th>
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<td>SIADH</td>
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<td>Low/N</td>
<td>&gt;60</td>
<td>&lt;275</td>
<td>&gt;500</td>
<td>&gt;1.020</td>
<td>&lt; 1ml/kg/hr</td>
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<tr>
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<td>High</td>
<td>&gt;120</td>
<td>&lt;275</td>
<td>&gt;300</td>
<td>&gt;1.010</td>
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<td>N/High</td>
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<td>&lt;275</td>
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<td>High</td>
<td>&lt;20</td>
<td>&gt;275</td>
<td>&gt;300</td>
<td>&gt;1.020</td>
<td>&lt; 1ml/kg/hr</td>
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A. Hyponatremia:

Definition:
- Mild Hyponatraemia Sodium (Na) <135mmol/L
- Moderate hyponatraemia requiring intervention Na <130mmol/L
- Severe hyponatraemia requiring intervention Na <125mmol/L or symptomatic

Normal daily requirements:
- Sodium (Na) 1 – 3mmol/kg/day
Aetiology:
- Hypovolaemia – GI losses, diuretic.
- Fluid overload - All children having $3L/m^2/day$ of IV fluid should have a daily weight and daily UEC.
- Renal dysfunction – renal tubulopathy, nephrotic syndrome
- SIADH – pain, intracranial tumour, meningitis, encephalitis, post-operative neurosurgical patients, vinca alkaloids, morphine, carbamazepine, cyclophosphamide
- Cerebral salt wasting – head injury, brain tumour, post –op, subarachnoid haemorrhage
- Endocrine – Mineralocorticoid insufficiency ($↓Na$, $↑K$, $↓Glucose$), hypothyroidism

Check:
- BP (CVP depending on circumstances).
- Hydration status (weight and fluid balance).
- Urine output
- Serum Na, Cl, HCO3, urea, creatinine, osmolality, blood glucose.
- Urine Na, urea, creatinine, osmolality, specific gravity, glucose.

Management for hyponatraemia:
- Discuss with Consultant on – call if:
  - Sodium <130mmol/L and seizures
  - Sodium <130mmol/L and decreased level of consciousness
  - Sodium <125mmol/L
- Consider underlying cause before prescribing the rate of intravenous (IV) fluid infusion (i.e. fluid overload or SIADH will require fluid restriction whereas hypovolaemia will require fluid resuscitation).

Oral replacement (check with cBNF):
- Preferred route if tolerating feeds
- Sodium chloride (NaCl) oral preparation 30% (5mmol/ml oral solution)
- 1 month–18 years: according to requirements, generally 1–2mmol/kg daily in divided doses, higher doses may be needed in severe depletion
- Formula to calculate required daily Sodium:
  \[ \text{Dose (mmol)} = (130\text{mmol/l} – \text{actual Na concentration}) \times 0.6 \times \text{body weight (kg)} \]

SIADH/Fluid overload:
- Mild: Fluid restrict to urine output, replace with 0.9% Saline
- Symptomatic – see below
Acute/intravenous replacement:

- **Na <130mmol/l and asymptomatic:**
  - Use 0.9% sodium chloride as hydration fluid

- **Na <130mmol/l and symptomatic:**
  - If the patient is symptomatic (i.e. decreased conscious level or fitting) initially manage with fluid restriction. Hypertonic sodium chloride may be required for partial correction.
  - It may be necessary to correct acutely with fluid restriction +/- hypertonic sodium chloride.
  - If sodium chloride 2.7% is required, the deficit should be corrected slowly to avoid the risk of osmotic demyelination syndrome; the rise in plasma-sodium concentration should be <10mmol/l in 24 hours.

- **Equation for determining the dose of Hypertonic 2.7% Saline for patients:**

<table>
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<tr>
<th>Sodium Dose (mmol)</th>
<th>= (125 – measured sodium) x 0.6 x body weight (kg)</th>
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</table>

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<tr>
<th>Convert to volume:</th>
<th>mmol x 2.17 = ml of Saline 2.7%</th>
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</table>

  OR 3ml/kg 2.7% Sodium chloride IV over 30minutes (preferably by central line) should raise sodium by approximately 2 – 3mmol/l

- **Continuous infusional rate** 1-2ml/kg/hour of 2.7% Saline (approx. 0.5-1mmol/kg/hour and aim to correct to above 125mmol/L over 3-4 hours. Maximal infusional rate: 2ml/kg/hr of 2.7% Saline

- **Maximal concentration:** concentrations over 0.9% Sodium Chloride should be given via a central line

- **Monitoring** Monitor sodium on gas machine hourly. If sodium increases by more than 3mmol/L in 4 hours reduce the rate of infusion.

- **Recheck Na levels** When serum sodium is corrected to 125mmol/L continue correction with 0.9% sodium chloride

**Preparations:**

- 0.9% Sodium chloride (IV): 150mmol Na and Cl per 1000ml
- 2.7% Sodium chloride (IV): 460mmol Na and Cl per 1000ml (0.46mmol/ml)
- 30% Sodium chloride (oral): 25mmol Na and Cl per 5ml (5mmol/ml)
B. Hypokalaemia

Definition:
- Mild/moderate hypokalaemia: Serum Potassium (K) <3.5mmol/L
- Significant hypokalaemia: K <3.0mmol/L

Normal Daily requirements:
- Infants: 2 – 6 mmol/kg/day
- Children: 2 – 3 mmol/kg/day

Causes include:
- Urinary loss due to drugs (e.g. furosemide, liposomal amphotericin (Ambisone®), aminoglycosides, broad spectrum penicillins, platinum based agents).
- Loss in the stools from diarrhoea.
- Alkalosis
- Proximal tubular nephropathy (ifosfamide, Ambisone®), ↓K, ↓albumin

Assessment:
- Drug chart
- Hydration status (weight and fluid balance)
- Na, K, Urea, creatinine, HCO3

Management for hypokalaemia
- Measure potassium levels frequently – see below.
- Monitor renal function and urine output.
- Use Amiloride with Ambisone® to reduce potassium loss.
  - NB Amiloride can be renal toxic (refer to the Paediatric Haematology/Oncology Anti-fungal Guidelines for Amiloride doses).

Oral replacement (check with cBNF)
- Preferred route of replacement if tolerating feeds
- Starting dose 1 – 2mmol/kg/day in divided doses, adjust according to plasma concentration
Acute/intravenous replacement:

- **Dose:** 0.5 - 1mmol/kg (max. dose 30mmol) by IV infusion at maximum rate of 0.2mmol/kg/hour
- **Peripheral intravenous administration**
  - infusion rate: 0.08 – 0.2mmol/kg/hr maximum peripheral concentration 40mmol/l potassium chloride (KCL)
- **Central intravenous administration**
  - Higher concentrations of up to 0.5mmol/kg/hour can be used on Paediatric Intensive Care Unit (PICU), however ECG monitoring must ALWAYS occur at this rate
- **Maximal concentration** 80mmol/L through a central line, 40mmol/L through peripheral line. In severely fluid restricted patients (with central lines), higher concentrations may be used under specialist supervision. Discuss with PICU.
- **Monitoring:** ECG monitoring if potassium <2.5mmol/L and when giving high concentration replacement
  - Stop infusion if peaked T waves occur. Hyperkalaemia is characterised on ECG by tall, peaked waves, followed by widening of QRS bending into abnormal T waves. P waves flatten and PR interval prolongs
- **Recheck** Renal function and potassium level after 3 hours.
  - Continue to monitor potassium levels and renal function 4-6 hourly.
  - **NB** ensure Magnesium is replete, replace if low (Mg<0.5mmol/l)

**CAUTION:**

- IV potassium should only be given according to your hospital Intravenous Drug Administration Guidelines and by an IV competent nurse after he/she has read the relevant IV drug monograph. Additional training and supervision may be required before the nurse can give IV potassium.
- Potassium solutions for intravenous administration should be prescribed in concentrations that are currently available as commercially prepared, ready-to-use, diluted preparations. When preparing potassium containing bags always ensure that the contents in the bag are mixed well.
- IV potassium solutions can cause extravasation, therefore give potassium via a large peripheral vein or central line.

**Preparations:**

- **For intravenous fluid concentration of 10 – 40mmol/l prescribe commercially prepared, ready – to – use diluted preparation. Generally available pre-mixed infusions at ORH (this list may be subject to change)**
- **High Strength Potassium Chloride Injection, 15%:** 20mmol potassium in 10ml.
• Sando K® tablets (effervescent potassium, bicarbonate and chloride): 12mmol potassium/tablet
• Slow K 600mg® tablets (potassium chloride): 8mmol potassium/tablet
• Kay-Cee-L® syrup (potassium chloride): 1mmol/ml

C. Hypomagnesaemia

Definition:
• Replacement Mg <0.7mmol/L
• Consider correction in patients on ciclosporin Mg <0.8mmol/L

Normal Daily Requirement
• Approximately 0.08 – 0.2mmol/kg/day

Causes:
• Proximal tubulopathy - drugs (furosemide, cisplatin, amphotericin, carboplatin, ifosfamide, aminoglycosides ciclosporin, proton pup inhibitors).
• Malnutrition and refeeding syndrome
• Endocrine - Hyperparathyroidism, hyperaldosterism
• Excessive GI losses

Management
• Magnesium is poorly absorbed and therefore in patients with serum levels below 0.5mmol/L or unable to tolerate oral preparations magnesium should be considered for intravenously magnesium
• Serum Mg levels do not accurately reflect total body stores. Treatment must therefore be tailored to symptoms

Oral replacement with magnesium glycerophosphate (as per cBNF):
Child 1 month – 12 years: 0.2mmol/kg/dose Magnesium tds
Child 12 – 18 years: 4-8mmol/dose Magnesium tds

Acute/Intravenous replacement with magnesium sulphate:
• Dose:
  o 0.2mmol/kg elemental Magnesium in 50ml Saline 0.9% over 1 hour
  o 0.4mmol/kg elemental Magnesium in 100ml Saline 0.9% over 2 hr
  o 0.6mmol/kg elemental Magnesium in 150ml Saline 0.9% over 2 hr
  o Doses may be escalated as required to maintain serum magnesium above 0.5mmol/L (Discuss with the Consultant).
• Infusional rate: max rate of magnesium sulphate 2.4mmol/kg/hr
• Maximal concentrations:
  o Dilute to concentration of 10% (40mmol in 100ml) with saline 0.9% or glucose run over 20-30min
- **Monitoring** renal function and urine output.
- **Recheck** Magnesium levels after 8 – 12 hours after end of infusion.

**Magnesium Preparations:**
- Magnesium sulphate 1g is equivalent to 4mmol magnesium.
- Magnesium sulphate injection (50%): 1g (4mmol Mg) in 2ml
- Magnesium sulphate injection 50%: 5g (20mmol Mg) in 10ml
- Magnesium glycerophosphate tablets (unlicensed product) (4mmol of magnesium/tablet) Magnesium glycerophosphate solution (unlicensed product) (1mmol/ml of magnesium)
- **NB:** Magnesium glycerophosphate tablets can be dispersed in water immediately before administration.

**D. Hypocalcaemia**

**Definition:**
- Serum Ca\(^{2+}\)<2.5mmol/l
- Ionised (Blood gas) Ca\(^{2+}\)<1.1mmol/l

**Normal daily requirement:**
- Approximately 0.05 – 0.1mmol/kg/day (5 – 33mmol/day)
- Increases with age

**Causes:**
- Usually a phenomenon secondary to hyperphosphataemia – esp. Tumour lysis syndrome
- Drugs: denosumab, cisplatin, carboplatin, pamidronate, furosemide
- Renal failure
- The total body calcium is usually normal so treatment is aimed at reducing the serum phosphate. In particular try to avoid IV calcium as this leads to deposition of calcium phosphate crystals in the veins, kidneys and throughout the body.

**Assessment:**
- Hydration status (weight and fluid balance)
- Ca, Mg, Albumin, PO\(_4\)
- Ionised calcium may be obtained from the gas machine: normal range 1.15-1.29 mmol/L.
Management of hypocalcaemia:
- NB hypocalcaemia is usually short lived and if patient is asymptomatic, there is no need to treat, particularly as treatment may result in deposition of Calcium phosphate crystals in the kidneys.
- IV replacement used for symptomatic patients, ie. tetany, fits

Oral replacement (check cBNF)
- Initial Dose is (adjust according to response):
  - 1 month – 4 years 0.25mmol/kg/dose four times per day (qds)
  - 5 – 12 years 0.2mmol/kg/dose qds
  - 12 – 18 years 10mmol qds.

Acute/intravenous replacement:
- **Dose**: 1 month – 18 years: 0.11mmol/kg (0.5ml/kg calcium gluconate 10%) max 4.5mmol (20ml calcium gluconate 10%).
- **Infusional rate**
  - **Via Central line**: undiluted slow IV bolus over 5 – 10 minutes
  - **Via peripheral administration**: for intravenous infusions dilute the 10% solution to at least 0.045mmol/ml (i.e. 1 in 5 dilution) with glucose 5% or sodium chloride 0.9%. Administer as slowly as possible, preferably at a rate of not greater than 0.045mmol/kg/hour
- **Maximal concentration** undiluted 10% Calcium gluconate can be given peripherally
- **Monitoring** ECG if hyperkalaemic
- **Recheck levels**

**CAUTIONS:**
Avoid calcium chloride as may produce local vein toxicity.
**DO NOT ADMINISTER Ca in the same line a Sodium Bicarbonate/Phosphate**

Preparations:
- Calcium gluconate injection, 10%: (2.2mmol Calcium in 10ml)
- Calcium gluconate 1gram effervescent tablet: 2.23mmol calcium/tablet.
- Sandocal 1000 effervescent tablets: 25mmol calcium/tablet.
- Calcium Sandoz syrup: 2.7mmol calcium in 5ml (only for children <1 year, due to manufacturer supply restrictions or pending special exceptions application to the manufacturer).

**E. Hypophosphataemia**

**Definition**
- Phosphate level <1mmol/L
Normal daily requirements

- Approximately 0.2 – 0.5 mmol/kg/day (3.2 – 34 mmol/day)
- Requirements increase with age

Causes

- Proximal tubular nephropathy
- Drugs e.g. cisplatin and ifosfamide, rarely ranitidine and valproate.
- Alkalosis (especially respiratory) and acute increases in glucose intake will increase phosphate movement into cells.

Assessment:

- Nutritional status (weight, calorie intake)
- Ca, PO₄, albumin
- Tubular Renal reabsorption of phosphate (TRP)
  \[
  \text{Normal Range: } 85 - 95\%, >95\% \text{ in hypophosphataemia}
  \]

Management:

- Asymptomatic hypophosphataemia usually does not require treatment
- An acute, significant drop in serum phosphate (>50-60% of normal) may cause muscle weakness, paraesthesias, cranial nerve palsies and reduced deep tendon reflexes.
- Prolonged hypophosphataemia in children may lead to rickets and delayed growth in addition to muscle effects, and if severe, haemolytic anaemia or rhabdomyolysis can occur

Oral replacement (adjust according to response):

- 1 month-5 years: 2-3 mmol/kg/day (max 48 mmol/day) in 2-4 divided doses
- 5-18 years: 2-3 mmol/kg/day (max 97 mmol/day) in 2-4 divided doses

Acute/intravenous replacement:

- Dose:
  - Total Daily Dose (mmol) = (1.5 mmol/l – actual concentration) x 0.6 x BW (kg)
  - OR
  - If losses are recent and uncomplicated: 0.08 mmol/kg over 6 hr as phosphate
  - If serum phosphorus 0.5 - 1 mmol/L: 0.16 - 0.24 mmol/kg as phosphate
If serum phosphorus <0.5mmol/L: 0.36mmol/kg as phosphate

- **Infusional rate** maximum rate 0.05mmol/kg/hour (in an emergency and in intensive care the rate can be increased to 0.5mmol/kg/hour via a central line)
- **Maximal concentration** (via CENTRAL line only): 20ml of sodium glycerophosphate (20mmol) in 30ml of 5% glucose or 0.9% sodium chloride
- **Monitoring** renal function, phosphate and potassium levels
- **Recheck phosphate** 6 hours after end of infusion

**Preparations:**
- Sodium glycerophosphate (IV) 20mmol (of phosphate) in 20ml injection
- Phosphate Sandoz: 16.1mmol phosphate per tablet
  Phosphate oral solution: 0.5mmol phosphate in 1ml

**F. Hypoalbuminaemia**

**Definition**
- Serum albumin <30g/L
- Consider replacement <20g/L

**Normal daily requirement**

**Cause**
- Reduced production – asparaginase in ALL
- Malnutrition
- Renal loss – nephrotic, nephritic, tubulopathy
- Stool loss

**Check**
- Nutritional assessment (weight, fluid balance, oedema)
- Albumin, LFT, renal function
- Urine dipstix (consider morning urine protein/creatinine ratio if protein ≥2+)
- Stool elastase

**Management**
- **Discuss with on call Consultant prior to initiating treatment**
- Only treat if severe symptoms e.g. severe oedema or ascites.
- **Dose:** 0.5g/kg 20% Albumin (maximum dose 40g, reduce dose in liver failure)
  Give furosemide (0.5 -1mg/kg) half way through infusion.
- **Infusional rate** Give over 4-5 hours depending on dose, slower in liver failure
- **Maximal concentration** 20% albumin
- **Monitoring** Blood pressure and saturations every 30 minutes throughout infusion and 1 hour after completion
• If significant hypertension or 20% increase in baseline BP, stop infusion and reassess.
• Watch for signs of fluid overload. Increased respiratory rate is a good indicator of fluid overload, consider further Furosemide.
• Recheck albumin on daily basis

CAUTION Human albumin solution (HAS) can cause significant side effects:
  - Acute pulmonary oedema
  - Fluid overload and hypertension

G. Hyperkalaemia

Definition:
• Mild Hyperkalaemia >5.5mmol/L – observe no acute interventions unless symptomatic
• Hyperkalaemia >6mmol/L
• Hyperkalaemia >5.5mmol/L with associated renal failure/ECG changes

Causes:
• Oral supplementation
• Tumour Lysis Syndrome, rhabdomyolysis
• Renal failure
• Metabolic Acidosis
• Consider the potential for pseudohyperkalaemia (e.g. sample lysis/sample taken from a line used to infuse potassium)
• Drugs that interfere with potassium excretion (amiloride, spironolactone)
• Mineralocorticoid deficiency (hypoaldosteronism states)

Assessment:
• Drug charts – oral supplements and nephrotoxic drugs
• UEC, uric acid
• Blood gas – assess pH, lactate, HCO₃, Base excess

Management of Hyperkalaemia:
• COMMENCE NEBULISED SALBUTAMOL IMMEDIATELY RECHECK UEC AND VBG
  - <25kg: Salbutamol 2.5mg
  - 26 – 50kg: Salbutamol 5mg
  - >50kg: Salbutamol 10mg
• Discuss with Consultant on – call, continue salbutamol nebulisers while awaiting results
• ECG rhythm strip
- Arrhythmias or K >7mmol/L: IV calcium gluconate (0.5ml/kg Calcium Gluconate 10% max. 20ml)
- If acidotic: half correct with 4.2% Sodium Bicarbonate (0.5mmol/l)
- Calculation for half - correction:

<table>
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<tr>
<th>Total (mmol) for half correction</th>
<th>Base excess x 0.3 x body wt (kg)</th>
<th>2</th>
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</table>

Convert to Volume of 4.2% NaBic = (Half correction mmol) x 2 ml IV over 20min

Emergency correction = 1mmol/kg 4.2% NaBic IV over 20 minutes

CAUTION:
- Sodium Bicarbonate 4.2% (0.5mEq/ml) is preferred concentration
- DO NOT GIVE NaBic and Ca²⁺ via same line – will lead to precipitation
- If not controlled: discuss with PICU for admission and glucose/insulin
  - Children over 1 month:
    - Soluble insulin rate: 0.05-0.2units/kg/hr WITH
    - Glucose 0.5-1g/kg/hour (5-10ml/kg of glucose 10% or 2.5-5ml/kg of glucose 20%
- Admit to PICU for dialysis if interventions not working
- Calcium resononium/Kayexalate® - this is not an emergency intervention
  - Child 1 month- 18 years: 0.5-1g/kg (max 60g) daily in divided doses
  - NB: One gram of resin exchanges 1mmol/l Na for 1mmol/k

Preparations:
- INJECTION 4.2% (0.5mmol of sodium and bicarbonate in 1ml) 10ml
- Calcium Resonium® (Calcium polystyrene sulphonate resin) 300g powder
- Soluble insulin (human) 50units in 50ml pre-filled syringe
- Calcium gluconate injection, 10%:( 2.2mmol Calcium in 10ml)

H. Hypercalcaemia

Definition
- Corrected Ca²⁺ >3mmol/L

Causes:
- Malignancy – ALL, bone metastases
- Paraneoplastic – ectopic related – PTH production
- Endocrine – Hyperparathyroidism, Addison’s disease
Assessment:
- Check oral supplements
- UEC, Ca, PO4, PTH
- Blood gas machine ionised calcium (normal range 1.15 - 1.29mmol/l)

Management of Hypercalcaemia:
- Discuss all hypercalcaemic patients with Consultant on – call
- Hyperhydration with 0.9% sodium chloride – at least 3L/m²/day.
- Promote calcium excretion with diuretics furosemide 1 – 2mg/kg/dose IV tds
- Consider:
  - Steroids for lymphoproliferative conditions
  - Bisphosphonates – discuss with Endocrine team

REFERENCES:

1. The Children’s Hospital Oakland Hematology/Oncology Handbook. Caroline Hastings
4. BNF for Children 2013-2014
5. Paediatric and neonatal dosage handbook. Carol Taketomo et al. 20th Edition

Review

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<th>Revision</th>
<th>Date</th>
<th>Version</th>
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<td>New doc</td>
<td>June 2010</td>
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<tr>
<td>Dr Shaun Wilson, Paed Oncology Consultant</td>
<td>Format change Major upgrade in definitions Additions to management guides References added</td>
<td>Sept 2015</td>
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