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BAPEN Position Statement on Electrolyte and Vitamin Replacement in Adult patients with severe malnutrition, including people with Eating Disorders and other related conditions who are undergoing refeeding.

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Introduction

The Royal College of Psychiatrists recently reported an 79% increase in hospital admissions in adults with eating disorders (ED) in the last five years[1]. Many of these patients will be at high risk of refeeding syndrome according to the criteria in the Medical Emergencies in Eating Disorders (MEED)[2] guidelines and NICE CG32[3] and managed on general medical wards. While serious but rare consequences of inappropriate refeeding including death are well publicised, more common problems related to fluid overload can be overlooked but lead to serious morbidity and prolonged length of stay[1, 4, 5.] These often relate to poor fluid and electrolyte management during refeeding and apply to all patients at high risk of refeeding syndrome, not just those with eating disorders. Metabolically stressed patients may be at highest risk of fluid and electrolyte disturbance. The importance of identifying and addressing the underlying causes of malnutrition cannot be understated and guidance on this is provided in NICE CG32[3] and MEED[2].

Key Points

- Plasma levels of electrolytes such as potassium (K), magnesium (Mg) and phosphate (PO_4) do not reflect whole body stores in severely malnourished patients. For example, 98% of K is intracellular and there can be significant depletion with normal plasma levels[1,2,3,6]. Potassium can leave the cell passively so plasma levels can be maintained while a significant intracellular deficit develops.
- The risk of dangerous fluid overload in refeeding patients is often overlooked[1]. During starvation activity of the cell membrane sodium-potassium-adenosine triphosphatase (ATPase) pump is significantly reduced, leading to accumulation of sodium (Na) and water inside cells. Re-activation of cell membrane pumps in refeeding liberates large amounts of water and Na from cells – enough to induce oedema in healthy volunteers[7,8]. Consequences of fluid overload are summarised in Table 1
- Prefeeding electrolyte replacement (attempting to normalise plasma levels before staring nutrition support) is not recommended as energy and insulin are required to replenish the intracellular deficits[1,6, 9,]. Electrolytes given without carbohydrate are likely to just give a transient increase in plasma levels before being excreted. The transient rise in plasma levels that results from giving electrolytes without carbohydrate can lead to a false sense of security as the intracellular deficit will persist.
- The belief that intravenous (IV) K should not be given in glucose 5% due to the risk of 'driving it into the cells' is flawed as the deficit is intracellular and cannot be corrected without energy and insulin[6],[9].
- Thiamine can be depleted in 18 days with poor intake[1,10,11]. People with a high alcohol intake have an increased risk of thiamine deficiency[11]. Initiating feeding where thiamine is depleted can lead to the development of Wernicke's encephalopathy, that may progress to the permanent brain injury Korsakoff's psychosis without adequate thiamine replacement[1,10, 12]. Symptoms of Wernicke's encephalopathy include confusion, ataxia and nystagmus[12].
- Feeding without adequate thiamine may lead to lactic acidosis that can increase excretion of K, Mg and PO_4 [13].
- Many standard policies for the treatment of hypokalaemia and hypophosphataemia, outside of critical care areas, are not suitable in patients at high risk of refeeding syndrome as they often advocate giving relatively small amounts of electrolyte replacement in large amounts of IV sodium chloride 0.9%[14].
- Sodium (Na) excretion is greatly reduced in refeeding [15], increasing the risk of fluid overload. The risks of circulatory overload which include pulmonary oedema, increased respiratory rate and tachycardia are summarised in Table 1.

- Several studies have shown that oral K supplementation is as effective as IV provision[16,17], however, patients with ED should be carefully observed to ensure they take It and do not vomit.
- Patients at high risk of refeeding problems who require parenteral nutrition (PN) may be at particularly high risk of fluid overload if they do not have gastrointestinal fluid losses and are given separate electrolyte replacement in large fluid volumes.
- PN is very rarely required, and usually not recommended in patients with ED. Where significant gastrointestinal (GI) symptoms are reported, assessment for dysmotility should be considered, especially in patients with ED who may have undiagnosed GI motility issues contributing to their malnutrition. The BSG have produced guidance on assessment and management of dysmotility[18].
- **Table 1 Consequences of Fluid Overload on Organ Function in Humans[4,5,]**

Organ System	Complications
Heart	Myocardial oedema Tachycardia Conduction disturbance Diastolic dysfunction Arrhythmia Impaired contractility Heart Failure
Kidneys	Reduced renal blood flow Decreased Glomerular Filtration Rate Acute Kidney Injury Uraemia Salt and water retention
Lungs	Increased respiratory rate Pulmonary oedema Pleural Effusion Impaired gas exchange Increased work of breathing
Skin / Muscle	Oedema Delayed wound healing Impaired mobility
Brain	Cognitive Impairment Delirium
Gastrointestinal tract	Increased permeability Bacterial translocation Malabsorption Bowel oedema Ileus Increased complications and mortality in abdominal surgery
Liver	Hepatic congestion and cholestasis Impaired synthetic function

Recommendations

- Patients at high risk of refeeding as per page 78 (table 8) of the MEED[2] guidelines or NICE CG32[3] should be started at around 10kcal/kg/day, with energy provision built up rapidly to meet or exceed requirements by around day 4 and a maximum of day 7[1,3]. Failing to meet full energy target by day 7 may lead to the potentially fatal underfeeding syndrome[2].
- MEED suggests that high refeeding risk ED patients who do not have systemic Illness can be started at 10 - 20kcal/kg/day' and the Parenteral and Enteral Nutrition Group of the British Dietetic Association (PENG) have proposed that feeding can start at 10 – 20kcal/kg/day in all high risk patients[19]. However, in acutely unwell hospitalised patients, it is recommended that feeding commences at the lower end of this range on day 1, to ensure compliance with current NICE guidance[3].
- Prophylactic provision of electrolytes to levels of 2-4mmol/kg/day K, 0.3-0.6mmol/kg/day PO_4 and Mg 0.2 – 0.4mmol/kg/day is recommended unless plasma levels are high, until plasma levels are stable in the normal range, and patients are established on full energy requirement [1,3].
- 0.2mmol/kg/day Mg should be the target for IV replacement, and 0.4mmol/kg/day for oral replacement.
- Prophylactic oral electrolyte preparations are recommended to allow rapid build-up of feeding without excess provision of sodium and fluid. Prophylactic oral electrolyte replacement can avoid the need for IV preparations which can be associated with very large amounts of fluid and Na. See table 2 for suggested provision in 30-40kg patents with normal renal function[1].
- It is recommended that euvolaemic patients who are refeeding without high fluid losses receive 20ml fluid/kg/day and <1mmol Na /kg/day [12].
- Daily or twice daily (in the highest risk and/or unstable patients) monitoring of plasma urea and electrolytes (U&E), chloride (Cl) Mg, PO_4 and adjusted calcium should be carried out[2, 3]until the patient is at goal rate of nutrition support. Frequency can then be reduced as per clinical need to daily or 2-3 times a week.
- Glucose monitoring is advised for all patients six times a day until they are at goal rate of nutrition support. Frequency can then be reduced to twice daily if blood glucose levels are stable. If there is a change in infusion time or feed rate, increase monitoring to four times a day for 48 hours, then reduce back down to twice daily if blood glucose levels are stable.
- Monitoring Na and Cl can give important information about hydration status and for guiding optimum choice of diluents for electrolytes and medicines. Hyponatraemia could indicate excess use of IV glucose 5% or GI losses that need replacement. Hyperchloraemia can result from the use of IV NaCl 0.9%[20,21]. Hyperchloraemia should be avoided as it causes constriction of renal arteries and reduced glomerular filtration rate, potentially exacerbating fluid overload associated with refeeding[20, 21].
- It has been suggested that drops in plasma electrolyte levels to approximately K< 2.5mmol/l, Mg<0.4mmol/l or PO_4 <0.4mmol/l from normal levels after the commencement of feeding can be regarded as confirmation that refeeding has occurred[22]. It is therefore recommended that increases in feeding should not be withheld unless K<2.5mmol/l, Mg <0.4mmol/l or PO_4 <0.4mmol/l, provided that electrolytes are supplemented as recommended above.

- Adjusted calcium (adjusted Ca) can drop in refeeding as a result of PO_4 provision. When adjusted Ca <2.0mmol/l, seek advice from an expert such as a Clinical Chemist or member of the nutrition support team.
- For malnourished patients with obesity and a BMI >30kg/m^2, it is recommended that electrolyte provision is based on ideal body weight (IDW)[1]. There are various formulae for estimating IDW, however the use of one that takes into account the optimum BMI for an Individual based on clinical judgement is recommended, such as that described by Peterson[23]
- Remember to consider the electrolyte content of oral nutrition supplements (ONS), enteral feeds and PN when prescribing electrolyte supplementation. This can usually be found on the container label.
- Check the patient is not prescribed other medicines that can interfere with serum electrolyte handling e.g., diuretics, proton pump inhibitors, laxatives, corticosteroids, IV iron preparations and antacids.

Table 2 Recommended prophylactic oral electrolyte provision for 30-40kg patients at high risk of refeeding problems with normal renal function[1]

Electrolyte	Example preparation*	Typical Dose	Provision/day (mmol)
Potassium	Sando K® effervescent tablet (12mmol/tablet)	2 tablets tds	72mmol K
Phosphate	Phosphate Sandoz® effervescent tablet (16mmol/tablet)	1 tablet bd	32mmol PO_4
Magnesium	Magnaspartate® powder (10mol/sachet)	1 sachet bd	20mmol Mg
	Neomag® chewable tablet (4mmol/tablet)	2 tablets bd	16mmol Mg
	Magnesium Kora Healthcare tablet (4mmol/tablet)	2 tablets bd	16mmol Mg

*Specials/unlicensed products may also be available. Ask your local pharmacy team for advice.

Intravenous Electrolytes

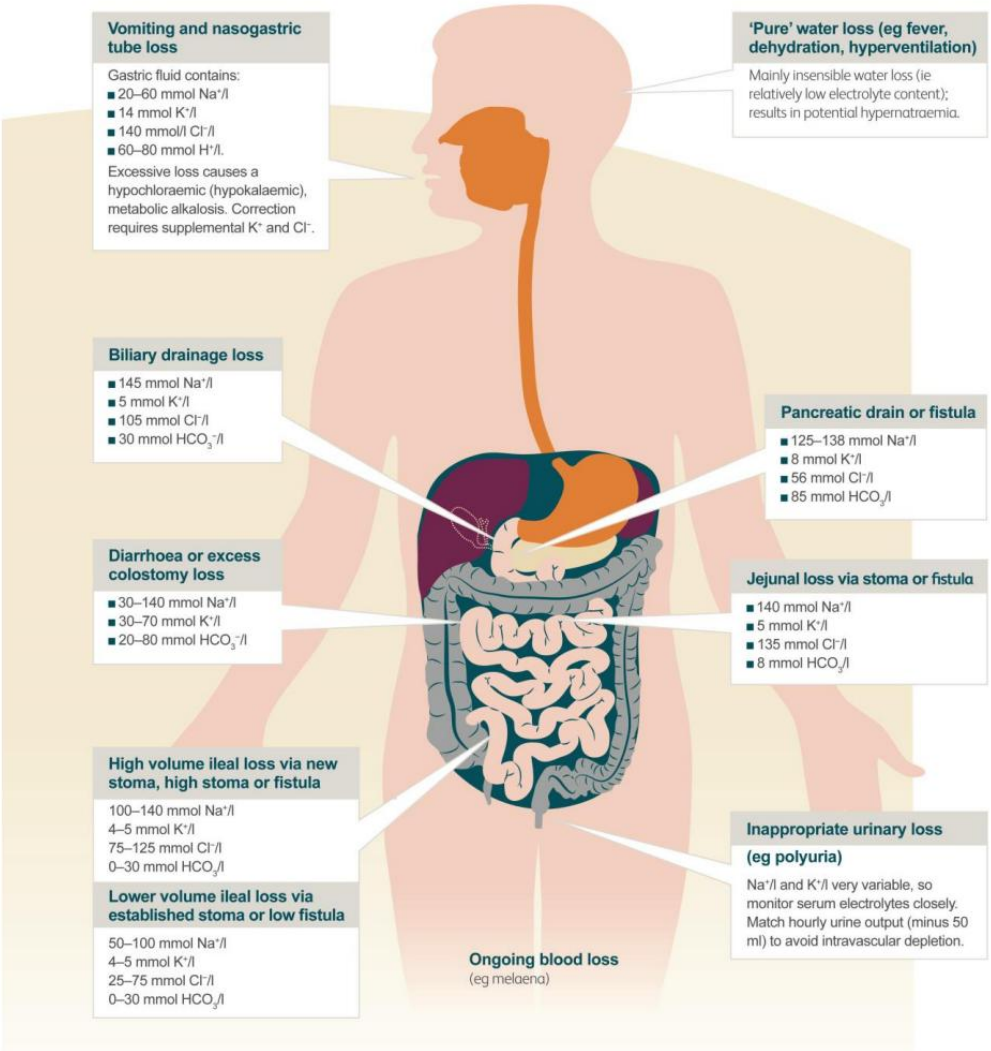
- Intravenous electrolytes may be required where the gut is not functioning or is inaccessible, or where plasma levels are very low, for example K<2.5mmol/l, PO_4 <0.4mmol/l or Mg <0.4mmol/l.
- When IV electrolyte provision is deemed necessary, it is recommended that where possible patients are transferred to a high dependency or similar unit for provision of concentrated electrolytes [1, 24].
- Extreme caution should be taken when giving IV electrolytes in NaCl 0.9% due to the risk of Na and fluid overload. 40mmol K in 1000ml NaCl 0.9% provides only 40 mmol K but 154mmol Na, 194mmol chloride (Cl) – this is 4-5 times recommended amounts of Na and Cl [14]. See table 3 for the risks of excessive provision of NaCl 0.9%[19]
- Check the patient is not receiving excessive amounts of NaCl 0.9% through dilution of other IV medicines. Ask your local pharmacy team if these can be diluted in glucose 5% or diluted in small volumes.
- Hyperchloraemia constricts renal arteries, reduces glomerular filtration rate, and depletes K from cells [20,21].

- Where non-concentrated electrolytes are used, glucose 5% is probably the superior diluent as the fluid load can be rapidly excreted[25]. The risk of hyponatraemia and energy content (200kcal/l) must be taken into account[22].
- If a central line is in place, concentrated K can be given as per local policies. Do not exceed 10 – 20mmolK per hour.
- If patients have high gastrointestinal losses e.g., vomiting, diarrhoea, nasogastric (NG) drainage, NaCl 0.9% is likely to the best diluent[24,26]. See figure 1 diagram of ongoing losses NICE CG174[26].
- Hyponatraemia can be common in patients with EDs a result of water loading or purging such as vomiting or laxative abuse[2]. It is imperative to determine the cause in patients requiring electrolytes, as fluid restriction would be the treatment in those with water loading because large volumes of IV fluid would be harmful. In those with hyponatraemia due to purging or gastrointestinal (GI) losses such as those from diarrhoea, vomiting and drains, NaCl 0.9% can be considered as a vehicle for electrolyte provision.
- Phosphate can be delivered intravenously using a Phosphate Polyfusor (50mmol/500ml) or dilution of concentrated phosphate injections such as sodium glycerophosphate. Note these preparations also contain Na +/- K in addition to PO_4. For example, 500ml of a Phosphate Polyfusor contains: 50mmol phosphate, 81mmol sodium, 9.5mmol potassium. Glucose 5% may be suitable for dilution of concentrate phosphate injections. Take care with concentration and infusion duration (check local policies). Concentrations greater than 10mmol/100ml should be given by a central route. Infusion times outside of critical care areas are usually 12hrs.
- Examples of ways to give 20mmol phosphate IV would be 200ml Polyfusor over 12 hours or 20mmol PO_4 as sodium glycerophosphate in 250ml for central administration over 12 hours or 20mmol PO_4 as sodium glycerophosphate in 500ml for peripheral administration over 12 hours.
- Mg preparation doses are referred to in grams or mmol. 1g Mg = 4mmol Mg.
- The recommended dose for IV Mg is 0.2mmol/kg/day. It can be given in relatively small volumes e.g. 8mmol in 100ml is adequate for a 40kg patient. Concentrations greater than 5% (5g in 100ml) should be given centrally. 4mmol (1g) may be given over 1-2 hours, although local policies may vary.
- The NICE[3] recommended levels of prophylactic electrolytes should be added to PN bags for patients at high risk of refeeding syndrome. Standard bags should only be used where electrolytes can be given in fluids to replace GI losses, or on units where concentrated IV electrolyte preparations are available.
- Repeated daily doses of intravenous infusions are likely to be needed to correct severe deficiencies, and one single dose is unlikely to be sufficient. Once or twice daily infusions of different electrolytes may be required with once/twice daily plasma monitoring.

Figure 1. Diagram of Ongoing Losses NICE CG174[26]

NICE National Institute for Health and Care Excellence

Diagram of ongoing losses



Micronutrients

- IV thiamine can be given as either;
  a. Vitamins B+C Intravenous High Potency concentrate for solution for infusion (1 pair is one 5 mL ampoule containing thiamine 250 mg, riboflavin 4 mg and pyridoxine 50 mg, and one 5 mL ampoule containing ascorbic acid 500 mg, nicotinamide 160 mg and glucose 1000 mg) formerly available as Pabrinex®, 1 pair once a day for 5 days.
  b. Thiamine Hydrochloride available as a licenced 250mg/2ml solution or 250mg/5ml for injection, once a day for 5 days. The 250mg/2ml preparation can also be given IM which may be an advantage where very strict fluid restriction is required, if IV access not available such as in community hospitals or prisons, or where it is suspected the patient may interfere with the infusion. The 250ml/2ml preparation is more suitable for I.M use due to its small volume. Check product information for excipients such as benzyl alcohol, which is used as a preservative, as it can be an irritant when administered IM.
- For patients with a history of high alcohol intake or symptoms of Wernicke's encephalopathy, higher doses will be required. Vitamins B+C Intravenous High Potency concentrate for solution for infusion 2 pairs three times a day (or 1500mg IV thiamine) is usually recommended for 5 days or until symptoms of Wernicke's encephalopathy resolve. Refer to local guidelines as there may be variations and discuss with local substance misuse team if required.
- IV thiamine can be stopped after 5 days or when feeding is fully established, provided no symptoms of Wernicke's encephalopathy have developed during refeeding
- Oral thiamine should follow parenteral dosing regimen until feeding regimen is fully established, up to maximum total of 10 days, unless required for other indications.

Table 3: **Adverse events related to intravenous fluid therapy with NaCl 0.9%**[20]

Metabolic	• Hyperchloraemic acidosis • ↑ Need for buffers to correct acidosis • Hypoalbuminaemia[24]
Body water	• Possible damage to endothelial glycocalyx • ↑Interstitial fluid volume leading to oedema
Gastrointestinal	• Gastrointestinal oedema, intestinal stretch • Ileus, impaired anastomotic healing
Renal	• Renal oedema and capsular stretch leading to intrarenal tissue hypertension • Renal vasoconstriction, ↓renal blood flow and tissue perfusion • ↓Glomerular filtration rate, urine volume, and sodium excretion
Haematological	• ↑Intraoperative blood loss • ↑Need for blood product transfusion
Clinical outcomes	• ↑Postoperative complications • ↑Mortality • ↑Incidence of acute kidney injury and need for renal replacement therapy.

*Disclaimer: BAPEN Position Statements/Guidelines have been prepared as guidance only to assist qualified healthcare professionals in the decision-making processes surrounding nutritional care. Users of these materials may only do so on the condition that they exercise their own professional knowledge and skills when applying such guidance to specific circumstances. Anyone without the appropriate qualifications must seek the advice of a qualified healthcare professional before taking, or refraining from, any action on the basis of the policies or guidance. BAPEN does not (i) owe a duty of care to users of the policies or guidance who are not qualified healthcare professionals; and (ii) cannot accept liability to anyone using these policies or guidance.

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