Guidelines for the prevention of Re-feeding Syndrome in Adult Acute Hospital Inpatients

FAO: All ward staff including nurses, doctors, pharmacists & dietitians

Scope: Identification & initial management of adult in-patients at potential risk of re-feeding syndrome (whether commencing oral, enteral or parenteral nutrition)

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These guidelines are to be read in conjunction with:

- National Institute of Clinical Excellence (NICE)
  Nutrition support in adults: Clinical guideline 32 (2006)
  https://www.nice.org.uk/guidance/cg32

  Best practice advice on the care of adults who are malnourished or at nutritional risk.

- Oral Feeding Difficulties and Dilemmas – report of a working party.
  Royal College Physicians January 2010
  https://www.rcplondon.ac.uk/projects/outputs/oral-feeding-difficulties-and-dilemmas

- Management of really sick patients with Anorexia Nervosa (MARSIPAN) – College report CR162.
  Royal College of Psychiatrists and Royal College of Physicians, April 2014.
  http://www.rcpsych.ac.uk/usefulresources/publications/collegereports/cr/cr189.aspx

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Background

Re-feeding syndrome is a set of **potentially fatal** adverse reactions occurring in the malnourished patient if nutrition is given too quickly or in amounts that exceed their metabolic capacity. These adverse reactions may stem from a variety of processes which are triggered by re-feeding, including:

- sudden electrolyte & fluid shifts
- altered glucose metabolism
- severe micronutrient (particularly thiamine) deficiency

However re-feeding syndrome can be prevented. Therefore it is important that patients at risk of re-feeding syndrome be identified, assessed and managed appropriately – see below.

Clinical features of re-feeding syndrome

Re-feeding syndrome affects **multiple organ systems** and therefore signs & symptoms can include any of the following:

- Cardiac arrhythmias
- Confusion, impaired consciousness, tremor, ataxia
- Weakness, paralysis (can affect respiratory muscles), myalgia, rhabdomyolysis
- Abdominal pain, constipation & ileus
- Fluid overload, or intravascular hypovolaemia

Re-feeding syndrome can also be characterised by **markedly deranged biochemistry**, in particular:

- Hypophosphataemia
- Hypokalaemia
- Hypomagnesaemia (possibly also refractory hypokalaemia, hypocalcaemia)

There may also be hyponatraemia, hyperglycaemia and acid-base disturbances.

Pathogenesis of re-feeding syndrome

Starvation causes adaptive reductions in cellular activity and organ function, accompanied by electrolyte and micronutrient depletion. Insulin levels fall and glucagon levels rise, resulting in a switch from carbohydrate to protein / fat metabolism.

Re-feeding (whether by oral, enteral or parenteral route) triggers a switch from fat to carbohydrate metabolism, with consequent insulin release, and increased uptake of phosphate, potassium, magnesium and water into cells. This results in the biochemical abnormalities and clinical features listed above.

Prevention

Re-feeding syndrome can be prevented by:

1) Identification of patients at risk of re-feeding syndrome:
    a. Assess patients for risk (page 2)
    b. Patients at risk should be discussed with a senior member of the parent medical/surgical team (registrar, or above)
    c. If appropriate, consider referral to dietitian

2) Careful management with medical, dietetic & pharmacist input, to include:
    a. Immediate vitamin supplementation (page 3)
    b. An appropriate re-feeding regimen (page 3)
    c. Electrolyte monitoring & management (page 4)

Identification of those at risk

Assess risk

- Complete **MUST screening tool**
- Baseline biochemistry, including:
  - urea & electrolytes *and* glucose
  - magnesium, phosphate & calcium / albumin levels

Patients at "high risk" may fit either:

Any **one** of the following	Any **two** of the following
• BMI <16 kg/m^2 • Weight loss >15% over 3-6 months • Poor intake for 10+ days • Low potassium, magnesium or phosphate prior to feeding	• BMI <18 kg/m^2 • Weight loss >10% over 3-6 months • Poor intake for 5-9 days • History of alcohol excess, insulin, chemotherapy, antacids or diuretics

Potential pitfalls

Note that the following patients **may still be at risk** of re-feeding syndrome:

- Patients with reference range levels of potassium, magnesium & phosphate prior to re-feeding
- Patients with reference range, or elevated BMIs
- Patients who are re-fed orally. Although starvation usually causes reduced appetite, **re-feeding syndrome can occur in patients fed orally, enterally or parenterally.**

Alert parent medical team - is nutritional support appropriate?

- Patients deemed to be at "high risk" of re-feeding syndrome require a cautious reintroduction of nutritional support (see next page)
- Such patients should be brought to the attention of a ***senior*** member (registrar, or above) of the parent medical / surgical team
- **Eating disorders**: assessment & management can be complex. Seek advice from psychological medicine **early** in an admission. Refer to MARSIPAN guidelines.

NO → Continue to monitor patient as per MUST

YES

Refer to Dietitian

Determine the most suitable feeding routes(s)

viable GI tract & SALT Assessment

feeding by GI tract not possible

Oral
(safe swallow)
consider supplementary NG feeding if necessary

Enteral nutrition
(unsafe swallow)
Consider nasogastric (NG) feeding

Parenteral nutrition
arrange appropriate venous access

Commence nutrition and re-feeding management

If a decision is made to initiate enteral / parenteral re-feeding, dietetic advice should be sought. If such advice is not immediately available (e.g. out-of-hours), this guideline details *provisional* re-feeding regimens

Management of patients at risk of re-feeding syndrome

All patients at risk of re-feeding syndrome should receive:

- Immediate replacement of thiamine – *before re-feeding, or IV dextrose*
- An appropriate initial re-feeding regimen which will vary depending on:
  - Patient weight (dry weight – marked oedema can be misleading)
  - Route of feeding: oral, enteral or parenteral
- Restoration of circulatory volume & electrolytes – followed by regular monitoring of both electrolytes and fluid balance status

Note – Initiation of feeding should **not** be delayed until electrolyte and fluid replacement have been achieved. Instead both should be started in tandem.

Replace vitamins

Start 10-day course of:

- Thiamine 100 mg, oral, three-times daily
- Forceval 1 capsule, oral, once daily
  OR
- Pabrinex 1 pair, IV, once daily
  OR
- Alcohol withdrawal: Pabrinex 2 pairs IV, for first 3 days*

*Management of Alcohol Withdrawal – Local Guidelines

Start nutrition

- In the absence of dietetic advice (i.e. out-of-hours):
  Consider an initial re-feeding rate of:
  - **10 kcal/kg/day** (~30% of total energy requirements)
  - **Seek dietetic input** thereafter

  For extreme cases (BMI <14, negligible intake >15 days), consider:
  - initial re-feeding at **5 kcal/kg/day**
  - continuous cardiac monitoring
- Increase nutrition slowly to meet full requirements by 4-7 days:
  - Any increase in feed should be dependent on trends in biochemistry
  - The more rapidly calories are delivered, the greater the risk of re-feeding syndrome
  - See re-feeding regimens (pages 5-8)

Replace & monitor electrolytes

- Potassium, magnesium & phosphate supplementation from the outset – unless levels are already high
- For guidance on electrolyte replacement, see page 4
- Check U&Es, magnesium, calcium, glucose & phosphate daily until stable (may take 7-10 days), 1-2 x weekly thereafter
- **Bedside glucose (BMs) 2 – 3x daily**. Consider referral to **diabetes team** if ≥2 glucose levels >10 mmol/L

Restore circulatory volume

Closely monitor fluid balance. Re-feeding tends to cause sodium & water retention so:

- Keep fluid input low but sufficient to maintain renal function
- Restrict sodium replacement
- Maintain a fluid balance chart

Beware of **very malnourished, dehydrated** patients with **renal impairment**:

- They may have initially **reference range or high potassium and phosphate levels** which can change in hours to very low levels due to the combined effects of dehydration and re-feeding
- It is **easy to overlook significant renal impairment in patients with very low BMI and recent starvation** who have very low creatinine and urea production, and may therefore have only modestly raised plasma creatinine and urea levels.

Potassium, phosphate & magnesium replacement

- Patients at risk of re-feeding syndrome may have total body deficits of these electrolytes despite initial reference range blood test results. Hence national guidelines recommend potassium, magnesium and phosphate supplementation from the outset of re-feeding, even if results are within the reference range.
- **However over-zealous replacement of these electrolytes (particularly potassium) is dangerous** – especially in **renal impairment**. It is therefore important to:
    - Monitor electrolytes daily
    - Consider ***total*** electrolyte replacement from all sources, including:
        - prescribed medicines
        - IV fluids
        - nutritional support
    - *Seek advice from a senior member of your surgical / medical team (registrar or above) if there is any doubt regarding appropriate replacement*

Potassium level	Replacement over 24 hr*
2.5 – 3.5 mmol/L	2 tablets Sando-K (12 mmol per tablet), three times a day OR 0.18% sodium chloride, 4% glucose, 0.3% potassium 500 mL (20 mmol potassium) at 50 – 80 mL/hr
<2.5 mmol/L	0.18% sodium chloride, 4% glucose, 0.3% potassium 1 L (40 mmol potassium) at max. 100 mL/hr

***Seek senior advice in patients with eGFR < 30 mL/min**

Phosphate level	Replacement over 24 hr*
0.3 – 0.5 mmol/L	1 tablet Phosphate-Sandoz (16 mmol per tablet), twice daily OR Phosphate Polyfusor 100 mL (10 mmol phosphate) at 10 mL/hr (discard remaining solution in bag)
<0.3 mmol/L	Phosphate Polyfusor 250 mL (25 mmol phosphate) at 25 mL/hr (discard remaining solution in bag)

***Seek senior advice in patients with eGFR < 30 mL/min, or if hypercalcaemia.** (500 mL of Polyfusor contains: phosphate 50 mmol, potassium 9.5 mmol, sodium 81 mmol.)

Magnesium level	Replacement over 24 hr*
0.4 – 0.7 mmol/L	1 sachet Magnesium Aspartate (10 mmol per sachet) twice daily
<0.4 mmol/L	20 mmol magnesium sulphate in 500 mL 5% dextrose, at 50 – 80 mL/hr

***Seek senior advice in patients with eGFR < 30 mL/min, or where heart block suspected.** (Oral replacement is frequently not tolerated therefore consider starting at 1 sachet daily, or if necessary using IV replacement.)

Oral nutrition for patients at high risk of re-feeding syndrome

Vitamin replacement – prescribe for 10 days

- Thiamine 100mg, oral, three times daily
- Forceval 1 capsule, oral, once daily

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Encourage oral intake

Do not commence oral nutritional supplements (ONS) unless advised by a dietitian

Patients on polymeric diet – limit to 1 x 220ml ONS*/day until review by dietitian (provides 330kcal, 13.8g of protein)
*oral nutritional supplement eg. Ensure Plus or Fortisip

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Monitoring & electrolyte replacement

- **Monitor daily** until stable: U&Es, magnesium, calcium, phosphate & glucose
- **Replace electrolytes** (see page 4)
- **Closely monitor fluid balance** – aim to keep fluid input low but sufficient to maintain renal function. (Consider fluid-balance chart and daily review.)

Enteral nutrition for patients at high risk of re-feeding syndrome

Vitamin replacement – prescribe for 10 days

Able to swallow tablets

- Thiamine 100mg, oral, three times daily
- Forceval 1 capsule, oral, once daily
  (Consider soluble preparation)

Enteral administration

- Contact pharmacy for advice

Not able to swallow tablets

- Pabrinex 1 pair, IV, once daily

OR

- Alcohol withdrawal 2 pair, IV, once daily for the first 3 days

*Management of Alcohol Withdrawal – Local Guidelines

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Continuous enteral feeding

Give 50 mL water
before & after each feed

Day 1
Nutrison 1.0 at 35 ml/hour for 10 hours
Day 2
Nutrison 1.0 at 50 ml/hour for 10 hours

OR

Bolus Feeding

Feed during the day,
give 50 ml water before & after feed

Day 1
Ensure Plus (or Fortisip) 110 ml x 2
Day 2
Ensure Plus (or Fortisip) 220 ml x 2

Maintain until review by a dietitian

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Monitoring & electrolyte replacement

- **Monitor daily** until stable: U&Es, magnesium, calcium, phosphate & glucose
- **Bedside blood glucose monitoring** – consider once to twice daily monitoring
- **Replace electrolytes** (see page 4)
- **Closely monitor fluid balance** – aim to keep fluid input low but sufficient to maintain renal function. (Consider a fluid balance chart and daily review.)

Parenteral nutrition for patients at high risk of re-feeding syndrome

Vitamin replacement – prescribe for 10 days

IV Pabrinex
- one pair daily*
- 30 min prior to initiation of feed

(* For alcohol withdrawal: 2 pairs for the first 3 days. See Management of Alcohol Withdrawal – Local Guidelines.)

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N.B. If you are unsure, or inexperienced, in prescribing parenteral nutrition (PN) – contact your Registrar or Consultant.

Inappropriate administration of PN to any patient (but particularly those at risk of re-feeding syndrome) is dangerous.

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Parenteral feeding

Refer to dietetics for nutritional assessment

Typical re-feeding regimen:

Day 1: 30% of requirements

Day 2: 50% of requirements

Patients should not normally be started on parenteral feeding without dietetic involvement. If feeding is commenced out of hours**, ensure referral is made when dietetic support becomes available**

In the absence of dietetic advice or specialist pharmacist advice:
- Contact Pharmacy to inform them of the decision to commence Parenteral feeding
- Consider **a maximum of 400 kcal** (use total kcal, **not** non-protein kcal) over first 24 hours until specialist advice is obtained
  ** If patient is less than 40kg then do not start feeding until reviewed by a Dietitian or Specialist Pharmacist**

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Monitoring & electrolyte replacement

- **Monitor biochemistry** daily until stable (1-2x weekly thereafter): U&Es, magnesium, calcium, phosphate & glucose
- **Bedside blood glucose** monitoring 2 – 3 times daily
- **Replace electrolytes** (see page 4)
- **Closely monitor fluid balance** – aim to keep fluid input low but sufficient to maintain renal function. Keep a fluid balance chart.

References / further reading

1. British Association for Parenteral and Enteral Nutrition (2003). Malnutrition Universal Screening Tool: 'MUST', Redditch: BAPEN. (Available on the NHS Lothian intranet: MUST)

2. National Institute for Health and Clinical Excellence (2006). Nutrition support in adults Oral nutrition support, enteral tube feeding and parenteral nutrition, NICE guideline (CG32).

3. British Association for Parenteral and Enteral Nutrition (2012). Refeeding syndrome: Identification of those at risk – Decision Tree, Redditch: BAPEN.

4. NHS Lothian (2015) Guidelines for Basic IV Fluid & Electrolyte Prescription in Adults.

5. NHS Lothian (2011) Management of Alcohol Withdrawal.

7. NHS Lothian (2015) Administration of Parenteral Nutrition Interim Guidelines

8. The Royal Colleges of Psychiatrists, Physicians and Pathologists (2014). MARSIPAN: Management of Really Sick Patients with Anorexia Nervosa, London: RCPsych.

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