Re-feeding Syndrome Guideline

**What is re-feeding?**

Re-feeding syndrome is a description of the fluid and electrolyte shifts from the extracellular to intracellular compartments that take place in malnourished patients undergoing refeeding.

During starvation, insulin concentrations are low as liver stores of glycogen are mobilized. The glycogen is rapidly converted into glucose and gluconeogenesis activated, resulting in protein and lipid breakdown. Free fatty acids and ketones become the major source of energy. When feeding is recommenced there is a switch back to a carbohydrate based energy sources which results in insulin release. This stimulates cellular uptake of glucose, phosphate, potassium and water and anabolic protein synthesis. This process results in severe hypophosphataemia often accompanied by hypokalaemia and hypomagnesaemia. This can happen with both parenteral and enteral feeding.

**Patients at Risk**

- Alcoholic Liver Disease (ALD)
- Chronic Malnutrition (e.g. self neglect)
- Eating Disorders (e.g. Anorexia Nervosa)
- Prolonged Fasting (7-10 days + evidence of stress)
- Chronic Antacid Users (bind Minerals)
- Chronic Diuretic Users
- Oncology Patients on Chemotherapy
- Patients with Altered Insulin Requirements (watch diabetics)

**Clinical Consequences**

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<td>Respiratory</td>
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Updated from Wishaw General Hospital – Refeeding Syndrome Guidelines 2006
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### Hypokalaemia (Low K)

- **Cardiac**
  - Cardiac Arrhythmia
  - Cardiac Arrest

- **Neuromuscular**
  - Weakness, Paralysis,
  - Rhabdomyolysis

- **Renal**
  - Decreased Urinary Concentrating Ability
  - Polyuria and Polydipsia
  - Decreased GFR

- **GI**
  - Constipation, Ileus

- **Hepatic**
  - Exacerbation of hepatic encephalopathy

- **Respiratory**
  - Respiratory Depression

### Hypomagnesaemia (Low Mg)

- **Cardiac**
  - Tachycardia
  - Cardiac Arrhythmia

- **Neuromuscular**
  - Ataxia, Confusion, Muscle Tremors, Weakness, Tetany

- **GI**
  - Abdominal pain, Anorexia, Diarrhoea, Constipation

### Altered Glucose Metabolism

### Fluid Balance Abnormalities

### Vitamin Deficiency

### Assessment and management

- Recommend U&Es checked/corrected (especially K, Mg, PO₄)

- Gradually increase Kcal content. Give 5-10 Kcal/Kg for the first 24h. The Kabiven 5g parenteral feed which is available on the wards, contains 1000kcal in 1440ml. Therefore initially only part of bag may be required. Increase gradually within the first week to full feeding with careful monitoring of electrolytes (K, Mg, PO₄, Ca).

- For high risk patients starting enteral nutrition give thiamine 100mg 3 times a day and vitamin B compound strong 2 tablets 3 times a day orally or a pair of Pabrinex® ampoules intravenously once daily and multivitamin/trace element supplement (Forceval®) for first 10 days of feeding. For patients receiving TPN give a pair of Pabrinex® ampoules intravenously before feeding commences. Multivitamins and trace elements will be added to TPN daily by pharmacy.

- Monitor glucose especially in DM patients

- Monitor fluid balance carefully
Monitoring

• Take a **baseline** (Day 1) sample prior to starting any feeding regime – request U&E, LFT, Mg, PO₄, Ca, Glucose and CRP (to assess acute phase response)
• Commence enteral/ parenteral feeding
• Repeat U&E, LFT, Mg, PO₄, Ca, and Glucose on Days 2 and 3 – a significant reduction in phosphate should alert to the possibility of re-feeding syndrome.
• Check tolerance and observe patient
• Check temperature, stool, fluid balance and drug charts regularly
• Repeat U&E, LFT, Mg, PO₄, Ca, and Glucose at least twice weekly.
  **More frequent monitoring will be required in high-risk individuals; those who fail to stabilise biochemically or clinically and those displaying re-feeding.**

**Phosphate Replacement (normal dietary intake 25mmol/day)**

There have been no randomised controlled trials for the treatment of re-feeding syndrome, and the optimal regimen therefore remains to be determined. The amount of phosphate supplementation depends on the result, the anticipated requirement, the renal function. In renal failure, the use of haemofiltration, and if it is likely to be continuous, or stopped abruptly, are important.

**Severe (serum phosphate <0.3 mmol/L) - replace intravenously**

• Glycophos® solution (20 mL) is recommended; this contains
  - 20 mmol phosphate (1 mmol/mL)
  - 40 mmol sodium (2mmol/mL)
• 20 mL of Glycophos® (20 mmol phosphate) should be added to 500ml of sodium chloride 0.9% or glucose 5% and given over 12 hours. **If renal function poor i.e. <20mls/min, give 50% of this dose over 12hours.**
• If patient is fluid restricted, hypernatraemic or a faster rate of administration required, contact pharmacy.
• This regimen should not be given to individuals with hypercalcaemia because of the risk of metastatic calcification.

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• If after 12-24 hours the serum phosphate remains low (<0.64 mmol/l) or falls, further phosphate should be administered.

Moderate (serum phosphate 0.3 - 0.5 mmol/L)
• Phosphate-Sandoz® dispersible tablets can be given orally or via enteral tube for supplementation
• Each tablet contains 16 mmol phosphate, 3 mmol potassium, 20 mmol sodium
• Moderate asymptomatic hypophosphataemia can be managed with 1-2 tablets three times daily
• If patients are symptomatic or nil by mouth replace intravenously as above and recheck serum phosphate after 24 hours

Mild (serum phosphate 0.5 mmol/L - 0.69 mmol/L)
• No treatment required but recheck serum phosphate after 24 hours

Monitoring
Serum phosphate and calcium levels should be monitored every 12-24 hours during IV administration. Monitor renal function regularly.

Adverse effects
Oral: Diarrhoea is a common side effect and may necessitate a reduction in dose
IV: Hypotension, hyperphosphataemia, hypocalcaemia, hypernatraemia, dehydration, metastatic calcification

Magnesium replacement (normal dietary intake 15-20mmol/day)

Moderate- severe hypomagnesaemia (<0.3mmol/l) or symptomatic of hypomagnesaemia
Treat with intravenous magnesium - Magnesium Sulphate 50% (2mmol/ml)
• 10ml (20mmol) in 500ml sodium chloride 0.9% of glucose 5% over 12-24 hours
• Contact pharmacy if patient is fluid restricted, has renal impairment (eGFR <20ml/min) or a faster rate of administration is required.
• Check serum magnesium daily.
• Magnesium is mainly an intracellular ion and most of the magnesium administered intravenously will be excreted in the urine
• Infusion may require to be repeated for up to 5 days to replete deficit

_Mild hypomagnesaemia (0.3-0.7mmol/l) (Asymptomatic)_
• Magnesium Glycerophosphate (4mmol Mg per tablet) – 2 tablets TID for 2 weeks
• Use may be limited by diarrhoea – switch to intravenous regimen
• Check magnesium level daily

**Monitoring**
Serum magnesium levels should be monitored every 12-24 hours during IV administration. Monitor renal function regularly.

**Adverse effects**
Elderly patients and those with renal impairment are at risk of hypermagnesaemia. Treatment should be discontinued if the following signs appear
• Hypotension
• Bradycardia
• Respiratory depression
• ECG abnormalities
• Depressed mental state

**Potassium replacement** (Normal dietary intake 50-100mmol/day)

**Oral potassium supplementation**

1. For serum K⁺ 3.0 - 3.5 mmol/L (approximate potassium deficit 200 mmol):
   
   Sando-K® (12mmol/tab) 2 tablets 3 times daily  
   Or  
   Slow K® (8mmol/tab) 3tabs 3 times daily (risk of GI ulceration, avoid if GI motility poor)
2. Serum K⁺ 2.5 - 2.9 mmol/L and ECG normal (approximate potassium deficit 200 - 400 mmol):
   Sando-K® (12mmol/tab) 3 tablets 3 times daily

Note
- Monitor serum K⁺ daily until serum K⁺ > 2.9 mmol/L and then manage as above.
- Once serum K⁺ stable or if serum K⁺ > 4.5 mmol/L, reassess requirement for supplementation

3. Serum K⁺ < 2.5 mmol/L (approximate deficit > 400 mmol) or <3.5mmol/L with cardiac arrhythmia: *Intravenous supplementation is usually required.*
   - Intravenous potassium supplementation is indicated if patients cannot eat, are unlikely to absorb oral potassium or have profound hypokalaemia
   - Where possible, use pre-prepared infusion bags. These are available as:
     - 20 mmol KCl in 500 ml sodium chloride 0.9% or 5% glucose
     - 40 mmol KCl in 500ml sodium chloride 0.9% or 5% glucose
   - Sodium chloride 0.9% preferred as glucose increases insulin secretion and can lower serum K.
   - The rate of infusion should not normally exceed 10 mmol/hour
   - 10 ml ampoules of potassium chloride containing 20 mmol potassium per ampoule are only available in intensive care areas and should not be used in ward areas unless in exceptional circumstances and under close supervision. These must be ordered in the controlled drug requisition book.
   - If concentrations other than those mentioned above are required, contact your Clinical Pharmacist or Medicines Information for advice.

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