

Refeeding Syndrome: Guidelines

Cape Town Metropole Paediatric Interest Group

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Contents

0.	Paediatric Working Group Developers Summary	5
1.	Summary: Re-feeding Guidelines	6
1.1	Summary table of Recommendations for the Management of Refeeding Syndrome	7
2.	Aim of Guidelines	12
2.1	Objectives	12
3.	Introduction	12
4.	Anthropometry	13
5.	Biochemical	13
5.1	Potassium	13
5.2	Phosphorus	14
5.3	Oncotic Pressure	14
6.	Clinical	14
6.1	Patient Group Characteristics	15
6.2	Infection	15
6.3	Losses	15
7.	Dietary	15
7.1	Recommendations for nutrition intervention	15
7.2	Protein and Energy Intake	16
7.3	Replacement therapy in the depleted patient	16
7.4	Monitoring	19
7.5	Enteral, parenteral or oral nutrition support	17
7.6	Initial refeeding	17
7.8	Rehabilitation Phase	17
7.9	Protein	17
7.10	Carbohydrate	18
7.11	Fat	18
7.12	Electrolyte and vitamin supplementation	18
7.13	General	19
8.	Summary	19
9.	Appendix 1: Dietary reference values energy and protein, Schofield equation and Fluid requirements	20
10.	References	22

0. Paediatric Working Group Guidelines: Developers Summary

Scope and Purpose

The Guidelines for Refeeding Syndrome have been developed by the Western Cape Paediatric Nutrition Working Group in response to the need for evidence-based guidelines with respect to the nutrition management of this condition.

The aim of this Guideline is to provide an evidence based nutrition management resource tool, which may be used by health professionals involved in the prescription and supply of nutrition support to infants or children with refeeding syndrome.

This Guideline uses an “A, B, C, D” approach e.g. Anthropometry, Biochemistry, Clinical and Dietary, to provide a step by step reference as to how to approach nutrition support.

These guidelines outline nutrition support in children with refeeding syndrome from the ages of 0 – 18 years of age. They are not meant to be prescriptive and there may be individual case variations.

Stakeholder Involvement

Members of the Paediatric Working Group are outlined in table 1:

Table 1: Paediatric Working Group Members and Reviewers

	Principal Author	Affiliations
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Rigour of Development

A Pubmed search was completed using key words such as refeeding syndrome. Table 1 was used to define the type of articles desired. Sixteen articles were identified using the key words. The review include papers graded as being 13 grade 2 and 3 grade 1 levels of evidence.

Grading of levels of evidence (LOE) according to the Scottish Intercollegiate Guideline Network (SIGN) 2000

Grading	Level of evidence
1+++	High quality meta analyses, systematic reviews of RCT's or RCT's with very low risk of bias
1+	Well conducted meta analyses, systematic review of RCT's or RCT's with low risk of bias
1-	Meta analyses, systematic reviews of RCT's or RCT's with a high risk of bias
2++	High quality systematic reviews of case controlled or cohort studies
2+	Well conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal
3	Non-analytical studies e.g. case reports, case series. Evidence from non analytical studies e.g. case reports, case series
4	Evidence from expert opinion

The principle author was responsible for compiling the refeeding guideline, which was circulated amongst members of the working group in addition some of the ad hoc members.

All guidelines went through a process of first to third drafts. The recommendations within the guidelines were drafted following a review of the literature and discussions within the group.

All benefits and potential harm of the nutrition recommendations within the guidelines have been discussed and reviewed by the panel at length. The recommendations provided within the text and summary tables are referenced and evidence based.

This guideline has been reviewed by pharmacists who are considered to be experts in their field. Comments received have been incorporated into the clinical guidelines.

This guideline will be reviewed in 2009 and updated accordingly.

Clarity and Presentation

The format of this clinical guideline aims to direct the health professional through a logical Nutrition Care Plan approach using A, B, C, D e.g. Anthropometry, Biochemistry, Clinical and Dietary using a series of summary tables, which can be used as a quick reference abridged version for the key recommendations. In addition to these tables the full text may be consulted as required.

A variety of management options have been present targeting clients within the Public and Private Health Care sector. The guideline provides a stratified management approach and identifies current nutrition support systems through which they could be implemented.

Applicability

The working group did not perceive any potential barriers as all nutrition support strategies are currently available within Public and Private Health Care centres and are available on national tenders. All cost implications have been considered and the most cost effective nutrition management strategies have been recommended.

Within the Nutrition Care Plan Summary Tables appropriate review processes have been identified. In addition all tools are presented with an audit process.

Editorial Independence

The principal author, working group and or reviewers did not receive any funding to complete these guidelines and no conflicts of interest are recorded by the team.

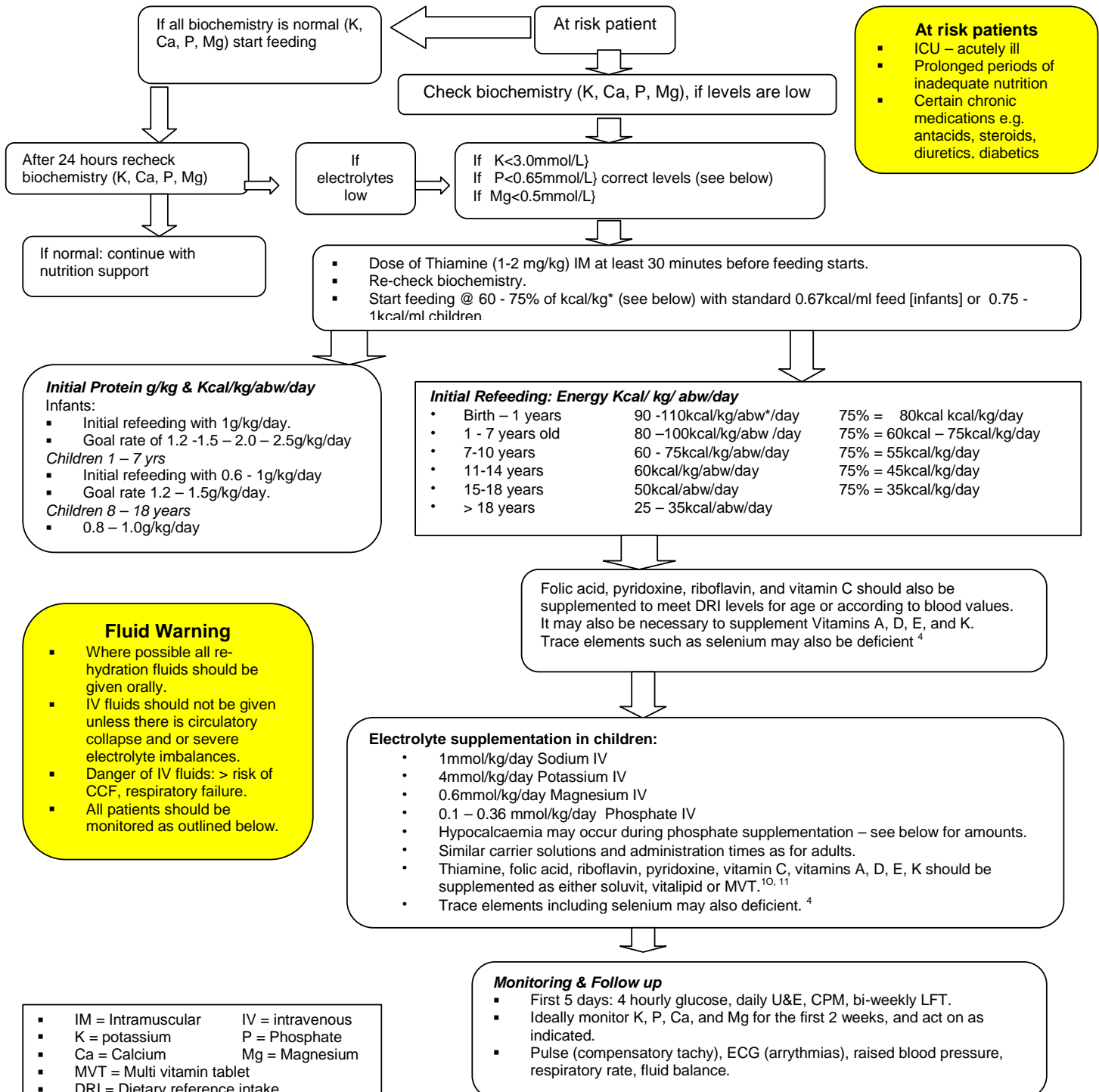
1. Summary: Re-feeding Guidelines ^{4, 7, 12, 18, 19}

Refeeding Syndrome can be defined as:

- Severe fluid and electrolyte shifts and related metabolic implications in malnourished patients undergoing refeeding (via the enteral or parenteral route).

The signs are:

- Hypophosphataemia, hypokalaemia, hypomagnesaemia, altered glucose metabolism, fluid balance abnormalities and vitamin deficiency especially thiamine.



1.1 Summary table of Recommendations for the Management of Refeeding Syndrome

Summary of Recommendations for the Management of Refeeding Syndrome ^{4, 5, 6 7,9,18,19}	
Recommendation	Comment
Overview	
<ul style="list-style-type: none"> It is important that fluid and electrolyte imbalances are corrected prior to commencing enteral or parenteral nutrition. Intravenous replacement is most efficacious as a slow infusion over 6 – 12 hours. Oral replacement of electrolytes such as magnesium, phosphorous and potassium may cause diarrhoea and is poorly absorbed. If levels are abnormally low administer replacement treatment prior to commencing nutrition support including thiamine. Once replacement therapy is complete re-check levels again. Replacement treatment should be given each time electrolyte levels are found to be abnormal. Replacement therapy requires the clinical judgement of the doctor and pharmacist on an individual patient basis. 	
Anthropometry^{4, 5, 6 7,9,18, 19}	
<ul style="list-style-type: none"> A complete anthropometrical review should be completed including. Severe malnutrition can be diagnosed when there is: <p><i>Daily weights</i></p> <ul style="list-style-type: none"> First 3 – 5 days post refeeding: 	<ul style="list-style-type: none"> Weight (wt) Height (ht) Head circumference (HC) < 3 years of age Mid upper arm circumference Weight , height and HC should be plotted on an age appropriate growth chart. < 5th or 3rd centile [with downward crossing of centiles or growth failure] Or < 60% expected weight for age (EWA) Or <-2 – 3 SD wt-for-age, wt-for-ht Or downward crossing of 2 or more centiles. Initial weight gain may be reflective of oedema and fluid retention and potential congestive cardiac failure and not an improvement in nutritional status.

Biochemistry ^{4, 5, 6 7,9,10, 11,18, 19}	
Recommended biochemistry monitoring, baseline and daily for first 5 days of refeeding.	<ul style="list-style-type: none"> Daily urea and electrolytes (U & E's) [sodium, potassium, urea, creatinine] Daily magnesium (Mg), phosphate (PO₄), calcium (Ca) Baseline & bi-weekly liver function tests (LFT's) [Albumin] Daily Glucose
<ul style="list-style-type: none"> Low phosphorous (serum <0.65mmol/l) 	<ol style="list-style-type: none"> If serum phosphate is <0.65mmol/l this is severe and requires correcting with intravenous phosphate [<i>Monobasic/ Dibasic Potassium Phosphate – expressed as phosphate</i>]. Physiological saline (0.9%) or half strength saline (if hypernatraemia is a problem) or 5% dextrose may be used as the carrier solution. Administer: 0.1 – 0.36mmol/kg/day up to 1.5mmol/kg/day Phosphate IV [Max 70mmol/day] 1ml Potassium Phosphate contains 1.4mmols phosphate & 2mmol potassium IV over 12 hours if the phosphate is < 0.65mmol. Infusions can be repeated every 12 hours with 12 hourly monitoring of plasma calcium, potassium and phosphate. Phosphate replacement can be stopped when plasma phosphate has risen by 0.32mmol/l to 0.9mmol/l in order to minimise risk of hypocalcaemia. (<i>NOTE: IV phosphate should not be given to hypercalcaemic patients</i>) Do not mix with calcium containing fluids. Shake bag well. Monitor urine output. Oral phosphate e.g. Joules solution may result in diarrhoea.
<ul style="list-style-type: none"> Low magnesium (<0.5mmol/l) 	<ol style="list-style-type: none"> Administer: 0.6mmol/kg/day Magnesium Sulphate (IV) [Dose expressed as Magnesium] IV 0.2 – 0.4 mmol/kg/12 hourly Magnesium sulphate (Mg SO₄) comes as 1ml = 0.5g or 2mmol. Oral magnesium is poorly absorbed due to GI side effects of large doses. Refractory hypokalaemia may occur during the treatment of hypomagnesaemia. Plasma Calcium should also be checked. NB: <i>Separate IV lines must be used for the administration of Magnesium and Phosphorus. The two electrolytes are incompatible and will precipitate out of the solution.</i>
<ul style="list-style-type: none"> Low potassium (<3.0mmol/l) 	<ol style="list-style-type: none"> Administer: Potassium 0.3mmol/kg/hr (max 0.4mmol/kg/hr) for 4 – 6 hours, then 2-4mmol/kg/day. Maintenance 2 – 4 mmol/kg/day. If peripheral IV: max 0.5mmol/kg. Potassium Chloride solution: 2mmol = 1 ml Monitor ECG for arrhythmias during replacement therapy.
<ul style="list-style-type: none"> Low Calcium (<1.75mmol/l :pre-term infant, <1.9mmol/l: term infant, <2mmol/l: older children & adults) 	<ol style="list-style-type: none"> Most mild hypocalcaemia may be managed without IV supplementation. Oral replacement = 400mg bd. <i>Children:</i> If IV Calcium is required (Ca Gluconate or Ca Chloride) administered as a diluted solution of either normal saline or 5% dextrose e.g. 10% Ca Gluconate diluted to 2% solution. For serious hypocalcaemia (convulsions/ arrhythmias) give Ca Chloride at 0.1 – 0.2mmol/kg/hr (10 – 20mg) of a 10% solution/kg/dose, 4 – 6hourly as required. For less severe cases (muscle cramps, parasthesia) give Ca Chloride at 0.05mmol/kg/hr. 10mmol of 10% Ca gluconate contains 0.23mmol Ca/ ml. Calcium gluconate 10% solution provide 200 – 500mg or 2 – 5ml/kg/day 6 hourly. Reduce infusion rate once desired level has been reached. All patients receiving IV Ca should be on a cardiac monitor. <i>Monitor IV site:</i> high risk of extravasation burns and venous thrombosis. Addition of 0.1mmol heparin, 1000U/ml, to each 10ml of Ca gluconate reduces the risk of thrombosis. Do not administer Calcium and NaHCO₃ in same IV tubing. Never give Ca intramuscularly (IM) or sub cutaneously (SC).
<ul style="list-style-type: none"> Thiamine 	<ol style="list-style-type: none"> Administer: (1-2mg/kg) IM. 1ml (equivalent to 100mg thiamine) should be administered in 50-100ml 5% dextrose over 30 minutes. This should be administered prior to refeeding as a stat dose. This should be repeated daily for 48 hours or until oral thiamine can be administered. Thiamine should be given weekly thereafter. Repeated injections or large doses (>400mg in adults) have been associated with anaphylaxis. Facilities for treating anaphylaxis should be available.
<ul style="list-style-type: none"> Other Vitamins 	<ol style="list-style-type: none"> Vitamin B complex (IV) if oral route is unavailable and a multivitamin with trace elements should be prescribed for daily intake.

<ul style="list-style-type: none"> • Monitoring 	<ul style="list-style-type: none"> • All patients receiving magnesium, phosphorus, calcium and potassium will require close monitoring for changes in clinical condition. • All of the above may cause possible respiratory, muscular and cardiac changes. • Appropriate monitoring will be required for all patients even after the initial phase of refeeding is completed.
<p>Supplements available IV & Oral:</p> <ul style="list-style-type: none"> • Phosphate IV [Potassium phosphate] • Potassium prep IV • Potassium prep - oral • Phosphorus oral prep • Magnesium sulphate IV prep • Magnesium oral prep • Calcium prep oral • Calcium prep IV 	<ul style="list-style-type: none"> • Monobasic Dibasic Potassium Phosphate • Potassium Chloride or Monobasic Dibasic Potassium Phosphate • Slow K ® or Plenish K ® Paeds: Pot Chloride 500mg/5ml • Phosphate sandoz • Generic • Slow mag • Calcium gluconate or Calcium Sandoz • Calcium chloride or Calcium gluconate (both are generics)

Clinical^{4, 5, 6 7,9,18, 19}

<p><i>Refeeding syndrome is likely to occur in patients who have had:</i></p>	<ul style="list-style-type: none"> • Prolonged periods of sub optimal nutrition intake over days or weeks prior to hospital admission, • Experienced significant weight loss prior to hospital admission in both the obese or underweight patient, • Experienced significant diarrhoea or vomiting in the week leading up to institution of nutrition support, • Prolonged period of nil by mouth for > 7-10 days, or poor nutrition intake during hospital stay with evidence of stress and depletion, • Hyperglycaemia/ insulin requirements, diabetic patients, • Chronic antacid users – these bind minerals, therefore levels may be low, • Chronic diuretic users, • Oncology or chemotherapy patients, • Chronic alcoholics [adolescents], • Anorexia nervosa, • Classic severe malnutrition with or without oedema, • Some critically ill patients, • Some acutely ill patients.
<p><i>Cardiac Status should be monitored by completing the following measurements:</i></p>	<ul style="list-style-type: none"> • Pulse (compensatory tachycardia) • ECG daily (arrhythmia) • Raised blood pressure • Increased respiratory rate • Fluid balance • Electrolyte status.

Dietary ^{4, 5, 6 7,9,18,19}			
Energy			
Comment	Age Group	Initial Refeeding [7 – 10 days] [60 – 75% of recommended daily intake (DRV)] Appendix 1	Rehabilitation Phase [> 10 days] [For “catch up” growth 1.2 – 1.5 x DRV]
<ul style="list-style-type: none">Provision of calories should be done gradually during first 5 – 7 days.*Start with 60 -75% of abw/kcal/kg as outlined above for the first 24hrs, then increase gradually within the first week to full feeding, with careful monitoring and replenishing of electrolytes as required.	<ul style="list-style-type: none">Birth – 1 years	<ul style="list-style-type: none">80kcal kcal/kg/day	<ul style="list-style-type: none">90 -110kcal/kg/abw*/day
	<ul style="list-style-type: none">1 - 7 years old	<ul style="list-style-type: none">60kcal – 75kcal/kg/day	<ul style="list-style-type: none">80 –100kcal/kg/abw* /day
	<ul style="list-style-type: none">7-10 years	<ul style="list-style-type: none">55kcal/kg/day	<ul style="list-style-type: none">60 - 75kcal/kg/abw*/day
	<ul style="list-style-type: none">11-14 years	<ul style="list-style-type: none">45kcal/kg/day	<ul style="list-style-type: none">60 kcal/kg/abw*/day
	<ul style="list-style-type: none">15-18 years	<ul style="list-style-type: none">35kcal/kg/day	<ul style="list-style-type: none">50 kcal/abw*/day
	<ul style="list-style-type: none">> 18 years	<ul style="list-style-type: none">20 – 25kcal//kg/day	<ul style="list-style-type: none">25-35 kcal/abw*/day
	Energy to macro & micronutrient ratio <i>For every: 200 – 250kcal it is necessary to provide to ensure protein sparing and sufficient micronutrients for growth:</i> <ul style="list-style-type: none">6.25g protein1.8 mmol calcium2.9 mmol phosphorus1.0 mmol magnesium10 mmol potassium7 mmol sodium and chloride1.2mg Zinc		
Protein			
Infants:ABW <i>High biological value protein</i>	<ul style="list-style-type: none">0 – 12 months	<ul style="list-style-type: none">0.5 - 1g/kg/dayMonitor for signs of acidosis & uraemia.	<ul style="list-style-type: none">1.2 -1.5 – 2.0 – 2.5g/kg/dayA minimum of 7 – 9% of total energy is required for anabolism to occur.
Children: ABW <i>High biological value protein</i>	<ul style="list-style-type: none">1 – 7 years	<ul style="list-style-type: none">0.6 – 1g/kg/dayMonitor for signs of acidosis, hypernatraemia, azotaemia and hypertonic dehydration & uraemia.	<ul style="list-style-type: none">1,2 – 1.5g/kg/dayA minimum of 7 – 9% of total energy is required for anabolism to occur.
	<ul style="list-style-type: none">8 – 18 years	<ul style="list-style-type: none">0.6 – 1g/kg/dayMonitor for signs of acidosis, hypernatraemia, azotaemia and hypertonic dehydration & uraemia.	<ul style="list-style-type: none">0.8 – 1g/kg/dayRequired for anabolism to occur.
Fluid:[Appendix 1] <ul style="list-style-type: none">	<ul style="list-style-type: none">Infants: 130ml/kg/day [100ml/kg/day if the child has severe oedema]Children: 100ml/kg/day [80ml/kg/day if the child has severe oedema]Oral route should be used where possible.IV for circulatory collapse and replacement of severe electrolyte depletion.If lower volumes of feeds are required in order to not exceed protein recommendations, the remainder of feeds should be given as maintenance fluid e.g. Sorol		
General: <ul style="list-style-type: none">Dilution of feeds is not recommended.Ready to use or hang feeds should be given where possible.	Infants <ul style="list-style-type: none">A lactose containing milk should be given where possible and only in the event of severe diarrhoea should a lactose and sucrose free alternative be considered. Children <ul style="list-style-type: none">Lactose and sucrose free feed should be considered if milk based feeds induce diarrhoea with positive faecal reducing substances.		

Refeeding Syndrome

2. Aim

The aim of these guidelines is to outline appropriate nutrition care practices for the management of children with refeeding syndrome.

Nutrition management usually aims to maintain haemodynamic stability, manage electrolyte abnormalities as they occur and improve nutrition status where appropriate.¹

2.1 Objectives

The objectives of these guidelines are to:

- Provide appropriate management strategies for the provision of calories, protein and electrolyte replacement in the refeeding phase.

3. Introduction

Definition

Refeeding syndrome can be defined as severe fluid and electrolyte imbalances (especially, but not exclusively, of phosphate) with metabolic abnormalities in malnourished patients receiving enteral, parenteral or oral feeds.^{1, 19}

During starvation there is a change in the hormonal milieu in addition to a reduction in basal metabolic rate, conservation of protein, prolongation of organ function, preferential catabolism of skeletal muscle and loss of visceral cell mass.¹⁸

The concentration of insulin is decreased whilst glucagons increases resulting in the conversions of glycogen to glucose in addition to gluconeogenesis from lipid and protein stores. Free fatty acids and ketone bodies replace glucose as the primary sources of energy.¹⁹

As feeds (parenteral or enteral) are initiated in a starving child the protective mechanisms starvation (ketosis) are disrupted.¹⁸ There is a rapid shift from fat metabolism (ketosis) to the utilization of carbohydrate. Excess glucose evokes a release of insulin, which acts as a driving mechanism causing an increased uptake of glucose, phosphate, potassium, magnesium, water into the cell in addition to stimulating protein synthesis. This often results in a precipitous drop in serum electrolytes and fluid shifts¹⁹

Fluid shifts may result in congestive cardiac failure, dehydration or overload, hypotension, pre-renal failure and sudden death. Carbohydrate can result in the retention of sodium and water.

The complications arising from this can be life threatening, so judicious use of protein and calories is advised.¹⁸

Refeeding syndrome can also be defined as a decrease in phosphate to levels below 0.65mmol/l. Severe hypophosphataemia has been reported to occur in 0.8% of all hospitalized patients, but is not exclusively seen in the malnourished patient and may occur in the acutely ill patient and or in those receiving some medications e.g.

antacids, glucocorticoids etc.^{2,3} Hypokalaemia, hypomagnesaemia, altered glucose metabolism and vitamin deficiencies may also be seen. This may lead to cardiac, respiratory, neuromuscular, renal, haematological, hepatic and gastrointestinal problems.

Some patients appear to be more pre-disposed to refeeding syndrome than others. Refeeding syndrome can occur in some patients after only 48 hours of starvation.⁴

4. Anthropometry

A complete anthropometrical review should be completed including:

- Weight (wt)
- Height (ht)
- Head circumference (HC) < 3 years of age
- Mid upper arm circumference

Weight, height and HC should be plotted on an age appropriate growth chart. Expected Wt-for-age, Ht-for-age, Wt-for-Ht and HC-for age should be plotted. Severe malnutrition can be diagnosed when there is:

- < 5th or 3rd centile [with downward crossing of centiles or growth failure]
- Or < 60% expected weight for age (EWA)
- Or < -2 – 3 SD wt-for-age and or wt-for-ht
- Or downward crossing of 2 or more centiles.^{4, 8}

In the first 3 – 5 days post refeeding daily weight should be annotated in the medical notes, as an increase in weight gain is unlikely to be a positive improvement in nutrition status. Weight loss or maintenance should be aimed for during the first 2 – 3 days post refeeding.¹⁸

Daily weights

Initial weight gain may be reflective of oedema and fluid retention and potential congestive cardiac failure and **not** an improvement in nutritional status.⁵

5. Biochemical

Patients with refeeding syndrome often suffer precipitous drops in certain electrolytes increasing the risk of respiratory and cardiac arrest/ failure. Serum levels of calcium, magnesium and phosphorus are often normal prior to refeeding but precipitously drop as feeds are commenced. Serum levels in the high risk patients should be reviewed at least daily if not more often in severe cases.

5.1 Potassium

Potassium should be corrected progressively through a slowly administered, (over 6 – 12 hours), intravenous (IV) solution whilst monitoring renal and cardiac function. Rapid correction is dangerous where the fixing capacity of potassium remains low as a result of low glucose intake, reduced muscle mass and protein synthesis. During the early stages of refeeding excess potassium may result in hyperkalaemia and cardiac arrhythmias.^{18,19}

5.2 Phosphorus

Phosphorus depletion should also be corrected slowly intravenously over a period of 6 – 12 hours with concomitant monitoring of neurological and renal function. It is recommended that at least 0.5mmol/kg be administered per day. Phosphate should be increased proportionally to any increases in the total protein and energy intakes up to an amount of 1.0mmol/kg. Blood and urea should be monitored daily for signs of toxicity e.g. hyperphosphataemia and phosphaturia.^{18,191}

Recommended biochemistry monitoring to be done at baseline and daily for the first 5 days of refeeding:

- Daily urea and electrolytes (U & E's) [sodium, potassium, urea, creatinine]
- Daily magnesium (Mg), phosphate (PO₄), calcium (Ca)
- Baseline and bi-weekly liver function tests (LFT's) [Albumin]
- 4 hourly Glucose for first week, daily thereafter.^{5, 6}

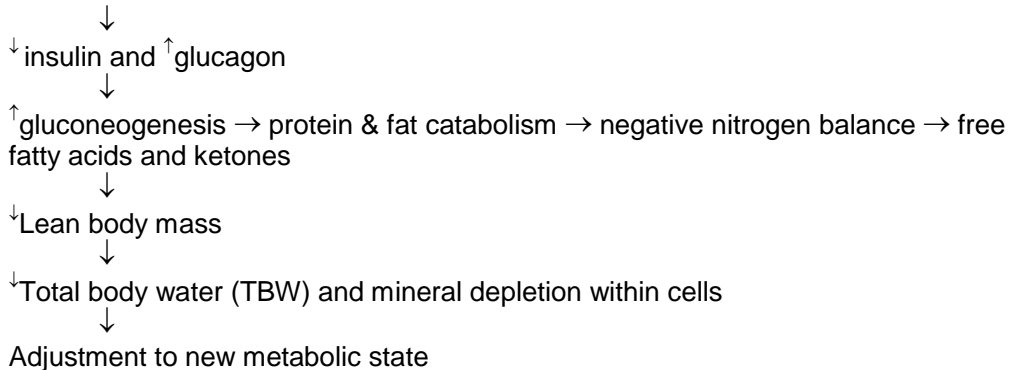
5.3 Oncotic Pressure

Oncotic pressure may be maintained by providing an infusion of macromolecules such as albumin (1g/kg at a slow infusion rate and if required twice per day, appropriate diuretic cover should be provided).¹⁸

6.Clinical

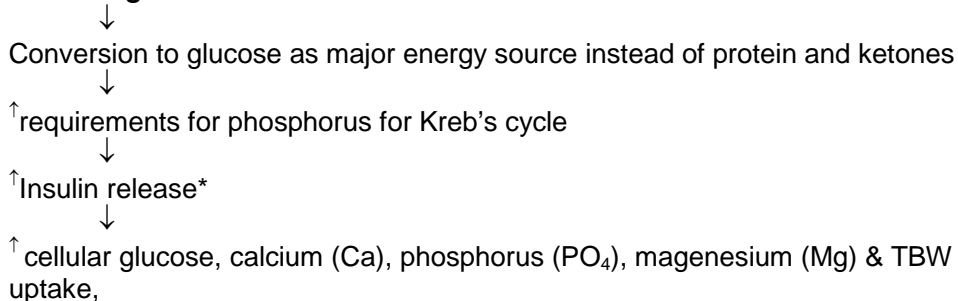
Pathogenesis of refeeding syndrome

Starvation



NB: Serum concentration of electrolytes may be normal due to adjustments in renal rate of excretion.

Refeeding



↑ protein synthesis and utilization of thiamine



Intracellular shifts of Ca, PO₄, Mg resulting in extracellular depletion of Ca, PO₄, Mg

*Insulin release stimulates the sodium potassium ATPase pump (which requires magnesium as a co-factor). This drives potassium into the cells and moves sodium out. Carbohydrate load and insulin release stimulate phosphate shifts into the cells and phosphate depletion is associated with increased urinary magnesium excretion. This leads to low extracellular phosphate, magnesium and potassium and may precipitate the symptoms of refeeding syndrome.

Thiamine is an essential coenzyme in carbohydrate metabolism. The symptoms of thiamine deficiency, e.g. Wernicke's encephalopathy, can be precipitated by feeding with carbohydrate in a vitamin B depleted patient.

Clinical symptoms include respiratory and cardiac failure.

6.1 Patient Group Characteristics

Refeeding syndrome is likely to occur in patients who have had:

- Prolonged periods of sub optimal nutrition intake over days or weeks prior to hospital admission,
- Experienced significant weight loss or growth faltering prior to hospital admission in both the obese or underweight patient,
- Experienced significant diarrhoea or vomiting in the week leading up to institution of nutrition support,
- Prolonged period of nil by mouth i.e. > 7-10 days,
- Or poor nutrition intake during hospital stay with evidence of stress and depletion,
- Hyperglycaemia/ insulin requirements, diabetic patients,
- Chronic antacid users – these bind minerals, therefore levels may be low.
- Chronic diuretic users,
- Oncology or chemotherapy patients,
- Chronic alcoholics, [Adolescents]
- ICU or acutely ill,
- Anorexia nervosa,
- Classic severe malnutrition with or without oedema
- Children with growth failure or > 5% weight loss in the previous month. ^{7,18,19}

6.2 Infection

Children with severe malnutrition are at high risk of infections which should be aggressively treated. All children should receive anti-helminthic medication as a routine from 6 months of age.

6.3 Losses

Uncontrolled losses through the skin and obligatory losses in addition to GIT, intraperitoneal or intestinal fluid retention should be monitored and controlled.

7. Dietary

7.1 Recommendations for nutrition intervention⁷

How to avoid the refeeding syndrome:

1. Be aware of at risk patients – checking serum electrolytes prior to and following the commencement of nutrition support.

2. Test and correct electrolyte abnormalities before initiating nutritional support whether enteral, oral or parenteral.
3. Carefully restore circulatory volume, monitor pulse rate, intake and output.
4. Provide sufficient Thiamine, Vitamin B complex, feeding
5. Increase calorie intake slowly.
6. Administer vitamins regularly.
7. Monitor electrolytes over the first week of refeeding include, phosphorus, potassium, magnesium, glucose and urinary electrolytes.

7.2 Protein and Energy Intake

During the initial refeeding phase catabolism usually continues due to the slow re-introduction of protein and energy. Large protein intakes may result in hyperammonaemia and or metabolic acidosis as result of renal capacity for hydrogen (H^+) and phosphate ions being exceeded.¹⁸

An intake of 0.5g – 1g of protein per kg from either parenteral nutrition or enteral nutrition is sufficient to maintain the amino acid pool. Protein intake may be increased during the rehabilitation phase with a view to allow repletion of somatic and visceral stores. It is important to provide a sufficient energy: protein ratio e.g. 1g amino acids requires 30 – 40kcal.¹⁸

There is a fine balance between macro and micronutrient requirements. Deficits will become evident through clinical and laboratory results. These deficits may be prevented by providing macro- and micronutrients in the following proportions:

For every 200 – 250kcal provide:

- 1g Nitrogen or 6.25g protein
- 1.8 mmol calcium
- 2.9 mmol phosphorus
- 1.0 mmol magnesium
- 10 mmol potassium
- 7 mmol sodium and chloride
- 1.2mg zinc¹⁸

7.3 Replacement therapy in the depleted patient

Initiation of nutrition support should be done cautiously with a small amount of nutrition support given during the first week of refeeding e.g. In children, provide of caloric requirements over the first 3 days, on days 3-5 and full requirements by days 5-7.⁴

7.4 Monitoring

Initially, prior to refeeding and during the first 3-5 days of feeding regular assessment of the following is required:¹⁸

- Administration rates of fluids (feeds and IV preparations)
- Temperature
- Cardiac and respiratory function
- Urinary volume
- Weight twice daily
- Output

As the osmotic load is increased during the first 5 days, urine load is increased urine should be checked for osmolality, pH, glucose and protein. During the first 5 days glucose should be measured 4 hourly then daily thereafter. Plasma and urinary ions should be measured daily until they have normalized. Calcium, phosphorus, magnesium, liver function tests and haematocrits should be measured initially twice weekly during the refeeding phase and weekly during the rehabilitation phase.¹⁸

Cardiac Status should be monitored by completing the following measurements:

- Pulse (compensatory tachycardia)
- ECG daily⁶
- Raised blood pressure⁸

7.5 Enteral, parenteral or oral nutrition support

A nutrition support team or multi-disciplinary team, including a dietitian, nurse, pharmacist and doctor should advise on the regimen and rate of feeding for patients at risk of refeeding syndrome or in those who have developed it.¹⁸

7.6 Initial refeeding

In particularly severe cases of refeeding syndrome cautious use of calories is advised. It is recommended that for the first week, 75% of total daily requirements for actual body weight (abw)* be used.^{4,8} In severe cases theoretical requirements of 60% should only be given, based on hydration status.¹⁸

• Birth – 1 years	90 -110kcal/kg/abw*/day	75% = 80kcal kcal/kg/day ¹⁹
• 1 - 7 years old	80 –100kcal/kg/abw /day	75% = 60kcal – 75kcal/kg/day
• 7-10 years	60 - 75kcal/kg/abw/day	75% = 55kcal/kg/day
• 11-14 years	60kcal/kg/abw/day	75% = 45kcal/kg/day
• 15-18 years	50kcal/abw/day	75% = 35kcal/kg/day
• > 18 years	25-35kcal/abw/day	75% = 20 – 25kcal//kg/day ^{4, 7}

If this is tolerated it may be gradually increased up to the goal calorie rate. It must be recognized that each case is individual and may require adjustments of up to 30% less of the average rates indicated above. It is recommended that for infants feeds which provide 0.67 kcal/ml are used in the initial refeeding phase to a volume of 130ml/kg or 100ml/kg if there is severe oedema. For children > 1 year of age, a 0.75 – 1 kcal/ml feed may be used as long as the amount of energy/ calories (kcal) provided in the volume prescribed does not exceed the recommendations for total energy intake.^{4, 7,18}

It is important not to fluid overload these patients as this may precipitate congestive cardiac failure. Where possible oral or enteral fluids should be provided. When IV electrolyte therapy is provided care should be taken to monitor vital signs regularly during each hour.

7.8 Rehabilitation Phase

Energy dense feeds in infants (1kcal/ml) and in children > 1 year of age (1.5kcal/ml) should only be used after the refeeding phase is complete (after at least 7 days). Following the refeeding phase, an additional 1.2 – 1.5 x DRV [Appendix 1] may be added on to the total calories for weight gain and/or an additional 500kcal in children older than 15 years of age.⁸

7.9 Protein

Excessive amounts of protein should not be given in the initial refeeding phase as this can result in acidosis, azotaemia, hypertonic dehydration and hypernatraemia. A protein source of high biological value should be used e.g. cow's milk based protein source.^{4,6,9, 19}

Check consistency of bullets – circles/ squares

Infants: Initial refeeding with:

- 0.5 - 1g/kg/day.

Rehabilitation phase:

- 1.2 -1.5 – 2.0 – 2.5g/ABW/kg/day should be reached for anabolism to occur.

Children: Initial refeeding with:

- 0.6 – 1.0g/kg/day.

Rehabilitation phase:

- 1 – 7 years old: 1.2-1.5g/ABW/day for anabolism to occur.
- 8 – 18 years old: 0.8 – 1g/kg should be used for older children

7.10 Carbohydrate

The intake of glucose represses gluconeogenesis, which may result in hyperglycaemia resulting in hyperosmolar, non-ketotic coma, keto-acidosis and acidosis, osmotic diuresis and dehydration. Glucose should be given cautiously in incremental doses.¹⁹

In the rehabilitation phase it is also important that maximal glucose oxidation rates are not exceeded i.e.:

Infants

- 8-9mg/kg/min [11.5g –12.9g/kg/day]
- Max 12.5mg/min/kg [18g/kg/day]

Toddlers

- 7mg/kg/min [10g/kg/day]

Adolescents

- 4mg/kg/min [5.7g/kg/day]²²

7.11 Fat

The upper limits of fat oxidation are difficult to determine. Parenteral lipid intake should not exceed 3 – 4 g/kg/day in infants and 2 – 3 g/kg/day in older infants.²⁰

7.12 Electrolyte and vitamin supplementation

An imbalance of micronutrients may be as a result of excesses or deficiencies. Refeeding syndrome is primarily associated with deficiencies of some micronutrients. *Table 1* describes some of the clinical features of micronutrient deficiencies commonly associated with this syndrome.^{13,14,15}

Table 1: Clinical features of micronutrient deficiencies ^{13,14,15}

Micronutrient	Clinical Features of deficiency
Thiamine	Beri-beri, muscle tenderness, foot/ wrist drop, sensory neuropathy; <i>Cardiomyopathy</i> → congestive heart failure→oedema. <i>Wernicke – Korsakoff syndrome</i> : Confusion, ataxia, ophthalmoplegia, psychosis.
Potassium	Decreased cardiac contractility, cardiac arrhythmia, hypotension, cardiac arrest, ileus, constipation, weakness, paralysis, confusion, parathesia, rhabdomyolysis, respiratory depression, glucose intolerance, metabolic alkalosis.
Phosphorus	Respiratory insufficiency, decreased cardiac contractility, haematological abnormalities, osteomalacia, bone pain, behavioural changes, peripheral neuropathy, muscle weakness, myalgia
Magnesium	Muscle fasciculation/ tremors, muscle weakness, cardiac arrhythmias (depressed ST- & T changes), personality changes, neurological abnormalities, rickets (secondary to impaired calcium metabolism)
Calcium	Osteoporosis/ rickets, increased blood pressure, tetany: parathesia of lips, tongue, hands & feet, muscle aching, Chvostek's sign [facial twitching], Trousseau's sign: carpopedal spasm, cardiac arrhythmias, depression, psychosis, myoclonic jerks, cyanosis.
Sodium	Dehydration, anorexia, vomiting, mental apathy, muscle cramps, seizures
Selenium	Cardiomyopathy, skeletal myopathy, macrocytosis and hair depigmentation

Before enteral or parenteral nutrition is commenced calcium, magnesium and phosphate levels should be checked. If levels are abnormally low administer replacement treatment prior to commencing nutrition support. [*Summary Algorithm or tables*] Thiamine (1-2 mg/kg) should be administered intramuscularly (IM) at least 30 minutes prior to commencing refeeding.^{4,8}

Once replacement therapy is complete re-check levels again. Replacement treatment should be given each time electrolyte levels are found to be abnormal.^{4,8, 18}

7.13 General

A lactose containing milk should be given where possible and only in the event of severe diarrhoea should a lactose and sucrose free alternative be considered with positive faecal reducing substances.¹⁸

8. Summary

Refeeding syndrome represents a significant risk of morbidity and mortality in some patients with features of starvation. Meticulous attention to the replacement of electrolyte imbalances and slow re-introduction of calories and protein will decrease the risk of cardiac and respiratory failure.

9. Appendix 1

Energy Calculations

Table 1: Selected Dietary Reference Values (DRV's) for Infants and Children requiring Oral/Enteral Nutrition ²²

Age	Weight (kg)	KJ/kg/day	Kcal/kg/day	Protein g/kg/day
Males				
0 – 3months	5.1	420 – 480	100 – 115	2.1
4 – 6	7.2	400	95	1.6
7 – 9	8.9	400	95	1.5
10 – 12	9.6	400	95	1.5
1 – 3 years	12.9	400	95	1.1
4 – 6	19.0	380	90	1.1
7 – 10		8240/day	1970/day	28.3g/day
11 – 14		9270/day	2220/day	42.1g/day
15 – 18		11510/day	2755/day	55.2g/day
Females				
0 – 3 months	4.8	420 – 480	100 – 115	2.1
4 – 6	6.8	400	95	1.6
7 – 9	8.1	400	95	1.5
10 – 12	9.1	400	95	1.5
1 – 3 years	12.3	400	95	1.1
4 – 6	17.2	380	90	1.1
7 – 10		7280/day	1740/day	28.3g/day
11 – 14		7920/day	1845/day	42.1g/day
15 - 18		8830/day	2110/day	45.4g/day

Table 2: Schofield Equation for Calculating Resting Metabolic Rate (RMR) – Kcal/day ²²

Age (yr)	Male	Female
< 3	$0.167(W) + 1517.4(H) - 617.6$	$16.252(W) + 1023.2(H) - 413.5$
3 – 10	$19.59(W) + 130.3(H) + 414.9$	$16.696(W) + 161.8(H) + 371.2$
10 – 18	$16.25(W) + 317.2(H) + 515.5$	$8.365(W) + 465(H) + 200.0$
> 18	$15.057(W) + 10.04(H) + 705.8$	$13.623(W) + 283(H) + 98.2$

*Weight (W) in kilograms (kg); Height (H) in metres (m)

Table 3: FAO/WHO/UNU kcal/day ²²

Age (yr)	Male	Female
3 – 10	$22.7 (W) + 495$	$22.5 (W) + 499$
10 - 18	$17.5 (W) + 651$	$12.2 (W) + 746$

*Weight (W) in kilograms (kg)

PHYSICAL ACTIVITY FACTORS ¹	
ACTIVITY	ACTIVITY FACTOR (AF)
• Sleeping (ICU, Sedation and muscle relaxation)	1.0
Hospitalized	
• Non Ambulant	1.2
• Ambulant	1.3
At Home	
• Relatively inactive	1.4
• Very active	1.9
STRESS FACTORS	
DISEASE	STRESS FACTOR
Trauma	
• Little (long bone fracture)	1.2
• Central Nervous System	1.3
• Moderate to severe (multiple)	1.5
Sepsis	
• Moderate	1.3
• Severe	1.6

Table 4: Fluid Requirements

Age (years)	ml/kg actual weight
Premature	180-200
0-1	150
1-3	100
3-6	90
7-10	70
10-15	60
Other formula for calculating fluid requirements	
Weight	Fluid volume per 24 hours*
Premature <2kg	150ml/kg
Neonates and infants - 2-10kg	100ml/kg for the first 10kg
Infants and children - 10-20kg	1000ml + 50ml/kg over 10kg
Children >20kg	1500ml + 20ml/kg over 20kg
Total Volume = IV + Enteral intake	

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