

Prevention of Electrolyte Disorders Refeeding Syndrome

Outline – Refeeding Syndrome

- **What is refeeding syndrome?**
- **What Electrolytes and minerals are involved?**
- **Who is at risk?**
- **How to manage and prevent?**

Outline – Refeeding Syndrome

- **What is refeeding syndrome?**
- **What Electrolytes and minerals are involved?**
- **Who is at high risk?**
- **How to manage and prevent?**

Refeeding Syndrome

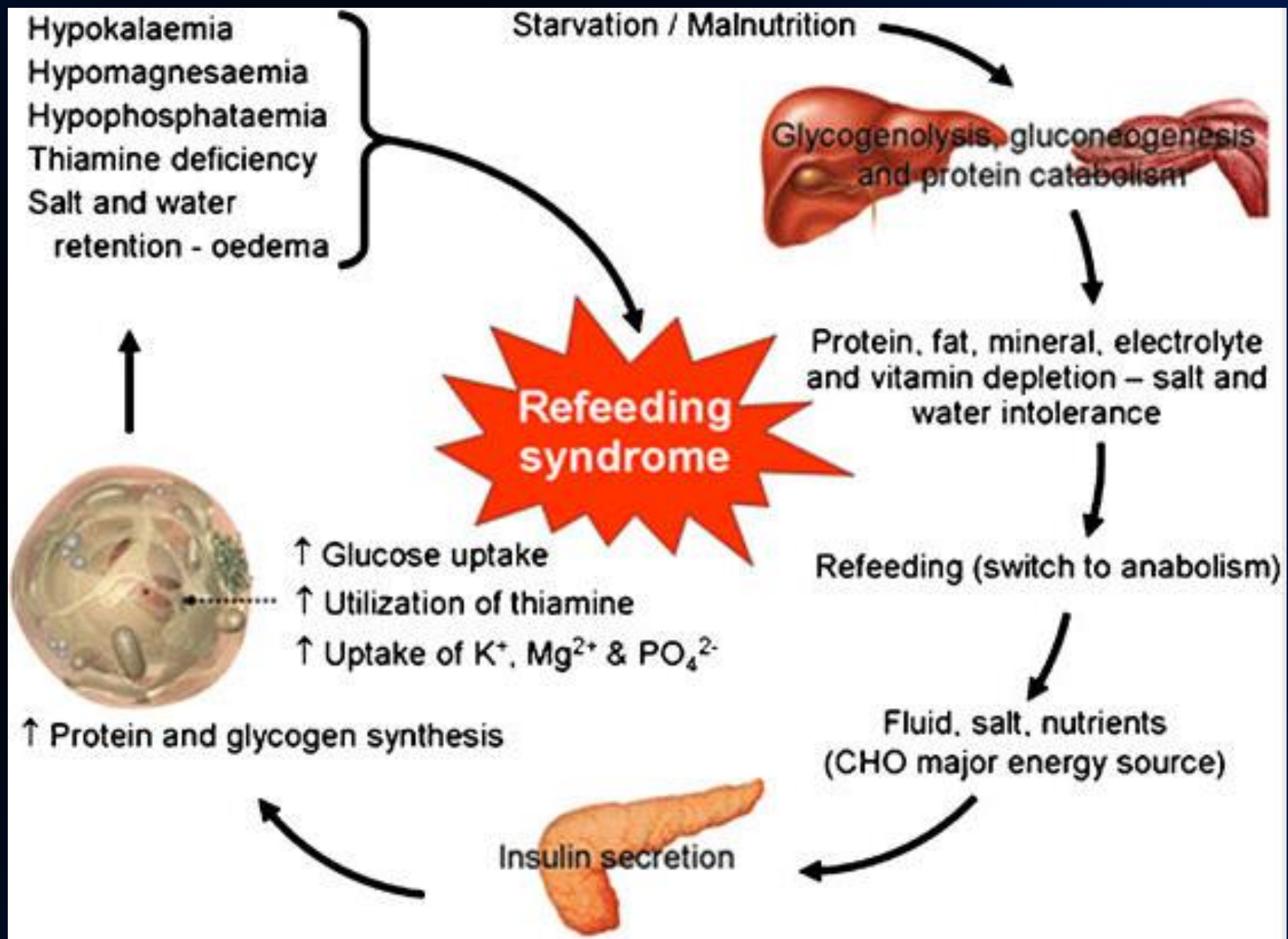
- **Metabolic and hormonal changes caused by over-rapid or unbalanced nutrition support in malnourished patients**
- **Whether enterally or parenterally**
- **Result in**
 - **Micronutrient deficiencies**
 - **Fluid and electrolyte imbalance**
 - **Disturbances of organ function → Death**

Incidence - ??

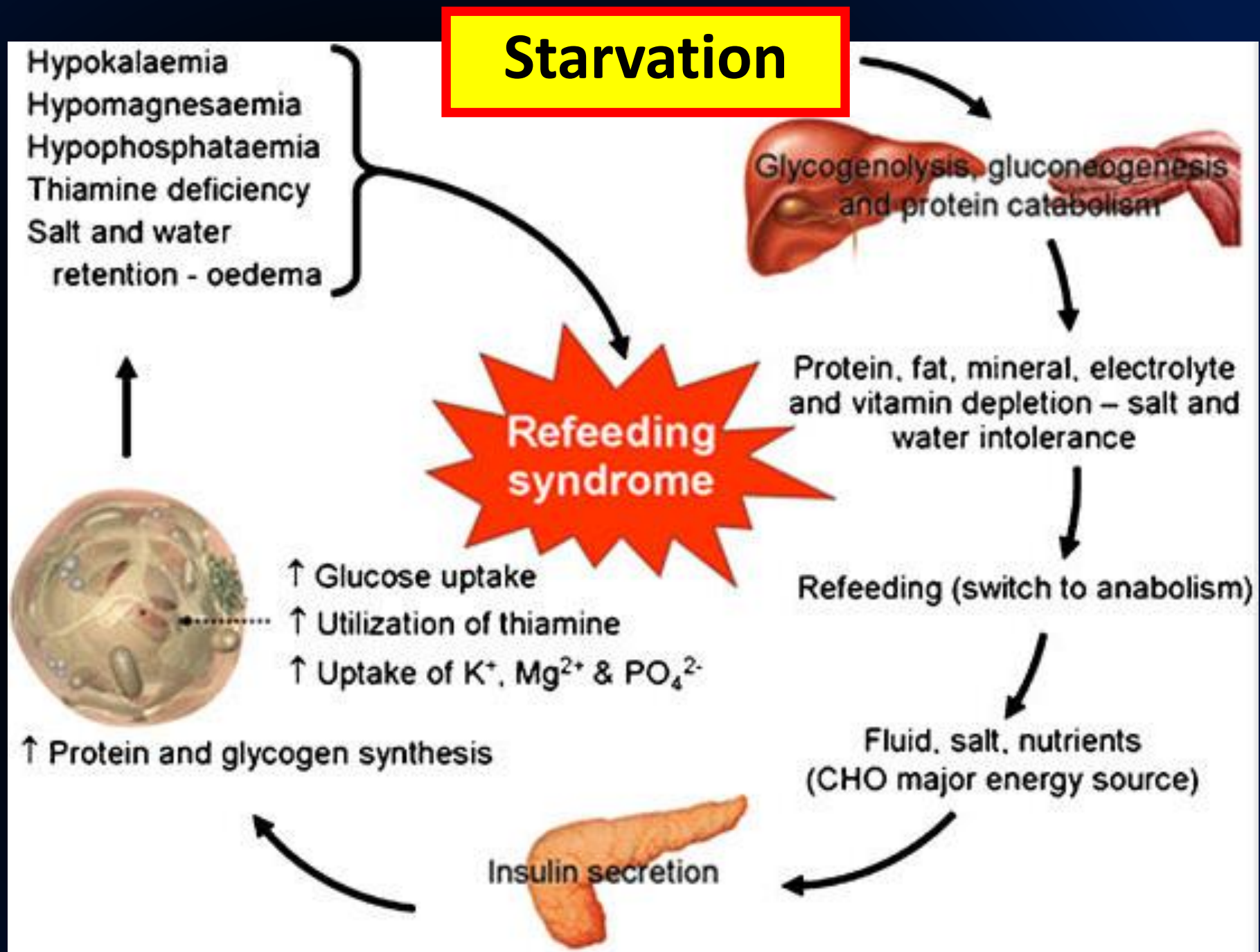
- **Lack of a universally accepted definition**
- **Often not recognized**

Pathophysiology

Pathogenesis of Refeeding Syndrome

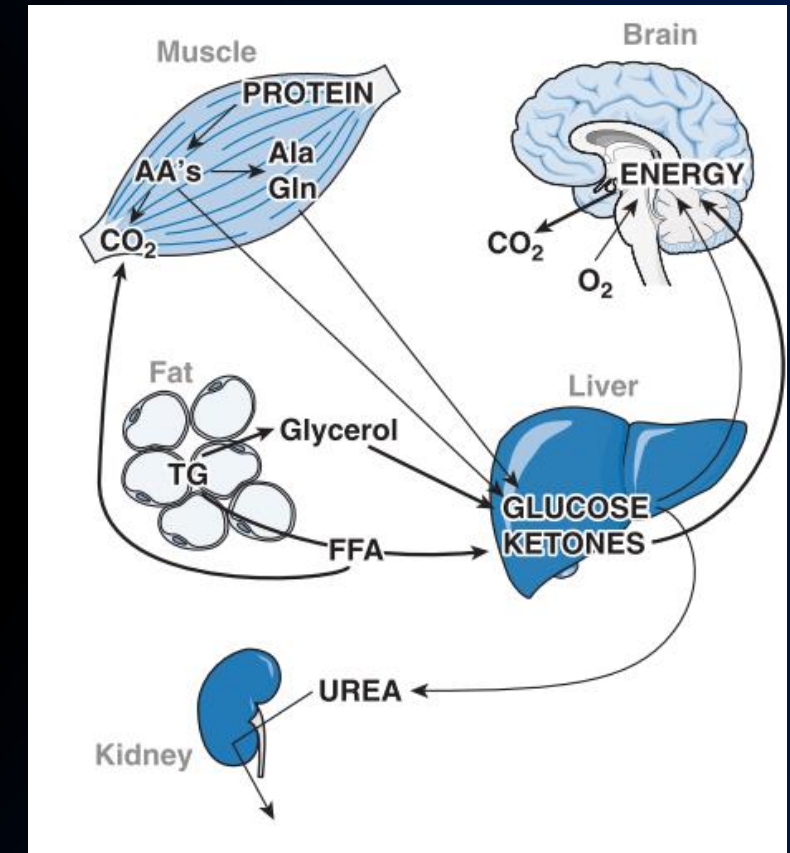


Pathogenesis of Refeeding Syndrome

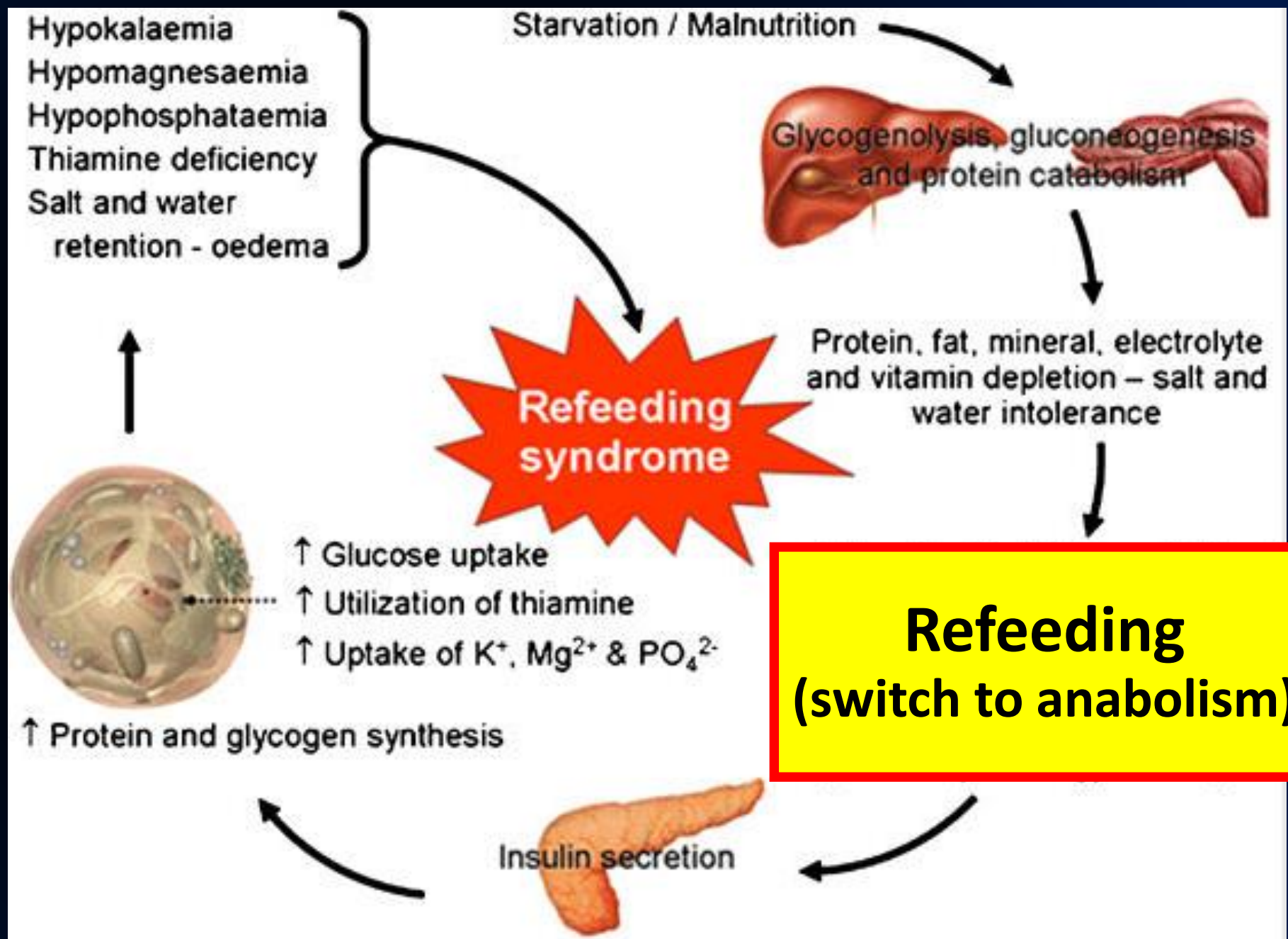


Starvation

- Basal metabolic rate decreases 20-25%
- **Body switches from using carbohydrate to protein in fasting state and fat in starvation state as the main source of energy**
- **Brain's switching from a glucose-based to a ketone-based fuel supply**
- **Intracellular minerals become depleted, while serum concentrations may remain normal**



Pathogenesis of Refeeding Syndrome



Refeeding (Major Energy => Carbohydrate)

- **Increased Insulin**

1. **Stimulate glycogen, fat, and protein synthesis**

- Requires minerals (phosphate and magnesium) and cofactors (thiamine) for phosphorylation and ATP synthesis

- Phosphate and magnesium are taken up into the cells

2. **Stimulate potassium and glucose absorption into the cells through the sodium-potassium ATPase symporter**

- Cause a decrease in serum phosphate, magnesium, and potassium

- Clinical features occur as a result of the functional deficits of these electrolytes and the rapid change in basal metabolic rate

Clinical Features

Clinical Manifestations of Electrolyte Abnormalities Associated with Refeeding Syndrome

**Hypophosphatemia
($\text{PO}_4^{3-} < 0.8 \text{ mmol/L}$)**

Cardiovascular	<ul style="list-style-type: none">- Cardiomyopathy- Heart failure- Arrhythmia
Respiratory	<ul style="list-style-type: none">- Respiratory failure- Pulmonary edema
Skeleton	<ul style="list-style-type: none">- Rhabdomyolysis- Weakness- Myalgia
Hematology	<ul style="list-style-type: none">- Hemolysis- Leukocyte and platelet dysfunction
Neurological	<ul style="list-style-type: none">- Delirium- Seizure

Clinical Manifestations of Electrolyte Abnormalities Associated with Refeeding Syndrome

**Hypokalemia
(K⁺ < 3.5 mmol/L)**

Cardiovascular	<ul style="list-style-type: none">- Ventricular arrhythmia- Brady/tachycardia- Cardiac arrest
Respiratory	<ul style="list-style-type: none">- Hypoventilation- Respiratory failure
Skeleton	<ul style="list-style-type: none">- Weakness/Fatigue- Muscle twitching
Gastrointestinal	<ul style="list-style-type: none">- Ileus- Constipation
Metabolic	<ul style="list-style-type: none">- Metabolic Alkalosis

Clinical Manifestations of Electrolyte Abnormalities Associated with Refeeding Syndrome

**Hypomagnesemia
(Mg²⁺ < 0.7 mmol/L)**

Cardiovascular	- Arrhythmias - Heart failure
Respiratory	- Hypoventilation - Respiratory failure
Skeleton	- Muscle cramps - Weakness/Fatigue
Neurological	- Seizure - Paresthesia
Gastrointestinal	- Ileus - Constipation
Metabolic	- Hypocalcemia

1. Classical Re-Feeding Syndrome

- **Acute circulatory fluid overload or depletion**
- **Pulmonary edema**
- **Cardiac failure / Arrhythmias**
- **Hyperglycemia**
- **Lactic acidosis**

2. Wernicke-Korsakoff Syndrome

- **Disorientation**
- **Ophthalmoplegia / nystagmus**
- **Ataxia**
- **Short-term memory impairment**
- **Confabulation**

1. Classical Re-Feeding Syndrome

- Acute circulatory fluid overload or depletion
- Pulmonary edema
- Cardiac failure / Arrhythmias
- Hyperglycemia
- Lactic acidosis

**Electrolyte
Abnormalities**

2. Wernicke-Korsakoff Syndrome

- Disorientation
- Ophthalmoplegia / nystagmus
- Ataxia
- Short-term memory impairment
- Confabulation

**Thiamine
Deficiency**

What Electrolytes and Minerals are Involved in Pathogenesis of Refeeding Syndrome ?

Phosphorus - - Hallmark

Magnesium

Potassium

Sodium

Outline – Refeeding Syndrome

- What is refeeding syndrome?
- What Electrolytes and minerals are involved?
- **Who is at high risk?**
- How to manage and prevent?

Malnourished Patients at Particular Risk of Developing Refeeding Syndrome

Unintentional weight loss

- Loss of >5% of body weight in 1 month
- Loss of >7.5% of body weight in 3 months
- Loss of >10% of body weight in 6 months

Low nutrient intake

- Patients starved for >7 days
- Prolonged hypocaloric feeding or fasting
- Chronic swallowing problems and other neurological disorders
- Anorexia nervosa
- Chronic alcoholism
- Depression in the elderly
- Patients with cancer
- Chronic infectious diseases (AIDS, tuberculosis)
- During convalescence from catabolic illness
- Postoperative patients
- Diabetic hyperosmolar states
- Morbid obesity with profound weight loss
- Homelessness, social deprivation
- Idiosyncratic/eccentric diets
- Hunger strikers

Increased nutrient losses/decreased nutrient absorption

- Significant vomiting and/or diarrhoea
- Dysfunction or inflammation of the gastrointestinal tract
- Chronic pancreatitis
- Chronic antacid users (these bind minerals)
- Chronic high-dose diuretic users
- After bariatric surgery

Malnourished Patients at Particular Risk of Developing Refeeding Syndrome

Unintentional weight loss

- Loss of >5% of body weight in 1 month
- Loss of >7.5% of body weight in 3 months
- Loss of >10% of body weight in 6 months

Low nutrient intake

- Patients starved for >7 days
- Prolonged hypocaloric feeding or fasting
- Chronic swallowing problems and other neurological disorders
- Anorexia nervosa
- Chronic alcoholism
- Depression in the elderly
- Patients with cancer
- Chronic infectious diseases (AIDS, tuberculosis)
- During convalescence from catabolic illness
- Postoperative patients
- Diabetic hyperosmolar states
- Morbid obesity with profound weight loss
- Homelessness, social deprivation
- Idiosyncratic/eccentric diets
- Hunger strikers

Increased nutrient losses/decreased nutrient absorption

- Significant vomiting and/or diarrhoea
- Dysfunction or inflammation of the gastrointestinal tract
- Chronic pancreatitis
- Chronic antacid users (these bind minerals)
- Chronic high-dose diuretic users
- After bariatric surgery

Malnourished Patients at Particular Risk of Developing Refeeding Syndrome

Unintentional weight loss

- Loss of >5% of body weight in 1 month
- Loss of >7.5% of body weight in 3 months
- Loss of >10% of body weight in 6 months

Low nutrient intake

- Patients starved for >7 days
- Prolonged hypocaloric feeding or fasting
- Chronic swallowing problems and other neurological disorders
- Anorexia nervosa
- Chronic alcoholism
- Depression in the elderly
- Patients with cancer
- Chronic infectious diseases (AIDS, tuberculosis)
- During convalescence from catabolic illness
- Postoperative patients
- Diabetic hyperosmolar states
- Morbid obesity with profound weight loss
- Homelessness, social deprivation
- Idiosyncratic/eccentric diets
- Hunger strikers

Increased nutrient losses/decreased nutrient absorption

- Significant vomiting and/or diarrhoea
- Dysfunction or inflammation of the gastrointestinal tract
- Chronic pancreatitis
- Chronic antacid users (these bind minerals)
- Chronic high-dose diuretic users
- After bariatric surgery

National Institute for Health and Care Excellence (NICE 2006)

Criteria for Identifying Patient at High Risk of Refeeding Problems

	≥ 1 criteria	≥ 2 criteria
BMI (kg/m²)	< 16	< 18.5
Unintentional weight loss in previous 3-6 months (%)	> 15	> 10
Little or no nutritional intake (days)	> 10	> 5
Low level of serum electrolyte before feeding <ul style="list-style-type: none"> - Phosphate - Potassium - Magnesium 	+	-
Alcohol or drug uses <ul style="list-style-type: none"> - Insulin - Chemotherapy - Antacids - Diuretics 	-	+

Outline – Refeeding Syndrome

- What is refeeding syndrome?
- What Electrolytes and minerals are involved?
- Who is at high risk?
- **How to manage and prevent?**

Management

“There are no internationally validated guidelines for the treatment of the refeeding syndrome”



National Collaborating Centre
for Acute Care

Nutrition Support for Adults Oral Nutrition Support, Enteral Tube Feeding and Parenteral Nutrition

METHODS, EVIDENCE & GUIDANCE

**National Institute for Clinical Excellence
(NICE) 2006**

FEBRUARY 2006
Commissioned by the National Institute for
Clinical Excellence

NICE 2006 Recommendation for Clinical Practice Patients at High Risk of Refeeding Syndrome

Macronutrients - Calories Intake (All Routes)

- ***Start*** - 10 kcal/kg/d
- 5 kcal/kg/d (if BMI < 14 kg/m² or no food intake > 15 d)
- ***Slowly Increase over 4-7 days to meet the full target***

Micronutrients – Vitamins and Trace Elements

- **Providing immediately before and during the first 10 days of oral thiamine 200–300 mg daily**
- **Vitamin B co strong 1-2 tab, three times a day (or full dose daily intravenous vitamin B preparation)**
- **Multivitamin/trace element supplement once daily**

NICE 2006 Recommendation for Clinical Practice Patients at High Risk of Refeeding Syndrome

Electrolytes

- Oral or intravenous supplementation of potassium, phosphate and magnesium unless pre-feeding plasma levels are high
 - Phosphate 0.3-0.6 mmol/kg/d
 - Magnesium 0.2 mmol/kg/d (IV), 0.4 mmol/kg/d (oral)
 - Potassium 2-4 mmol/kg/d
- Pre-feeding correction of low plasma levels is unnecessary

Fluid

- Carefully restoring circulatory volume
- Monitoring fluid balance and overall clinical status closely

Head & Neck

Review

Refeeding syndrome

Hisham Mehanna*¹, Pa

these articles see bmj.com

Refeeding to prevent

Hisham M Mehanna,^{1,2} J

Check
K⁺, Ca²⁺
PO₄, Mg²⁺

Before feed starts, administer
Thiamine 200-300mg daily orally and
Vit B co strong 1-2 tablets 3 times daily
(Or full dose intravenous Vitamin B)
and multivitamin/trace element
supplement once daily

Start feeding 10Kcals/kg/day *
Slowly increase feeding over 4 - 7 days

Rehydrate carefully and supplement
and /or correct K⁺, PO₄, Ca²⁺, Mg²⁺
levels :
K⁺ 2 - 4mmol/kg/day
PO₄ 0.3-0.6 mmol/kg/day,
Mg²⁺ 0.2 mmol/kg/day IV or 0.4
mmol/kg/day oral

Monitor K⁺, PO₄, Ca²⁺ and Mg²⁺ for the
first 2 weeks and act on as appropriate

Figure 1

Guidelines for management. * if severely malnourished, e.g. BMI less than 14 kg/m or negligible intake for 2 weeks or more, start feeding at maximum of 5 kcal/kg/day. Adapted from NICE [14] and British Association of Parenteral and Enteral Nutrition guidelines [15].



BioMed Central

Open Access

management and Jane Travis³

Mehanna H Head & Neck Oncology 2009, 1:4

REVIEW

, and how

HM Mehanna BMJ 2008;336:1495-8

REVIEW

Nutrition in clinical refeeding syndrome: illustration of prevention and treatment

Z Stanga^{1,2}, A Brunner^{1,3}, M Leuenberger^{1,4}, M G. Müller^{1,5}

Days 1–3

1. Energy (by all routes): start at 42 kJ/kg/day (10 kcal/kg/day) and slowly increase to 63 kJ/kg/day (15 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.
2. Electrolytes: measure serum concentrations basally, 4–6 h later, and daily during feeding (see below). Supplement prophylactically (unless pre-feeding plasma levels are high), in most cases by the intravenous route initially. Amounts depend on patient size and plasma concentrations, but usual daily requirements are:
 - Phosphate 0.5–0.8 mmol/kg/day
 - Potassium 1–3 mmol/kg/day
 - Magnesium 0.3–0.4 mmol/kg/day. Levels should be monitored frequently and supplements increased if necessary.
3. Fluid: restrict to sufficient to maintain renal function, to replace deficits or losses, and avoid weight gain, that is achieve zero balance. Patients usually need 20–30 ml/kg/day.
4. Salt: restrict sodium to <1 mmol/kg/day. If oedema develops, restrict further.
5. Minerals and trace elements: 100% DRI. Iron should not be supplemented in the first week.
6. Vitamins 200% DRI. Give 200–300 mg thiamine i.v. at least 30 min before feeding, and 200–300 mg daily i.v. or orally till day 3.
7. Monitor daily
 - Body weight (fluid balance).
 - Clinical examination: oedema, blood pressure, pulse rate, cardiovascular and respiratory systems.
 - Biochemistry: phosphate, magnesium, potassium, sodium, calcium, glucose, urea, creatinine, (thiamine).
 - Preferably ECG-monitoring in severe cases.

Days 4–6

1. Energy (by all routes): 63–84 kJ/kg/day (15–20 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.
2. Electrolytes: continue supplementation as above, giving more or less according to plasma concentrations. If the refeeding syndrome is already established, aim to restore normal levels. If
 - PO_4^{2-} <0.6 mmol/l—give 30–50 mmol phosphate (eg. Phosphates Polyfusor) i.v. over 12 h.
 - Mg^{2+} <0.5 mmol/l—give 24 mmol MgSO_4 i.v. over 12 h.
 - K^+ <3.5 mmol/l—give >20–40 mmol KCl i.v. over 4 h.Remeasure and repeat if necessary.
3. Minerals and vitamins: as for days 1–3.
4. Fluid: depending on hydration, weight change and losses. Patients usually need 25–30 ml/kg/day.
5. Monitor daily: as for days 1–3.

Days 7–10

1. Energy (by all routes): 84–132 kJ/kg/day (20–30 kcal/kg/day); 50–60% carbohydrates, 30–40% fat, and 15–20% protein.
2. Electrolytes, minerals and vitamins: as above. Iron should be supplemented from day 7 onwards

Clinical Nutrition (2008) 62, 687–694

Group All rights reserved 0954-3007/08 \$30.00

Refeeding guidelines for

kin⁴, SP Allison⁵ and DN Lobo⁵

TABLE 4: Refeeding regime for patients at risk of RFS [5, 29].

Day	Calorie intake (All feeding routes)	Supplements
Day 1	10 kcal/kg/day For extreme cases (BMI < 14 kg/m ² or no food >15 days) 5 kcal/kg/day Carbohydrate: 50–60% Fat: 30–40% Protein: 15–20%	Prophylactic supplement PO ₄ ²⁻ : 0.5–0.8 mmol/kg/day K ⁺ : 1–3 mmol/kg/day Mg ²⁺ : 0.3–0.4 mmol/kg/day Na ⁺ : <1 mmol/kg/day (restricted) IV fluids-Restricted, maintain “zero” balance IV Thiamine + vitamin B complex 30 minutes prior to feeding
Day 2–4	Increase by 5 kcal/kg/day If low or no tolerance stop or keep minimal feeding regime	Check all biochemistry and correct any abnormality Thiamine + vitamin B complex orally or IV till day 3 Monitoring as required (Table 3)
Day 5–7	20–30 kcal/kg/day	Check electrolytes, renal and liver functions and minerals Fluid: maintain zero balance Consider iron supplement from day 7
Day 8–10	30 kcal/kg/day or increase to full requirement	Monitor as required (Table 3)

If RFS is suspected based on clinical and biochemical assessment or the patient develops intolerance to artificial nutritional support, the energetic intake should be reduced or stopped.

Feeding rate should be increased to meet full requirements for fluid, electrolytes, vitamins, and minerals if the patient is clinically and biochemically stable.



IrSPEN GUIDELINE DOCUMENT No. 1:

**Prevention and Treatment of
Refeeding Syndrome
in the Acute Care Setting**

Dr. Karen Boland, Damodar Solanki, and Carmel O'Hanlon
On behalf of IrSPEN's Standards and Guidelines Committee

High risk: 1 or more major risk factors

- BMI < 16kg/m²
- Unintentional weight loss of >15% in the previous 3-6 months
- Little or no nutritional intake for >10 days
- Low levels of potassium, phosphate and magnesium prior to refeeding

Extreme risk: one of the following

- BMI < 14 kg/m²
- Very little or no nutrient intake for >15 days

High risk: 2 or more minor risk factors

- BMI < 18.5kg/m²
- Unintentional weight loss of >10% in the previous 3-6 months
- Little or no nutritional intake for >5 days
- History of alcohol abuse* or drugs including insulin, diuretics, chemotherapy or antacids.

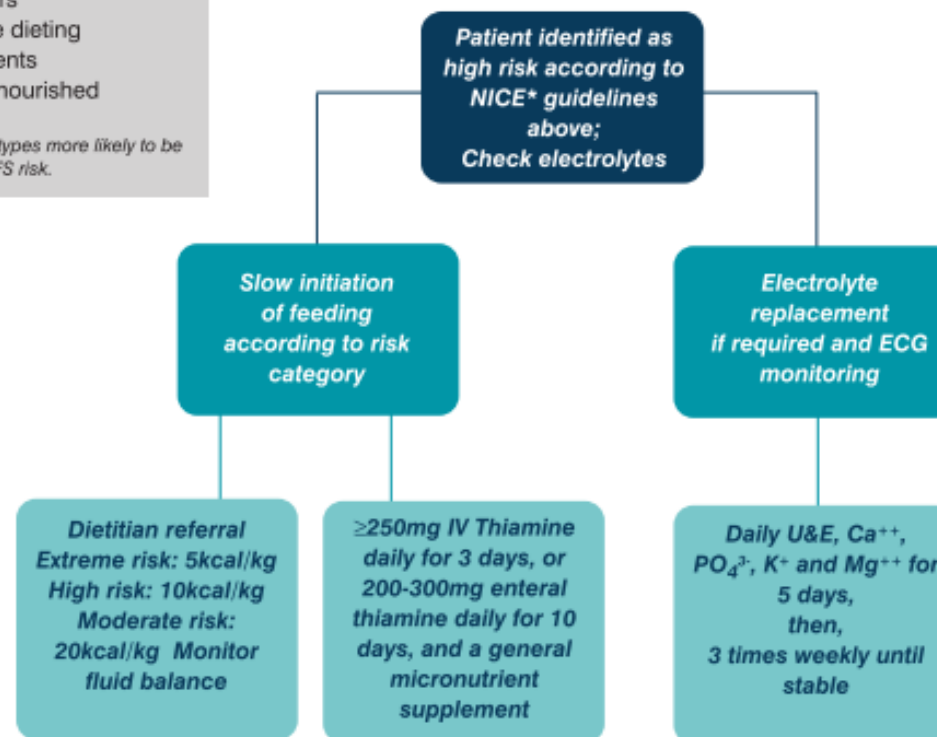
*See local guidelines on management of alcohol withdrawal for guidance on thiamine supplementation.

Moderate risk: 1 of the top 3 factors above

Risk by patient category*

- Chronic alcohol abuse
- Elderly living alone
- Chronic GI symptoms
- Chronic debilitating disease
- Eating disorders
- Chronic severe dieting
- Oncology patients
- Obviously malnourished

*Indicates patient types more likely to be associated with RFS risk.



Recommendation for phosphate and magnesium supplementation

Mineral	Dose
Phosphate	
Maintenance requirement	0.3-0.6 mmol/kg/day orally
Mild hypophosphataemia (1.9-2.6 mg/dL)	0.3-0.6 mmol/kg/day orally
Moderate hypophosphataemia (1-1.8 mg/dL)	9 mmol infused into peripheral vein over 12 hours
Severe hypophosphataemia (< 1 mg/dL)	18 mmol infused into peripheral vein over 12 hours
Magnesium	
Maintenance requirement	0.2 mmol/kg/day intravenously (or 0.4 mmol/kg/day orally)
Mild to moderate hypomagnesaemia (0.5-0.7 mmol/l)	Initially 0.5 mmol/kg/day over 24 hours intravenously, then 0.25 mmol/kg/day for 5 days intravenously
Severe hypomagnesaemia (<0.5 mmol/l)	24 mmol over 6 hours intravenously, then as for mild to moderate hypomagnesaemia (above)

Phosphorus Supplements (Parenteral)

Inorganic Phosphate

- **Dipotassium phosphate (K_2HPO_4)**
 - PO_4^{3-} 0.5 mmol/mL
 - K^+ 1 mmol/mL

Organic Phosphate

- **Fructose 1,6 phosphate (Esafosfina)**
 - PO_4^{3-} 0.45 mmol/mL
- **Sodium Glycerophosphate (Glycophos)**
 - PO_4^{3-} 1 mmol/mL
 - Na^+ 2 mmol/mL

Recommendation for phosphate and magnesium supplementation

Mineral	Dose
Phosphate	
Maintenance requirement	0.3-0.6 mmol/kg/day orally
Mild hypophosphataemia (0.6-0.85 mmol/l)	0.3-0.6 mmol/kg/day orally
Moderate hypophosphataemia (0.3-0.6 mmol/l)	9 mmol infused into peripheral vein over 12 hours
Severe hypophosphataemia (<0.3 mmol/l)	18 mmol infused into peripheral vein over 12 hours
Magnesium	
Maintenance requirement	0.2 mmol/kg/day intravenously (or 0.4 mmol/kg/day orally)
Mild to moderate hypomagnesaemia (1.2-1.6 mg/dL)	Initially 0.5 mmol/kg/day over 24 hours intravenously, then 0.25 mmol/kg/day for 5 days intravenously
Severe hypomagnesaemia (< 1.2 mg/dL)	24 mmol over 6 hours intravenously, then as for mild to moderate hypomagnesaemia (above)

Serum Potassium (mmol/L)	Recommendation for Replacement
<i>Critical deficit</i> < 2.0 or < 2.5 + ECG changes	- Central IV KCL 10 mEq/100mL NSS replace in intensive setting (max rate 20 mEq/hr)
<i>Severe deficit</i> 2-2.5 no ECG changes	- Peripheral IV 40 mmol/1L - Check serum K at 8 hr (if repeat 40 mmol/1L)
<i>Moderate deficit</i> 2.5-3.0	- Peripheral IV 40 mmol/1L - Check serum K at 8 hr (if repeat 20 mmol/500mL)
<i>Mild deficit</i> 3.1-3.5	- Oral replacement - Peripheral IV 20 mmol IV/500 mL (if intolerance to oral)

- **Cardiac monitoring if rate > 10 mEq/hr**
- **Maximal rate : peripheral = 10 mEq/hr, central = 20 mEq/hr**
- **Maximal IV dose = 200 mEq/24 hr**
- **Maximal concentration for peripheral vein = 60-80 mEq/L**

Daily Parenteral Electrolyte and Mineral Requirements

Electrolyte/ Mineral	Preterm/ Neonates	Infants/ Children		Adults	
Sodium	2-5	2-5	mEq/kg/d	1-2	mEq/kg/d
Potassium	2-4	2-4	mEq/kg/d	1-2	mEq/kg/d
Calcium	2-4	0.5-4	mEq/kg/d	10-15	mEq/d
Magnesium	0.3-0.5	0.3-0.5	mEq/kg/d	8-24	mEq/d
Phosphorus	1-2	0.5-2	mmol/kg/d	20-40	mmol/d
Acetate	As needed to maintain acid-base balance				
Chloride					

Note : Based on normal age-related organ function and normal losses

Take Home Messages

- **Aware of at risk individuals**
- **Appropriate feeding regimen**
 - **Calories : slowly increase over a week**
 - **Vitamins and trace elements : esp. thiamine**
 - **Supplementation of the electrolytes : PO_4^{3-} , Mg^{2+} , K^+**
 - **Carefully restoring circulatory volume**
- **Monitoring during refeeding**