The Refeeding Syndrome: how often does it occur and how can it be managed?

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The Lennard-Jones
Intestinal Failure Unit

Incidence

- Unknown
- No agreed definition
- Low electrolytes OR % reduction
- Clinical Observations
- “Symptomatic” vs “Biochemical” refeeding

Occurrence of Refeeding

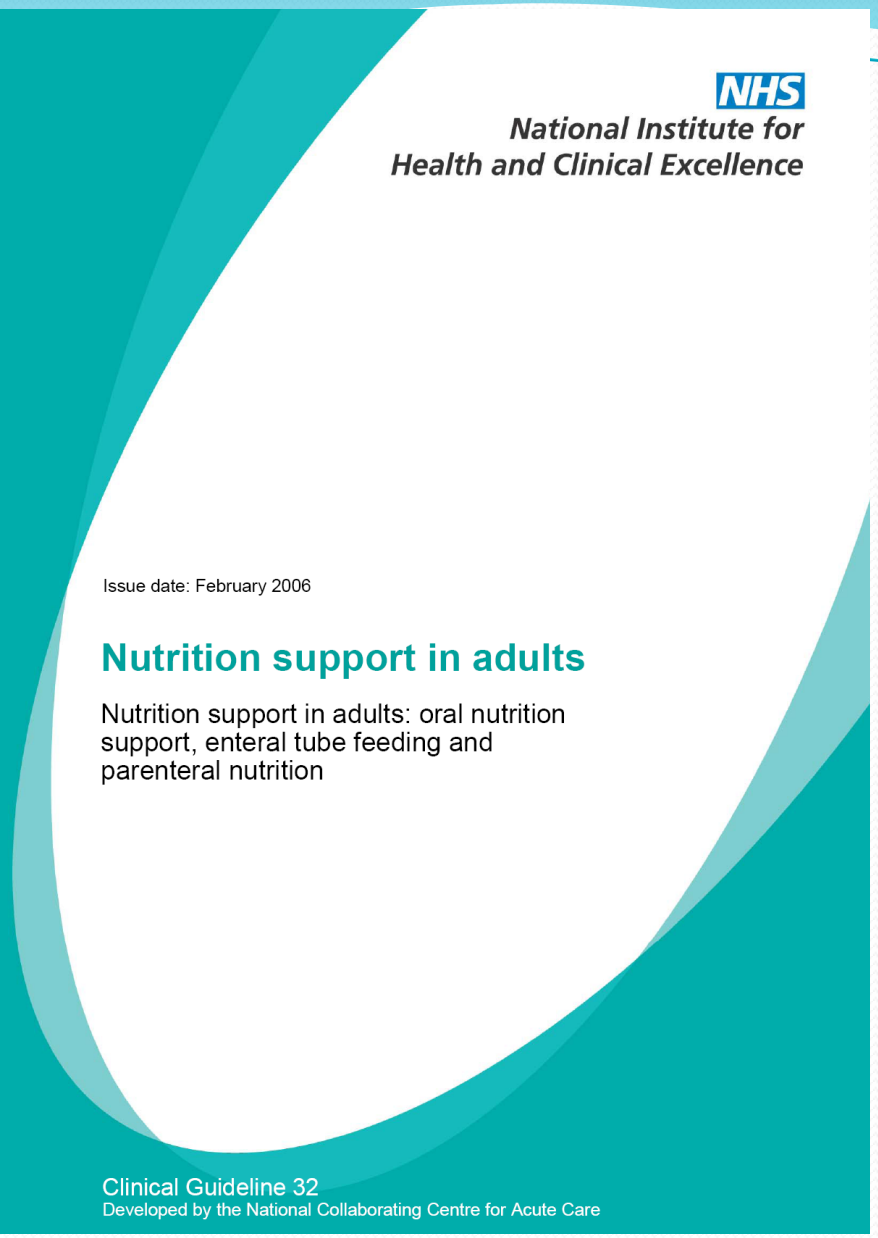
- Prospective cohort study
- 243 patients starting EN or PN
- 133 at high risk of refeeding according to NICE
- Observed ↓ electrolytes & clinical observations
  - K<2.5, PO4 <0.32, Mg <0.5
  - Peripheral oedema or acute circulatory overload
  - Disturbances to organ function inc respiratory or cardiac failure & pulmonary oedema

Rio et al (2013) BMJ Open:3:e002173. doi:10.1136

Occurrence of Refeeding

- Predictors of refeeding (sensitivity of 67%):
  - Poor intake for >10 days
  - Weight loss of >15%
  - Low serum magnesium
- No deaths attributable to refeeding
- Rare survivable phenomena
- Starvation is the most reliable predictor

Rio et al (2013) BMJ Open:3:e002173. doi:10.1136



D Grade Evidence

National Collaborating Centre for Acute Care, Feb 2006. Nutrition support in adults oral nutrition support, enteral tube feeding and parenteral nutrition

Patients at High Risk (NICE 2006)

- Patient has one or more of the following:
  - BMI <16kg/m^2
  - Unintentional weight loss >15% over 3-6 months
  - Little or no nutritional intake for >10 days
  - Low levels of potassium, phosphate or magnesium prior to feeding

OR

- Patient has two or more of the following:
  - BMI less than 18.5kg/m^2
  - Unintentional weight loss >10% over 3-6 months
  - Little or no nutritional intake for >5 day
  - A history of alcohol abuse or drugs including insulin, chemotherapy, antacids & diuretics

D Grade Evidence

How to feed patients at risk (NICE 2006)

- **High risk**
- ***Consider*** starting nutrition support at a maximum of 10kcal/kg increasing levels slowly to meet or exceed needs by 4 -7 days
- ***Consider*** restoring circulatory volume and monitoring fluid balance and overall clinical status closely

- **Extreme high risk**
- ***Consider*** using only 5 kcal/kg/day and monitoring cardiac rhythm continually in these patients

D Grade Evidence

How to feed patients at risk (NICE 2006)

- ***Consider* providing immediately before and during the first 10 days of feeding**:
  - Oral thiamine 200-300 mg/day
  - Vitamin B co strong 1or 2 tablets tds **OR**
  - Full dose intravenous vitamin B preparation if necessary
  - A balanced multivitamin/trace element supplement

- ***Consider* providing oral, enteral or intravenous supplements of:**

D Grade Evidence

  - Potassium = 2 - 4mmol/kg/day
  - Phosphate = 0.3 - 0.6mmol/kg/day
  - Magnesium = IV 0.2 or oral 0.4mmol/kg/day (unless pre-feeding plasma levels are high)
  - Pre feeding correction of low plasma levels unnecessary

Other Guidelines

Reference	Energy	Protein	Electrolytes	Fluid	Micro nutrients
Solomen & Kirby (1990) *JPEN*, 14:90	20kcal/kg	1.2-1.5g	_	_	_
Dewar & Horvath (2001) *A Pocket Guide to Clinical Nutrition*	20kcal/kg	_	Replenish as required	_	Thiamine IV 48hrs → Oral & Forceval
Crook *et al* (2001) *Nutrition.* 7:632	20kcal/kg	1.2-1.5g	Replenish as required	_	Thiamine IV 48hrs → Oral
Kraft *et al* (2005) *Nutr Clin Pract.* 20:625	25% of requirements	_	10 -15mmol of PO4/1000kcal Replenish as required	<1L/d	Thiamine IV 50-100mg/d or 100mg PO 5-7d & multivitamin
Stanga *et al* (2008) *Eur J Clin Nutr.* 62:687	10kcal/kg 50-60% CHO 30-40% Fat	10-20%	KCL: 1-3mmol/kg Mg 0.3-0.4mmol/kg PO4 0.5-0.8mmol/kg Na <1mmol/kg	20-30ml /kg	100% Thiamine IV 200-300 for 72hrs

Attitudes to NICE Refeeding Guidelines

- Unpublished survey of HCP
- 44% of doctors followed the guidance vs. 70% of dietitians
- 39% thought guidance was safe practice
- 36% thought excessively cautious
- Obstacle to providing adequate nutrition
- Other never seen refeeding despite providing 100% requirement from day 1

De Silva *et al* (2008) *BMJ,* 337:67

Dietetic Practice in Refeeding

- Questionnaire including 3 case studies
- 30.8% response rate, 89.8% had read NICE
- 66.9% changed practice based on NICE
- 89.5% do not wait for normal biochemistry
- Feed increased over 3-4 days
- 75% supplement electrolytes reactively
- Current practice is inconsistent but 20kcal/kg common
- Common themes: lack of evidence, overcautious & exacerbate malnutrition vs. better safe than sorry
- Clinical Judgment
- Advice on supplementation confusing or difficult to follow and often impractical.

Wagstaff (2011) *JHND* 24:505

ESPEN Guidelines for PN & EN

- PN
  - Geriatrics – strict monitoring required
  - Hepatology – Additional K, PO4 & Mg
  - Pancreas – Appropriate supplements
  - Surgery – Care increasing calories & protein
- EN
  - Gastroenterology & Renal – mentioned but no advice

Marsipan Report (2010)

- Joint report – Royal College of Physicians & Royal College of Psychiatrists working group
- Recommendation 8
- The key tasks of the in patient team are to:
  - safely re-feed the patient
  - avoid re-feeding syndrome caused by too rapid re-feeding
  - avoid underfeeding syndrome caused by too cautious rates of re-feeding

Refeeding in Anorexia Nervosa

- 33 in-patients with anorexia nervosa
  - Mean BMI 11.3±0.7kg/m^2,REE 777±145kcal/d
- Treatment:
  - Oral/enteral thiamine & B vitamins bd before feeding
  - IV 5-10% glucose ~20-40ml/hr (n=29)
  - NG feeding over 24 hr (n=30), ONS (n=3)

Gentile et al (2010) *Clin Nutr* 29:627

Refeeding in Anorexia Nervosa

	Time			
	Day 0	7 days	15 days	30 days
Measured kcal/expenditure – kcal/day	776 ± 145			
Enteral feeding regimen – kcal/day	806 ± 269	1002 ± 270	1133 ± 420	1154 ± 420
Oral diet – kcal/day	431 ± 331 (25)[b]	707 ± 320	890 ± 314	1162 ± 387
Glucose[c] kcal/day – i.v.[d] infusion	171 ± 56 (29)	186 ± 91 (28)	189 ± 113 (21)	194 ± 88 (15)
Phosphate mEq/day – i.v./oral	39.9 ± 24.8 (26)	45.0 ± 32.0 (25)	46.5 ± 32.0 (23)	32.5 ± 26.9 (23)
Potassium mEq/day – i.v./oral	33.0 ± 19.2 (21)	29.9 ± 13.9 (16)	29.7 ± 20.9 (15)	20 ± 8.2 (16)
Body weight – kg	29.1 ± 3.2	30.3 ± 3.8	31.35 ± 2.8	32.3 ± 2.9
BMI[f] – kg/m^2	11.3 ± 0.7	11.8 ± 0.7	12.2 ± 0.9	12.6 ± 0.9
Δ Body weight[g] – kg	0	1.2 ± 1.3	2.3 ± 1.8	3.2 ± 2.2

Day 1

NG feeding & glucose & oral food = Total kcal day 1 => 40kcal/kg

Majority supplemented with IV/oral phosphate (n=26) & potassium (n=21) and occasionally magnesium (n=3)

Gentile et al (2010) *Clin Nutr* 29:627

Refeeding Audit

Aims

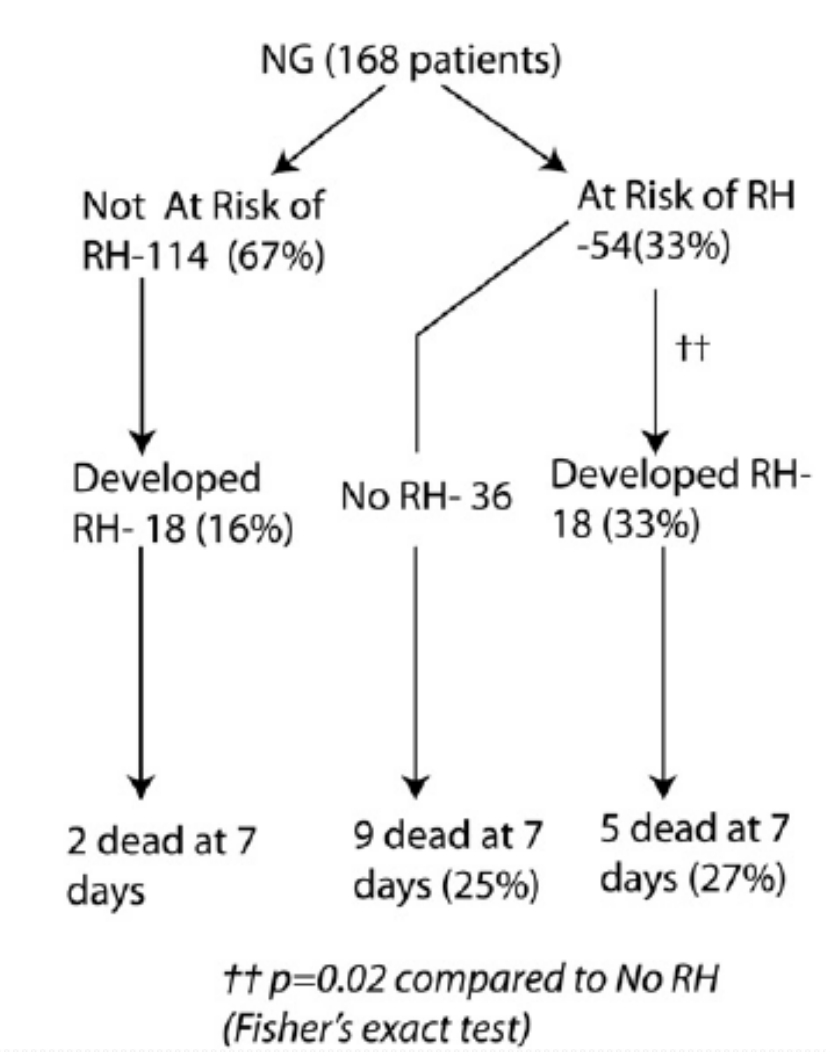
- Determine the overall & comparative incidence of refeeding hypophosphataemia (RH) between EN & PN
- Assessment of the number of patients progressing to RH in those deemed at risk according to NICE (2006)
- Determine mortality at one week of those with RH
- Assess sensitivity & specificity of NICE guidelines

Zeki, Culkin, Gabe & Nightingale (2011) *Clin Nutr*, 30: 365

Method

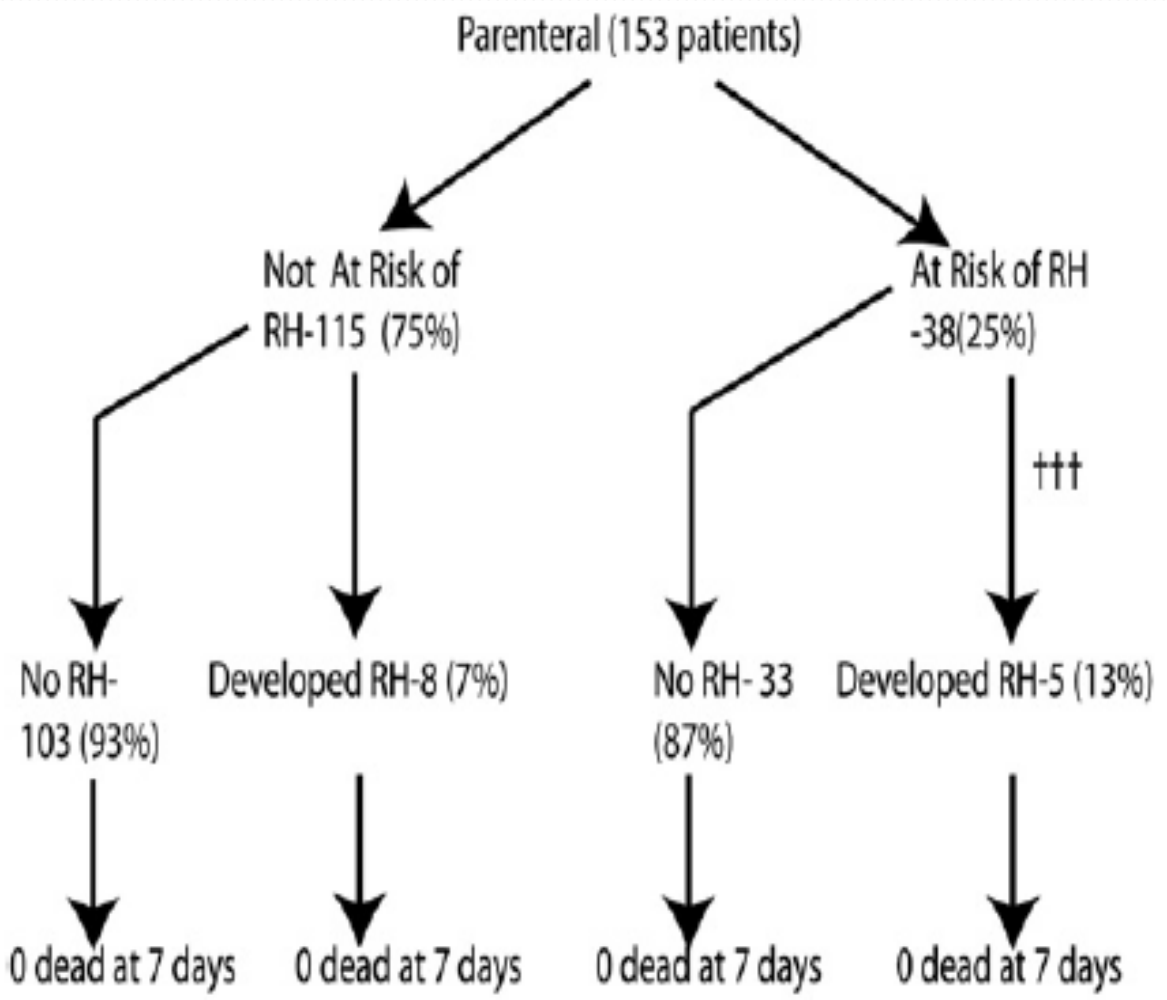
- Retrospective study using dietetic record cards
- Inclusion: All patients referred for EN or PN over a 12 month period
- Exclusion: Serum phosphate of <0.6mmol/L & ICU
- Refeeding hypophosphatemia: ↓ in serum phosphate to <0.6mmol/L during the first 7 days of feeding

Results – Enteral



- Significant association between being at risk of RH and developing RH (p=0.02)
- No difference in mortality between those deemed at risk of RH and developing RH compared to those who did not develop RH (p=0.53)

Results – Parenteral



- No significant associations between being at risk of RH and developing RH (p=0.31)

Results

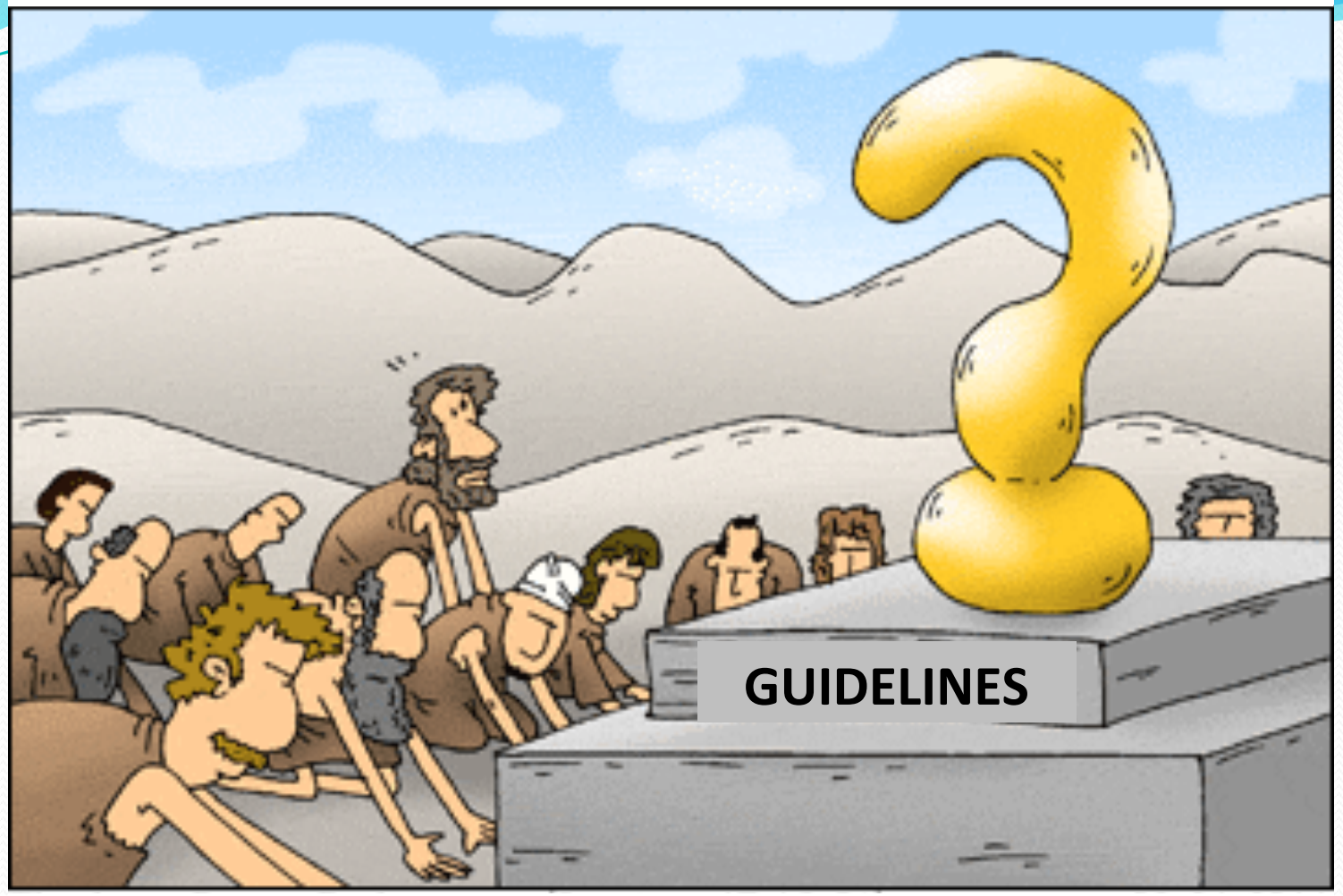
- Death was more common in EN compared to PN ($p<0.001$)
- No association between developing RH and death in EN and/or PN ($p=0.73$)
- At risk EN patients more likely to develop RH than PN ($p=0.003$)

Specificity & Sensitivity

- Specificity measures the proportion of negatives which are correctly identified (i.e. the % of patients correctly identified as not experiencing RH)
- Sensitivity measures the proportion of actual positives which are correctly identified as such (i.e. the % of patients correctly identified as experiencing RH)
- Parenteral
  - Moderate specificity (0.76) & poor sensitivity (0.5)
- Enteral
  - Moderate specificity (0.73) & poor sensitivity (0.38)

Discussion

- A third of patients were at risk of RH using NICE criteria
- A quarter developed RH but more common in EN
- Possible causes include:
  - Inadequate phosphate in enteral feeds
  - Lack of prophylactic supplementation
  - Poor absorption in the gut
  - Incretin effect? ↑ Insulin secretion from enteral vs. parenteral delivery of glucose
  - Experienced Nutrition Team prescribing PN
- RH may be common but not association with mortality


GUIDELINES

The Challenge

R C T

Disclaimer

- The following case study was used to illustrate the current practice at St Mark's hospital.
- The cautious approach of the NICE guidelines is not followed
- Usually feed to EER

Case Study

- Male age 27
- Crohn's disease diagnosed 2000
- SB resection 2002 & 2009
- Previous EN via PEG
- Resistant to medical intervention
- BO x 2/day semi formed
- Ht 1.88, Wt = 49kg, O/E oedema ~6kg
- Estimated dry wt 43kg, estimated BMI=12.2kg/m^2
- Usual wt 55kg 3/12 ago, % wt loss 21.8%
- TST <5th, MAMC <5th, Handgrip 21kg <85% normal

Biochemistry

Date	WCC	Na	K	Cr	Urea	CRP	ALT	AP	Bili	Alb	Ca	Mg	PO4
19/9/12	**4.2**	137	**3.3**	**41**	**2.7**	**59**	18	148	4	**7**	**1.85**	**<0.27**	0.87
20/9/12	**3.7**	137	**2.6**	**41**	**2.3**	**-**	22	**174**	5	**7**	**1.80**	**0.43**	0.86

Receiving IV fluids with electrolytes (40mmol Mg & 80mmol KCL) before CVC inserted

IV Thiamine given before feeding as enteral route compromised

Risk of Refeeding

Patients with any **one** of the following:	Yes	No
BMI <16kg/m^2		
Unintentional weight loss >15% in 3-6/12		
Very little or no food for > 10 days		
Low levels of K, PO4 or Mg before feeding		
Patients with **2 or more** of the following:	Yes	No
BMI <18.5kg/m^2		
Unintentional weight loss >10% in 3-6/12		
Very little or no food for > 5 days		
History of alcohol, insulin, chemotherapy, antacids or diuretics		

Risk of Refeeding

Patients with any **one** of the following:	Yes	No
BMI <16kg/m^2	√	
Unintentional weight loss >15% in 3-6/12	√	
Very little or no food for > 10 days		X
Low levels of K, PO4 or Mg before feeding	√	
Patients with **2 or more** of the following:	Yes	No
BMI <18.5kg/m^2	√	
Unintentional weight loss >10% in 3-6/12	√	
Very little or no food for > 5 days	√	
History of alcohol, insulin, chemotherapy, antacids or diuretics		X

Calculated PN Requirements

- BMR = 1233kcal + stress 0% (apyrexic & CRP 59) + activity 20% = 247kcal = Total = 1480kcal
- N_2 = 0.3g/kg = 12.9g/day (depleted)
- Fluid = 35ml/kg = 1505ml
- GOR = 991kcal
- Sodium 1-1.5mmol/kg = 43-65mmol
- Potassium 1-1.5mmol/kg = 43-65mmol
- Calcium 0.1-0.15mmol/kg = 4.3-6.5mmol
- Magnesium 0.1-0.2mmol/kg = 4.3-8.6mmol
- Phosphate 0.5-0.7mmol/kg = 21.5-30mmol

Requirements

	Calculated requirements	NICE	Prescribed
Energy (kcal)	1480	215	1400
Kcal/kg	**-**	**5**	**32**
Glucose (kcal)	991	?	400
Lipid (kcal)	?	?	1000
Nitrogen (g)	12.9	6.5	9
K (mmol)	43-65	86-172	100
Na (mmol)	43-65	?	60
PO4 (mmol)	21.5-30	12.9-25.8	30
Mg (mmol)	4.3-8.6	4.3-8.6	30

PN & Biochemistry

Date	N2	Glucose	Lipid	Na	K	Mg	Ca	PO4	Volume	Rate
21/9/12	9	400	1000	60	100	30	6	30	1500	24
24/9/12	9	800	571	60	100	30	6	30	1500	20
27/9/12	9	1000	571	60	80	30	6	30	1500	16

Date	WCC	Na	K	Cr	Urea	CRP	ALT	AP	Bili	Alb	Ca	Mg	PO4
20/9/12	3.7	137	**2.6**	**41**	**2.3**	**-**	22	**174**	5	**7**	**1.80**	**0.43**	0.86
21/9/12	4.1	135	4.2	**41**	**1.1**	**63**	24	**162**	7	**12**	**1.46**	**-**	**0.70**
22/9/12	3.1	**132**	4.0	**45**	**0.8**	**100**	18	146	5	**9**	**2.14**	0.98	0.94
23/9/12	3.0	134	4.3	**46**	**1.1**	**103**	15	148	6	**8**	2.23	1.02	1.11
24/9/12	-	**131**	4.1	**42**	**1.1**	**95**	-	-	-	**-**	**-**	0.78	-
26/9/12	5.3	134	4.9	**45**	**1.4**	**104**	16	**309**	7	**8**	**-**	**0.54**	1.14

Outcome

- At extreme high risk of refeeding according to NICE but no evidence of refeeding
- 50:50 mix of lipid:glucose
- Electrolytes improved before feeding
- BG 4.2-5.9mmol/L
- Biochemical vs. symptomatic refeeding
- Recommendation: Kcal/kg → Glucose kcal/kg

Buddha & Goldilocks

Thank you for your attention