Entry Level Clinical Nutrition
Part XVII

Insulin – part II:
Carbohydate:protein imbalances and the refeeding syndrome

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60 MINUTES

60 Minutes – Sunday, April 1, 2012

Is sugar toxic?

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Mark Lenzi dies at 43; American diving champion - latimes.com Page 1 of 1

latimes.com/news/obituaries/la-me-mark-lenzi-20120410,0,4422006.story

latimes.com

Mark Lenzi dies at 43; American diving champion

Inspired by Greg Louganis' performance at the '84 Games, Lenzi switched from wrestling to diving and quickly became a star, winning gold in the 1992 Olympic 3-meter springboard event.

Associated Press

April 10, 2012

Mark Lenzi, the 1992 Olympic 3-meter springboard champion and the last American male diver to win Olympic gold, died Monday in Greenville, N.C. He was 43.

Lenzi's alma mater, Indiana University, announced his death but did not provide the cause. His mother, Ellie, told the family's hometown newspaper, the Free Lance-Star of Fredricksburg, Va., that Lenzi had been hospitalized the last two weeks because of fainting spells caused by low blood pressure.

Four years after his gold-medal performance in Barcelona, Lenzi earned a bronze medal at the 1996 Atlanta Olympics and became the first diver to score 100 points on a single dive.

Lenzi was wrestling in high school when he was suddenly captivated by Greg Louganis' remarkable Olympics performance at the 1984 Los Angeles Games. Lenzi changed sports, diving right into his new passion.

"…Lenzi had been hospitalized the last two weeks because of fainting spells caused by low blood pressure."

Lenzi's impressive resume includes 18 international springboard championships. He was the first diver to score more than 700 points in an 11-dive competition on the 3-meter board and the first American to successfully complete a forward, 4 1/2 somersault in competition.

Lenzi, who struggled with post-Olympic depression, went into coaching after his diving career ended.

Survivors include his wife, mother, three siblings and grandmother.

news.obits@latimes.com

http://www.latimes.com/news/obituaries/la-me-mark-lenzi-20120410,0,5827103,print.story 4/10/2012

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Tuesday, April 10, 2012

B2 Daily Hampshire Gazette • gazettenet.com

OBITUARIES

James E. Bodmer Jr., engineer, scuba diver

Dead at 50

AMHERST — James Ellis Bod-

He was born Nov. 23, 1961, in Abington, Pa., and was baptized in League City, Texas, United Methodist Church. He went to James H. Ross Elementary School, Webster Intermediate School and graduated from Clear Creek High School, where he played the tuba in the marching band.

James joined the U.S. Marine Corps soon after and he graduated with top honors in his class from the USMC Radar Technician School in Memphis, Tenn.

After he was honorably discharged, he attended the University of Arizona while working as a telemetry technician for the U.S. Army. He earned a

ested in the development of rich internet applications, server side Web applications and relational databases.

On a personal note, James participated in the Rustman Triathlon in 1989 and 1990. He was an avid scuba diver and photographer and was a past president

remote operators and maintainers with enhanced situational awareness of the sensor equipment. He worked closely with MIT Lincoln Laboratories to coordinate and implement this project to give all RTS radars improved reliability and enhanced troubleshooting capabilities.

He was very much into computer technology and was inter-

cousins.

The family will receive friends for visitation Wednesday, April 11, from 5 to 8 p.m. at Pat H. Foley & Co. A celebration of James' life will be held at 9:30 a.m. on Thursday, April 12, in the chapel of Pat H. Foley & Co. Interment will follow at Houston National Cemetery, 10401 Veterans Memorial Drive, Houston, TX 77038.

"On a personal note, James participated in the Rustman Triathlon in 1989 and 1990. He was an avid scuba diver and photographer and was a past president of the ROI-Namur Dolphin's Club. James also hiked the Appalachian Trail with his father every year."

John F. McNulty Jr., hard worker

S. Hadley trainer dies

Dead at 57

By ETTA WALSH
Contributing Writer

SOUTH HADLEY — The unexpected death of popular South Hadley High School athletic trainer Peter R. Krasnor on Friday sent shock waves through the school as students, staff and athletic officials mourned the loss of a man described as physically fit and a role model.

"It was quite a shock to everyone," Dale Carey, chairman of the School Committee, said in a telephone interview Monday.

In his seven years as athletic trainer at South Hadley High School, Krasnor proved to be not only a highly qualified professional, but also

nor, Desautels said.

"They did that on their own," he said. "They contacted all their friends. That's the impact he had on student athletes."

Scammons said the vigil attracted current South Hadley athletes along with those who had already graduated.

"One of the great things about Peter was that he was a father figure to some students, a mentor," the football coach said. "He was also a fan, someone who really enjoyed athletics, who encouraged students."

died Friday at Baystate Medical Center. No cause of death has been made public.

Eric Scammons, football coach at the school, said Krasnor "was in phenomenal physical shape."

"He was a body builder," Scammons said. "He had run marathons. He was just really in good shape. For him to pass so suddenly is really a shock."

"He always preached wellness. He preached staying in shape," said Desautels, adding that Krasnor practiced what he preached.

"He was extremely passionate about his job," the athletic director said. "He was very, very thorough in his

sionate about his job," Desautels said. "He really, really enjoyed everything he did. Every day, he came in with a smile and left with a smile."

Krasnor was a Springfield native. He attended Classical High School and earned a bachelor's degree in athletic training from Bridgewater State University and a master's degree in exercise physiology from Springfield College, according to his obituary.

He worked as an athletic trainer in schools in South Hadley, Longmeadow, Springfield and Chicopee. He leaves his mother, Marion, daughter Rachael and brothers Carl and Richard.

"'He was a body builder,'" Scammons said. 'He had run marathons. He was just really in good shape. For him to pass so suddenly is really a shock."

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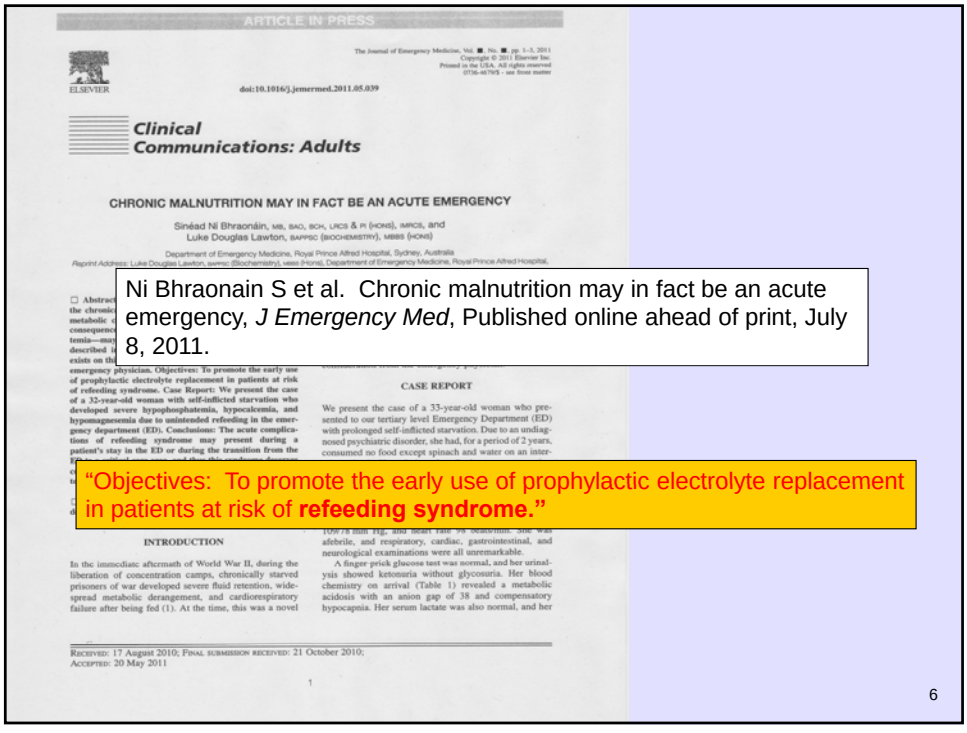

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Clinical Communications: Adults

CHRONIC MALNUTRITION MAY IN FACT BE AN ACUTE EMERGENCY

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Reprint Address: Luke Douglas Lawton, BAPPSC (Biochemistry), MBBS (Hons), Department of Emergency Medicine, Royal Prince Alfred Hospital,

☐ Abstract

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emergency physician. Objectives: To promote the early use of prophylactic electrolyte replacement in patients at risk of refeeding syndrome. Case Report: We present the case of a 32-year-old woman with self-inflicted starvation who developed severe hypophosphatemia, hypocalcemia, and hypomagnesemia due to unintended refeeding in the emergency department (ED). Conclusions: The acute complications of refeeding syndrome may present during a patient's stay in the ED or during the transition from the

Ni Bhraonain S et al. Chronic malnutrition may in fact be an acute emergency, *J Emergency Med*, Published online ahead of print, July 8, 2011.

"Objectives: To promote the early use of prophylactic electrolyte replacement in patients at risk of **refeeding syndrome."**

INTRODUCTION

In the immediate aftermath of World War II, during the liberation of concentration camps, chronically starved prisoners of war developed severe fluid retention, widespread metabolic derangement, and cardiorespiratory failure after being fed (1). At the time, this was a novel

CASE REPORT

We present the case of a 33-year-old woman who presented to our tertiary level Emergency Department (ED) with prolonged self-inflicted starvation. Due to an undiagnosed psychiatric disorder, she had, for a period of 2 years, consumed no food except spinach and water on an inter-

109/78 mm Hg, and heart rate 93 beats/min. She was afebrile, and respiratory, cardiac, gastrointestinal, and neurological examinations were all unremarkable.

A finger prick glucose test was normal, and her urinalysis showed ketonuria without glycosuria. Her blood chemistry on arrival (Table 1) revealed a metabolic acidosis with an anion gap of 38 and compensatory hypocapnia. Her serum lactate was also normal, and her

RECEIVED: 17 August 2010; FINAL SUBMISSION RECEIVED: 21 October 2010;
ACCEPTED: 20 May 2011

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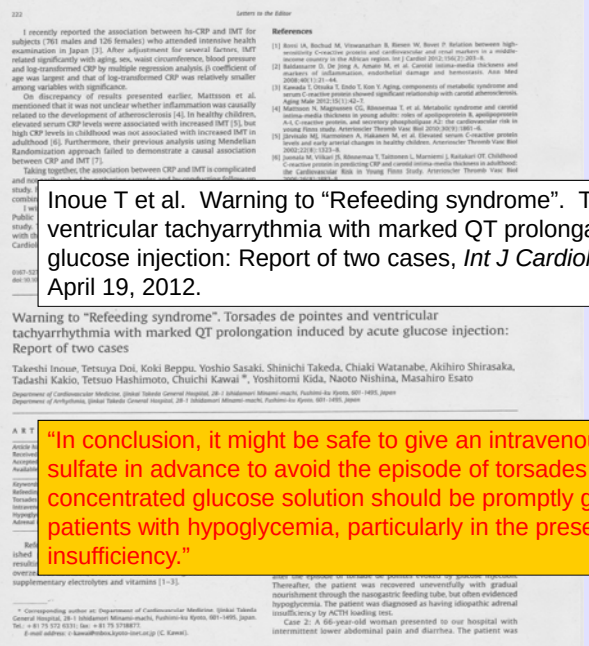

Warning to "Refeeding syndrome". Torsades de pointes and ventricular tachyarrhythmia with marked QT prolongation induced by acute glucose injection: Report of two cases

Takeshi Inoue, Tetsuya Doi, Koki Beppu, Yoshio Sasaki, Shinichi Takeda, Chiaki Watanabe, Akihiro Shirasaka, Tadashi Kakio, Tetsuo Hashimoto, Chuichi Kawai *, Yoshitomi Kida, Naoto Nishina, Masahiro Esato

Inoue T et al. Warning to "Refeeding syndrome". Torsades de pointes and ventricular tachyarrhythmia with marked QT prolongation induced by acute glucose injection: Report of two cases, *Int J Cardiol*, Vol. 156, No. 2, pp. 222-4, April 19, 2012.

"In conclusion, it might be safe to give an intravenous infusion of magnesium sulfate in advance to avoid the episode of torsades de pointes when highly concentrated glucose solution should be promptly given intravenously in patients with hypoglycemia, particularly in the presence of adrenal insufficiency."

7

Could classic "carb loading" in certain susceptible athletes be contributing to torsades de pointes?

8

Quality of life issues are the major concerns more than ever now.

9

The New York Times

September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

By KEVIN SACK

SEATTLE — This summer, medical students from the University of Washington took a long look under the hood of the health care system they are about to inherit, and many returned to campus last week with their eyes wide open and their idealism tempered.

Jacob R… more th… eschew… Olsgaar… treatme…

Summer of work exposes medical students to system's ills, *The New York Times, September 9, 2009*

The students learned not only to deliver babies and suture wounds, but also to order unnecessary tests as protection against lawsuits, to hector specialists into seeing Medicaid patients, to match patients with prescriptions on Wal-Mart's $4 list. And they saw firsthand what Mr. Olsgaard called "a tidal wave of chronic disease" — diabetes, hypertension, obesity, depression — that left many questioning how much any one physician could really accomplish.

"I often wondered what we were actually doing to help people," Mr. Olsgaard said.

Not sur… devalue…

"…a tidal wave of chronic illness…"

"You ha… reimbur… treatments they can afford early instead of waiting until there's a catastrophic surgery. It's pretty simple."

For 21 years, the University of Washington School of Medicine has dispatched its rising second-year students across the Northwest to provide primary care in rural or underserved areas. The monthlong program is elective, but a record number of students took part this year — 117 from a class of 216.

The school has a cooperative agreement to train medical students from Alaska, Idaho, Montana and Wyoming, none of which has a medical college of its own. The summer program is one of several vehicles, along with loan forgiveness enticements, designed to lure students back to their home states to practice in areas with a shortage of primary care givers.

This year, the students set out as negotiations were intensifying in Washington over wholesale changes to the health care system they will soon be joining. Whether there will be improvements to the system remains to be seen, but few students returned thinking there was little to fix.

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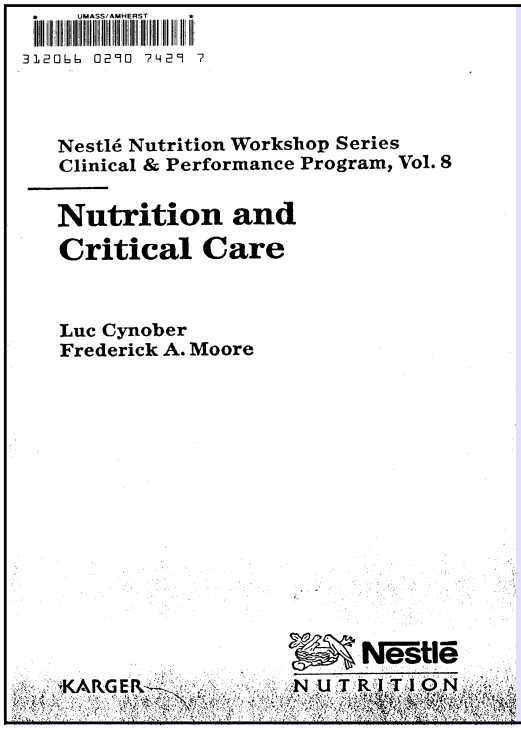

Baracos VE. Overview on metabolic adaptation to stress, pp. 1-13.

"An understanding of the nature of stress is fundamental to the rational design of nutrient mixtures to feed patients whose homeostasis has been altered by one or more stressors."

"All stresses may be presumed to be associated with characteristic modifications in the metabolism of lipids, carbohydrates, amino acids, and micronutrients."

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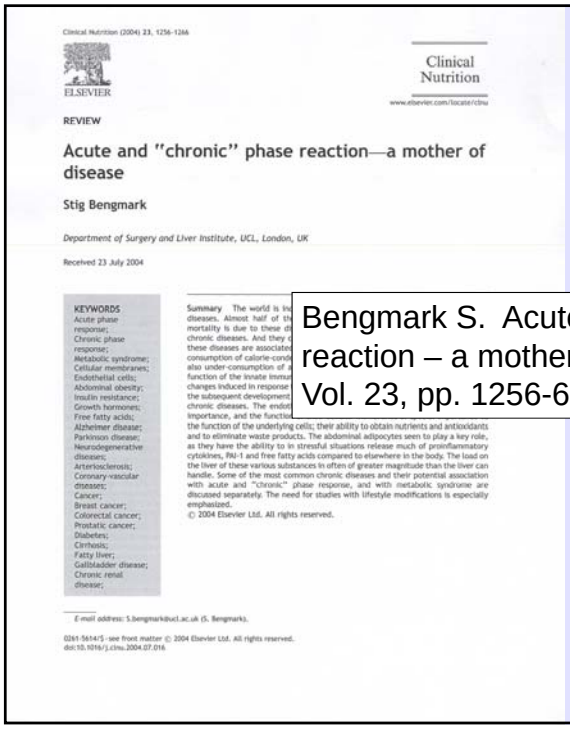

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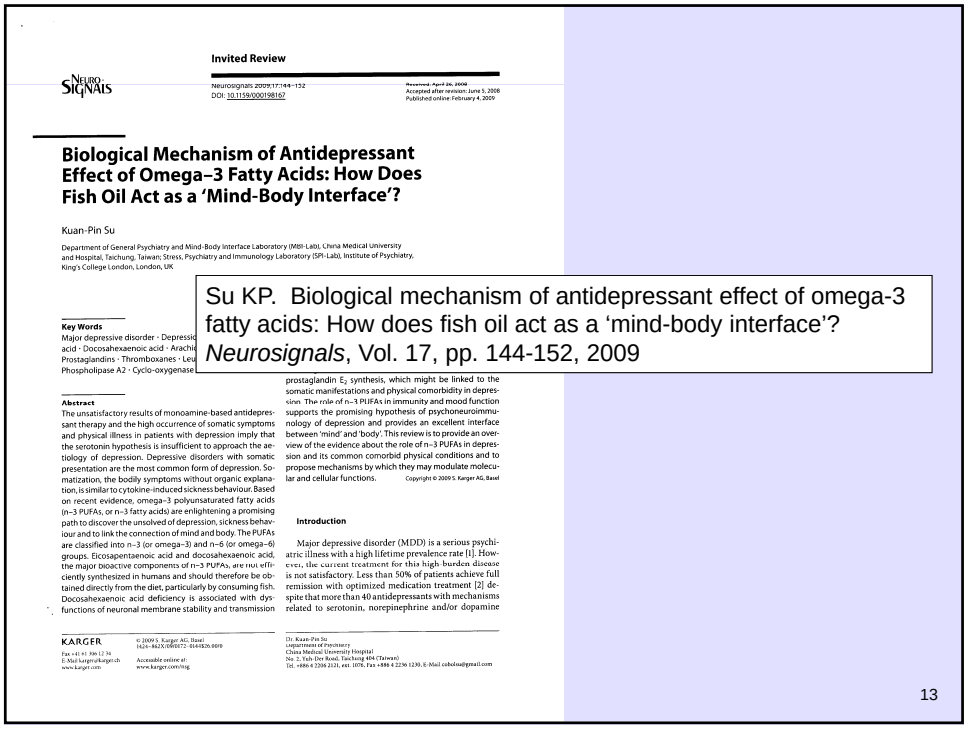

Invited Review

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Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a 'Mind-Body Interface'?

Kuan-Pin Su

Department of General Psychiatry and Mind-Body Interface Laboratory (MBI-Lab), China Medical University and Hospital, Taichung, Taiwan; Stress, Psychiatry and Immunology Laboratory (SPI-Lab), Institute of Psychiatry, King's College London, London, UK

Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a 'mind-body interface'? *Neurosignals*, Vol. 17, pp. 144-152, 2009

Key Words
Major depressive disorder · Depressi
acid · Docosahexaenoic acid · Arachi
Prostaglandins · Thromboxanes · Leu
Phospholipase A2 · Cyclo-oxygenase

Abstract
The unsatisfactory results of monoamine-based antidepressant therapy and the high occurrence of somatic symptoms and physical illness in patients with depression imply that the serotonin hypothesis is insufficient to approach the aetiology of depression. Depressive disorders with somatic presentation are the most common form of depression. Somatization, the bodily symptoms without organic explanation, is similar to cytokine-induced sickness behaviour. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFAs, or n-3 fatty acids) are enlightening a promising path to discover the unsolved of depression, sickness behaviour and to link the connection of mind and body. The PUFAs are classified into n-3 (or omega-3) and n-6 (or omega-6) groups. Eicosapentaenoic acid and docosahexaenoic acid, the major bioactive components of n-3 PUFAs, are not efficiently synthesized in humans and should therefore be obtained directly from the diet, particularly by consuming fish. Docosahexaenoic acid deficiency is associated with dysfunctions of neuronal membrane stability and transmission prostaglandin E_2 synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFAs in immunity and mood function supports the promising hypothesis of psychoneuroimmunology of depression and provides an excellent interface between 'mind' and 'body'. This review is to provide an overview of the evidence about the role of n-3 PUFAs in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions.

Introduction

Major depressive disorder (MDD) is a serious psychiatric illness with a high lifetime prevalence rate [1]. However, the current treatment for this high-burden disease is not satisfactory. Less than 50% of patients achieve full remission with optimized medication treatment [2] despite that more than 40 antidepressants with mechanisms related to serotonin, norepinephrine and/or dopamine

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Table 1. Overlapping of symptoms of acute sickness behaviour associated with IFN-α therapy and the somatic symptoms in MDD

Symptoms	Prevalence in IFN-α therapy [a], %	Prevalence in MDD [b], %
Fatigue/asthenia	39–90	73
Headache	27–67	33[e]
Gastrointestinal symptoms	50[c, 1]	34–47[f]
Psychomotor slowing	40[c]	59–65[f]
Insomnia	20–39[d]	63
Irritability	35[d]	50
Arthralgia	9–36	31[e]
Musculoskeletal pain	26–32	62–80[g, 2]
Abdominal pain	15–20	21[e]
Anorexia	13–19	40
Anxiety	13–18[d]	57
Poor concentration	14[d]	51

[a] [46], unless otherwise specified; [b] [99], unless otherwise specified; [c] [100]; [d] [101]; [e] [102]; [f] [103]; [g] [104].
[1] Nausea, vomiting, bowel problems.
[2] Result from depressed inpatient population.

Key metabolic imbalances seen with the acute phase response

- Metabolic acidosis
- Loss of lean body mass (sarcopenia)
- Insulin resistance
- Inflamm-aging (Increased innate immunity and decreased adaptive immunity)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction/gut atrophy
- Deficiencies of key micronutrients such as zinc, selenium, and vitamin D

15

Underlying hypotheses of Entry Level Clinical Nutrition:

- Chief complaints in chronically ill patients are not diseases but responses that have gone on too long (Allostatic load).
- The metabolic imbalances that combine to form this response have been well defined by critical care nutritionists.

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Entry Level Clinical Nutrition:

A new model of functional medicine that incorporates allostatic load and the "chronic" acute phase response

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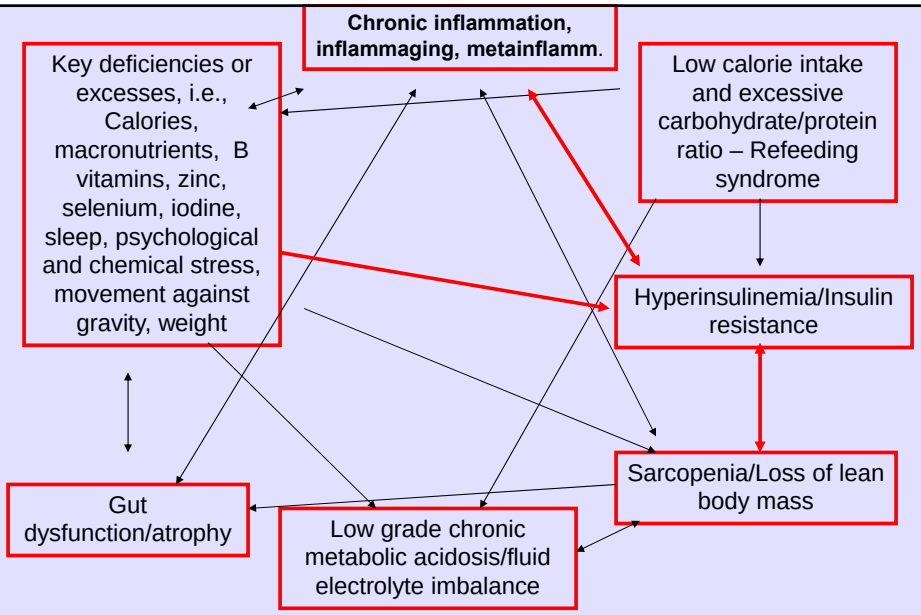

THE CREATION OF THE EXCESSIVE CATABOLIC PHYSIOLOGY "RESPONSE"

18

Is reactive hypoglycemia a mild form of refeeding syndrome?

19

What is reactive hypoglycemia?

20

According to Maria Collazo-Clavel, MD from the Mayo Clinic Website

- **"Reactive hypoglycemia (or alimentary hypoglycemia) is low blood sugar that occurs after a meal — usually one to three hours after eating."**
- **"Low blood sugar (hypoglycemia) usually occurs while fasting."**
- **"Signs and symptoms of reactive hypoglycemia may include hunger, weakness, shakiness, sleepiness, lightheadedness, anxiety and confusion."**

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Dr. Collazo-Cavell's recommendations

- **"Avoid or limit sugary foods, especially on an empty stomach."**
- **"Be sure to eat food if you're consuming alcohol and avoid using sugary soft drinks as mixers."**

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Refeeding syndrome

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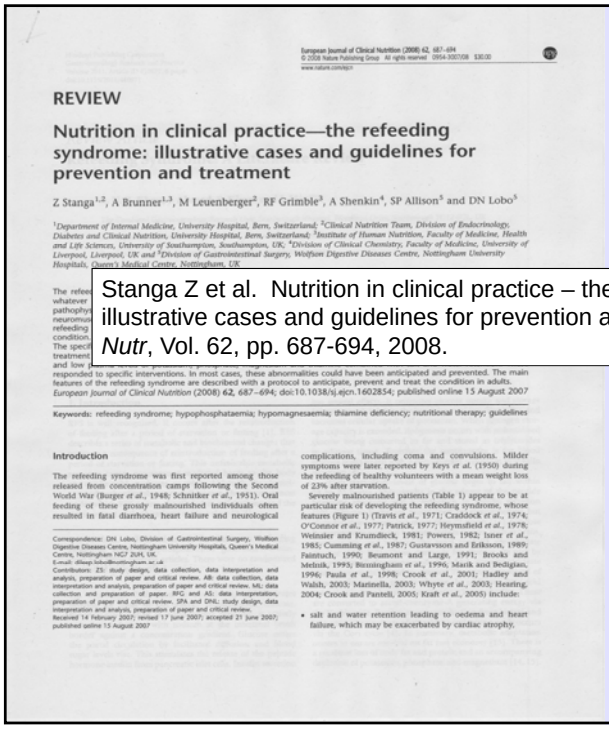

European Journal of Clinical Nutrition (2008) 62, 687–694

0954-3007/08 $30.00
www.nature.com/ejcn

REVIEW

Nutrition in clinical practice—the refeeding syndrome: illustrative cases and guidelines for prevention and treatment

Z Stanga[1,2], A Brunner[1,3], M Leuenberger[2], RF Grimble[3], A Shenkin[4], SP Allison[5] and DN Lobo[5]

[1]*Department of Internal Medicine, University Hospital, Bern, Switzerland;* [2]*Clinical Nutrition Team, Division of Endocrinology, Diabetes and Clinical Nutrition, University Hospital, Bern, Switzerland;* [3]*Institute of Human Nutrition, Faculty of Medicine, Health and Life Sciences, University of Southampton, Southampton, UK;* [4]*Division of Clinical Chemistry, Faculty of Medicine, University of Liverpool, Liverpool, UK and* [5]*Division of Gastrointestinal Surgery, Wolfson Digestive Diseases Centre, Nottingham University Hospitals, Queen's Medical Centre, Nottingham, UK*

The refee
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responded to specific interventions. In most cases, these abnormalities could have been anticipated and prevented. The main features of the refeeding syndrome are described with a protocol to anticipate, prevent and treat the condition in adults.
European Journal of Clinical Nutrition (2008) 62, 687–694; doi:10.1038/sj.ejcn.1602854; published online 15 August 2007

Keywords: refeeding syndrome; hypophosphataemia; hypomagnesaemia; thiamine deficiency; nutritional therapy; guidelines

Introduction

The refeeding syndrome was first reported among those released from concentration camps following the Second World War (Burger *et al.*, 1948; Schnitker *et al.*, 1951). Oral feeding of these grossly malnourished individuals often resulted in fatal diarrhoea, heart failure and neurological complications, including coma and convulsions. Milder symptoms were later reported by Keys *et al.* (1950) during the refeeding of healthy volunteers with a mean weight loss of 23% after starvation.

Severely malnourished patients (Table 1) appear to be at particular risk of developing the refeeding syndrome, whose features (Figure 1) (Travis *et al.*, 1971; Craddock *et al.*, 1974; O'Connor *et al.*, 1977; Patrick, 1977; Heymsfield *et al.*, 1978; Weinsier and Krumdieck, 1981; Powers, 1982; Isner *et al.*, 1985; Cumming *et al.*, 1987; Gustavsson and Eriksson, 1989; Faintuch, 1990; Beumont and Large, 1991; Brooks and Melnik, 1993; Buzzinghams *et al.*, 1996; Marik and Bedigian, 1996; Paula *et al.*, 1998; Crook *et al.*, 2001; Hadley and Walsh, 2003; Marinella, 2003; Whyte *et al.*, 2003; Hearing, 2004; Crook and Pantell, 2005; Kraft *et al.*, 2005) include:

- salt and water retention leading to oedema and heart failure, which may be exacerbated by cardiac atrophy.

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E-mail: dilwyn.lobo@nottingham.ac.uk
Contributors: ZS: study design, data collection, data interpretation and analysis, preparation of paper and critical review. AB: data collection, data interpretation and analysis, preparation of paper and critical review. ML: data collection and preparation of paper. RFG and AS: data interpretation, preparation of paper and critical review. SPA and DNL: study design, data interpretation and analysis, preparation of paper and critical review.
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Stanga Z et al. Nutrition in clinical practice – the refeeding syndrome: illustrative cases and guidelines for prevention and treatment, *Eur J Clin Nutr*, Vol. 62, pp. 687-694, 2008.

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- “The refeeding syndrome was first reported among those released from concentration camps following the Second World War.”
- “Oral feeding of these grossly malnourished individuals often resulted in fatal diarrhea, heart failure and neurological complications, including coma and convulsions.”
- “Milder symptoms were later reported by *Keys et al.* during the refeeding of healthy volunteers with a mean weight loss of 23% after starvation.”

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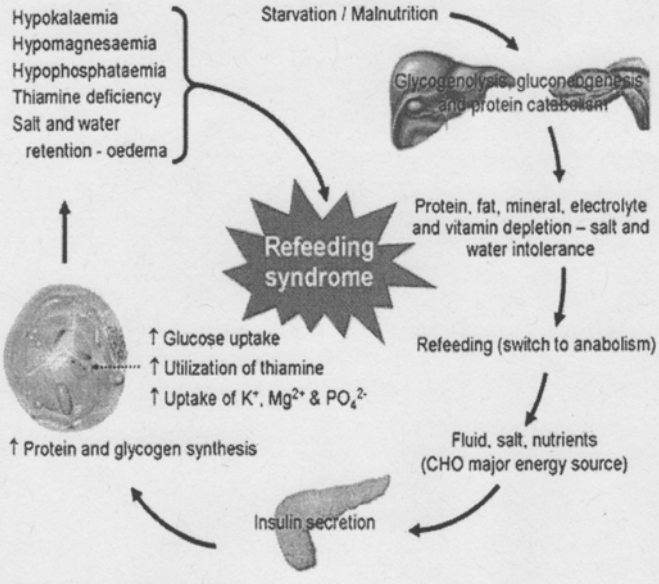

Figure 1 Pathogenesis and features of the refeeding syndrome.

pean Journal of Clinical Nutrition

Table 1 Some groups of malnourished patients at particular risk of developing the 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

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Contributing factors to occurrence of refeeding syndrome

- “Common factors include the severity of the underlying malnutrition, overaggressive nutritional support in the early stages with adequate supplements of phosphate, thiamine, potassium and magnesium, and associated conditions that exacerbate micronutrient, electrolyte and mineral deficiencies, for example alcoholism, gastrointestinal disorders, and poor or eccentric diets.”

28

Metabolic sequence

- “During starvation, phosphate and potassium are lost from the cell in proportion to the breakdown of glycogen and protein, potassium being the main intracellular cation balancing the negative charges on proteins.”

29

- “There is, therefore, no clinical deficiency of these electrolytes until catabolism is abruptly reversed and resynthesis of glycogen and protein begins, creating a sudden demand for inorganic phosphate for phosphorylation and adenosine triphosphate (ATP) synthesis and for potassium to balance the negative charges on protein and glycogen.”

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- “Magnesium, being involved in ATP synthesis, is also taken up by the cells.”
- “Upon the introduction of carbohydrate, insulin is released into the blood stream and there is a shift of metabolism from fat to carbohydrate.”
- Acute thiamin deficiency may be precipitated, especially in patients suffering from chronic alcoholism, since diminished thiamine reserves are rapidly used up, as carbohydrate metabolism is accelerated.”

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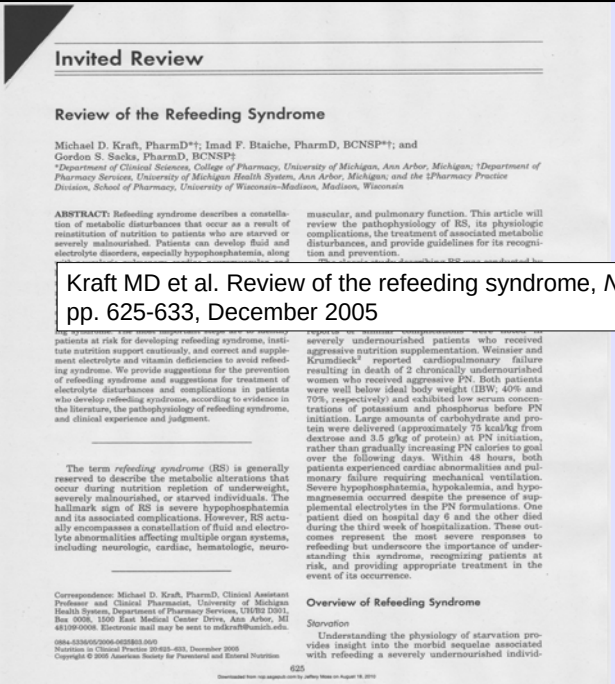

Invited Review

Review of the Refeeding Syndrome

Michael D. Kraft, PharmD*†; Imad F. Btaiche, PharmD, BCNSP*†; and Gordon S. Sacks, PharmD, BCNSP‡

*Department of Clinical Sciences, College of Pharmacy, University of Michigan, Ann Arbor, Michigan; †Department of Pharmacy Services, University of Michigan Health System, Ann Arbor, Michigan; and the ‡Pharmacy Practice Division, School of Pharmacy, University of Wisconsin–Madison, Madison, Wisconsin

ABSTRACT: Refeeding syndrome describes a constellation of metabolic disturbances that occur as a result of reinstitution of nutrition to patients who are starved or severely malnourished. Patients can develop fluid and electrolyte disorders, especially hypophosphatemia, along

muscular, and pulmonary function. This article will review the pathophysiology of RS, its physiologic complications, the treatment of associated metabolic disturbances, and provide guidelines for its recognition and prevention.

patients at risk for developing refeeding syndrome, institute nutrition support cautiously, and correct and supplement electrolyte and vitamin deficiencies to avoid refeeding syndrome. We provide suggestions for the prevention of refeeding syndrome and suggestions for treatment of electrolyte disturbances and complications in patients who develop refeeding syndrome, according to evidence in the literature, the pathophysiology of refeeding syndrome, and clinical experience and judgment.

The term *refeeding syndrome* (RS) is generally reserved to describe the metabolic alterations that occur during nutrition repletion of underweight, severely malnourished, or starved individuals. The hallmark sign of RS is severe hypophosphatemia and its associated complications. However, RS actually encompasses a constellation of fluid and electrolyte abnormalities affecting multiple organ systems, including neurologic, cardiac, hematologic, neuro-

severely undernourished patients who received aggressive nutrition supplementation. Weinsier and Krumdieck[2] reported cardiopulmonary failure resulting in death of 2 chronically undernourished women who received aggressive PN. Both patients were well below ideal body weight (IBW; 40% and 70%, respectively) and exhibited low serum concentrations of potassium and phosphorus before PN initiation. Large amounts of carbohydrate and protein were delivered (approximately 75 kcal/kg from dextrose and 3.5 g/kg of protein) at PN initiation, rather than gradually increasing PN calories to goal over the following days. Within 48 hours, both patients experienced cardiac abnormalities and pulmonary failure requiring mechanical ventilation. Severe hypophosphatemia, hypokalemia, and hypomagnesemia occurred despite the presence of supplemental electrolytes in the PN formulations. One patient died on hospital day 6 and the other died during the third week of hospitalization. These outcomes represent the most severe responses to refeeding but underscore the importance of understanding this syndrome, recognizing patients at risk, and providing appropriate treatment in the event of its occurrence.

Overview of Refeeding Syndrome

Starvation

Understanding the physiology of starvation provides insight into the morbid sequelae associated with refeeding a severely undernourished individ-

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- **“Refeeding syndrome describes a constellation of metabolic disturbances that occur as a result of reinstitution of nutrition to patients who are starved or severely malnourished.”**
- **“Patients can develop fluid and electrolyte disorders, especially hypophosphatemia, along with neurologic, pulmonary, cardiac, neuromuscular, and hematologic complications.”**

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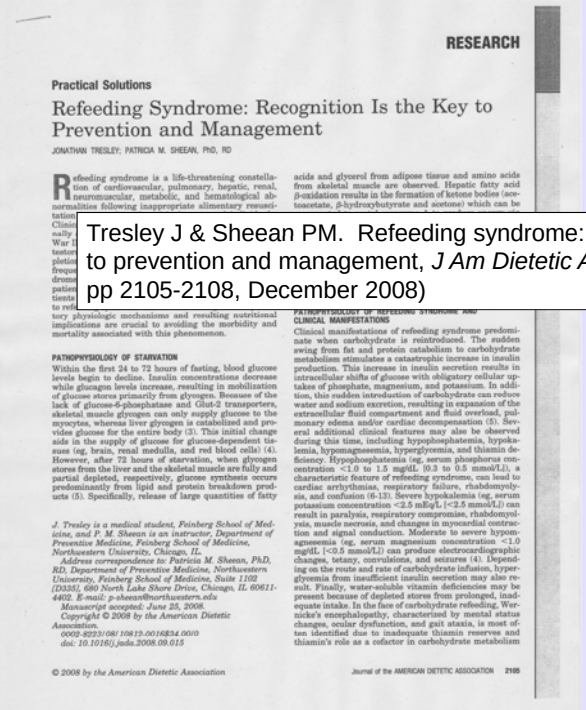

RESEARCH

Practical Solutions

Refeeding Syndrome: Recognition Is the Key to Prevention and Management

JONATHAN TRESLEY; PATRICIA M. SHEEAN, PhD, RD

Refeeding syndrome is a life-threatening constellation of cardiovascular, pulmonary, hepatic, renal, neuromuscular, metabolic, and hematological abnormalities following inappropriate alimentary resuscitation

tory physiologic mechanisms and resulting nutritional implications are crucial to avoiding the morbidity and mortality associated with this phenomenon.

PATHOPHYSIOLOGY OF STARVATION

Within the first 24 to 72 hours of fasting, blood glucose levels begin to decline. Insulin concentrations decrease while glucagon levels increase, resulting in mobilization of glucose stores primarily from glycogen. Because of the lack of glucose-6-phosphatase and Glut-2 transporters, skeletal muscle glycogen can only supply glucose to the myocytes, whereas liver glycogen is catabolized and provides glucose for the entire body (3). This initial change aids in the supply of glucose for glucose-dependent tissues (eg, brain, renal medulla, and red blood cells) (4). However, after 72 hours of starvation, when glycogen stores from the liver and the skeletal muscle are fully and partial depleted, respectively, glucose synthesis occurs predominantly from lipid and protein breakdown products (5). Specifically, release of large quantities of fatty acids and glycerol from adipose tissue and amino acids from skeletal muscle are observed. Hepatic fatty acid β-oxidation results in the formation of ketone bodies (acetoacetate, β-hydroxybutyrate and acetone) which can be

PATHOPHYSIOLOGY OF REFEEDING SYNDROME AND CLINICAL MANIFESTATIONS

Clinical manifestations of refeeding syndrome predominate when carbohydrate is reintroduced. The sudden swing from fat and protein catabolism to carbohydrate metabolism stimulates a catastrophic increase in insulin production. This increase in insulin secretion results in intracellular shifts of glucose with obligatory cellular uptakes of phosphate, magnesium, and potassium. In addition, this sudden introduction of carbohydrate can reduce water and sodium excretion, resulting in expansion of the extracellular fluid compartment and fluid overload, pulmonary edema and/or cardiac decompensation (5). Several additional clinical features may also be observed during this time, including hypophosphatemia, hypokalemia, hypomagnesemia, hyperglycemia, and thiamin deficiency. Hypophosphatemia (eg, serum phosphorus concentration <1.0 to 1.5 mg/dL [0.3 to 0.5 mmol/L]), a characteristic feature of refeeding syndrome, can lead to cardiac arrhythmias, respiratory failure, rhabdomyolysis, and confusion (6-13). Severe hypokalemia (eg, serum potassium concentration <2.5 mEq/L [<2.5 mmol/L]) can result in paralysis, respiratory compromise, rhabdomyolysis, muscle necrosis, and changes in myocardial contraction and signal conduction. Moderate to severe hypomagnesemia (eg, serum magnesium concentration <1.0 mg/dL [<0.5 mmol/L]) can produce electrocardiographic changes, tetany, convulsions, and seizures (4). Depending on the route and rate of carbohydrate infusion, hyperglycemia from insufficient insulin secretion may also result. Finally, water-soluble vitamin deficiencies may be present because of depleted stores from prolonged, inadequate intake. In the face of carbohydrate refeeding, Wernicke's encephalopathy, characterized by mental status changes, ocular dysfunction, and gait ataxia, is most often identified due to inadequate thiamin reserves and thiamin's role as a cofactor in carbohydrate metabolism

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- **"Today, anorexia nervosa is one of the more frequent clinical presentations at risk of refeeding syndrome; however, malnourished elderly patients, oncology patients receiving chemotherapy, and postoperative patients may also be at risk."**
- **"Recognizing individuals prone to refeeding syndrome and understanding the compensatory physiologic mechanisms and resulting nutritional implications are crucial to avoiding the morbidity and mortality associated with this phenomenon."**

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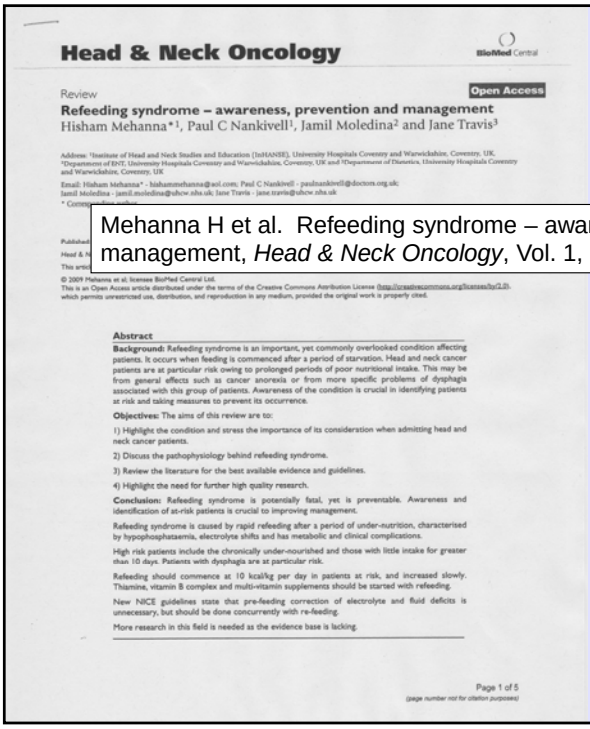

Head & Neck Oncology

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Review

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Refeeding syndrome – awareness, prevention and management

Hisham Mehanna*[1], Paul C Nankivell[1], Jamil Moledina[2] and Jane Travis[3]

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Email: Hisham Mehanna* - hishammehanna@aol.com; Paul C Nankivell - paulnankivell@doctors.org.uk; Jamil Moledina - jamil.moledina@uhcw.nhs.uk; Jane Travis - jane.travis@uhcw.nhs.uk

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Abstract

Background: Refeeding syndrome is an important, yet commonly overlooked condition affecting patients. It occurs when feeding is commenced after a period of starvation. Head and neck cancer patients are at particular risk owing to prolonged periods of poor nutritional intake. This may be from general effects such as cancer anorexia or from more specific problems of dysphagia associated with this group of patients. Awareness of the condition is crucial in identifying patients at risk and taking measures to prevent its occurrence.

Objectives: The aims of this review are to:

1) Highlight the condition and stress the importance of its consideration when admitting head and neck cancer patients.

2) Discuss the pathophysiology behind refeeding syndrome.

3) Review the literature for the best available evidence and guidelines.

4) Highlight the need for further high quality research.

Conclusion: Refeeding syndrome is potentially fatal, yet is preventable. Awareness and identification of at-risk patients is crucial to improving management.

Refeeding syndrome is caused by rapid refeeding after a period of under-nutrition, characterised by hypophosphataemia, electrolyte shifts and has metabolic and clinical complications.

High risk patients include the chronically under-nourished and those with little intake for greater than 10 days. Patients with dysphagia are at particular risk.

Refeeding should commence at 10 kcal/kg per day in patients at risk, and increased slowly. Thiamine, vitamin B complex and multi-vitamin supplements should be started with refeeding.

New NICE guidelines state that pre-feeding correction of electrolyte and fluid deficits is unnecessary, but should be done concurrently with re-feeding.

More research in this field is needed as the evidence base is lacking.

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- **“On refeeding, the absorbed glucose leads to increased blood glucose levels, which increase insulin and decrease glucagon secretion.”**
- **“The net result of these changes is the synthesis of glycogen, fat and protein.”**
- **“This anabolic state requires minerals such as phosphate and magnesium and cofactors such as thiamine.”**
- **“Insulin stimulates absorption of potassium into the cells (via the Na-K ATPase symporter), with both magnesium and phosphate also taken up.”**
- **“Water is drawn into the intracellular compartment by osmosis.”**
- **“This decreases serum levels of phosphate, potassium and magnesium further, and results in the clinical features of refeeding syndrome.”**

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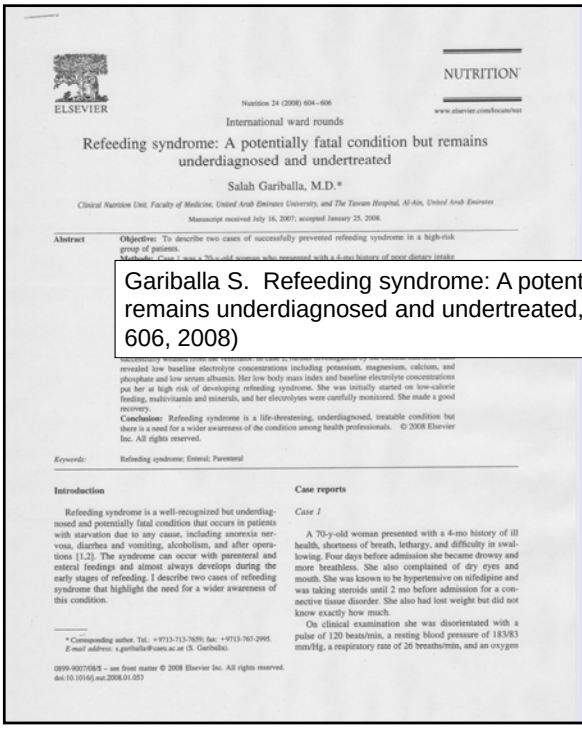

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International ward rounds

Refeeding syndrome: A potentially fatal condition but remains underdiagnosed and undertreated

Salah Gariballa, M.D.*

Clinical Nutrition Unit, Faculty of Medicine, United Arab Emirates University, and The Tawam Hospital, Al-Ain, United Arab Emirates

Manuscript received July 16, 2007; accepted January 25, 2008.

Abstract **Objective:** To describe two cases of successfully prevented refeeding syndrome in a high-risk group of patients.

Methods: Case 1 was a 70-y-old woman who presented with a 4-mo history of poor dietary intake

revealed low baseline electrolyte concentrations including potassium, magnesium, calcium, and phosphate and low serum albumin. Her low body mass index and baseline electrolyte concentrations put her at high risk of developing refeeding syndrome. She was initially started on low-calorie feeding, multivitamin and minerals, and her electrolytes were carefully monitored. She made a good recovery.

Conclusion: Refeeding syndrome is a life-threatening, underdiagnosed, treatable condition but there is a need for a wider awareness of the condition among health professionals. © 2008 Elsevier Inc. All rights reserved.

Keywords: Refeeding syndrome; Enteral; Parenteral

Introduction

Refeeding syndrome is a well-recognized but underdiagnosed and potentially fatal condition that occurs in patients with starvation due to any cause, including anorexia nervosa, diarrhea and vomiting, alcoholism, and after operations [1,2]. The syndrome can occur with parenteral and enteral feedings and almost always develops during the early stages of refeeding. I describe two cases of refeeding syndrome that highlight the need for a wider awareness of this condition.

Case reports

Case 1

A 70-y-old woman presented with a 4-mo history of ill health, shortness of breath, lethargy, and difficulty in swallowing. Four days before admission she became drowsy and more breathless. She also complained of dry eyes and mouth. She was known to be hypertensive on nifedipine and was taking steroids until 2 mo before admission for a connective tissue disorder. She also had lost weight but did not know exactly how much.

On clinical examination she was disorientated with a pulse of 120 beats/min, a resting blood pressure of 183/83 mm/Hg, a respiratory rate of 26 breaths/min, and an oxygen

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Gariballa S. Refeeding syndrome: A potentially fatal condition but remains underdiagnosed and undertreated, *Nutrition*, Vol. 24, pp. 604-606, 2008)

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- **“When patients start to refeed after a period of starvation, a sudden shift from fat to carbohydrate occurs.”**
- **“A glucose load stimulates insulin release, causing increased cellular uptake of glucose, phosphate, potassium, magnesium, and water and protein synthesis.”**
- **“This cellular uptake of phosphate, potassium, and magnesium results in a dramatic decrease of concentrations.”**
- **“Decreased levels of such important minerals can lead to altered myocardial function, cardiac arrhythmias, hemolytic anemia, liver dysfunction, neuromuscular abnormalities, acute respiratory failure, gastrointestinal and renal disorders, and death.”**

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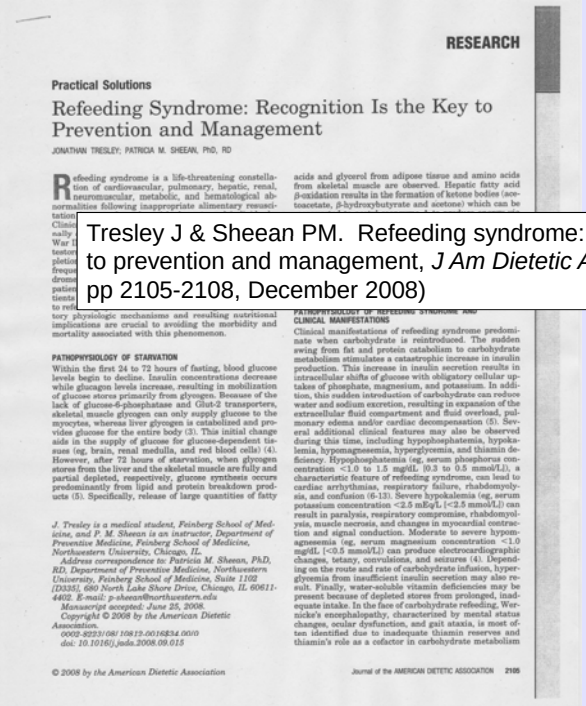

RESEARCH

Practical Solutions

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Refeeding syndrome is a life-threatening constellation of cardiovascular, pulmonary, hepatic, renal, neuromuscular, metabolic, and hematological abnormalities following inappropriate alimentary resuscitation

PATHOPHYSIOLOGY OF STARVATION

Within the first 24 to 72 hours of fasting, blood glucose levels begin to decline. Insulin concentrations decrease while glucagon levels increase, resulting in mobilization of glucose stores primarily from glycogen. Because of the lack of glucose-6-phosphatase and Glut-2 transporters, skeletal muscle glycogen can only supply glucose to the myocytes, whereas liver glycogen is catabolized and provides glucose for the entire body (3). This initial change aids in the supply of glucose for glucose-dependent tissues (eg, brain, renal medulla, and red blood cells) (4). However, after 72 hours of starvation, when glycogen stores from the liver and the skeletal muscle are fully and partial depleted, respectively, glucose synthesis occurs predominantly from lipid and protein breakdown products (5). Specifically, release of large quantities of fatty acids and glycerol from adipose tissue and amino acids from skeletal muscle are observed. Hepatic fatty acid β-oxidation results in the formation of ketone bodies (acetoacetate, β-hydroxybutyrate and acetone) which can be

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Clinical manifestations of refeeding syndrome predominate when carbohydrate is reintroduced. The sudden swing from fat and protein catabolism to carbohydrate metabolism stimulates a catastrophic increase in insulin production. This increase in insulin secretion results in intracellular shifts of glucose with obligatory cellular uptakes of phosphate, magnesium, and potassium. In addition, this sudden introduction of carbohydrate can reduce water and sodium excretion, resulting in expansion of the extracellular fluid compartment and fluid overload, pulmonary edema and/or cardiac decompensation (5). Several additional clinical features may also be observed during this time, including hypophosphatemia, hypokalemia, hypomagnesemia, hyperglycemia, and thiamin deficiency. Hypophosphatemia (eg, serum phosphorus concentration <1.0 to 1.5 mg/dL [0.3 to 0.5 mmol/L]), a characteristic feature of refeeding syndrome, can lead to cardiac arrhythmias, respiratory failure, rhabdomyolysis, and confusion (6-13). Severe hypokalemia (eg, serum potassium concentration <2.5 mEq/L [<2.5 mmol/L]) can result in paralysis, respiratory compromise, rhabdomyolysis, muscle necrosis, and changes in myocardial contraction and signal conduction. Moderate to severe hypomagnesemia (eg, serum magnesium concentration <1.0 mg/dL [<0.5 mmol/L]) can produce electrocardiographic changes, tetany, convulsions, and seizures (4). Depending on the route and rate of carbohydrate infusion, hyperglycemia from insufficient insulin secretion may also result. Finally, water-soluble vitamin deficiencies may be present because of depleted stores from prolonged, inadequate intake. In the face of carbohydrate refeeding, Wernicke's encephalopathy, characterized by mental status changes, ocular dysfunction, and gait ataxia, is most often identified due to inadequate thiamin reserves and thiamin's role as a cofactor in carbohydrate metabolism

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40

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41

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- **"…water soluble vitamin deficiencies may be present because of depleted stores from prolonged, inadequate intake."**
- **"In the face of carbohydrate refeeding, Wernicke's encephalopathy, characterized by mental status changes, ocular dysfunction, and gait ataxia, is most often identified due to inadequate thiamin reserves and thiamin's role as a cofactor in carbohydrate metabolism."**

43

- **"…after 72 hours of starvation, when glycogen stores from the liver and the skeletal muscle are fully and partially depleted, respectively, glucose synthesis occurs predominantly from lipid and protein breakdown products."**
- **"Specifically, release of large quantities of fatty acids and glycerol from adipose tissue and amino acids from skeletal muscle are observed."**
- **"Hepatic fatty acid β-oxidation results in the formation of ketone bodies (acetoacetate, β-hydroxybutyrate, and acetone) which can be reconverted to acetyl-coenzyme A to produce energy via the Krebs cycle."**

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- **“Energy in the form of glucose is also synthesized from endogenous glycerol, the gluconeogenic amino acids (primarily alanine and glutamine) and lactate and pyruvate produced by glycolysis via the Cori cycle.”**
- **“Overall, this adaptation to altered sources of energy can result in profound fat and muscle wasting, in addition to total body depletion of electrolytes, magnesium, potassium, and phosphate.”**

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- **“Optimal treatment generally includes a conservative approach to nutritional repletion, although no one technique has been reported to be superior. The clinical mantra of ‘start low and go slow’ has been advocated.”**

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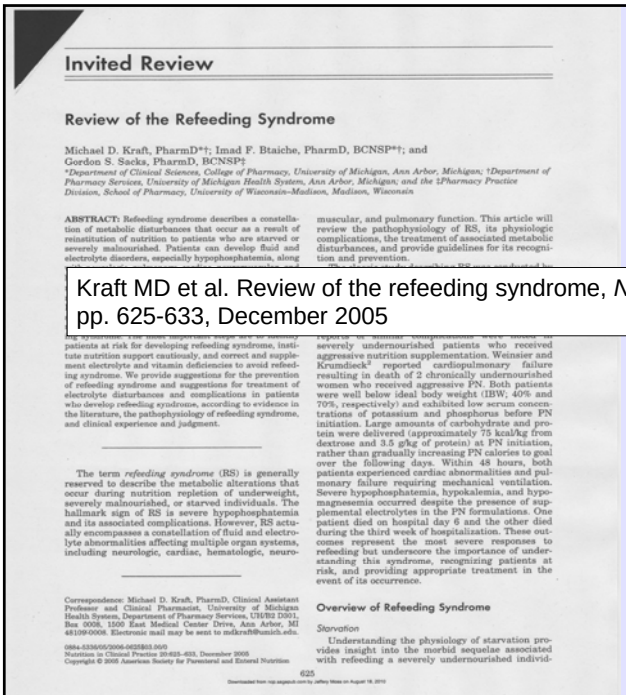

Invited Review

Review of the Refeeding Syndrome

Michael D. Kraft, PharmD*†; Imad F. Btaiche, PharmD, BCNSP*†; and Gordon S. Sacks, PharmD, BCNSP‡

*Department of Clinical Sciences, College of Pharmacy, University of Michigan, Ann Arbor, Michigan; †Department of Pharmacy Services, University of Michigan Health System, Ann Arbor, Michigan; and the ‡Pharmacy Practice Division, School of Pharmacy, University of Wisconsin–Madison, Madison, Wisconsin

ABSTRACT: Refeeding syndrome describes a constellation of metabolic disturbances that occur as a result of reinstitution of nutrition to patients who are starved or severely malnourished. Patients can develop fluid and electrolyte disorders, especially hypophosphatemia, along

muscular, and pulmonary function. This article will review the pathophysiology of RS, its physiologic complications, the treatment of associated metabolic disturbances, and provide guidelines for its recognition and prevention.

patients at risk for developing refeeding syndrome, institute nutrition support cautiously, and correct and supplement electrolyte and vitamin deficiencies to avoid refeeding syndrome. We provide suggestions for the prevention of refeeding syndrome and suggestions for treatment of electrolyte disturbances and complications in patients who develop refeeding syndrome, according to evidence in the literature, the pathophysiology of refeeding syndrome, and clinical experience and judgment.

The term *refeeding syndrome* (RS) is generally reserved to describe the metabolic alterations that occur during nutrition repletion of underweight, severely malnourished, or starved individuals. The hallmark sign of RS is severe hypophosphatemia and its associated complications. However, RS actually encompasses a constellation of fluid and electrolyte abnormalities affecting multiple organ systems, including neurologic, cardiac, hematologic, neuro-

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Overview of Refeeding Syndrome

Starvation

Understanding the physiology of starvation provides insight into the morbid sequelae associated with refeeding a severely undernourished individ-

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- **"If a patient manifests signs and symptoms of refeeding syndrome, nutrition support should be started with great caution."**
- **"All electrolyte abnormalities should be adequately treated and supplemental electrolytes provided in the nutrition formulation above what was previously provided when refeeding syndrome symptoms developed."**
- **"Multivitamins should also be supplemented…"**

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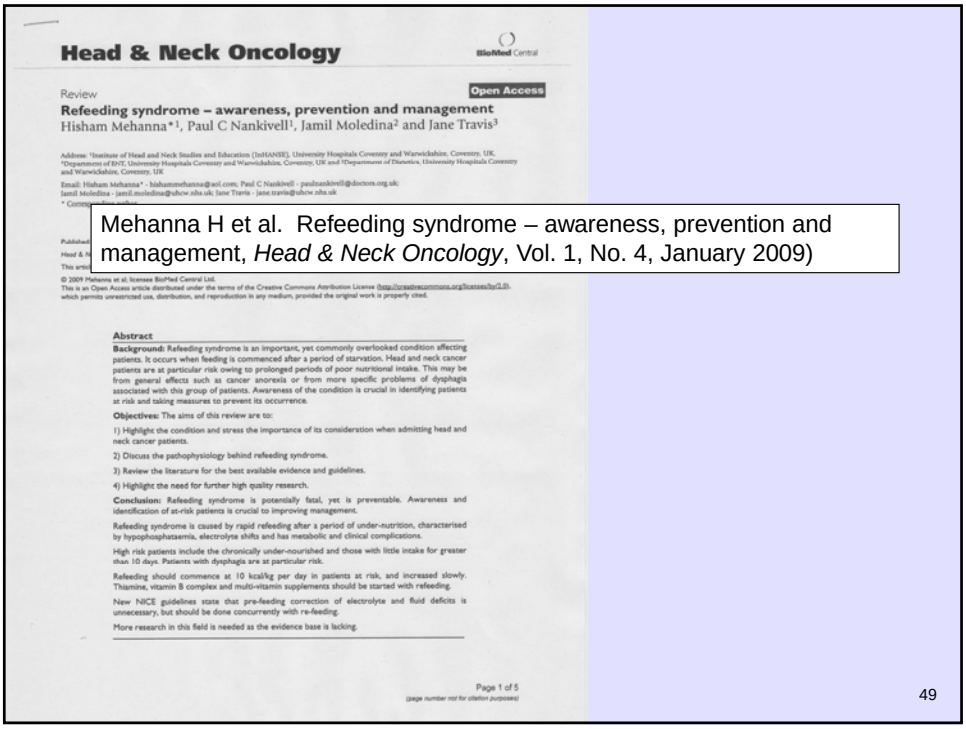

Head & Neck Oncology

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Review

Open Access

Refeeding syndrome – awareness, prevention and management

Hisham Mehanna*[1], Paul C Nankivell[1], Jamil Moledina[2] and Jane Travis[3]

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Abstract

Background: Refeeding syndrome is an important, yet commonly overlooked condition affecting patients. It occurs when feeding is commenced after a period of starvation. Head and neck cancer patients are at particular risk owing to prolonged periods of poor nutritional intake. This may be from general effects such as cancer anorexia or from more specific problems of dysphagia associated with this group of patients. Awareness of the condition is crucial in identifying patients at risk and taking measures to prevent its occurrence.

Objectives: The aims of this review are to:

1) Highlight the condition and stress the importance of its consideration when admitting head and neck cancer patients.

2) Discuss the pathophysiology behind refeeding syndrome.

3) Review the literature for the best available evidence and guidelines.

4) Highlight the need for further high quality research.

Conclusion: Refeeding syndrome is potentially fatal, yet is preventable. Awareness and identification of at-risk patients is crucial to improving management.

Refeeding syndrome is caused by rapid refeeding after a period of under-nutrition, characterised by hypophosphataemia, electrolyte shifts and has metabolic and clinical complications.

High risk patients include the chronically under-nourished and those with little intake for greater than 10 days. Patients with dysphagia are at particular risk.

Refeeding should commence at 10 kcal/kg per day in patients at risk, and increased slowly. Thiamine, vitamin B complex and multi-vitamin supplements should be started with refeeding.

New NICE guidelines state that pre-feeding correction of electrolyte and fluid deficits is unnecessary, but should be done concurrently with re-feeding.

More research in this field is needed as the evidence base is lacking.

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"Vitamin replacement should be started right away, in particular thiamine…"

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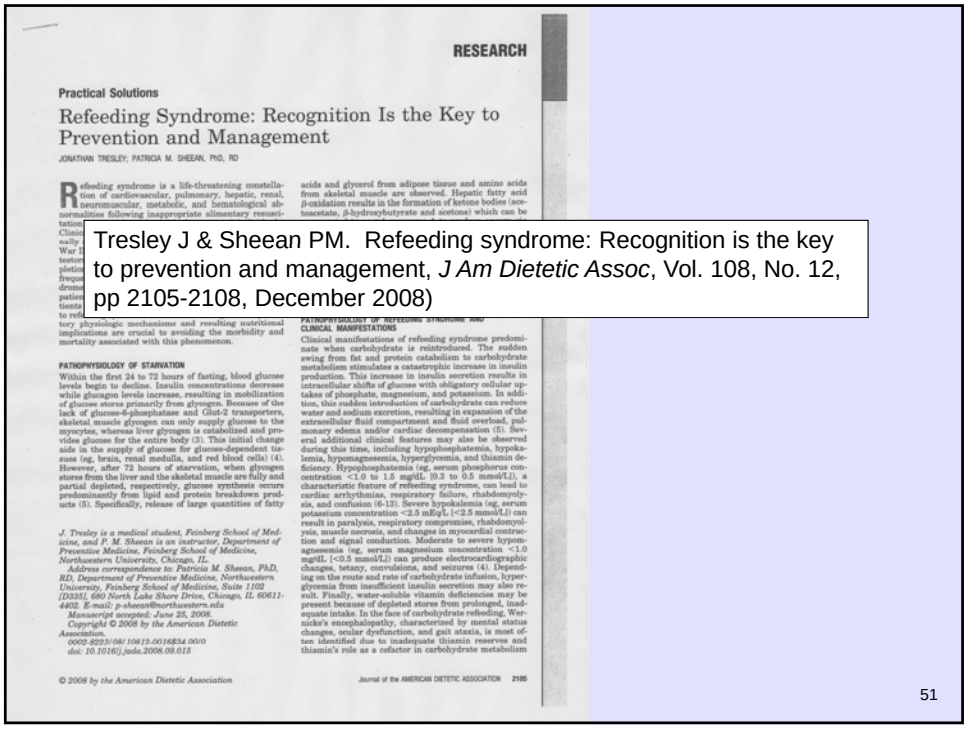

RESEARCH

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PATHOPHYSIOLOGY OF REFEEDING SYNDROME AND CLINICAL MANIFESTATIONS

Clinical manifestations of refeeding syndrome predominate when carbohydrate is reintroduced. The sudden swing from fat and protein catabolism to carbohydrate metabolism stimulates a catastrophic increase in insulin production. This increase in insulin secretion results in intracellular shifts of glucose with obligatory cellular uptakes of phosphate, magnesium, and potassium. In addition, this sudden introduction of carbohydrate can reduce water and sodium excretion, resulting in expansion of the extracellular fluid compartment and fluid overload, pulmonary edema and/or cardiac decompensation (5). Several additional clinical features may also be observed during this time, including hypophosphatemia, hypokalemia, hypomagnesemia, hyperglycemia, and thiamin deficiency. Hypophosphatemia (eg, serum phosphorus concentration <1.0 to 1.5 mg/dL [0.3 to 0.5 mmol/L]), a characteristic feature of refeeding syndrome, can lead to cardiac arrhythmias, respiratory failure, rhabdomyolysis, and confusion (6-13). Severe hypokalemia (eg, serum potassium concentration <2.5 mEq/L [<2.5 mmol/L]) can result in paralysis, respiratory compromise, rhabdomyolysis, muscle necrosis, and changes in myocardial contraction and signal conduction. Moderate to severe hypomagnesemia (eg, serum magnesium concentration <1.0 mg/dL [<0.5 mmol/L]) can produce electrocardiographic changes, tetany, convulsions, and seizures (4). Depending on the route and rate of carbohydrate infusion, hyperglycemia from insufficient insulin secretion may also result. Finally, water-soluble vitamin deficiencies may be present because of depleted stores from prolonged, inadequate intake. In the face of carbohydrate refeeding, Wernicke's encephalopathy, characterized by mental status changes, ocular dysfunction, and gait ataxia, is most often identified due to inadequate thiamin reserves and thiamin's role as a cofactor in carbohydrate metabolism

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- **"Currently, it is advised to begin feeding at 20 kcal/kg/day or about half of estimated needs with 1.0 to 1.5 g/kg/day protein and careful attention to correction of electrolyte abnormalities."**
- **"A low sodium diet and fluid restriction of 1L/day may also help to prevent fluid overload. To detect fluid overload, daily weights, heart rate, and rhythm should be monitored."**
- **"Once electrolytes are stable, it is appropriate to advance feeding by 200 to 300 kcal every 2 to 3 days, pending stable blood electrolytes."**
- **"However, weight gain of more than 2 to 3 lb/week is indicative of fluid retention and all of these clinical guidelines must be tailored to the individual case."**

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Thank you!!

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