

Entry Level Clinical Nutrition Part XVIII

More on carbohydrate-protein imbalances and the refeeding syndrome

Jeffrey Moss, DDS, CNS, DACBN

jeffmoss@mossnutrition.com

413-530-0858 (cell)

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60 MINUTES

60 Minutes – Sunday, April 1, 2012

Is sugar toxic?



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**Nestlé Nutrition Workshop Series
Clinical & Performance Program, Vol. 8**

**Nutrition and
Critical Care**

**Luc Cynober
Frederick A. Moore**




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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REVIEW

Acute and "chronic" phase reaction—a mother of disease

Stig Bengmark

Department of Surgery and Liver Institute, UCL, London, UK

Received 23 July 2004

KEYWORDS

Acute phase response;
Chronic phase response;
Metabolic syndrome;
Cellular membranes;
Endothelial cells;
Abdominal obesity;
Insulin resistance;
Growth hormones;
Free fatty acids;
Alzheimer disease;
Parkinson disease;
Neurodegenerative diseases;
Atherosclerosis;
Coronary-vascular disease;
Cancer;
Breast cancer;
Colorectal cancer;
Prostatic cancer;
Diabetes;
Cirrhosis;
Fatty liver;
Gallbladder disease;
Chronic renal disease;

Summary The world is in diseases. Almost half of the mortality is due to these chronic diseases. And they are these diseases are associated consumption of calorie could also under consumption of a function of the innate immune changes induced in response the subsequent development chronic diseases. The end of importance, and the function of the underlying cells; their ability to obtain nutrients and antioxidants and to eliminate waste products. The abdominal adipocytes seem to play a key role, as they have the ability to in stressful situations release much of proinflammatory cytokines, TNF- α and free fatty acids compared to elsewhere in the body. The load on the liver of these various substances is often of greater magnitude than the liver can handle. Some of the most common chronic diseases and their potential association with acute and "chronic" phase responses, and with metabolic syndrome are discussed separately. The need for studies with lifestyle modifications is especially emphasized.

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Bengmark S. Acute and "chronic" phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004

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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 (MB-Lab), China Medical University and Hospital, Taichung, Taiwan; Stress, Psychiatry and Immunology Laboratory (SPI-Lab), Institute of Psychiatry, King's College London, London, UK

Key Words

Major depressive disorder · Depression · Docosahexaenoic acid · Arachidonic acid · Prostaglandins · Thromboxanes · Leukotrienes · 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 E₂ 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.

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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, noradrenaline and/or dopamine

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E-Mail: karger@karger.ch

www.karger.com

Dr. Kuan-Pin Su

MD, PhD, Department of Psychiatry
China Medical University Hospital
No. 2, Yuh-Der Road, Taichung 404, Taiwan
Tel.: +886 4 2206 2121, ext. 1078; Fax: +886 4 2206 1230; E-Mail: kpsu@cmu.edu.tw

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 ^c
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

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Underlying hypotheses of Entry Level Clinical Nutrition:

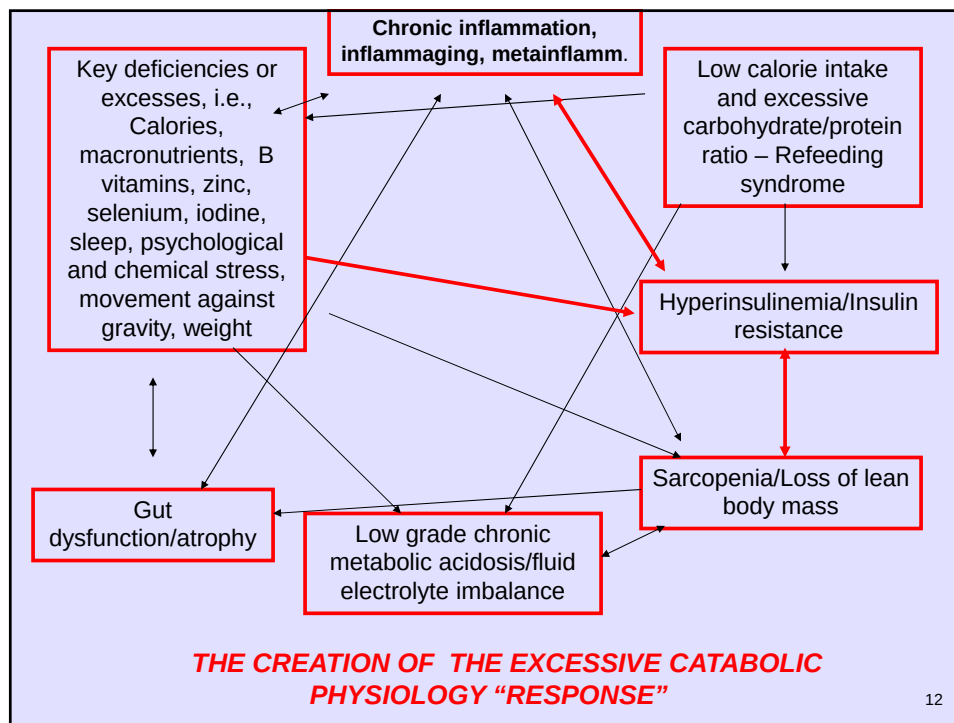
- Chief complaints in chronically ill patients are not diseases but responses that have gone on too long (Allostatic load).
- The metabolic imbalances that combine to form this response have been well defined by critical care nutritionists.

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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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Is reactive hypoglycemia a
mild form of refeeding
syndrome?

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What is reactive
hypoglycemia?

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**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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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 Leuenberger², RF Grimble¹, A Shenkin⁴, SP Allison⁵ and DN Lobo⁵

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

The refeeding syndrome is a life-threatening condition. The specific treatment is to provide a low-calorie, low-protein, low-fat diet.

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.

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/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; Schatzker *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.

Seventy malnourished patients (Table 1) appear to be at particular risk of developing the refeeding syndrome, whose features (Figure 1) (Davis *et al.*, 1971; Chadlock *et al.*, 1974; O'Connor *et al.*, 1977; Patrick, 1977; Heymsfield *et al.*, 1978; Weinberger and Knudsen, 1981; Powers, 1982; Loner *et al.*, 1983; Cummings *et al.*, 1987; Gusterson and Eriksson, 1989; Fomon, 1990; Beaumont and Large, 1991; Brooks and Jendryak, 1993; Boushaghian *et al.*, 1996; Mark and Redigan, 1996; Paula *et al.*, 1998; Crook *et al.*, 2001; Hadley and Walsh, 2003; Mastrolia, 2003; Whyte *et al.*, 2003; Heering, 2004; Crook and Parnell, 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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- “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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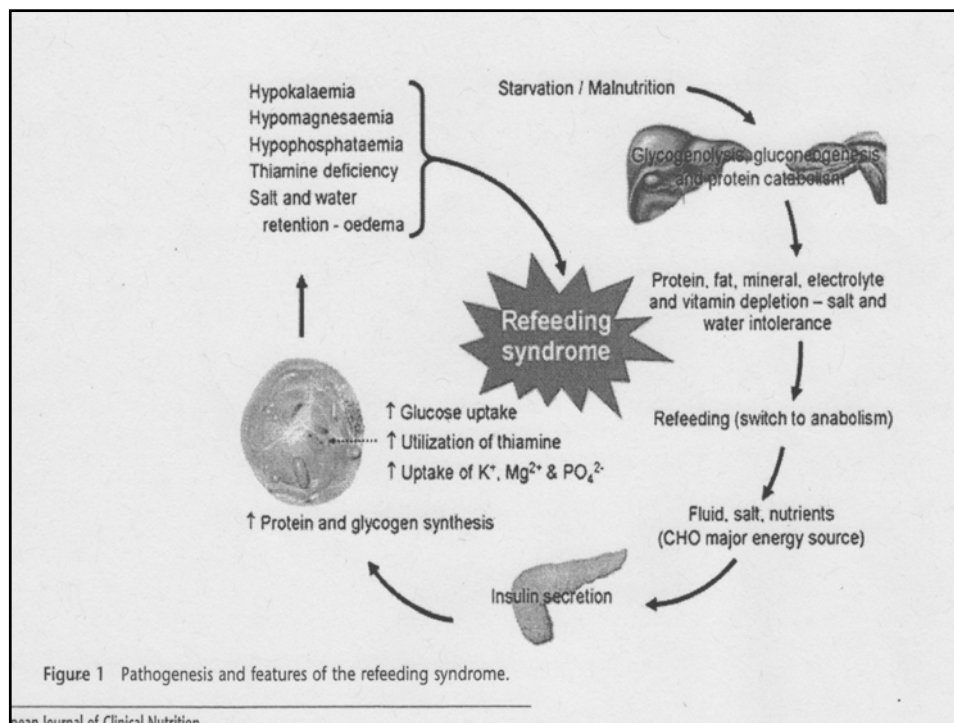


Table 1 Some groups of malnourished patients at particular risk of developing the refeeding syndrome

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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Review Article

Refeeding Syndrome: A Literature Review

L. U. R. Khan, J. Ahmed, S. Khan, and J. MacFie

The Combined Gastroenterology Research Unit, Scarborough Hospital, Woodland Drive, Scarborough YO12 6QL, UK

Correspondence should be addressed to J. Ahmed, djag@hotmail.co.uk

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Khan LUR et al. Refeeding syndrome: A literature review, *Gastroenterol Res Pract*, Vol. 2011, Article ID 410971, 2010

preliminary to using to inform treatment and research; this review estimates the percentage of patients who develop the refeeding syndrome. A management strategy is described. The importance of a multidisciplinary approach is emphasized.

1. Introduction

RFS is well recognized. It occurs after the reintroduction of feeding after a period of starvation or fasting [1]. RFS describes a series of metabolic and biochemical changes that occur as a consequence of reintroduction of feeding after a period of starvation or fasting. This unfavorable metabolic response causes nonimmune-mediated harm to the body and can be mild, moderate, or severe. Although the physiology and pathophysiology are well known, the circumstances under which RFS occurs, the clinical manifestations, and the management of these patients are less clear [2, 3].

1.1. Methods. A PubMed search for the terms "refeeding syndrome" AND "hypophosphatemia" generated two hundred and seven separate articles. There were no randomized controlled trials identified.

1.2. Physiology. With food in abundance, carbohydrates provide for most of our energy requirements. Glucose, the principal product of carbohydrate digestion, is actively cotransported along with sodium at the intestinal brush border against a concentration gradient. Glucose enters the portal circulation by facilitated diffusion and blood sugar levels rise. This stimulates the release of the peptide hormone insulin from pancreatic β cells. Insulin secretion

has several effects. It promotes glucose uptake and storage (glycogenesis), inhibits the breakdown of fat (lipolysis), and increases cellular uptake of potassium. When glycogen storage capacity is exceeded, lipogenesis occurs with nonoxidized glucose being converted to fat and stored as triglycerides in adipose tissue. Together, the consequence is for blood glucose levels to fall with a concomitant reduction in insulin secretion [4].

With starvation, levels of glucose begin to fall within 24 to 72 hours. This results in the release of the peptide hormone glucagon and a reduction in insulin secretion [10]. Glucose levels are maintained by glycogenolysis but glycogen stores rarely last more than 72 hours [11]. Glucose homeostasis is essential because certain tissues, such as brain, erythrocytes, and cells of the renal medulla are obligate glucose users [12]. These demands for glucose are met by the process of gluconeogenesis by which noncarbohydrate sources are metabolized to glucose. The most important of these is the muscle protein alanine. In addition, fatty acid oxidation in liver hepatocytes generates ketone bodies. These are converted to acetyl-coenzyme-A generating energy via the Krebs cycle. Further energy production from lactate and pyruvate (the products of glycolysis) and amino acids occurs via the Citric cycle [4]. In summary, metabolic adaptation occurs to ensure survival on fat fuel economy [13]. There is a resultant loss of body fat and protein and an accompanying depletion of potassium, phosphate, and magnesium [14, 15].

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- **“RFS describes a series of metabolic and biochemical changes that occur as a consequence of reintroduction of feeding after a period of starvation or fasting.”**
- **“This unfavorable metabolic response causes nonimmune-mediated harm to the body and can be mild moderate, or severe.”**

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- **“With food in abundance, carbohydrates provide for most of our energy requirements.”**
- **“Glucose, the principal product of carbohydrate ingestion, is actively cotransported along with sodium at the intestinal brush border against a concentration gradient.”**
- **“Insulin secretion has several effects. It promotes glucose uptake and storage (glycogenesis), inhibits the breakdown of fats (lipolysis), and increases cellular uptake of potassium.”**

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- **“When glycogen storage capacity is exceeded, lipogenesis occurs with nonoxidised glucose being converted to fat and stored as triglycerides in adipose tissue.”**
- **“Together, the consequence is for blood glucose levels to fall with a concomitant reduction in insulin secretion.”**

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What happens when caloric intake is suboptimal?

- **“Glucose levels are maintained by glycogenolysis but glycogen stores rarely last more than 72 hours.”**
- **“These demands for glucose are met by the process of gluconeogenesis by which noncarbohydrate sources are metabolized to glucose. The most important of these is the muscle amino acid alanine.”**

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- **“In addition, fatty acid oxidation in liver hepatocytes generates ketone bodies. These are converted to acetyl-coenzyme-A generating energy via the Krebs cycle.”**
- **“Further energy production from lactate and pyruvate (the products of glycolysis) and amino acids occurs via the Cori cycle.”**

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- **“In summary, metabolic adaptation occurs to ensure survival on fat fuel economy.”**
- **“There is a resultant loss of body fat and protein and an accompanying depletion of potassium, phosphate, and magnesium.”**
- **“Homeostatic mechanisms maintain serum concentrations of these ions at the expense of intracellular stores.”**
- **“Serum levels may remain normal despite a marked reduction in total body levels.”**

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- **“The reintroduction of nutrition to a starved or fasted individual results in a rapid decline in both gluconeogenesis and anaerobic metabolisms.”**
- **“This is mediated by the rapid increase in serum insulin that occurs on refeeding.”**
- **“Insulin stimulates the movement of extracellular potassium, phosphate, and magnesium to the intracellular compartment.”**
- **“Depleted intracellular stores and a large concentration gradient ensure a rapid fall in the extracellular concentration of these ions.”**

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- **“Osmotic neutrality must be maintained resulting in the retention of sodium and water.”**
- **“Reactivation of carbohydrate-dependent metabolic pathways increases demand for thiamine, a cofactor required for cellular enzymatic reactions.”**
- **“The deficiencies of phosphate, magnesium, potassium, and thiamine occur to varying degrees and have different effects in different patients.”**

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“...RFS is not defined by a clear set of signs and symptoms but is considered an arbitrary term referring to a wide spectrum of biochemical abnormalities and clinical consequences.”

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Prevalence of situations that where RFS is a significant risk

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- **“In 2005 Hise et al. estimated that 30% to 50% of hospitalized patients are malnourished.”**
- **“Morley in 2002 estimated the prevalence of malnutrition is 1% to 15% in patients attending outpatient, 25% to 60% in the institutionalized patients, and it is 35% to 60% in hospitalized patients.”**

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- **“Symptoms of RFS are variable, unpredictable, may occur without warning, and may occur late.”**
- **“Symptoms occur because changes in serum electrolytes affect the cell membrane potential impairing function in nerve, cardiac, and skeletal muscle cells.”**
- **“The variable picture in RFS reflects the type and severity of biochemical abnormality present.”**
- **“With mild derangements in these electrolytes, there may be no symptoms.”**
- **“More often, the spectrum of presentation ranges from simple nausea, vomiting, and lethargy to respiratory insufficiency, cardiac failure, hypotension, arrhythmias, delirium, coma, and death.”**

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Treatment considerations: Fluid & electrolytes first

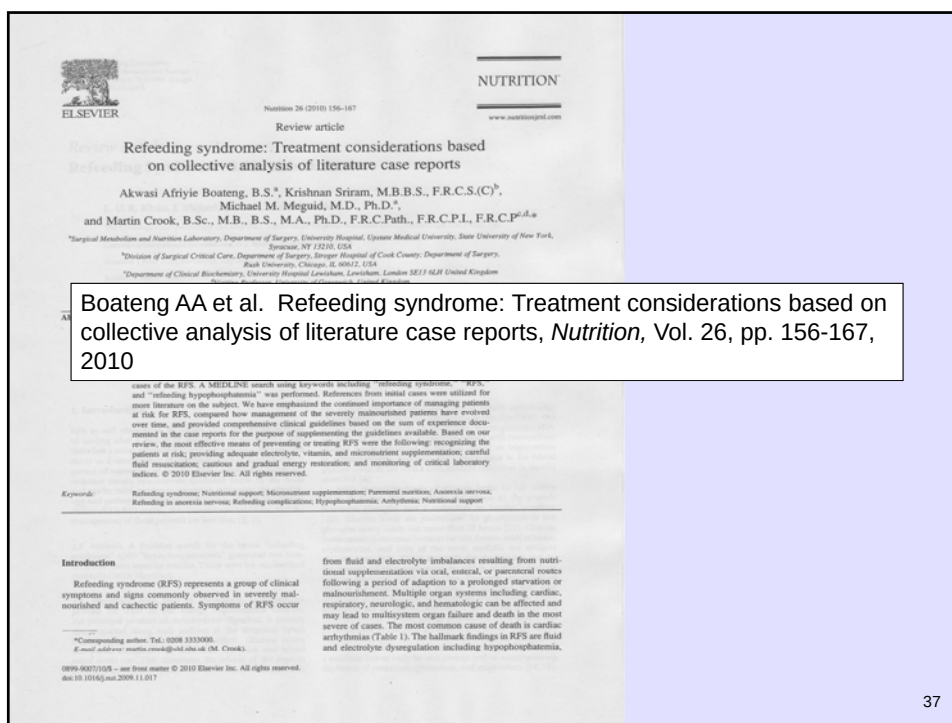
- **“The view that correction of electrolyte abnormalities must occur before commencement of feeding has been revised and recent National Institute of Health and Clinical Excellence in the United Kingdom guidelines indicate that feeding and correction of biochemical abnormalities can occur in tandem without deleterious effects to the patient.”**

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Final thoughts from Khan et al.

- **“It is important to emphasize that RFS does not represent a singular condition or syndrome.”**
- **“Rather it describes an illness spectrum that occurs under particular circumstances within high-risk populations.”**
- **“Improved understanding of energetic requirements in healthy and sick patients will help improve understanding and allow for developing novel strategies to minimize risk of RFS to patients.”**

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- **“The hallmark findings in refeeding syndrome (RFS) are fluid and electrolyte dysregulation including hypophosphatemia, hypokalemia, hypomagnesemia, abnormalities in glucose metabolism, vitamin (importantly thiamine), and trace element deficiencies.”**
- **“RFS can be viewed as spectrum disorder where symptoms range from mild to severe depending on the degree of starvation or malnourishment and the form of management employed.”**

- **“Without replacement, intracellular and extracellular ions including PO_4^{3-} , K^+ , Mg^{2+} , and Na are lost over time, although their measured concentrations may remain falsely normal mainly because of concurrent loss of total body water that also accompanies malnourishment.”**
- **“Importantly, the falsely normal concentration of these ions is not simply due to excess total body water, since they may occur in normally hydrated individuals or individuals with only mild water retention.”**
- **“Once adaptation has occurred, survival can be effectively sustained for months, the exact duration being variable among individuals and proportional to amount of available fat stores.”**

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- **Sudden introduction of seemingly adequate nutrition during this time can be interpreted by the body as ‘stressful.’”**
- **“Dormant enzymes are suddenly activated in the context of relative nutrient and cofactor deficiency.”**
- **“This deficiency of micro- and macromolecules is enhanced at the onset of increased enzymatic activity, precipitating signs and symptoms of RFS.”**

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Hypophosphatemia

- ***“Hypophosphatemia results from cellular uptake of phosphorus (P) and inorganic phosphates (PO₄³⁻) under the influence of insulin for synthesis of ATP, DNA, RNA, proteins, and 2,3-diphosphoglycerate and from increased phosphorylation of glucose.”***

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Hyperglycemia

- ***“Hyperglycemia results from glucose introduction into a starved system adapted to fat metabolism.”***
- ***“Infections become more common as hyperglycemia disrupts neutrophilic function, leading to a functional neutropenic state.”***

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Hypomagnesemia

- ***“Hypomagnesemia results from cellular uptake of magnesium (Mg) after feeding.”***
- ***“Mg is essential for many cellular processes and all cellular processes involving ATP.”***
- ***“Hypomagnesemia is also an important mediator of both hypocalcemia and hypokalemia.”***

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Hypokalemia

- ***“Hypokalemia results from cellular uptake of potassium (K), induced by insulin produced in response to the nutritional load.”***

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Fluid overload

- ***“Fluid overload occurs from the sodium (Na) retention effects of hyperglycemia and hyperinsulinemia.”***

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Vitamin deficiency

- ***“Vitamin deficiency results from the rapid depletion of vitamins after onset of refeeding due to their role in various biochemical functions.”***
- ***“For example, thiamine is necessary for glucose metabolism but its stores are depleted during starvation.”***
- ***“Sudden introduction of glucose drives already depleted thiamine stores to a nadir, precipitating Wernicke’s encephalopathy and lactic acidosis.”***

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Trace element deficiency

- ***“Trace element deficiency also results from increased enzymatic activity during the anabolic process.”***
- **“For example, the importance of trace elements such as zinc and selenium as functional components of many enzymes involved in DNA/RNA metabolism and oxidative-reduction processes is well known.”**

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Diagnostic indicators

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Phosphorus

- “Serum phosphorus levels can be monitored along with Mg, K, Na, and Ca. Hypophosphatemia plays a key role in the pathogenesis of RFS.”
- “Thus maintenance of serum P levels in the normal range (3.0 – 4.5 mg/dL or 1 – 1.4 mM/L) is essential in the management of RFS and may resolve most of the symptoms.”

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Potassium

- “Correction of K is relatively simple to accomplish and the target level should be >3.5 mEq/L (3.5 mM/L) (normal level: 3.5 – 5.0).”

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Thiamine

- **“Vitamin B1 (thiamine) is not stored in sufficient amounts and, since it is needed for glycolysis, it must be provided before or along with glucose administration.”**
- **“Deficiency in thiamine also causes a buildup of pyruvic and lactic acids...”**

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Lab test interpretation and the acute phase response

- **“The clinician must keep in mind that it is often difficult when interpreting levels in patients with acute phase response.”**

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Dosing considerations

- “In addition to the recommended daily reference intake of supplements, it may be necessary to provide surplus amounts based on the clinical scenario.”
- “For instance, folate and thiamine may be needed in higher doses during the refeeding period in pregnancy.”

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Macronutrient supplementation

- “Carbohydrate supplementation must not exceed 7 g/kg/d (28 kcal/kg/d) in the healthy individual.”
- “Nutrition must be started at no more than 10 kcal/kg/d in patients at risk, and as low as 5 kcal/kg/d in less stable patients.”
- “Calories should be given slowly and calories increased in a stepwise manner to 15-20 kcal/kg/d from days 4 to 10.”

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Caloric intake

- **“We recommend advancing calories by 200-300 kcal every 3-4 d; however, slower calorie advancement may be necessary in those who fail to improve clinically.”**

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Concerns about liver enzymes

- **“Abnormal values in hepatic enzymes (alanine transaminase and aspartate transaminase) have been associated with refeeding complications, which justifies monitoring.”**

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Does this occur in the outpatient setting?

- **“RFS may occur in the outpatient setting during oral feeding; therefore, the caretaker must discourage binging in severely starved patients.”**

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**Hypothesis:
Could refeeding syndrome be
a major contributing factor for
sudden cardiac death?**

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Bloomberg News – May 1, 2012
Norway Swimming Champion Alexander Dale Oen Dies While Training

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Importance of Postprandial Glucose Control

DAVID S. BELL, MD, Birmingham, Ala

ABSTRACT: Although a traditional goal of glycemic control in the treatment of diabetes mellitus is to normalize fasting plasma glucose, emerging data indicate that modulation of postprandial plasma glucose levels plays an important role in overall glycemic control. This article reviews the evidence linking postprandial glucose levels with long-term indices of diabetes control, such as glycosylated hemoglobin, lipid abnormalities, and the risk of microvascular and macrovascular complications. Early in the development of type 2 diabetes, the initial burst of insulin release in response to food intake is compromised, allowing postprandial hyperglycemia to develop. Meal-associated hyperglycemia further contributes to increase insulin resistance and decrease insulin production. Evidence of a strong correlation between high postprandial glycemic levels and the development of vascular complications underscores the importance of postprandial glucose control.

THE GOAL in type 2 diabetes is to normalize fasting plasma glucose and glycosylated hemoglobin (HbA_{1c}) levels. In patients with well-controlled diabetes (HbA_{1c} <7%, or within 1% of normal) or glucose intolerance (fasting plasma glucose level <126 mg/dL and a 2-hour plasma glucose of 140 to 200 mg/dL after 75 g of oral glucose), postprandial hyperglycemia has a greater effect on HbA_{1c} than fasting glucose levels. Jovanovic¹ recently reported that the postprandial glucose level at 1 hour is the best predictor of HbA_{1c} in patients with well-controlled type 2 diabetes mellitus. In addition, a French study of patients with type 2 diabetes showed that glucose concentrations at 2 and 5 hours after a meal were better predictors of the HbA_{1c} than prebreakfast or prelaunch values.² Therefore, in patients with elevated HbA_{1c}, the postprandial plasma glucose levels may play a disproportionate role in the genesis of both microvascular and macrovascular complications of diabetes.

The recent change in plasma glucose threshold for the diagnosis of diabetes was based on evidence such as that from the United Kingdom Prospective Diabetes Study, which showed that 50% of patients with type 2 diabetes already had one or more chronic complications by the time it was diagnosed.³ The standard for diagnosis is still a plasma glucose level >200 mg/dL at 2

a fasting plasma glucose value of 126 mg/dL. In addition, 52% of patients with fasting plasma glucose <126 mg/dL still have postprandial levels >200 mg/dL. Therefore, patients with fasting glucose levels between 110 and 126 mg/dL should undergo a 2-hour, 75-g glucose challenge to assess their postprandial glucose levels, since early detection and treatment can delay or prevent the onset of complications.⁴

WHY IS GLUCOSE CONTROL SO IMPORTANT?

In the fasting state, the suppression of insulin production and stimulation of glucagon production control the concentration of blood glucose. These processes allow the liver to mobilize glucose from its glycogen stores and synthesize glucose from amino acids and pyruvate (gluconeogenesis). In addition, when insulin levels are low, the uptake of glucose by muscle is mini-

KEY POINTS

- Modulation of postprandial plasma glucose plays an important role in overall glycemic control.
- A strong correlation between high postprandial glucose level and the development of vascular complications.
- First phase insulin release is lost early in the development of type 2 diabetes, leading to postprandial hyperglycemia, increased insulin resistance, and decreased insulin production.
- With loss of the first phase insulin release, an exaggerated second phase insulin release in response to the postprandial hyperglycemia can cause postprandial hypoglycemia.
- Emerging drugs that reduce postprandial hyperglycemia include nateglinide, pramlintide, and glucagon-like insulinotropic peptide.

From the Department of Medicine, University of Alabama at Birmingham School of Medicine, Birmingham, Ala.
Reprint requests to David S. Bell, MD, University of Alabama at Birmingham, Department of Medicine, 1808 7th Ave S, Room 513, Birmingham, AL 35294.

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- “The Honolulu Heart Study found that the risk of CAD correlated with plasma glucose levels measured 1 hour after a 50-g glucose load.”
- “The incidence of CAD was twice as high in patients with postprandial glucose levels between 157 and 189 mg/dL as in those with levels <144 mg/dL, and the incidence of sudden death was doubled with postprandial plasma glucose levels >151 mg/dL.”

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- “The Whitehall Study of British male civil servants showed that plasma glucose levels >96 mg/dL 2 hours after a meal were associated with a two-fold increase in mortality from CAD.”
- “Another British study, the Islington Diabetes Survey, reported that the incidence of major CAD (defined as major electrocardiographic changes or myocardial infarction) was 17% in subjects with a 2-hour postprandial glucose level between 120 and 180 mg/dL compared with 9% in subjects with levels <120 mg/dL.”

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- “The Oslo Study indicated that the nonfasting plasma glucose level was a predictor of fatal stroke in diabetic patients, with the risk increasing by 13% for each 18-mg/dL elevation in postprandial glucose.”
- “Overexposure to insulin in response to postprandial hyperglycemia has been shown to be a risk factor for cardiovascular events.”

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- “The Paris Prospective Study found that postprandial hyperinsulinemia was a better predictor for fatal CAD than either hyperglycemia or diabetes.”
- “Similarly, the Helsinki Policeman Study revealed an independent association between fatal and nonfatal CAD events and 1- and 2-hour postprandial insulin levels that was stronger than that with fasting plasma insulin levels.”

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“Finally, a recent report suggested an association between postprandial levels and intellectual function in elderly Alzheimer’s patients who were not ApoE4 positive.”

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Look for Warning Signs of Sudden Death in Kids

By Nancy Walsh, Staff Writer, MedPage Today
Published: March 26, 2012

Reviewed by Robert Jaeger, MD, Associate Clinical Professor of Medicine, University of California, San Francisco.

Take Posttest

Action Points

- Awareness of warning signs and family history are crucial for the prevention of sudden cardiac arrest in young people.
- Note that the statement recommends that clinicians recognize the warning signs and symptoms of sudden cardiac arrest, including those that may be incorrectly attributed to noncardiac diseases and, thus, delay correct diagnosis.

Awareness of warning signs and family history are crucial for the prevention of sudden cardiac arrest in young people, according to a new policy statement from the American Academy of Pediatrics.



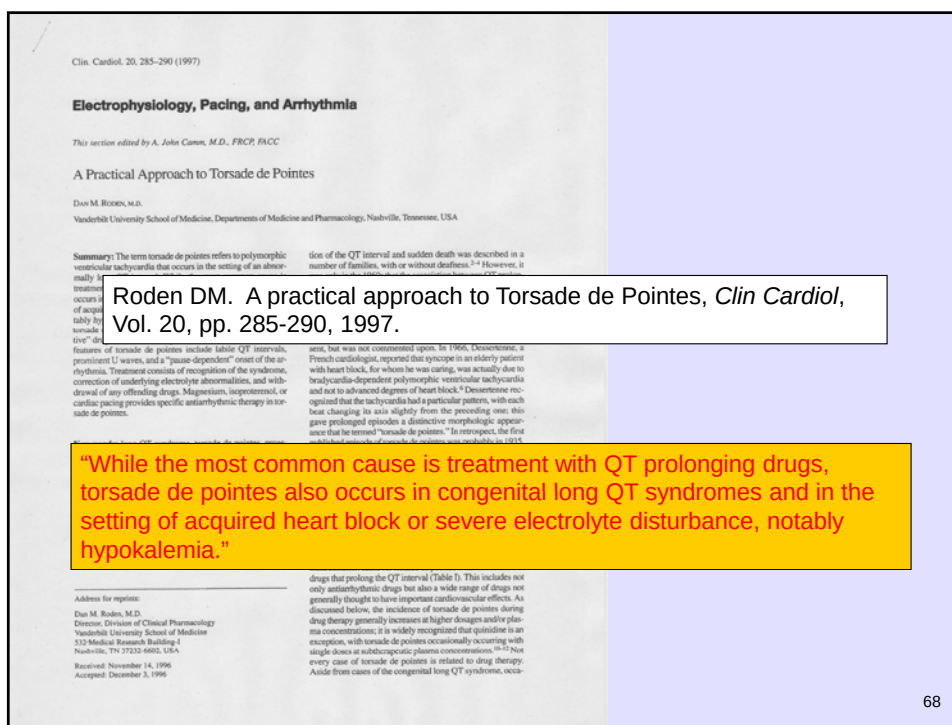
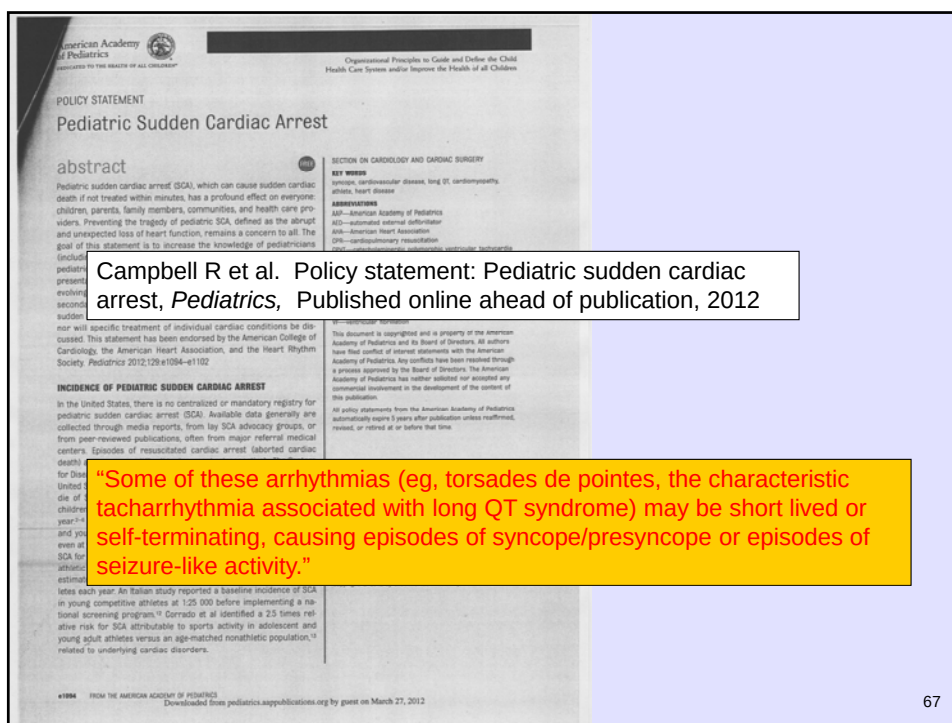
“The most common underlying causes of sudden cardiac arrest in this age group are structural or functional disorders such as hypertrophic cardiomyopathy and coronary artery anomalies, and primary cardiac electrical disorders such as familial long QT syndrome and Wolff-Parkinson-White syndrome.”

sudden cardiac arrest in children.

The most common underlying causes of sudden cardiac arrest in this age group are

“A history of fainting or having a seizure, especially during exercise.”

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- ***“...serum potassium should be kept in the high normal range.”***
- ***“Intravenous administration of 1-2 g magnesium sulfate appears to prevent recurrences of torsade de pointes in most patients.”***

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Thank you!!

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