# *Nitrogen Imbalance in critically ill patients*

**essay**
**Submitted For Partial fulfillment**
**For Master degree in**
**Intensive Care**

**By**
***Ahmed Mahmod Moawad***

**(M.B. B.Ch.)**

Supervised by

## *Prof. Dr Sohair Abbas M. Sadek*

**Professor of Anesthesia and Intensive Care**

**Faculty of Medicine - Ain Shams University**

## *Prof. Dr. Heba Bahaa El Din El Serwi*

**Assistant professor of Anesthesia and Intensive Care**

**Faculty of Medicine - Ain Shams University**

## *Dr. Walid Ahmed AbdElrahman*

**Lecturer of Anesthesia and Intensive Care**

**Faculty of Medicine - Ain Shams University**

**Faculty of Medicine**

**Ain Shams University**

**2009**

# Acknowledgments

*First, thanks are all due to Allah for blessing this work until it has reached its end, as a part of his generous help throughout my life.*

*I would like to express my deepest gratitude to Prof.Dr Sohair Abbas M. Sadek, Professor ofAnesthesia and intensive care , Faculty of Medicine, Ain Shams University, for her great support and continous encouragement throughout this whole work. It is a great honor to work under her guidance and supervision.*

*I am truly grateful Prof.Dr Heba Bahaa El Din El serwi Assistant Professor of Anesthesia and intensive care, Faculty of Medicine, Ain Shams University, for her close supervision, sincere help, valuable suggestions and continous encouragement throughout the whole work.*

*I would like to express thanks and appreciation to Dr. Walid Ahmed AbdElrahman, lecturer of anesthesia and intensive care, Faculty of Medicine, Ain Shams University, for his great help throughout the whole work.*

# Contents

page

# List of abbreviations

**AAA: Aromatic Amino Acid**
**AMAs: American Medical Associations**
**AMA-NAG: American Medical Association National Adversory Group**
**APACHE: Acute Physiology And Chronic Health Evaluation**
**ARDS: Acute Respiratory Distress Syndrome**
**BCAAs: Branched Chain Amino Acids**
**BV : Biological Value**
**BMI: Body Mass Index**
**CDC: Catheter Dressing Care**
**CNS : Central Nervous System**
**CO2: Carbon Dioxide**
**CRBSIs: Catheter Related Colonizations And Blood Stream Infections**
**CVCs: Central Venous Catheters**
**DAH : Docosahexanoic Acid**
**DCH: Delayed Cutaneous Hypersensitivity**
**EPA : Eicosapentanoic Acid**
**FDA: Food And Drug Administration**
**GCS: Galasgow Coma Scale**
**ICU: Intensive Care Unit**
**ICVADs : Implantable Central Venous Access Devices**
**IV: Intra Venous**
**IVLE: The Infusion Rate For Intravenous Lipid Emulsion**
**LCTs:Long Chain Triglycerides**
**MCTs: Medium Chain Triglycerides**
**MODS: Multiple Organ Dysfunction Syndrome**
**PICCs: Peripherally Inserted Central Catheters**
**PRCTs: Prospective Randomized Controlled trials**
**PUFAs: PolyUnsaturated Fatty Acids**
**PVC:PolyVinyl Chloride**
**ROS: Reactive Oxygen Species**
**SAAs: Simple Amino Acids**
**SCFAs: Short Chain Fatty Acids**
**SGA : Subjective Global Assessment**
**SIRS: Systemic Inflammatory Response Syndrome**
**TISS: Therapeutic Intervention Scoring System**
**TPN : Total Parentral Nutrition**
**UK : United Kingdom**
**USA: United States of America**
**UUN : Urine Urea Nitrogen**

# Introduction

The role of nutrition in patient care became a part of mainstream medicine at about the end of the 1960s, with the publication of several papers that showed a benefit of nutritional support in the prevention of complications. Nutritional support can increase the risk of complications when given to well-nourished, obese and hyperglycemic patients. The avoidance of overfeeding and hyperglycemia is, therefore, of paramount importance ***(Jeejeebhoy, 2007)***.

Hypermetabolism and malnourishment are common in the intensive care unit. Malnutrition is associated with increased morbidity and mortality, and most intensive care unit patients receive specialized nutrition therapy to attenuate the effects of malnourishment. However, the optimal amount of energy to deliver is unknown, with some studies suggesting that full calorie feeding improves clinical outcomes but other studies concluding that caloric intake may not be important in determining outcome ***(Stapleton et al., 2007)***.

Protein catabolism is a hall mark of critical illness. The most common clinical method for assessing a patient's protein requirement is determination of nitrogen balance ***(Cheatham et al., 2007)***.

Nitrogen balance calculations are the single nutritional variable most consistently associated with improved patient outcome during critical illness. Achievement of a positive nitrogen balance is widely considered to be the primary goal of nutritional support ***(Eastern association for the surgery of trauma, 2008)***.

Early nutrition support, defined as within the first 24-48 h of ICU care, is recommended by clinical practice guidelines ***(Scurlock and Mechanick, 2008)***.

At about the end of the 1960s, the emphasis was on nutrition given by the parenteral route. Since then, a series of studies that compared parenteral nutrition with enteral nutrition have suggested that the enteral

route of feeding causes fewer complications than the parenteral route ***(Jeejeebhoy, 2007)***.

Intravenous nutrition plays an important supportive role in the management of the critically ill patient. Energy substrates consist of concentrated glucose and lipid solutions. The nitrogen requirement is supplied as L-amino acids. The water soluble vitamins and vitamin K should supplement intravenous nutrition with amounts at least to meet the recommended daily allowance. Additional supplementation of thiamine, folic acid and ascorbic acid are often administered in the critically ill patient ***(Atkinson and Worthley, 2003)***.

Enteral nutrition has emerged as the preferred route of feeding particularly in critical illness. By providing enteral nutrition instead of parenteral nutrition, the natural physiologic pathway is being followed and gut immunity preserved. However, obstacles such as upper gastrointestinal intolerance, hypoperfusion vasopressor support, and glycemic control make the task of initiating feeds a challenge ***(Widlicka, 2008)***. Experience with management of the many common complications of enteral access is a pre-requisite for successful long-term outcomes ***(Iyer and Crawley, 2007)***.

Early enteral nutrition is recommended for critically ill patients. Supplemental parenteral nutrition combined with enteral nutrition can be considered to cover the energy and protein targets when enteral nutrition alone fails to achieve the caloric goal ***(Heidegger et al., 2008)***.

Glutamine and arginine are both used as nutritional supplements in critically ill patients. Although glutamine has been shown to be beneficial for the metabolically stressed patient, considerations about arginine supplementation are not unanimously determined. The beneficial effects of free glutamine may depend on the route of administration but also on the metabolic fate of amino acids generated (e.g., citrulline, arginine).

Glutamine serves as a substrate for de novo citrulline and arginine synthesis ***(Vermeulen et al., 2007)***.

# Chapter 1

# Nutritional requirements

The metabolic response to critical illness is characterized by hypermetabolism, hyperglycemia, increased lipolysis, and net protein catabolism. Skeletal muscle protein is broken down and the amino acids are used for gluconeogenesis and protein synthesis. Synthesis of positive acute-phase proteins (e.g., C-reactive protein) is increased. These metabolic changes, along with bed rest and suboptimal nutrient intake, result in depletion of lean body mass. Nutritional support in the critically ill should provide nutrition consistent with the patient's medical condition, nutritional status, and available route of administration; prevent or treat macro- or micronutrient deficiencies; provide doses of nutrients compatible with current metabolism; avoid complications associated with the route of delivery; and improve patient outcomes related to their disease morbidity (body composition, tissue repair, organ function). The patient's response to nutritional support should be monitored so that adjustments can be made to avoid complications and ensure that the goals of nutritional support are met***(Cerra et al., 2007)***.

## CARBOHYDRATES

Carbohydrates are compounds of carbon, hydrogen, and oxygen. They are the chief source of calories in most diets. They are also the main energy source for the body in health and disease states, yielding 4 kcal /g. Carbohydrates play critical roles as constituents of DNA and RNA, coenzymes, glycoproteins, and glycolipids. Glucose is the most important carbohydrate, serving as an oxidative fuel for the brain, renal medulla, leukocytes, and erythrocytes ***(Frakenfield, 2001)***.

The minimum amount of exogenous glucose needed per day is thought to be between 100 and 150 grams. Optimal carbohydrate delivery

should be at a level to allow maximal protein sparing while minimizing hyperglycemia ***(Wilmore, 2004)***.

The amount of carbohydrate that can be safely provided to a critically ill patient is a function of the patient's ability to oxidize these carbohydrates. The rate of infusion has been suggested to be no more than 4 to 5 mg/kg/min. For patients who are diabetic or receiving steroid therapy, or who have stress-induced hyperglycemia, the carbohydrate infusion should be limited to 2.5 to 4.0 mg/kg/min initially until blood sugars are well controlled. Patients requiring total parental nutrition (TPN) who are at risk for developing refeeding syndrome should be initiated with no more than 100 to 150 g dextrose/d **.** Carbohydrate requirements have also been suggested as 30 to 70% of the total calories needed per day ***(Cerra et al., 2007)***.

## PROTEINS

Proteins are essential components of all living cells and are involved in almost every bodily function. Proteins function in tissue, cell, and organelle structure, as enzymes and hormones, and in molecules involved with cell-to-cell communication and in genetic material. The carbon in amino acids can be oxidized, yielding 4 kcal/g ***(Frakenfield, 2001)***.

Protein requirements in the critically ill have not been clearly defined but they generally range between 1.0 and 2.0 g/kg/d. In comparison to the dietary reference intake for protein in healthy adults (0.8 g/kg/d), most critically ill patients require almost twice as much protein. Some have suggested protein requirements in the critically ill to be as much as 1.5 to 2.0 g/kg/d ***( Keating, 2001)***.

However, there is little evidence that giving more than 1.0 to 1.5 g/kg/d has any further benefit. ***Ishibashi and associates (2008)*** suggest that 1 to 1.2 g/kg/d would provide for optimal protein provision in the first two weeks of critical illness. ***Larsson and colleagues (2000)*** also found that provision of 0.2 g nitrogen/kg/d (approximately 1.25 g protein/kg/d) was optimal in the first week post trauma. Providing an exogenous source of protein will reduce nitrogen loss, but protein sparing may not be further improved by providing greater than 1.5 g protein/kg/d ***(Shaw et al., 2007)***.

## LIPIDS

Fatty acids perform a wide variety of functions in the body. Fat serves as a source of calories (9 kcal/g) and is a major fuel source after carbohydrate stores are depleted. Fat serves to insulate the body and cushion organs. Fats play an important role in cell membrane structure; as a lubricant for body surfaces, joints, and mucus membranes; and in cell signaling components. Fat is also needed for fat-soluble vitamin digestion and absorption ***(Frakenfield, 2001)***.

The minimum amount of fat needed is only 2 to 4% of total calories. The only essential fatty acids are the long-chain fatty acids alpha-linolenic acid and linoleic acid. When fat is used as a source of calories, generally 15 to 30% of total calories can be provided as fat. The absolute maximum amount of fat is suggested to be no more than 2.5 g/kg/d, or less than 60% of total calories***(Cerra et al., 2007)***.

Some literature suggests that fat be further limited to 1 g/kg/d or less in critically ill patients. The infusion rate for intravenous lipid emulsions (IVLE) is also important to consider and should not exceed 0.11 g/kg/h to avoid metabolic complications. Contraindications to the use of IVLE include

egg allergy and hypertriglyceridemia. Provision of IVLE is generally considered safe as long as triglyceride concentrations are less than 400 mg/dl. There is no strong evidence to suggest a benefit in restricting IVLE for patients with thrombocytopenia***(Frakenfield, 2001; Battistella et al., 2007)***.

## MICRONUTRIENT SUPPLEMENTATION

All critically ill patients need micronutrient supplementation as soon as nutritional support is initiated enterally or parenterally. It is also possible to supply these micronutrients directly via the intravenous fluids of patients who are not yet at goal enteral or parenteral nutrition ***(Sriram and Cué, 2005)***.

### TIMING

The largest increases in reactive oxygen species (ROS) production occurs early in the course of acute illness. Likewise, decreased serum levels of micronutrients are seen in this period. In burns, early administration of micronutrients has been shown to be beneficial. It is therefore logical to conclude that micronutrient supplementation should begin early in the course of acute illness to offset the deleterious effects of ROS. During the first five to seven days, the emphasis is on antioxidant supplementation. After this period, routine micronutrient supplementation is provided ***(Berger et al., 2008)***.

### ROUTE

In critically ill patients, the intravenous route is the only reliable method by which micronutrients can be administered. Very few clinical trials have used the enteral route for micronutrient supplementation in

critically ill patients. Absorption by the enteral route in critically ill patients is unpredictable, due to hemodynamic instability, bowel edema, and alterations in blood supply. Vitamin E absorption is reduced in critically ill patients. Interactions between various micronutrients in normal individuals, discussed earlier, are even more complex in critically ill patients. Micronutrients are initially administered intravenously, either as a component of total parenteral nutrition or separately. When enteral feeding is initiated and tolerated, micronutrient supplementation can be provided enterally ***(Seeger et al., 2007)***.

## DOSE

Although firm conclusions and recommendations are not available, the additional modest doses of vitamins A (10,000 IU/d), E (50 to 60 IU/d), and C (500 mg/d) will benefit critically ill patients.

## MONITORING

Though serum levels can be used to detect deficiencies, they are not easy to obtain in most hospitals and may not reflect a true deficiency. There are no reliable laboratory indicators for vitamins and trace elements to determine adequacy of supplementation. Functional end points, such as using enzyme assays (alkaline phosphatase for Zn) are also not reliable ***(Sriram and Cué, 2005)***.