FACTORS THAT AFFECT NUTRITIONAL ADEQUACY IN MECHANICALLY VENTILATED PATIENTS RECEIVING ENTERAL NUTRITION SUPPORT

by

COLLEEN O'LEARY-KELLEY

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

in

NURSING

in the

GRADUATE DIVISION

of the

UNIVERSITY OF CALIFORNIA SAN FRANCISCO

Approved:

. . . .

. . . .

. . . .

Committee in Charge

Deposited in the Library, University of California San Francisco

. . . .

Date University Librarian

Degree Conferred: . . . .

Abstract

FACTORS THAT AFFECT NUTRITIONAL ADEQUACY IN MECHANICALLY VENTILATED PATIENTS RECEIVING ENTERAL NUTRITION SUPPORT

by

Colleen O'Leary-Kelley, RN, MS, PhD (c)

University of California, San Francisco, 2003

The purpose of this study was to examine the adequacy of enteral nutritional intake and the factors affecting its delivery in mechanically ventilated intensive care unit (ICU) patients. A prospective, descriptive design was used to study a convenience sample of 60 patients receiving enteral nutrition at goal rate. Patients were enrolled from intensive care units at 2 study sites. Caloric requirements were determined based upon the Harris-Benedict Equation (HBE). A total of 25 patients were also measured by indirect calorimetry. The enteral volume and kilocalories delivered, residual volumes, stool frequency, and duration of feeding interruptions were recorded for 3 consecutive days after the goal rate had been established.

A statistically significant difference was found between the HBE requirements ($M = 2{,}150$, $SD = 317$) and the average kilocalories received ($M = 1{,}410$, $SD = 731$; 95% confidence interval 573-905, $p < .001$). Forty-one patients (68.3%) received less than 90% of requirements, 18 (30%) received within 10% of requirements, and 1 patient received more than110% of required calories. However, for patients with indirect calorimetry measurements ($n = 25$), there was no significant difference between the measured requirements and mean kilocalories received ($p = .337$). Multiple linear-regression analysis determined that 70% of the variance in the required kilocalories (per HBE) received was explained by the 5 predictors in the model (F $_{5,53}$ = 25.335, $p < .001$, R^2 .705). Enteral feedings were often interrupted and the duration of feeding interruptions explained 45% of the variance within the context of the other 4 predictors. A number of factors limited the adequacy of enteral intake, as determined by HBE, which may potentially contribute to complications associated with underfeeding and overfeeding. Noteworthy is that the two methods used to determine nutritional requirements yielded different results related to adequacy of intake. This finding poses additional questions about the accuracy of methods commonly used to determine requirements. The study builds upon existing knowledge and provides direction to future research related to enteral nutrition in mechanically ventilated ICU patients.

[redacted]

6/6/03

Kathleen Puntillo, RN, DNSc, FAAN – Chair

Date

ACKNOWLEDGEMENTS

This dissertation represents the culmination of 7 years of graduate study and was only made possible through the combined efforts and support of several individuals. Dr. Kathleen Puntillo has provided perpetual support, first as my professor and subsequently as my as my doctoral studies advisor; a member of my qualifying examination committee; and finally, as the Chairperson for my dissertation committee. I truly appreciate her shared knowledge and dependable guidance and encouragement. Dr. Nancy Stotts served as the Chairperson for my qualifying examination and offered valuable support throughout the qualifying examination and dissertation process. I would also like to acknowledge Dr. Patricia Benner for her initial encouragement to pursue doctoral study. It is through my relationships with these outstanding nursing scholars that I have come to know the valuable collegial bond between doctoral student and professor. Dr. Bruce Wolfe served faithfully on both my qualifying examination and dissertation committees and has provided key support throughout the design and conduct of the study. Dr. Steven Paul provided essential support related to data analysis, power analysis, and statistics.

Many individuals at the Veteran's Affairs Palo Alto Health Care System extended tremendous assistance during several phases of the dissertation process. Dr. Marilyn Douglas mentored me throughout the data collection and post analysis phases of the study. Her insight and wealth of research experience is highly valued. Dr. Juliana Barr provided excellent guidance during the data collection, data input, and analysis. Her enthusiasm for nutrition research related to patient care within the hospital intensive care unit served to strengthen my resolve toward the ultimate completion of this study. I

would like to extend special thanks to the staff of the Respiratory Therapy Department, especially Brad Wee-Tom for his interest and support in helping to identify potential patients. I am also grateful for the assistance and nutrition consultation provided to me by Ampy Khorana. My heartfelt thanks go to the Pulmonary Therapy Department for use of the indirect calorimetry equipment, and especially to James Canfield for teaching me how to perform the indirect calorimetry measurements, and for helping me troubleshoot equipment problems. I am grateful for the support of Dr. Eran Geller, Medical Director of the Medical Surgical Intensive Care Unit and to Shirley Paulson, Bobette Nicholl, and Sandy Cardoza for facilitating my access to patients in the facility. I am genuinely grateful to all my professional nurse colleagues in the Medical Surgical Intensive Care Unit for their encouragement throughout my doctoral studies, and especially for their assistance during the data collection phase. Thanks are extended to Sheila Jun for her continual help in identifying potential patients. I am also grateful for the support of Dr. Patrick Kearns at the Santa Clara Valley Medical Center, and extend my sincere thanks to the nursing and dietary staff of the Medical Intensive Care Unit and Coronary Care Unit. I appreciate the willing assistance of Terri Sexton in performing all of the indirect calorimetry measurements for the study at that site.

To my fellow doctoral students, who helped me immensely throughout the program, my sincere thanks to you. I would like to acknowledge Gretchen Summer and Yoshimi Fukuoka, in particular, for their support. I extend special thanks to my dear friend and fellow doctoral student, Helen Daley for helping me keep my perspective and sense of humor through the years. The patients and families who consented to participate in this study must also be acknowledged. I truly appreciate their willingness to be a part of this research.

Finally, I would like to recognize the members of my family. Your love, support, and encouragement allowed me to successfully complete this life milestone. To my sons—Donovan, Edward, and Declan—thank you for your tolerance and for "propping me up" when I needed it most. To my husband, Michael, what can I say except thank you for cheering me along and for being there to share all the disappointments and joys along the way.

This study was conducted at the Veteran Affairs Palo Alto Health Care System, in Palo Alto, California and the Santa Clara Valley Medical Center in San Jose, California with funds provided through a predoctoral nurse fellowship sponsored by the Veteran's Affairs Office of Academic Affiliations. Additional support was provided by the National Institute of Nursing Research, National Institutes of Health, National Research Service Award, and a 2002 Sigma Theta Tau Research Award.

Table of Contents

Page

COPYRIGHT PAGE ii

ABSTRACT iii

ACKNOWLEDGEMENTS v

TABLE OF CONTENTS viii

LIST OF TABLES xii

LIST OF FIGURES xiii

CHAPTER I / THE STUDY PROBLEM 1

Statement of the Problem and Purpose of the Study 3

Significance 5

  Consequences of Malnutrition 5

  Adequate Nutritional Intake 7

CHAPTER II / REVIEW OF RELATED LITERATURE AND CONCEPTUAL FRAMEWORK 11

Physiological Background 11

  Malnutrition and Metabolic Response to Starvation 11

    The Early Phase 12

    The Late Phase 14

    Summary 15

  Metabolic Response to Illness or Injury 16

    Alterations in Substrate Metabolism 18

      Carbohydrate Metabolism 18

Page

Lipid Metabolism 18
Protein Metabolism 19
Summary 20
Respiratory Effects of Malnutrition 21
Respiratory Muscle 22
The Immune System 23
Summary 24
Review of Related Literature 25
Measures of Energy Expenditure 25
Indirect Calorimetry 26
Gas Exchange Methods 27
Variability and Precision 29
Validation Methods 30
The Fick Method 31
Predictive Equations 33
Summary 37
Effects of Underfeeding and Overfeeding in Critical Illness 38
Nutritional Adequacy 41
Effects of Accurate Assessment 41
Gastrointestinal Intolerance 45
Tube Factors 50
Factors Related to the Intensive Care Unit 51

Page

Summary of Research 55

Conceptual Framework 57

CHAPTER III / METHODOLOGY 59

Research Design, Setting and Study Sample 59

Human Subjects and Sampling Procedures 59

Participant Criteria and Sample Size 60

Measures 61

Instrumentation 61

Indirect Calorimetry 61

Harris-Benedict Equation and the Enteral Feeding Pump 63

Study Variables 64

Procedures 67

Data Collection 67

Data Analysis 69

CHAPTER IV / RESULTS 72

Characteristics of the Study Sample 72

Primary Aims 74

Secondary Aims 80

Summary of Results 84

CHAPTER V / DISCUSSION 85

The Study Sample 85

The Research Findings 88

Page

Kilocalories Received 88

Use of the Harris-Benedict Equation 88

Use of Indirect Calorimetry 89

Adequacy of Enteral Nutritional Intake 90

Influence of Specific Variables 94

Comparison of the Harris-Benedict Equation and Indirect Calorimetry 97

Analysis of Subsamples 99

Limitations of the Study 101

Implications and Recommendations 103

REFERENCES 106

APPENDIXES 128

APPENDIX A: CHR APPROVAL LETTER 128

APPENDIX B: HUMAN SUBJECTS CONSENT FORM 130

APPENDIX C: STUDY RECRUITMENT FLYER 135

APPENDIX D: DATA COLLECTION FORMS 137

List of Tables

Page

1. Flow / Volume Gas Specifications 63

2. Study Concepts 66

3. Demographics of the Study Sample 73

4. Nutritional Data for the Study Sample 74

5. Paired Samples *T*-Test Results 76

6. Nutritional Adequacy Categories 77

7. Correlations with Dependent Variable 78

8. Multiple Regression Summary Table 79

9. Paired Sample *T*-Test Measured Versus Estimated Energy Expenditure 80

10. Chi-Square and *T*-Test Results 83

List of Figures

Page

1. Conceptual Framework for Enteral Nutritional Adequacy 58

2. Normal Distribution Curve for Estimated Resting Energy Expenditure 75

3. Difference Between Estimated and Measured Energy Expenditure 81

CHAPTER I

THE STUDY PROBLEM

Nutrition plays a pivotal role in the maintenance of normal physiological function and optimal health (Daly et al., 1993). It represents a combination of biochemical and physiological processes that allow the body to receive, absorb, and use nutrients for growth and development and renewal of its vital components (Herrmann, 1995). Depletion of essential nutrients, resulting from prolonged periods of inadequate intake, can lead to a clinical diagnosis of malnutrition (Daly et al., 1993). Therefore, it is critical to maintain minimal nutritional requirements in the prevention of dietary deficiencies.

Although no universal definition of *malnutrition* exists, it is broadly defined as a disorder of body composition resulting from a deficit or excess of nutritional intake (Cerra et al., 1997). It includes several clinical conditions that occur in response to problems with nutrient intake, digestion, absorption, metabolism, and excretion (Daly et al., 1993). Malnutrition represents a continuum that begins in one or more of these areas and progresses to clinical and functional changes ultimately affecting morbidity and mortality. In acutely ill patients, prevalence of malnutrition ranges from 30% to 60% (McWhirter & Pennington, 1994; Naber et al., 1997). One study found that 43% of patients admitted to an intensive care unit (ICU) were malnourished according to their serum albumin level and weight status (Giner, Laviano, Meguid, & Gleason, 1996). Moreover, it is difficult to determine a causal link between malnutrition and outcome because presence of the condition may simply reflect the severity of the underlying disease (Weinsier & Heimburger, 1997).

Acutely ill, malnourished patients typically experience a 2.6 to 3.4 times the number and extent of medical complications observed in normally nourished patients, as well as 3.8 times the mortality rate (Reilly, Hull, Alpert, Waller, & Bringardener, 1988). Malnutrition may be preexistent or develop as a result of disease factors during the course of hospitalization. Progressive malnutrition leads to weight loss, muscle wasting, decreased wound healing, alterations in visceral proteins, and economical complications due to the need for increased care costs (Chima et al., 1997; Daly et al., 1993). Decreased respiratory muscle function can also result, as well as reduced ventilatory drive and compromised pulmonary defense mechanisms (Rochester, 1986b). Respiratory failure may develop in malnourished patients independent of the presence of preexisting pulmonary disease (Murciano et al., 1994).

Patients who develop acute respiratory failure may require mechanical ventilatory support that precludes oral nutritional intake. Prolonged mechanical ventilation limits respiratory muscle work and often leads to atrophy and ventilator dependence (Shikora & Benotti, 1997). While most patients can be removed from mechanical ventilation, between 5% to 10% become chronically ventilator dependent and require more than 50% of all critical care resources available (Cohen & Booth, 1994). Malnutrition is common in mechanically ventilated ICU patients (Bartlett et al., 1982; Driver & LeBrun, 1980; Shikora & Benotti, 1997). Additionally, poor nutritional status limits ventilatory drive and contributes to respiratory muscle weakness and fatigue (Knebel, 1992).

Nutrition support is the provision of oral, enteral, or parenteral nutrients. It is an essential adjunct in the prevention and management of malnutrition in critically ill patients. Goals for nutrition support in mechanically ventilated ICU patients are the same as those for all critically ill patients—the provision of enough support for body requirements, to minimize complications, and to promote rapid recovery. Accurate assessment of requirements and monitoring the adequacy of nutritional intake can prevent serious complications of nutrition support such as underfeeding and overfeeding. Related literature indicates a preference for enteral nutrition over parenteral methods (Kudsk et al., 1992; Moore, Moore, Jones, McCroskey, & Peterson, 1989). However, an insufficient number of randomized, prospective, controlled trials prevents a comprehensive meta-analysis of these two methods across a wide patient population with a variety of illnesses (Braunschweig, Levy, Sheean, & Wang, 2001). Advantages of enteral nutrition include lower cost, enhanced maintenance of gut mucosal integrity, reduced infection, and decreased length of hospital stays (August et al., 2002). Consequently, enteral nutrition methods are preferred when nutrition support is indicated. However, some critical care studies indicate that it may be difficult to meet full nutrient requirements with enteral nutrition (Adam & Batson, 1997; Kemper, Weissman, & Hyman, 1992). For mechanically ventilated ICU patients, multiple barriers exist that limit the adequacy of nutritional intake with this method. To maximize the benefits of enteral support, it must be carefully prescribed and delivered in amounts that will improve nutritional status and while avoiding complications associated with underfeeding and overfeeding (McClave, 1997).

Statement of the Problem and Purpose of the Study

Several factors influence the adequacy of enteral nutritional intake in ICU patients. Specifically, these patients may not receive adequate nutrition support because nutrient demands may be considerably increased due to the underlying illness or injury

(McClave, 1997; Shikora & Benotti, 1997), or enteral feedings are interrupted because of gastrointestinal (GI) dysfunction, tube-placement issues, or necessary tests or other procedures (Campbell, Branson, Burke, & Covington, 1994; Cerra et al., 1997). As mentioned earlier, enteral nutrition is generally preferred over parenteral nutrition and has demonstrated improved outcomes with less clinical complications. However, despite the known benefits, enterally fed patients often do not receive nutrition in amounts adequate to meet their energy requirements (Cerra et al., 1997). Greater effort is needed toward improving the adequacy of enteral nutritional intake. Few advances have been made in this regard, and adequate enteral nutrition in ICU patients remains highly inconsistent (Daly et al., 1993). It is essential to explicate the factors that influence the adequacy of nutritional intake to form a firmer foundation for improved intervention. Understanding the importance of adequate enteral nutritional intake, as well as these factors that influence proper intervention with this method, are critical in the development evidence-based nutrition support for mechanically ventilated ICU patients.

The purpose of this prospective study was to examine the adequacy of enteral nutritional intake and the factors affecting its delivery in mechanically ventilated ICU patients. The following four primary aims guided this research:

1. Determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by the Harris-Benedict Equation (HBE).
2. Determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by indirect calorimetry.
3. Determine the percentage of patients who received adequate enteral nutrition kilocalories, the percentage underfed, and the percentage overfed.

4. Examine the influence of specific factors on the percentage of required enteral nutrition actually received.

The following two secondary aims also guided this research:

1. Determine the difference between kilocalories determined necessary by indirect calorimetry compared to HBE in those patients with indirect calorimetry measurements.
2. Determine the differences in demographic variables between patients able to be measured by indirect calorimetry and those who were not.

Significance

Consequences of Malnutrition

Malnutrition is associated with poor clinical outcomes and complications resulting in increased health care costs (Chima et al., 1997; Klein et al., 1997; Reilly et al., 1988; Robinson, Goldstein, & Levine, 1987). This condition prolongs the length of ICU and hospital stays and serves to increase morbidity and mortality (Cerra et al., 1997; Shikora & Benotti, 1997). Malnutrition also leads to a depletion of body cell mass, as well as impaired tissue and organ function. It is associated with the development of a wide variety of complications in hospitalized patients (Daly et al., 1993) including delayed wound healing (Kay, Moreland, & Schmitter, 1987), development of pressure sores (Myers, Takaguchi, Slavish, & Rose, 1990), and increased morbidity and mortality compared to normally nourished patients (Reilly et al., 1988; Sullivan & Walls, 1994).

In a retrospective study conducted by Reilly and colleagues (1988), the medical charts of 771 patients within two hospitals were reviewed to assess the effects of malnutrition on care costs. Based upon specific nutritional criteria at the time of admission, the likelihood of malnutrition was determined in advance for each patient.

Criteria included serum albumin level, total lymphocyte count, cachectic appearance, and percentage of weight loss within the 3 months preceding admission. Fifty-nine percent of the medical charts reviewed by Reilly et al. indicated increased likelihood of malnutrition compared to 48% of the surgical charts. Malnourished patients were 2.6 to 3.4 times more likely to experience minor or major complications. Minor complications included bacteremia, wound infection, atelectasis, or urinary tract infection. Major complications included sepsis, wound dehiscence, pneumonia, renal failure, repeat surgery, and death. Patients with malnutrition experienced longer hospital stays (i.e., 1.1 to 12.8 excess days) than those who maintained higher levels of nutrition. Additionally, costs associated with the medical care of patients with malnutrition were significantly increased ($p < .0001$) compared to those without the condition.

Malnutrition also often leads to decreased respiratory muscle strength and function, as well as diminished pulmonary immune competence (Kelly et al., 1984; Niederman et al., 1984). In turn, decreased respiratory muscle strength may lead to pulmonary infection and can also impair weaning from mechanical ventilation (Bassili & Deitel, 1981; Larca & Greenbaum, 1982). Malnutrition is common in mechanically ventilated ICU patients, particularly those with chronic pulmonary disease (Bartlett et al., 1982; Driver & LeBrun, 1980; Shikora & Benotti, 1997). In one study, 60% of the patients with chronic obstructive pulmonary disease (COPD) who were admitted for acute respiratory failure, and 74% of those who required mechanical ventilation, were malnourished (Laaban et al., 1993). Prolonged mechanical ventilation limits respiratory muscle work and leads to atrophy and ventilator dependence (Shikora & Benotti, 1997). Poor nutritional status limits ventilatory drive and contributes to respiratory muscle weakness and fatigue (Knebel, 1992). Therefore, optimizing respiratory muscle function and nutritional intake are key priorities (Daly et al., 1993). The importance of this issue is highlighted by the American Association of Critical Care Nursing, which identified clinical research related to mechanical ventilation and nutrition support outcomes as a priority for critical care nursing as cited in Lindquist et al. (1993). Additionally, a National Institutes of Health consensus conference recommended research to determine the adequacy of nutrition support and its relationship to outcomes (Klein et al., 1997). Inadequate nutritional intake and the increased metabolism associated with critical illness or injury lead to malnutrition in the critically ill patient (Barton, 1994; Daly et al., 1993). In light of its prevalence, associated complications, and the direct and indirect costs of care, it is clear that malnutrition prevention should be a focus of both research and practice (Daly et al., 1993).

Adequate Nutritional Intake

Studies of a wide variety of patient populations have demonstrated positive outcomes from enteral nutritional support (Potter, Langhorne, & Roberts, 1998; Zaloga, 1999). In a meta-analysis of 32 randomized controlled studies, Potter and colleagues (1998) evaluated adult medical-surgical patients for nutritional status, the effectiveness of oral versus enteral nutrition toward improved body weight, and survival. Routine provision of oral or enteral nutrition improved the weight and anthropometrics of their patient sample; however, the data were insufficient to determine whether mortality was reduced by nutrition support. Nutrition support has demonstrated variable benefit in studies of critically ill patients with burns, trauma, sepsis, acute lung injury, and renal failure (Klein et al., 1997). In a review published by Zaloga (1999), 84% of 19 prospective, controlled studies reported improved clinical outcomes in critically ill patients who received early versus delayed enteral nutrition support. Early enteral nutrition has since been identified as a Level I recommendation for critically ill patients.

In spite of the available data in support of nutrition support, considerable debate exists surrounding such intervention in the management of critically ill patients (Koretz, 1995). Questions remain as to when to begin supplemental nutrition, how much to provide, how to measure requirements, the relative efficacy of enteral versus parenteral methods, and the efficacy of nutrition support on clinical outcomes. Few randomized, controlled clinical trials indicate a direct link between nutrition support and the health outcomes of critically ill patients. The long-term effects on morbidity and mortality are also yet to be determined (Potter et al., 1998).

Little direct evidence exists to confirm that nutrition support independently improves clinical outcomes or prevents complications in critically ill patients (Koretz, 1995). Given the relationship between malnutrition and respiratory function and the development of respiratory failure, the value of nutrition support is substantiated in the clinical management of mechanically ventilated ICU patients (Shikora & Benotti, 1997). A correlation has been shown between nutritional status and the ability to wean these patients from mechanical ventilation (Bassili & Deitel, 1981; Larca & Greenbaum, 1982). Practice guidelines advocate nutrition support in respiratory failure patients to limit the ongoing wasting of skeletal and respiratory muscles and support early identification and treatment of malnutrition while preventing overfeeding (Daly et al., 1993). Nutrition support provides nutrients to meet energy needs, protects organ function, and limits breakdown of muscle tissue (Posa, 1994). During the hypermetabolic phase of critical illness, nutrition support theoretically limits additional loss of lean muscle (Barton, 1994; Cerra, 1987). Once the acute illness resolves, nutrition support improves nitrogen balance and restores muscle mass, potentially improving the ability to wean from mechanical ventilation. It is recognized, however, that nutrition support combined with optimal weaning strategies is necessary to improve the likelihood of successful weaning (Shikora & Benotti, 1997).

Enteral nutrition is a key component in the management of ICU patients able to tolerate feeding into the GI tract (Heyland et al., 1995). The reported benefits of enteral nutrition over parenteral nutrition include preservation of intestinal mucosa, optimal nutrient utilization, safer administration, and reduced cost (Daly et al., 1993). Enteral nutrition is utilized more efficiently because of the first-pass effect that processes nutrients in the gut and liver before release into the systemic circulation. Maintenance of the normal intestinal structure prevents the entrance of bacteria through the intestinal wall into the bloodstream (Meijer, Muller, & van Leeuwen, 1996). Enteral nutrition promotes growth of GI mucosal cells and stimulates the production of secretory Immunoglobin A, which prevents attachment of bacteria to the intestinal lining (Takahashi & Kiyono, 1999). The inactive GI tract during critical illness or prolonged periods of parenteral nutrition theoretically leads to changes in the intestinal wall structure decreasing its integrity.

The safety benefits of enteral nutrition include avoidance of complications related to central lines such as pneumothorax and catheter sepsis (Kemper et al., 1992). Fewer infections were observed in trauma patients who received enteral nutrition compared to those fed parenterally (Moore et al., 1989). Although there are no randomized controlled studies confirming any direct cost benefit, enteral nutrition remains preferred for an assumed decrease in cost (August et al., 2002). Enteral nutrition is also purported to limit the hypermetabolic response to injury (Windsor et al., 1998), improve wound healing, and decrease septic morbidity (Moore et al., 1989). Reported benefits support a general preference for enteral over parenteral nutrition. However, enterally fed critically ill patients often do not receive nutrition in amounts adequate to meet energy requirements (Adam & Batson, 1997; Kemper et al., 1992). Although the adequacy of nutrient delivery is an intermediate endpoint of research, greater effort is needed to improve the adequacy of enteral nutrition support in critically ill patients (August et al., 2002). Few advances have been made toward this end, and enteral nutrition delivery practices remain highly variable and inconsistent (Adam & Batson, 1997). Examination of enteral nutrition adequacy, as well as factors that influence delivery, will provide the knowledge necessary to develop evidence-based practice strategies. Such strategies will, in turn, potentially and positively influence clinical outcomes for mechanically ventilated ICU patients.

CHAPTER II

REVIEW OF RELATED LITERATURE AND CONCEPTUAL FRAMEWORK

Physiological Background

Malnutrition and Metabolic Response to Starvation

Malnutrition represents a significant health risk and is a particular threat to those with respiratory disorders (McCarthy & Deal, 2002). Normal metabolic processes function optimally when nutrient intake is well balanced. These processes become negatively altered in the absence of an adequate and balanced diet and in the concurrent presence of stress, illness, or injury. A clear understanding of the differences between simple starvation and malnutrition coupled with the stress of illness or injury is essential in interpreting data collected from a complete nutritional assessment (Herrmann, 1995). Early detection of malnutrition may lead to treatment that can effectively decrease or prevent further complications.

Starvation is a specific adaptive response to inadequate nutrient intake and depletion of energy stores (Barton, 1994). The body attempts to maintain survival by providing enough glucose to tissues that require it as their main fuel source and by minimizing muscle protein loss (Stryer, 1995). The adaptation of starvation occurs as energy sources shift from carbohydrates to fat. The use of nutrients by the body also shifts from exogenous to endogenous sources (Welborn & Moldawer, 1995). Starvation is characterized by the use of alternate fuel sources, reduced protein wasting, and decreased energy expenditure (Barton, 1994). Prolonged starvation is limited by the amount of fat stores available and the rate of catabolism. A well-nourished individual has large stores of fuel reserves. Starvation can potentially continue for extended periods with little effect on health (Stryer, 1995). However, weight loss exceeding 10% to 20% generally results in a poor clinical outcome and significant morbidity (Daly et al., 1993).

The Early Phase

Untreated starvation generally progresses through three phases. Each phase is characterized by a specific hormone response and substrate utilization, which serves to supply energy and minimize protein breakdown. The early starvation phase begins after the first 24 hours of fasting (Daley & Bistrian, 1994). Metabolic alterations occur as a result of changes in hormone levels. The absence of food in the system results in low circulating glucose, followed by decreased insulin levels. The first priority of metabolism in starvation is to provide sufficient glucose to the brain and other tissues absolutely dependent upon it for fuel. Low insulin stimulates the release of catecholamines, cortisol, and glucagon, which in turn, stimulate changes that promote stable blood glucose levels. Increased levels of catabolic hormones are released, triggering glycogenolysis in the liver and glucose release in muscle (Stryer, 1995). Muscle glycogen cannot release glucose systemically because it lacks glucose 6-phosphatase. Therefore, liver glycogen releases glucose systemically and muscle glycogen releases glucose for use in the muscle.

Quantities of glycogen in the liver and muscle are small and supply approximately 600 to 1,000 kilocalories of energy (Stryer, 1995). Glycogen is used as a fuel source; however, it becomes depleted after several hours of fasting. Hepatic gluconeogenesis subsequently begins and proceeds to generate glucose rapidly from mobilized fat stores and endogenous proteins. The kidneys also supply glucose through gluconeogenesis. However, in the initial phase of starvation, the liver is the primary site of gluconeogenesis and only approximately 10% occurs in the kidney (Welborn & Moldawer, 1995).

Substrates for gluconeogenesis include lactate and alanine from muscle as well as glycerol from adipose tissue (Stryer, 1995). Low insulin levels also stimulate the release of lipase, which hydrolyzes triacylglycerol in fat stores into fatty acids and glycerol. Once mobilized, fatty acids and glycerol are transported to the liver. Fatty acids cannot be converted into glucose because acetyl CoA cannot be transformed into pyruvate (Stryer, 1995). However, the glycerol portion can be converted into glucose, but provides a limited amount for gluconeogenesis. Gluconeogenesis is the process that leads to the formation of glucose from noncarbohydrate sources. Proteolysis of skeletal muscle and intestinal protein provide the major source of substrate for gluconeogenesis. Large amounts of amino acids are released and converted to glucose during hepatic gluconeogenesis. The breakdown of endogenous protein causes a marked increase in urinary excretion of nitrogen and rapid weight loss within the early phase of starvation.

Liver and muscle are able to use alternate fuels to meet energy needs. The liver is able to use fatty acids and keto acids, and muscle can use fatty acids and ketone bodies in addition to glucose (Stryer, 1995). The brain, red blood cells, white blood cells, bone marrow, and renal medulla are dependent upon glucose for energy. The blood brain barrier does not allow passage of protein-bound fatty acids (Cahill, 1998). Consequently, unlike most other tissues, brain cells are unable to utilize fatty acids for energy. Low levels of insulin decrease the uptake of glucose in the muscle, but fatty acids enter muscle freely. Consequently, muscle shifts almost entirely from glucose to fatty acids for fuel. The increased beta oxidation of fatty acids in muscle mitochondria halts the conversion of pyruvate into acetyl CoA. Pyruvate is reduced to lactate. Muscle lactate and alanine are exported from muscle to the liver for conversion into glucose (Stryer, 1995). Lactate and alanine are both converted to glucose through a reaction known as the *Cori cycle*, wherein glucose is synthesized from these substances, released into the blood, and absorbed by skeletal muscle. In early starvation, the dominant processes are the mobilization of triacylglycerols in adipose tissue and gluconeogenesis by the liver. Additional mechanisms that occur during this initial phase are the insulin effect and Cori cycle (Long & Long, 1994). These compensatory mechanisms are insufficient; hence, protein catabolism predominates during this early starvation phase.

The Late Phase

Continued breakdown of muscle protein must be halted for survival. To limit the breakdown of additional protein for gluconeogenesis, the major fuel source shifts to fatty acids and glycerol in all tissues except obligate tissues using glucose. The oxidation of fat becomes the primary fuel source, decreasing the need for gluconeogenesis and resulting in decreased protein catabolism and ureagenesis (Barton, 1994). Increased lipolysis creates high levels of fatty acids in the bloodstream. In response, the liver begins to produce ketone bodies from the excess acetoacetate created by the fatty acid breakdown. Large quantities of acetoacetate and 3-hydro butyrate are formed by the liver and released into the blood within a few days of the onset of starvation. As the serum level rises, ketone levels in the cerebrospinal fluid also increase. This displaces glucose metabolism and the brain begins to consume acetoacetate in place of glucose (Cahill, 1998). During continued starvation, the brain and other tissues are able to adapt to ketones as an energy source. In late starvation, 75% of the fuel needs of the brain are met by ketone bodies (Stryer, 1995). Muscle, including heart muscle, also adapts to the use of ketones. This is one of the key adaptations of this phase, which serves to limit the breakdown of protein for glucose production.

Protein metabolism in the patient adapted to starvation is characterized by reduced protein synthesis and breakdown (Barton, 1994). Muscle releases less protein and the kidney also recycles glutamine for glucose production. In prolonged starvation, the kidney becomes more involved. As much as 45% of gluconeogenesis occurs in the kidney and 55% in the liver (Welborn & Moldawer, 1995). Weight loss slows and protein is spared by the adaptive processes during this late phase of starvation. Another adaptation is the decrease in metabolic rate that occurs as result of the decreased fat-free free mass (Saltzman, Mogensen, & Hassoun, 2002). Following prolonged starvation, ketone bodies remain the major fuel source of the brain and other tissues. There is a decreased need for glucose, which lessens the rate of muscle breakdown and enhances the likelihood of survival. Fat is the primary energy source until the fat stores are depleted and the fuel source shifts back to protein, which marks the premorbid phase of starvation (Long & Long, 1994). Without nutrition repletion, prolonged starvation leads to continued catabolism and eventual death. Refeeding should be started to halt catabolism and begin to rebuild lean tissue; however, this process should begin slowly in severely malnourished patients to avoid serious complications associated with rapid refeeding (Daley & Bistrian, 1994).

Summary

In the absence of adequate nutrient intake, hormonal changes occur which affect the balance of catabolism and anabolism. The metabolic changes and adaptations arise from the need to shift from an exogenous to an endogenous supply of energy (Welborn &

Moldawer, 1995). Glucose homeostasis and the sparing of protein are essential components of this response. During starvation, the body develops adaptive mechanisms that allow it to slowly adjust to the absence of food.

Metabolic Response to Illness or Injury

The metabolic response to acute illness and injury is associated with hypermetabolism and hypercatabolism. Hypermetabolism may occur in response to tissue injury, inflammation, infection, perfusion shock, or any process that causes vascular endothelial injury (Barton, 1994). A coordinated chain of events elicits a metabolic response observed in conditions ranging from elective surgery to massive trauma. Conditions commonly associated with hypermetabolism include burns, multiple trauma, sepsis, and pancreatitis (Leupold-DiCicco & Monturo, 1996). The magnitude of the metabolic response varies with the duration of the respective condition and is also proportional to the severity of the trauma and the amount of tissue injured.

In contrast to the specific responses that occur in unstressed starvation, hypermetabolism is a rapid, generalized, adaptive response that mobilizes energy to support immune function, inflammation, and tissue repair (Barton, 1994; Martindale, Shikora, Nishikawa, & Siepler, 2002). The impact on organ function, as well as on immune function at the cellular level, is significantly greater than in uncomplicated starvation (Herrmann, 1995). It is therefore important to distinguish between the effects of hypermetabolism and starvation in assessing patients for appropriate nutrition support. The metabolic changes that occur in response to acute illness or injury begin in the neuroendocrine system and are mediated by the sympathetic nervous system (Barton, 1994). These changes lead to rapid breakdown of protein and loss of lean body mass as they stimulate energy mobilization from endogenous stores. This response is characterized by hypermetabolism, hyperglycemia, and hypercatabolism (Barton, 1994; Buckley & Kudsk, 1994).

The hypermetabolic response was first described by Cuthbertson (1942) who introduced the "ebb phase" and the "flow phase" (p.434). This theory provides a framework within which to describe the concepts related to hypermetabolism. The initial ebb phase usually lasts 48 to 72 hours and is characterized by decreased metabolic rate, cardiac insufficiency, and hypothermia. The goal during this phase is to maintain blood flow and oxygenation to vital organs (Ackerman, Evans, & Ecklund, 1994). The flow phase follows resuscitation and is referred to as the hypermetabolic phase. It generally lasts for several days, but may persist if complications, such as sepsis, develop (Barton, 1994). The flow phase itself can be viewed with two sequences—the acute and the adaptive. In the acute sequence, catabolic processes predominate and are mediated by increased levels of cortisol, glucagon, catecholamines, and insulin (Buckley & Kudsk, 1994). These substances are collectively termed counterregulatory hormones because their effects are opposite to those of insulin. Inflammatory mediators and cytokines, such as interleukin-1, tumor necrosis factor, and interferon are also released during this phase (Barton, 1994). Clinical symptoms of hypermetabolism include fever, rapid heart and respiratory rates, and marked hyperglycemia. The acute phase generally peaks in 3 to 4 days and subsides in 7 to 10 days unless complications develop to prolong the response (Ackerman et al., 1994; Cerra, 1987). In the adaptive phase, anabolic processes begin and hormonal levels gradually diminish. The adaptive phase is associated with recovery and is characterized by a decrease in hypermetabolism.

Alterations in Substrate Metabolism

The flow phase of the hypermetabolic response is associated with several alterations in substrate metabolism that serve to mobilize energy for tissue repair. Glucose, protein, and lipid metabolism are affected as a result of the altered biochemical environment (Barton, 1994; Buckley & Kudsk, 1994). In contrast to starvation where glucose and fat are used as primary fuel sources, hypermetabolism processes rapidly deplete fat and protein stores (Cerra, 1987). The overall effect of this response is to increase oxygen consumption and redistribute amino acids and glucose from peripheral tissues into the central circulation.

Carbohydrate metabolism. Hepatic glucose production is elevated in response to the counter regulatory hormones producing profound hyperglycemia. Epinephrine release causes hyperglycemia through glycogenolysis and lipolysis (Long & Long, 1994). Hyperglycemia is also related to the production of excess glucose by increased gluconeogenesis and synthesis from lactate during the Cori cycle (Barton, 1994). Gluconeogenesis continues despite the presence of hyperglycemia and is refractory to exogenous glucose or insulin (Long & Long, 1994). The effects of insulin become suppressed, causing decreased cellular uptake of insulin, as well as insulin resistance. The changes in glucose utilization lead to an increased breakdown of fats and protein for energy (Barton, 1994).

Lipid metabolism. Lipolysis is increased during hypermetabolism as a result of the counterregulatory hormones and their blunting effects on insulin. High levels of catecholamines and decreased insulin levels result in a breakdown of triglycerides, producing free fatty acids and ketone bodies for energy use. If the rate of ketone production exceeds peripheral uptake, ketosis may result in acidosis (Leupold-DiCicco & Monturo, 1996). Normal lipid transport mechanisms are altered and lipid clearance decreases, potentially leading to hepatic failure. Alterations in lipid metabolism and the absence of dietary fat may lead to a deficiency in essential fatty acid (Barton, 1994).

Protein metabolism. Hypermetabolism is characterized by changes in both protein synthesis and protein catabolism. The rate of protein catabolism exceeds protein synthesis, which results in a rapid decrease in lean body mass and increases in urinary nitrogen losses, leading to a negative nitrogen balance (Leupold-DiCicco & Monturo, 1996). During critical illness, the liver preferentially increases the production of acute-phase proteins in response to inflammation and infection. These proteins include C-reactive protein, which support the inflammatory response, immune function, and wound healing (Barton, 1994). The synthesis of visceral proteins, such as albumin, is curtailed during this time to support synthesis and function of the acute-phase proteins (Spiekerman, 1995). During acute hypermetabolic conditions, such as severe stress, sepsis, and surgery and trauma, levels of C-reactive protein increase, triggering the acute sequence within the flow phase of illness or injury (Barton, 1994).

Protein breakdown is initially directed toward skeletal muscle, sparing visceral proteins for functions other than energy (Stryer, 1995). Skeletal muscle rapidly breaks down and mobilizes amino acids into the central circulation. These amino acids are subsequently used for gluconeogenesis that continues in spite of glucose or insulin infusion (Barton, 1994). Alanine and glutamine are the primary amino acids released from muscle during the initial phase of injury. During hypermetabolism, branched-chain amino acids within the intracellular muscle protein are broken down and used as a primary energy source for skeletal muscle (Buckley & Kudsk, 1994). As skeletal muscle is depleted, visceral organs are catabolized to provide amino acids. Nitrogen losses from protein catabolism may exceed 20 to 40 grams per day, depending upon the severity of injury. As the hypermetabolic phase resolves, nitrogen losses decrease to normal levels.

If there are complications such as those that occur with infection, the hypermetabolic phase persists as a result of the persistent changes in the hormonal environment. Impaired substrate utilization continues, despite provision of nutrition, and continued hypermetabolism leads to organ failure, adversely affecting morbidity and mortality (Cerra, 1987). Unlike simple starvation, the reversal of catabolism is not possible during hypermetabolism, even with the administration of large amounts of nutrients. Catabolism can only be stopped when the cause of the hypermetabolic response is controlled (Barton, 1994). Nutritional therapy during hypermetabolism is aimed at limiting nitrogen losses and providing enough energy and protein to maintain metabolic and immunologic responses.

Summary

Metabolic responses that occur during starvation and acute illness and injury lead to a malnourished state characterized by decreased muscle mass and visceral protein loss. The malnourished condition found in patients with severe stress and hypermetabolism differs from that observed in unstressed starvation. The lack of adequate nutrition is compounded by the inability of these patients to eat, as well as by the anorexia associated with the initial phase of acute illness (Daley & Bistrian, 1994; Herrmann, 1995). Catabolism increases rapidly and leads to significant depletion of skeletal muscle and visceral protein stores. The impact of this reaction on organ function, immune competence, and biochemical function at the cellular and molecular level is greater than that observed with unstressed starvation (Cerra, 1987).

Respiratory Effects of Malnutrition

Progressive malnutrition leads to structural and functional alterations in the lungs and respiratory muscles (Grant, 1994). The primary respiratory complications associated with malnutrition include decreased respiratory muscle structure and function, decreased ventilatory drive, and decreased pulmonary immune defenses. Availability of substrates at the cellular level is altered, which negatively impacts muscle contractility (Wilson, Rogers, & Hoffman, 1985). Alterations in the structure of muscle fibers, combined with changes in the size and length of the diaphragm, have profound effects on respiratory muscle mechanics (Pezza, Iermano, & Tufano, 1994). Other complications can include reduced ability to repair after injury and decreased surfactant production (Johnson, Chin, & Haponik, 1999).

The respiratory effects of malnutrition occur independent of the presence of underlying pulmonary disease. Respiratory abnormalities found in malnourished patients without concomitant lung disease (Braun, Arora, & Rochester, 1983; Murciano et al., 1994) are similar to those found in malnourished COPD patients in terms of muscle strength and endurance. At half the normal respiratory muscle strength, vital capacity is reduced to 65% of normal. A decrease in the maximal voluntary ventilation leads to reductions in respiratory muscle strength and endurance (Lewis & Belman, 1988). Consequences of altered respiratory muscle strength, ventilatory drive, and immune mechanisms can lead to hypercapnic respiratory failure, delayed weaning from mechanical ventilation, and increased susceptibility to pneumonia (Pingleton, 1996).

Adequate muscle strength and endurance are necessary for normal ventilation. When respiratory muscle strength falls below 50% of normal, ventilatory function remains adequate. However, ventilatory failure, as indicated by rising partial pressures of carbon dioxide, may occur when respiratory muscle strength falls to less than one third to one quarter of normal (Rochester, 1986a).

Respiratory Muscle

The diaphragm is a major respiratory muscle and is primarily involved with inspiration. It is composed of striated skeletal muscle, which is highly vascular with a central muscular tendon (Murray & Nadel, 1994). Weight loss is associated with reduced diaphragmatic mass in both humans (Arora & Rochester, 1982a) and animals (Kelsen, Ference, & Kapoor, 1985). Arora and Rochester (1982b) found that malnutrition is associated with diminished muscle strength and endurance. Individuals within their patient sample with significant weight loss were found to have maximal inspiratory and expiratory pressures of only 35% and 59% of normal, respectively. Vital capacity was 63% of predicted value, and minute volume was only 41% of predicted. This is significant when compared with the findings of Braun et al. (1983) in patients with polymyositis and other myopathies. These researchers found that maximal inspiratory pressures of less than 30% of normal led to respiratory failure and prolonged ventilator dependence.

Malnutrition is associated with mineral and electrolyte deficiencies that affect skeletal muscle and ventilatory function. The electrolytes of particular concern are phosphorus, potassium, and magnesium (Lewis & Belman, 1988). Low phosphorus is associated with respiratory muscle weakness, which may lead to respiratory muscle fatigue and failure (Rochester, 1986b). Hypophosphatemia may occur as a side effect of drugs such as steroids, theophylline, and lasix. It may also occur with malnutrition and renal disease (Pezza et al., 1994). Sensitivity to hypoxia and hypercapnia is also observed in early starvation (Grant, 1994). Early studies have shown that hypoxic drive is blunted in response to semistarvation (Doekel, Zwillich, Scoggin, Kryger, & Weil, 1976). Starvation is associated with a decreased metabolic rate and minute ventilation (Rothkopf, Stanislaus, Haverstick, Kvetan, & Askanazi, 1989). Doekel et al. (1976) administered hypocaloric feedings of 500 kilocalories per day (kcal/day) to healthy volunteers for 10 days and found a 20% reduction in metabolic rate and a 42% reduction in ventilatory response to hypoxia.

The Immune System

Malnutrition is associated with depressed cell-mediated and humoral immunity. Although the specific effects on the pulmonary immune system are not well characterized, nutritional factors may predispose pulmonary infection (Wilson, Rogers, & Openbrier, 1986). Animal studies have shown a decrease in the number of alveolar macrophages in malnourished rats compared to controls. Lung phagocytic activity and clearance of bacteria are also impaired (Rothkopf et al., 1989; Wilson et al., 1985). Niederman et al. (1984) documented that patients with tracheostomies and severe malnutrition experienced greater tracheal bacterial adherence and were more frequently colonized by pseudomonas species than well-nourished patients. This suggests that the airways of these patients were susceptible to colonization in response to altered nutritional status, and that poor nutritional status may predispose infection.

The lung tissue is continually undergoing a process of fiber repair and replacement. The fibers are made of elastins, fibronectins, and collagens that provide structure and allow for elasticity (Wilson et al., 1985). Damaged fibers are removed by enzymes or proteases, which are activated during the immune response process. When these destructive enzymes are not controlled, they eventually damage healthy lung tissue as well. This process is normally kept in balance by alpha-1-antitrypsin—one of the key antiproteases. It has been theorized that malnutrition may cause a deficiency of alpha-1-antitrypsin, promoting lung injury and destruction (Murray & Nadel, 1994). The balance of repair and destruction ensures an appropriate response to lung inflammation. Malnutrition or illness may deplete circulating antiproteases, resulting in unopposed protease activity. Subsequent pulmonary infections may cause an exaggerated amount of lung-fiber destruction, leading to weakened and structurally abnormal lung tissue (Piquette, Rennard, & Snider, 2000). It has been suggested in animal studies that nutritional deprivation is associated with decreased production of pulmonary surfactant (Wilson et al., 1985). Although it is difficult to relate animal research directly to clinical practice, malnourished patients may have a diminished capacity to produce surfactant, which can potentially lead to atelectasis and pulmonary infection.

Summary

It is clear that nutritional status and respiratory function are linked. Respiratory muscle weakness from inadequate nutrition may promote pulmonary failure (Pinard & Geller, 1995). This relationship is particularly important with respect to patients who become critically ill and require mechanical ventilatory support. The inability to consume nutrients may adversely affect nutritional status and increase morbidity and mortality.

Nutritional repletion has been associated with measurable improvement in respiratory muscle strength and endurance in COPD patients (Efthimiou, Fleming, Gomes, & Spiro, 1988). Although the role of nutrition therapy in patients with acute respiratory failure has not been definitively established, nutrition support is clearly indicated to meet energy requirements and limit further muscle breakdown (Daly et al., 1993).

Review of Related Literature

Measures of Energy Expenditure

The adequacy of nutrition support in mechanically ventilated patients begins with accurate assessment of energy needs. Determination of energy requirements is important for patients receiving either enteral or parenteral support, for those who are critically ill, and particularly for patients requiring mechanical ventilation (Weissman, Kemper, Askanazi, Hyman, & Kinney, 1986). Accurate measurement of required needs can prevent complications associated with overfeeding and underfeeding. Although energy expenditure is not absolutely equivalent with energy requirements, assessment of metabolic rate or energy expenditure is a key factor in designing nutrition support regimens (Ireton-Jones, 2002; Weissman & Kemper, 1995). A variety of methods are used in clinical practice to measure the energy requirements of critically ill patients.

Total energy expenditure (TEE) is the total amount of energy expended in 24 hours. Resting energy expenditure (REE) accounts for 75% to 90% of the TEE (Fuerer & Mullen, 1986). The remainder is accounted for by metabolism from nutrient intake, environment interaction, and physical activity. The difference between TEE and REE is reflected in energy from activity; consequently, REE plus an activity factor provides an estimate of TEE (Weissman & Kemper, 1995). Although not exactly equivalent, measured REE generally corresponds to the number of calories required and is expressed in terms of kilocalories per day. Several measures of energy expenditure are used in clinical practice, and the TEE can be either estimated or directly measured.

Indirect Calorimetry

Indirect calorimetry can be performed using either gas exchange methods or circulatory methods derived from the Fick equation. Indirect calorimetry provides information surrounding energy expenditure reflected by measures of REE, as well as information on substrate utilization as measured by a respiratory quotient (RQ) (McClave & Snider, 1992). It is based upon the principle that, as food is burned for energy, oxygen is consumed; heat is released; and carbon dioxide, water, and energy are produced (Weissman & Kemper, 1995). All energy is produced from the oxidation of protein, carbohydrate, and fat, and the amount of oxygen consumed and carbon dioxide produced are constant for each type of fuel (McClave & Snider, 1992; Porter & Cohen, 1996).

The RQ is a measure that can also be obtained using indirect calorimetry methods. It is the ratio of oxygen consumption (VO_2) to carbon dioxide production (VCO_2) and provides an indication of substrate utilization (McClave & Snider, 1992). The rates of metabolism of carbohydrate, fat, and protein yield different amounts of oxygen, carbon dioxide, and water. The RQ at steady state conditions reflects the net substrate utilization of the body. The normal physiologic range of the RQ in humans is approximately 0.67 to 1.25 (Weissman & Kemper, 1995). Oxidation of glucose is associated with an RQ of 1.0. The RQ for fat oxidation is 0.7, and protein metabolism has an RQ of approximately 0.8 (Fung, 2000). An RQ below 0.70 may indicate alcohol or ketone metabolism, and RQs greater than 1.0 reflect net lipogenesis, which may occur with excess glucose intake. The

RQ can be used to validate indirect calorimetry because measurements outside the normal physiologic range may indicate potential measurement errors (McClave & Snider, 1992).

Gas exchange methods. The gas exchange method determines energy expenditure indirectly by measuring pulmonary gas exchange—the VO_2 and VCO_2 of the entire body. Measurements of VO_2 and VCO_2 are converted to REE in kcal/day by applying the following Weir (1949) equation:

$$\text{REE ([kcal/ 24 hr])} = 3.941 \text{ x } VO_2 + 1.1 \text{ x } VCO_2 \text{ x } 1{,}440.$$

Gas exchange measurements are expressed in liters per minute and 1,440 is the number of minutes in a 24 hour period. Trained personnel perform the measurements using indirect calorimeters, also known as metabolic carts. The instruments are classified as either open-circuit or closed-circuit, based upon the method of VO_2 measurement incorporated (Branson, Lacy, & Berry, 1995). Open-circuit equipment determines VO_2 by measuring minute ventilation and the difference between inspired and expired gas concentrations. Closed-circuit calorimeters determine VO_2 by measuring volumetric change from a reservoir of oxygen over time. Open-circuit systems are currently used most often in clinical practice, and can also be used for spontaneously breathing patients as well as those supported by mechanical ventilation (McClave & Snider, 1992).

The accuracy of gas exchange measurements depends on several factors. Both open-circuit and closed-circuit methods are subject to technical errors in measurement, which may lead to inaccurate determination of REE (Weissman & Kemper, 1995). Equipment must be free of leaks because gas leaks in or out of the system cause dilution of the gases and can potentially lead to false measurement. The fraction of inspired oxygen must also be delivered at stable concentrations. High levels of positive-end expiratory pressure, gas volumes, and flow rates may also affect accuracy, as will temperature, pressure, and humidity of the gases (Campbell et al., 1994). Indirect calorimetry using gas exchange methods requires strict attention to detail. The metabolic cart must be calibrated according to the specifications outlined by the manufacturer. All patient activity must be minimized and environmental conditions strictly controlled during measurement. Gas measurements must be obtained while the patient is at rest in a steady state. The steady state measurements are subsequently averaged to determine REE (Weissman & Kemper, 1995).

The need for a steady state is to ensure measurement that clearly corresponds to energy expenditure (Fung, 2000). A steady state is more specifically defined as an interval of 5 consecutive minutes where VO_2 and VCO_2 change by less than 10% (McClave et al., 2003). Generally, 20 to 30 minutes of testing are required to achieve steady state measures during rest. These measures are then averaged with the REE measurements to provide the 24-hour REE (Weissman & Kemper, 1995). The 20- to 30-minute period of testing time is generally considered a stable and reliable measure of the 24-hour REE (Isbell, Klesges, Meyers, & Klesges, 1991). Frankenfield, Sarson, Blosser, Cooney, and Smith (1996) found no statistically significant differences in VO_2, VCO_2, RQ, or REE between protocols using 5 consecutive 1-minute measures versus 30 consecutive 1-minute readings. Other studies have indicated that increasing the frequency of testing is more useful in reducing error and approximating TEE than increasing the length of testing (Cunningham, Aeberhardt, Wiggs, & Phang, 1994; Leff, Hill, Yates, Cotsonis, & Heymsfield, 1987). Questions also remain with regard to how long and how often to measure, as well as the type of patients who should be measured (Branson et al., 1995; McClave & Snider, 1992). Generally, patients should be measured for as long as it is necessary to obtain measurement at a steady state. The measurement frequency is of particular concern for critically ill patients who display wide variation in metabolic state due to the physiological and environmental factors associated with critical illness and related treatment.

Variability and precision. Variability of energy expenditure in critically ill patients makes measurement of REE an important issue in determining caloric needs to avoid overfeeding and underfeeding. The variability of REE is related to several factors in both healthy individuals and critically ill patients. Basic factors are related to age, gender, body size, fat free mass, dietary intake, temperature, and circadian fluctuations (McClave & Snider, 1992; Weissman & Kemper, 1995). The variability of energy expenditure in critically ill patients is affected by disease state, severity of illness, medications, fever, activity, and routine nursing procedures (Swinamer, Phang, Jones, Grace, & King, 1988; Weissman et al., 1984; Weissman, Kemper, Elwyn et al., 1986; Weissman, Kemper, & Hyman, 1989). Studies with healthy volunteers indicate an average daily variation in REE of 12.5% (Leff et al., 1987). Critically ill patients demonstrate variations ranging from 10% below to 23% above steady state REE (Weissman, Kemper, Elwyn et al., 1986). An activity factor of 5% to 10% is usually added to the measured REE to calculate TEE in this patient population (Swinamer, Phang, Jones, Grace, & King, 1987; Weissman et al., 1989).

The reliability of indirect calorimetry is measured by evaluating the reproducibility of measured values. Mullen (1991) documented a 2% coefficient of variation in critically ill patients measured multiple times in a single day. A study by Rumpler, Seale, Conway, and Moe (1990) measured REE daily for 5 days in four males who were part of a larger nutrition study. The within-subject coefficient of variation was 3% when measured daily for 5 consecutive days and 4% when measured weekly over 1 month with the same study participant. Leff and colleagues (1987) examined the reliability of indirect calorimetry in 14 healthy volunteers. The average of several measurements taken for each participant on different days produced reliability correlation coefficients of .86 to .96. This was greater than any single measurement with correlation coefficients of .69 to .89. The study reported considerable variability in repeated measurements of energy expenditure; however, reliability was improved using serial measurements as opposed to single measurements.

Validation methods. Several methods are used to validate indirect calorimetry instruments. Direct calorimetry measures heat or caloric expenditure from the entire body and is an impractical, complex process, used generally in nutrition research (Weir, 1949). The indirect approach has been validated via comparison with direct calorimetry. A study conducted by Daly et al. (1985) found a correlation between indirect and direct calorimetry ($r = .81, p < .001$). The mean difference between the two methods was less than 3%.

Gas analyzers must be calibrated and checked at intervals between 4 and 6 months to prevent *calibration drift* (Branson et al., 1995). Two methods are commonly used to calibrate and determine clinical performance of the equipment. One method infuses precise amounts of gas into a lung simulator (Weissman, Sadar, & Kemper, 1994) and another uses combustion of a substance, such as butane, with a known RQ (Makita, Nunn, & Royston, 1990). The newest calorimeters have advanced technology that provides continuous measurement (Weissman et al., 1994). In vitro studies indicate that accurate measurements of VO_2 and VCO_2 have been obtained within a wide variety of simulated conditions. Quality of the test measurements is evaluated by determining whether RQ is in the normal physiological range, whether measured VO_2 is within plus or minus 10% of the mean value, and whether measured VCO_2 is within plus or minus 6% of the mean value (Campbell et al., 1994). Cumulative studies indicate that indirect calorimetry is a reliable and accurate instrument for the measurement of energy expenditure (Daly et al., 1985).

Several patient factors affect gas exchange measurements in the realm of intensive care. These include leaks surrounding the tracheal cuffs, the presence of chest tubes, or a bronchopleural fistula. Measurement is contraindicated in patients during peritoneal and hemodialysis because carbon dioxide is removed and cannot be measured by the indirect calorimeter (Campbell et al., 1994; Weissman & Kemper, 1995). Until recently, patients requiring more than 60% oxygen were not considered candidates for indirect calorimetry. Newer equipment is now accurate up to 80% oxygen, and some closed-circuit calorimeters have also demonstrated accuracy at levels of 100% oxygen (Branson et al., 1995).

The Fick method. The Fick method, which is also known as circulatory indirect calorimetry (CIC), is another method used to measure energy expenditure within the clinical setting. It measures oxygen utilization from arterial and mixed venous blood by applying the Fick equation. TEE is calculated to provide an estimate of kilocalories per 24 hours. (TEE = cardiac output [CO] x hemoglobin [Hb] x oxygen saturation of arterial blood [Sa02] – oxygen saturation of mixed venous blood (SV02) x constant 95.2).

$$TEE = CO \times Hb \times (Sa02 - Sv02) \times 95.2$$

The constant 95.2 is derived from 1.36 ml oxygen/gram of hemoglobin/deciliter, 10 deciliters/liter, 7.0 kilocalories/day per milliliter of oxygen consumed per minute (Van Way, 1999). The Fick method requires a pulmonary artery catheter and accurate CO measurements. It does not provide continuous or real-time measurements and VCO_2 and RQ calculations are not easily obtained. Accuracy and precision are limited because the method depends upon several factors including thermodilution CO and pulmonary and systemic arterial oxygen content (Weissman & Kemper, 1995).

The accuracy of thermodilution CO is affected by the temperature of the injectate and the number and timing of the injections. Under laboratory conditions, accuracy of thermodilution CO ranges between 7% and 13% (Thys, 1988). In clinical practice, error of thermodilution CO averages about 10% to 15% (Nadeau & Noble, 1986). The precision of CIC is influenced by the number of measurements and injection timing within the respiratory cycle. Error in laboratory measures of arterial and venous oxygen content is also a factor (Thys, 1988). The advantages of CIC are that it provides an easy alternative for measuring energy expenditure, especially for critical care patients with a pulmonary artery catheter already in place. Comparison studies have found a significant correlation between CIC and the gas exchange methods of indirect calorimetry (Brandi et al., 1992; Chiolero et al., 1994; Williams & Feunning, 1991). One such correlation was determined by Williams and Feunning in a sample of eight adult patients on mechanical ventilation within a hospital ICU ($r = 0.831, p < .0001$).

Brandi et al. (1992) compared indirect calorimetry with the Fick method in 26 postoperative trauma patients. Patients were excluded from the study if they required supplemental oxygen or mechanical ventilation. Measurements of VO_2 and energy expenditure by indirect calorimetry and the Fick method indicated a significant correlation ($r^2 = 0.93$ and $r^2 = 0.92$, respectively; $p <. 001$). However, VO_2 and VCO_2 values determined by indirect calorimetry were consistently higher than those calculated via the Fick method ($p < .01$). Measures of RQ were not correlated between methods ($r^2 = .06, p = .21$). Brandi and colleagues concluded that indirect calorimetry is more appropriate within clinical practice over the Fick method because of the increased accuracy in VCO_2 and RQ measurements.

Predictive Equations

Predictive equations are commonly used to estimate REE and caloric requirements in hospitalized patients. Over 100 formulas have been developed for clinical use and are frequently derived from the HBE (Fung, 2000). In the early 1900s, Harris and Benedict performed several studies on healthy volunteers to determine the daily energy expenditure of adults as cited in Frankenfield, Muth & Rowe(1998). Regression equations were calculated from these groups based upon their sex, body weight, age, and height. The HBE predicts minimal energy needs for a healthy individual at rest. Consequently, the equation incorporates data that may not be suitable for hospitalized patients.

The HBE (Harris & Benedict, 1919) provides a measure of basal energy expenditure (BEE), which represents basal metabolism in a resting and fasted state. The following equation represents the HBE for men:

$$BEE\ (kcal/24\ hr) = 66 + (13.7 \times wt) + (5.0 \times ht) - (6.7 \times age)$$

The following equation represents the HBE for women:

$$BEE\ (kcal/24\ hr) = 655 + (9.6 \times wt) + (1.8 \times ht) - (4.7 \times age).$$

The REE is derived from the calculated BEE through multiplying by a factor of 1.2, which allows for the thermic effect of food (Marino, 1998). To increase relevance in hospitalized patients, adjustment factors are added to the calculated REE to account for the influence of disease state on energy expenditure. Adjustment factors vary widely but range from 1.2 for mild stress, 1.4 for moderate stress, 1.6 for severe stress, and 2.1 for thermal injury (Long, Schaffel, Geiger, Schiller, & Blakemore, 1979).

In an effort to improve the accuracy of predictive equations, in patients with specific diseases or conditions, specialized equations have been developed (Moore & Angelillo, 1988; Sherman, 1994; Swinamer et al., 1990). Examination of these disease-specific formulas reveals that most have a tendency to overestimate or underestimate actual energy requirements because they do not account for severity of illness or the variability in REE (Mullen, 1991). Foster, Knox, Dempsey, and Mullen(1987) reviewed 191 published formulas for predicting energy expenditure. Many were based upon the original Harris-Benedict (1919) formula with added factors to account for specific illnesses and/or activities. They found that, in most patients, indirect calorimetry measurements yielded greater accuracy.

Other researchers have found advantages in using equations to determine energy requirements for specific patient populations. Ireton-Jones, Turner, Liepa, and Baxter (1992) developed an equation using physiologic variables in a group of 200 burn patients. The variables included age, weight, sex, diagnosis, and ventilatory status. Equations were developed for both spontaneously breathing and ventilator-dependent patients by applying stepwise multiple-regression analysis. The equations were tested on 100 patients and measured REE was not found to be significantly different from calculated energy expenditure ($p > .25$). Swinamer et al. (1990) also applied multiple-regression analysis to develop a predictive equation for mechanically ventilated critically ill patients. Indirect calorimetry was used to measure energy expenditure in a sample of 112 patients. Physiological variables including age, body surface area, vital signs, and illness severity scores were entered into the model. An equation was developed from the five variables that contributed more than 3% to the variance in energy expenditure. Whereas, HBE underestimated energy expenditure in 79 of the total 112 patients, the new equation deviated more than 15% from the measured REE in only 15 patient calculations.

In contrast, a study by Flancbaum, Choban, Sambucco, Verducci, and Burge (1999a) compared gas exchange indirect calorimetry; the Fick method; and four predictive equations, including HBE, to determine the reliability of measures in 36 critically ill patients. The patients were mechanically ventilated and receiving total parenteral nutrition. Metabolic measures were obtained using indirect calorimetry and simultaneous calculations using the Fick method. The results obtained from these measures were subsequently compared with four predictive equations calculated for each patient. The correlation between indirect calorimetry and all other methods was low. Mean REE by indirect calorimetry was 2,005 plus or minus 464 kcal/day and correlated poorly with the other methods tested ($r^2 = .057$ to 0.154).

Results from the Flancbaum et al. (1999) study did not confirm the findings of earlier studies indicating a strong correlation between indirect calorimetry and the Fick method (Brandi et al., 1992; Williams & Fuenning, 1991) or between indirect calorimetry and predictive equations (Swinamer et al., 1990). Limitations associated with the Fick method may account for the lack of correlation reported. The sample was comprised of critically ill patients with a broad range of illnesses. The lack of correlation with predictive equations may have been due to the differences between this sample and the patients from which the equations were derived. Data from this study support the use of indirect calorimetry over other methods for determining energy requirements in critically ill mechanically ventilated patients.

Many of the predictive formulas used in clinical practice were derived from populations of healthy nonobese individuals (Harris & Benedict, 1919). This limits their application in patient populations with variable degrees of illness and metabolism. Studies have shown that the HBE correctly predicts REE in only 50% of cases (Foster et al., 1987; Fuerer & Mullen, 1986; Weissman, Kemper, Askanazi et al., 1986). For most diseases, the HBE tends to underestimate energy expenditure by as much as 50% because of the multiple metabolic factors that affect REE (Swinamer et al., 1987).

The respective clinical situation must be thoroughly assessed before applying predictive equations (Weissman & Kemper, 1995). Clinicians must know what the equation predicts and from what patient population the formula was originally derived. An awareness of patient factors that can potentially affect the accuracy of predictive equations, such as changes in body weight, is also important in their use. A simple method of estimating energy requirements is to calculate 25 to 30 kcal/kilogram (Cerra et al., 1997; Daly et al., 1993). This simplified method of determining energy needs in hospitalized patients is generally accepted in clinical practice and has also been used frequently in clinical nutrition studies (McClave, Sexton et al., 1999). Its limitations are similar to other predictive methods that do not adequately account for the metabolic state or severity of disease.

Many critical care studies have compared estimates of energy expenditure using formulas versus indirect calorimetry. These comparative studies have been performed in mechanically ventilated patients with COPD (Branson, Hurst, Warner, Bower, & Arita, 1987; Moore & Angelillo, 1988), as well as in heterogenous samples (Makk et al., 1990; Weissman, Kemper, Elwyn et al., 1986). Indirect calorimetry is considered a more reliable method in critically ill patients, particularly in those with COPD (Branson et al., 1987).

Summary

Measurement of energy expenditure using indirect calorimetry is not required, nor practical, for all patients. The expense and complexity is not always realistic; however, indirect calorimetry is recommended as the primary method of energy measurement for patients with specific conditions (Campbell et al., 1994). It is highly recommended in patients who are underweight, or overweight, or who are amputees; difficult to wean from mechanical ventilation; or have been diagnosed with cancer, COPD, trauma, or sepsis and exhibit a poor response to nutrition support (Campbell et al., 1994; Porter & Cohen, 1996). In spite of these recommendations, use of indirect calorimetry has been limited in clinical practice due to the expense, availability of equipment, and the preferred use of standard predictive equations (Campbell & Kudsk, 1988).

Effects of Underfeeding and Overfeeding in Critical Illness

Although the exact percentage of calories needed to realize the benefits of enteral nutrition is unknown, nutrition should be provided in sufficient amounts based upon an accurate assessment of individual energy needs, which may vary considerably from acute illness through to recovery (Weissman et al., 1989). It is essential to avoid the hazards of underfeeding and overfeeding in critically ill patients, especially those requiring mechanical ventilation (Klein, Stanek, & Wiles, 1998; McClave, 1997). The consequences have been outlined in previous research (Bartlett et al., 1982; Driver & LeBrun, 1980; Kresowick et al., 1984). Inadequate nutritional intake leads to malnutrition and increases the potential for organ failure and ultimate death (Daly et al., 1993).

Retrospective research conducted by Driver and LeBrun (1980) was one of the earliest studies to examine the adequacy of nutrition support in mechanically ventilated patients. The study sample included 26 patients with respiratory failure requiring mechanical ventilatory support. Only 3 of the 26 patients received sufficient dietary intake to match minimal requirements. Albumin levels were decreased to less than 3.2 g/dl in 71% of the patients, and 54% died while intubated or shortly after extubation. This study used a very small heterogeneous sample of patients and was also limited by the lack of control inherent in retrospective analyses. In spite of its limitations, it emphasized the existence of malnutrition in mechanically ventilated patients and sparked further research. Subsequent studies reported high mortality rates due to the development of organ failure in heterogeneous groups of underfed ICU patients (Bartlett et al., 1982; Kresowick et al., 1984).

A descriptive study conducted by Bartlett et al. (1982) found a direct correlation between caloric deficits and mortality in 57 critically ill patients. This research examined the relationship between measured respiratory variables and the development of multiple organ failure. Those patients on mechanical ventilation with at least one vital organ failure, or those at risk for such organ failure and anticipated nutritional problems were selected for participation in the study. Exclusion criteria were not described, and description of the dependent variable—multiple organ failure—was not clear. Patients were measured once or twice daily by indirect calorimetry. The results were made available to physicians; however, nutrition orders were based upon estimated requirements. The type of nutrition support administered was not reported; however, most of the patients required parenteral nutrition because of GI intolerance or ileus. Cumulative caloric balances were determined upon discharge of the patients from the ICU. The patients were divided into three groups—those with positive caloric balance, a negative caloric balance between 0 and 10,000 kcal, and those with greater than a 10,000 kcal negative caloric balance.

The results of the Bartlett et al. (1982) research indicated that out of 57 patients, only 15 had a positive cumulative caloric balance. Twenty-eight had negative caloric balances between 0 and 10,000 kcal and 11 of these patients (39%) died. Fourteen patients had deficits greater that 10,000 calories, and 12 of these (86%) died. Three additional patients developed a 10,000-calorie deficit, but later received increased nutrition; two survived. Overall, 30 patients survived and 27 died. Higher caloric deficits correlated with higher mortality rates. The development of complications and organ failure—defined as sepsis, cardiac, renal, or hepatic failure—was consistently higher in patients with the greatest caloric deficit and who ultimately died.

As a follow up to the Bartlett et al. (1982) study, Kresowik and colleagues (1984) followed 61 surgical patients prospectively during their ICU stays. The timing of nutrition support was variable, and ventilatory status of the patients was not described. Twenty-six patients had positive cumulative caloric balances after 1 week in the ICU, and 35 had negative cumulative balances. The variables of age, sex, energy expenditure, diagnosis, severity of illness, and mortality were compared between the study groups, which were found to be similar in terms of all variables with the exception of ICU mortality. ICU mortality was 27% in the study group with positive cumulative caloric balance and 54% in the group with negative cumulative caloric balance ($p < .05$). Energy expenditure and Acute Physiology and Chronic Health Evaluation (APACHE) scores were similar between groups.

Nutrition support as a treatment during critical illness has gradually evolved. The provision of excess calories was once considered appropriate (Barton, 1994). Current data suggest that optimal nutrition support should be given early in the course of illness and should initially provide up to 80% of total caloric requirements with a balanced mix of nutrients (DeBiasse & Wilmore, 1994). New data suggest that, within the early hypermetabolic stages of critical illness, hypocaloric nutrition support may be beneficial in facilitating prevention of the organ failure commonly observed in such acute illness (Zaloga & Roberts, 1994).

Although less common than underfeeding, overfeeding may further stress critically ill patients and lead to metabolic complications and prolonged ventilatory support (Klein et al., 1998). The provision of nutrition support in excess of requirements occurs in up to 40% of all critically ill patients receiving such support (Guenst & Nelson, 1994; Makk et al., 1990). Overfeeding is associated with serious complications that often result in fluid-volume overload, hyperglycemia, hyperlipidemia, azotemia, hepatic dysfunction, and hyperosmolar states (Talpers, Romberger, Bunce, & Pingleton, 1992). Overfeeding total calories significantly increases the metabolic rate as a result of lipogenesis (Guenst & Nelson, 1994; McClave et al., 1998), and carbon dioxide production (Talpers et al., 1992), and impairs neutrophil function (McClave, 1997). Excess amounts of glucose or protein may increase respiratory muscle workload due to increased metabolic rate and ventilatory drive (Rochester, 1986b).

Nutritional Adequacy

Effects of Accurate Assessment

Determination of metabolic state is an important component of nutritional assessment (Cerra et al., 1997). There is wide variability in energy expenditure during illness or injury and throughout the recovery phase (Weissman, Kemper, Askanazi et al., 1986). Since nutritional requirements generally correspond with the level of energy expenditure, variation in energy expenditure during critical illness limits the accurate assessment of nutritional requirements. Energy expenditure varies as a result of multiple factors including medication, activity, mechanical ventilation, dietary intake, and illness severity (Weissman, Kemper, Elwyn et al., 1986). Increases in energy expenditure during critical illness plateau at approximately two times baseline REE (McClave & Snider, 1992). Most ICU patients are initially hypermetabolic; yet, some are hypometabolic—a response generally associated with a worse prognosis (McClave & Snider, 1994).

Makk and colleagues (1990) examined medical-surgical patients ($n = 26$) in a university hospital to compare the accuracy of indirect calorimetry and the HBE in determining nutritional requirements. The patients presented a variety of conditions including burns and trauma; 16 were on mechanical ventilators. Fourteen of the Makk et al. patient sample received parenteral nutrition, seven received enteral nutrition, and five were fasting. The degree of feeding adequacy was defined as the ratio of caloric intake to required intake times 100. Patients who received less than 90% of requirements were underfed, those who received greater than 110% of requirements were overfed, and those who received within 10% of requirements were considered adequately fed.

All of the patients under study in the Makk et al. research were measured once by indirect calorimetry. The HBE was calculated for each patient using ideal body weight or adjusted body weight as indicated. Sixty-two percent of the patients were found to be hypermetabolic, and 15% of patients were hypometabolic. A moderate correlation was found between the HBE and REE ($r = .52$) and was found to be statistically significant ($p < .01$). However, neither the HBE using adjusted body weight or ideal body weight proved more accurate in predictive power, and both calculations underestimated total REE. The degree of error increased when energy expenditure was higher. The addition of stress factors tended to overestimate requirements; consequently, nutrition administered on the basis of these calculations would lead to overfeeding.

Forty-seven percent of the patients in the Makk et al. (1990) study were underfed; 27% were overfed and only 32% received adequate feeding. The research thoroughly addressed energy expenditure and related factors in critically ill patients. The data are consistent with other studies within which the HBE was found to be inaccurate in patients with acute illness (Weissman, Kemper, Askanazi et al., 1986). This well-designed study showed the variability of energy expenditure in critically ill patients and the importance of measurement by indirect calorimetry. The limitations of this study were not addressed. The findings may have been limited by the sample size of 26 and, although it was not specific to enteral nutrition, it would have been interesting to determine the actual amount of nutrition support received by the patient sample. The investigators concluded that inaccurate nutritional assessment can potentially lead to overfeeding or underfeeding and that more accurate measurement may be indicated to provide optimal nutrition support.

McClave and colleagues (1998) examined enteral nutritional adequacy in patients admitted for long-term acute care. This multicenter study was conducted over a 9-week period at 30 long-term care hospitals within the United States. The research goal was to determine what percentage of patients within the total population was fed appropriately and the effects of feeding adequacy on clinical outcomes. The sample included patients receiving mechanical ventilatory support and enteral nutrition (*n* = 213). Patients on oral or parenteral nutrition were excluded from the study along with those with conditions precluding measurement by indirect calorimetry. Each patient was tested once by indirect calorimetry during steady state, and caloric intake over the preceding 24 hours was recorded from physician orders and intake and output records. Methods and instrument validity and reliability were thoroughly described. The degrees of feeding and metabolism were expressed in the same manner described by Makk et al. in their earlier 1990 study. The mean age of the patient sample was 70.1 plus or minus 14 years and 58.7% were male. Patient diagnoses included nonspecific respiratory failure in 59.4%, exacerbation of COPD in 28.4%, posttraumatic respiratory failure in 5.6%, pulmonary edema in 4.7%, and pneumonia in 1.9% of the cases. Approximately 48.4% of the patients were hypermetabolic and 20.6% were hypometabolic, compared to 62% and 15%, respectively, in the Makk et al. study (1990). This latter finding indicates variability in metabolic rates as patients progress from acute illness through to recovery. The critical illnesses of patients within long-term care facilities may be more chronic in nature and, hence, lower metabolic rates would be expected.

A comparison of measured requirements with physician orders revealed that 58.2% of the McClave et al. (1998) patients were overfed and 12.2% were underfed. Upon closer analysis of discrepancies noted in the intake and output records, it was found that 41.8% of the patients were overfed and 33% were underfed. Approximately 25% of the patients received feeding within 10% of their required calories. This finding was similar to the earlier research of Makk et al. (1990) in which only 25% to 32% of the participating patients under study received calories within 10% of the amount required. Both studies emphasized the importance of accurate measurement of energy requirements, especially with patients on mechanical ventilation. In terms of clinical outcome, McClave et al. (1998) found a significant inverse relationship between the degree of feeding and minute ventilation ($p = .001$, $R^2 = .05$). Minute ventilation increased in patients who received less than 100% of their nutritional requirements, and minute ventilation decreased in patients whose requirements were exceeded by up to

300%. Researchers hypothesized that increased minute ventilation in underfed patients may have resulted from decreased respiratory muscle strength from malnutrition.

The patients under study in the McClave et al. (1998) research were measured at a single point in time. It may be of interest to observe metabolic patterns over time, as well as the feeding adequacy in such patients. This study confirmed the findings of Makk et al. (1990), which demonstrated the importance of measuring energy expenditure in determining nutritional requirements. It also identified patient responses to underfeeding and overfeeding in a sample of mechanically ventilated patients in long-term care. It did not address why only 25% of the patient sample received adequate enteral intake. Avoidance of underfeeding and overfeeding is important in critically ill patients receiving enteral nutrition support. Nutritional needs should be assessed using indirect calorimetry when practical and possible. Additionally, individual assessment should also include whether each patient is actually receiving nutrition support as prescribed and whether the condition of the respective patient is improving. Research has shown that nutrition support should be based upon accurately measured requirements and reassessed at regular intervals during the recovery process (McClave & Snider, 1992).

Gastrointestinal Intolerance

Many factors having an impact on the adequacy of nutritional intake have been identified in recent research. These include GI issues, tube issues, and feeding interruptions due to ICU factors including testing and other procedures (Adam & Batson, 1997; Heyland et al., 1995; Kemper et al., 1992; McClave, Sexton et al., 1999; Montejo, 1999). Tolerance of enteral feeding is often reduced in the early phases of critical illness (Adam & Batson, 1997; Montejo, 1999). Gastric intolerance of enteral nutrition is a significant problem in ICU patients and a major factor limiting adequate enteral intake. Definitions of gastric intolerance vary but generally include high gastric residual volumes, diarrhea, vomiting, and abdominal distention (Montejo, 1999). These symptoms reflect the alterations in GI blood flow and decreased motility associated with critical illness (Cerra, 1987). Gastric intolerance is generally less frequent with small bowel feedings than with gastric enteral feeding (Cerra et al., 1997; Heyland, 1998; Kearns et al., 2000). Vasoactive and analgesic medications have also been shown to limit gastric tolerance of enteral nutrition (De Jonghe et al., 2001; Mentec et al., 2001). Morphine also decreases GI motility in mechanically ventilated patients receiving gastric feedings (Bosscha et al., 1998).

In a prospective study conducted in Great Britain, Adam and Batson (1997) examined the incidence of problems associated with enteral feeding in 193 patients in five ICUs. The heterogeneous sample was comprised of general medical (*n* = 36) and surgical (*n* = 21) patients, as well as patients with respiratory failure (*n* = 41). The remaining patients (*n* = 95) had cardiac, trauma, Acute Respiratory Distress Syndrome (ARDS), sepsis, and oncology diagnoses. The entire sample was fed by nasogastric (NG) tube, with the exception of two patients who received nasojejunal feedings. Patients receiving parenteral nutrition were excluded. Data collection began after the first 24 hours of enteral nutrition support. Calorie requirements were not measured, but were calculated as 25 kcal/kg/day for women, and 30 kcal/kg/day for men. The researchers acknowledged that given the high acuity of the patients in the study, this calculation may have underestimated requirements. On average, the patients received only 76% of the quantity prescribed. Two major factors for this were identified—GI complications and frequent interruptions for ICU procedures. The GI complications were defined as high gastric residual with no specific volume amounts stated, vomiting, and abdominal distention. The GI symptoms may have been related to the fact that all but two of the patients received NG feeding in this study. Although the standard time required to reach goal rate for each ICU was not detailed, the authors stated that the hospitals that used "fast start-up feeding regimens" (p. 265) demonstrated a significantly decreased incidence of GI complications, although the significance level was not documented. Two of the ICUs that used faster startup regimens had well-defined feeding protocols in place. This well-designed study was one of the first to examine a large sample of ICU patients receiving enteral nutrition support and the causes of feeding inadequacy.

In a prospective multicenter study conducted in Spain, Montejo (1999) evaluated the frequency of GI complications in 400 ICU patients receiving enteral nutrition. The GI complications were defined as abdominal distention, high gastric residuals, vomiting, diarrhea, regurgitation, and constipation. Sixty-two percent of patients developed one or more GI complications during feeding. As a result, enteral nutrition was subsequently withdrawn in 15.2% of these patients. Those with GI complications received less enteral feeding than patients without GI complications (63.1 ± 1.2% vs. 93.3 ± 0.3%, $p < .001$). They also experienced longer lengths of hospital stay (20.6 ± 1.2 days vs.15.2 ± 1.2, $p < .01$). Overall mortality for both groups was 25.5%. ICU mortality for patients with GI complications was higher compared to patients without GI complications (31.1% vs. 16.1%, $p < .001$). This was one of the first studies to demonstrate adverse clinical outcomes related to GI complications in enterally fed ICU patients.

McClave, Sexton, and coworkers (1999) conducted a prospective study within the ICUs of two university-based hospitals to evaluate factors affecting delivery of enteral tube feeding. The heterogeneous sample (*n* = 44) included medical, surgical, trauma, and neurological-injury patients. All of the patients, with the exception of two, were mechanically ventilated. Patients were excluded from the study if they were receiving parenteral or oral intake. Enteral feedings were infused by NG tube. No effort was made to place postpyloric feeding tubes. The ICU dietitian of each hospital determined required calories using a range of 25 to 35 kcal/kg/day. The physicians ordered the type and rate of enteral feeding. Data collected included the volume of formula delivered and percentage of calories received by the patients. Patient position, residual volume, flush volume, presence of blue food color in the oropharynx, and stool frequency were recorded every 4 hours. Frequency, duration, and reason for feeding interruptions were also recorded.

In the 44 patients studied in the McClave et al. (1999) research, the mean volume of the enteral feeding received was only 52% of goal, and only 14% of the patients reached 90% of goal feeding within 72 hours of start of feeding. The most common reason for feeding interruption was high gastric residual volume, defined as a volume greater than 200 ml. Feedings were held for gastric residual volume in 45% of the patients. In most cases, feedings were held when residual volume was greater than 200 ml; however, in 45% of the cases, feedings were held for volumes less than 200 ml for up to 4 hours at a time. Diarrhea, defined in the McClave, Sexton et al. study as more than "three stools per day or the need for an incontinence bag," occurred in 23 (52.3%) of patients (p.1253). However, feedings were not held due to diarrhea stools. In the 24 patients who were weighed at the beginning and end of the study, 54% lost weight; however, the amount was not documented. A decreased percentage of calories infused was correlated with decreased albumin levels ($r^2 = 0.13, p = .042$). This study highlighted the numerous factors associated with interruption of enteral feeding in an ICU.

Mentec and colleagues (2001) conducted a prospective study of 153 ICU patients receiving NG tube feeding. The purpose of the research was to investigate the frequency of, and risk factors for, increased gastric residual volume and upper GI intolerance. All of the patients received NG feeding. The sample included a mix of medical (92%), surgical (3%), and multiple trauma (4%) patients. The ventilatory status of the patients was not reported. The feeding goal for all patients was established at 25 kcal/kg/day. All patients reached goal rate by the first day of feeding. Gastric residual volume was measured by aspiration at the start of the enteral feeding, every 4 hours on days 1 through 5, and every 12 hours on days 6 through 20 or through the completion of enteral nutrition support. Gastric aspirate was returned to the patient unless it was greater than 500 ml. Enteral nutrition management was guided by the use of a specific protocol established by the respective ICU.

Mentec et al. (2001) defined upper GI intolerance as residual volume between 150 and 500 ml on two consecutive measurements, greater than 500 ml, or when vomiting occurred. The findings indicated that 104 patients had normal gastric residual volumes and 49 had increased gastric residual volumes. The independent risk factors for increased gastric residual volume included gastric residual volume greater than 20 ml at the onset of feeding, residual volume greater than 100 ml at any time during feeding, sedation of an unreported amount and type, and use of catecholamines. Although examination of nutritional adequacy was not a specific goal of the study, these researchers found that patients with increased gastric residual volumes had a significantly lower mean daily enteral intake compared to patients without GI complications (15 ± 8 kcal/kg/day vs. 20 ± 8 kcal/kg/day, $p = .0005$). Although not statistically significant, GI complications were also associated with longer ICU stays and higher ICU mortality.

Tube Factors

Tube patency or displacement problems are significant factors that impact adequacy of enteral intake. Critical care nursing research conducted by Stechmiller, Treolar, Derrico, Yarandi, and Guin (1994) examined the differences between calorie intake and caloric requirements in neurosurgical ICU patients. The frequency of feeding interruption was also recorded. All of the patients ($n = 53$) were mechanically ventilated and receiving enteral nutrition for at least 2 days. The HBE was used to estimate energy requirements. The neurosurgeon of the study site ordered the type and rate of enteral feeding formula. Propofol was recorded as an additional calorie source for 12 patients who required continuous infusion during the study period. During the first 8 days of feeding, 80% of the patients were underfed. There was a statistically significant difference between the number of calories prescribed and the number received (Days 1-5: $p = .001$; Days 6-7: $p = .003$, Day 8: $p = .01$). During the first 12 days of feeding, 77% of the patients were underfed. Stechmiller and colleagues reported that after day 12, feeding stabilized; however, no data were provided to substantiate this finding.

For the first 8 days, feeding interruptions were cited as the most common cause of underfeeding (Stechmiller et al. 1994). A total of 183 interruptions in feedings were observed. Thirty-one percent of these were due to medication administration, which involved 12 patients (24%) and, specifically administration of phenytoin. Feedings were held for 2-hour intervals with each ordered dose. The second most frequent cause of enteral feeding interruption was tube dislodgement (27%). This occurred 24 times in 31% of patients. Tube replacement took anywhere from 4 to 96 hours. Other reasons for feeding interruption included surgery (12%), ileus (9%), airway management (8%), bedside procedures (3%), and patient agitation (1%). This study examined factors that contribute to underfeeding in brain-injured ICU patients and revealed these patients received less nutrition than required. Tube location, confirmed by radiograph, was documented; however, the details on tube location were not addressed. Diarrhea was not reported as a reason for feeding interruption in the study, and Stechmiller et al. did not address other GI issues.

In the McClave, Sexton, et al. study (1999), tube displacement was the second most common cause for interruption of enteral tube feeding, occurring in 18 (41%) of the patients under study. The time required for tube replacement and radiographic confirmation often led to feeding delays of up to 8 hours. The inability to maintain enteral feeding access has been identified as a cause of feeding interruption in other studies (Adam & Batson, 1997; Heyland et al., 1995; Ott, Annis, Hatton, McClain, & Young, 1999).

Factors Related to the Intensive Care Unit

Several factors routine to the ICU setting lead to frequent interruptions in continuous tube feeding, limiting adequate nutritional intake (Adam & Batson, 1997; McClave, Sexton et al., 1999). Enteral feeding is routinely held in preparation for surgical or diagnostic procedures, weaning, hemodynamic instability, and various nursing care activities in an effort to decrease the risk of pulmonary aspiration of enteral formula. In 1992, Kemper and colleagues examined actual caloric intake compared to measured requirements in patients receiving nutrition support. The sample included 22 mechanically ventilated postoperative patients in a university hospital. The majority of the patients had undergone abdominal surgical procedures. Patients received total parenteral nutrition ($n = 8$), enteral nutrition ($n = 8$), or both ($n = 6$). REE was measured by indirect calorimetry and nutritional intake was recorded on a consistent basis. The patients who received parenteral, or enteral plus parenteral nutrition support received an average of 80% of measured requirements. Those exclusively on enteral nutrition support received 68% of caloric requirements. Variations in nutrient intake were recorded, which revealed more day-to-day variation within the enteral group (40% ± 56%) than in the parenteral group (12.2% ± 24%, $p < .001$). The study groups were not significantly different in age, sex, or diagnosis, and there was no variation in daily REE between them.

The Kemper et al. (1992) study found that inadequate intake was related to several factors including delayed initiation of enteral nutrition, mechanical problems with feeding tubes, gastric distention, and delayed gastric emptying. Problems related to procedure delays, weaning trials, or other critical care activities were also mentioned, but not addressed in detail. Diarrhea, although not quantified, was cited as a frequent problem. The feeding formulas used in the study were low-residue, isotonic formulas free of high fat concentrations. It is unknown whether the formulas contained soluble fiber which may impact the frequency and volume of diarrhea as cited in Fuhrman (1999). Kemper and colleagues addressed their physiologic rationale for preferring enteral nutrition support; however, their findings actually indicated that enteral feeding is less consistent than parenteral methods in critically ill patients. Although not a specific aim of the study, Kemper et al. identified slow initiation of feeding and tube problems as causes of inadequate enteral intake. The enteral route is presumed to be the best method physiologically, unless significant contraindications are present (Daly et al., 1993). However, as shown in similar research (De Jonghe et al., 2001; DeBiasse & Wilmore, 1994), this study found that it may be more effective to use a combination of parenteral and enteral nutrition to prevent caloric deficits.

A prospective cohort study by Heyland et al. (1995) examined enteral feeding practices and identified barriers to early feeding. The dependent variables were initiation and tolerance of enteral nutrition. The research was conducted in the medical-surgical ICUs of two tertiary hospitals. Ninety-nine consecutive patients who were expected to remain in the ICU for longer than 3 days and be unable to tolerate oral nutrition were enrolled in the study. They were followed for 21 days or until they tolerated enteral or oral nutrition, were discharged from ICU, or died. Heyland et al. examined factors related to initiation and tolerance of enteral feedings. Tolerance was defined as receiving 90% of estimated requirements for longer than 48 hours without GI problems. Seventy-three of 99 patients (74%) were started on enteral feedings an average of 3.1 days following ICU admission; however, some began the feedings as late as Day 18 of their ICU stay. Of 26 patients never started on enteral nutrition, 3 (12.5%) eventually tolerated oral nutrition, 14 (54%) were discharged from the ICU, 7 (27%) died, and two were followed for a maximum of 21 days.

Enteral nutrition was withheld due to the absence of bowel sounds in 27.0% of the Heyland et al. (1995) patient sample, due to high NG drainage in 16.9%, contraindication to enteral nutrition in 16.7%, tolerance of oral nutrition in 6.8%, and for no apparent reason in 5.1%. Independent variables significantly associated with starting enteral nutrition were the admitting diagnosis, abdominal surgery within 1 week of admission, the policies and procedures of the respective hospital, the presence of bowel sounds, or the current use of paralytic and vasoactive drugs. Of the 73 patients started on enteral feedings, 35 (48%) tolerated the feedings. Variables associated with intolerance in the univariate regression model included the use of paralytic and vasoactive drugs and gastric residuals greater than 150 ml. Use of paralytic drugs was the only independent factor that predicted intolerance to enteral nutrition ($p = .037$). The most common reasons for discontinuing feedings included: high gastric residuals, blocked tubes and delays in reinsertion, upcoming surgical or radiological procedures, or vomiting.

The study by Heyland and colleagues (1995) provided the first published survey of feeding practices in patients eligible for enteral nutrition. The research confirmed that GI problems are major barriers to successful enteral nutrition in critically ill patients. However, significant variation was observed in practices of prescribing enteral nutrition between the two hospitals that participated in the study. This was apparently not due to differences in the patient populations between the two facilities, but from a systematic difference between hospital physician practices. Energy requirements were calculated using estimates instead of indirect calorimetry. Examination of nutritional adequacy was not a primary aim of this study; hence, evaluation of which patients were underfed or overfed was not approached. A strength of this descriptive research study was that medical and nursing staffs were blinded to the study, which served to limit confounding via the Hawthorne effect. The findings are consistent with other research that described the association between GI dysfunction and intolerance to enteral feedings (Mentec et al., 2001; Montejo, 1999; Potter et al., 1998). The Heyland et al. (1995) study raises questions surrounding alternative ways of increasing tolerance. These may include feeding beyond the stomach or using prokinetic medications. The findings also demonstrate a need to challenge current beliefs surrounding enteral nutrition that are not evidence based.

McClave, Sexton, and coworkers (1999) found that feedings were withheld for 36 (83.7%) of the patients within their study sample. There were several reasons recorded including endoscopic and surgical procedures (39%), diagnostic procedures (27%), and routine nursing activities (30%). These researchers evaluated the reasons for feeding interruption to determine if any could be avoided. The avoidable reasons included withholding feeding for more than 2 hours for residual volume greater than 200 ml; taking more than 1.5 hours to replace a feeding tube; and withholding feeding for more than 4 hours before a surgical or endoscopic procedure, or a diagnostic test. Feedings were withheld for a mean of 20% of the total infusion time, and McClave et al. found interruptions in feeding were potentially avoidable 66% of the time.

Summary of Research

This body of research highlights the importance and complexity of nutritional management for ICU patients. It uncovers issues related to accurate assessment and delivery of optimal enteral nutrition in hospital ICUs. The studies reviewed were primarily descriptive and included heterogeneous samples. Nutritional requirements were primarily assessed using estimates rather than measurement methods such as indirect calorimetry. The HBE or other methods were commonly used to calculate requirements in most of the studies reviewed. A small number of the studies used indirect calorimetry to determine caloric requirements (Kemper et al., 1992; Makk et al., 1990; McClave et al., 1998; Ott et al., 1999). Although not all of the patients required mechanical ventilation, most of the critical care studies reviewed included mechanically ventilated patients. Enteral and parenteral methods of nutrition support were utilized in several of the studies (Kemper et al., 1992; Makk et al., 1990); however, the majority examined enteral nutrition support exclusively.

Three of the reviewed studies (Adam & Batson, 1997; Mentec et al., 2001; Montejo, 1999) were conducted in ICUs outside the United States. Differences in nutrition practice patterns and admission criteria may limit their generalizability to patient populations within this country. Few studies reported medication administration (Heyland et al., 1995; Makk et al., 1990; Mentec et al., 2001; Ott et al., 1999). Because medications affect gastric motility, it is important to record administration of specific medications such as catecholamines, opioids, and anesthetic agents.

Accurate assessment of metabolic state, GI tolerance, feeding tube issues, and factors related to clinical practice within the ICU environment impact enteral nutrition adequacy. Enteral nutrition is prescribed by physicians and monitored and delivered by nursing. Nursing activities have been shown to interrupt feeding, yet only two recently published nursing studies examined the adequacy of nutritional intake in ICU patients

(Briggs, 1996; Stechmiller et al., 1994).Given the complications of malnutrition, nursing research that examines issues related to nutritional adequacy in critically ill patients is absolutely essential.

Conceptual Framework

This current prospective descriptive study is based upon a conceptual framework in which adequacy of enteral nutritional intake is influenced by factors identified from current research. These factors are organized into the following four categories: assessment of energy requirements, GI factors, tube related factors, and ICU factors. The model illustrated in Figure 1 clarifies the relationships between the factors and the adequacy of enteral nutrition. It is based upon the review of current literature within the field of nutrition support. This model guided the development of the study aims that sought to determine the degree of nutritional adequacy and test the potential relationship of factors that influence it.

The concept of adequacy of enteral nutritional intake is defined as the amount of energy consumed compared to the amount required. Adequacy is further categorized as (a) underfed (i.e., less than 90% of requirements received), (b) adequately fed (i.e., plus or minus 10% of requirements received), (c) overfed (i.e., greater than 110% of requirements received). This same categorization has been outlined in previous research (Makk et al., 1990; McClave et al., 1998).

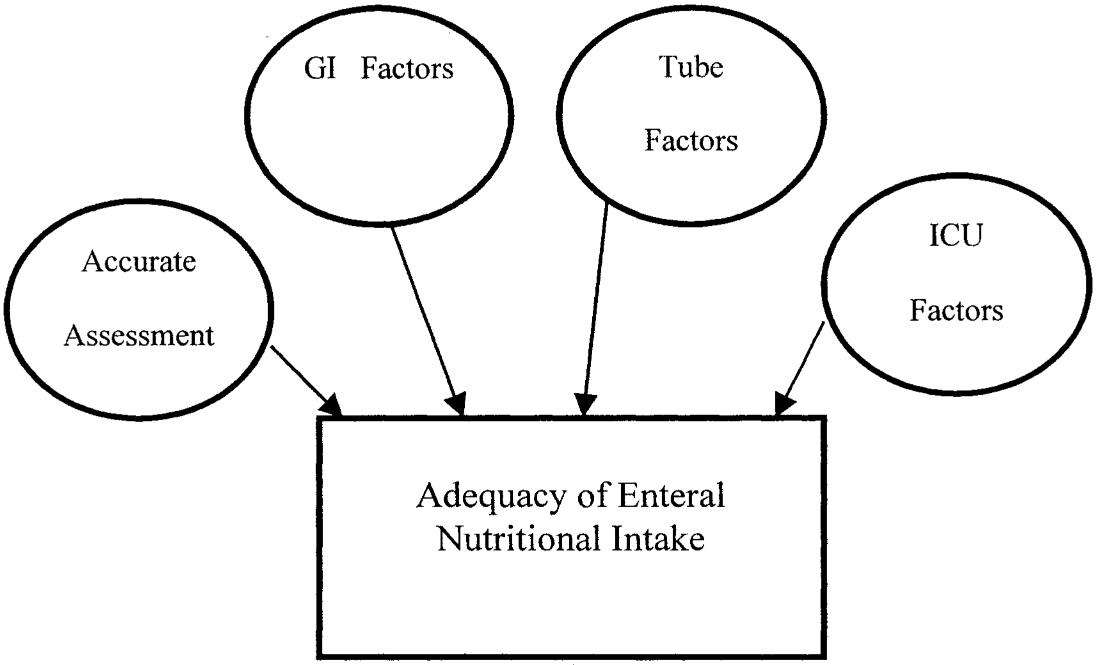

Figure 1. Conceptual Framework: depicts the influence of accurate assessment, gastrointestinal (GI) factors, tube factors, and intensive care unit (ICU) factors on the adequacy of enteral nutritional intake.

CHAPTER III

METHODOLOGY

Research Design, Setting, and Study Sample

This study incorporated a prospective descriptive design to examine the adequacy of enteral nutrition intake in mechanically ventilated ICU patients. It also examined the influence of specific factors on enteral nutrition delivery within this patient population. The research was conducted at the following two study sites: (a) the Medical-Surgical Intensive Care Unit (MSICU) of a northern California Veterans Affairs hospital, and (b) the coronary care unit and medical ICU of a northern California county hospital.

Human Subjects Assurance and Sampling Procedures

Prior to the initiation of this study, the research protocol was approved by the Nursing Research and Research and Development committees of the northern California Veterans Affairs hospital serving as the first study site. It was also approved by the Stanford University Panel on Medical Human Subjects, the Research and Human Subjects Review Committee of the northern California county hospital, serving as the second study site, and the Committee on Human Research for the University of California, San Francisco (see Appendix A). Eligible patients were screened and permission to seek consent for enrollment in the study was obtained from their respective physicians. Since mechanically ventilated ICU patients often require sedation, the study was explained to the legal next of kin when necessary, and written informed consent was obtained from either the patient or legal next of kin (see Appendix B).

The group studied was a convenience sample of mechanically ventilated adult patients receiving enteral nutrition support. Recruitment was conducted at two university-affiliated teaching hospitals within the San Francisco Bay Area. Patients were recruited from the 15-bed MSICUs of each study site. Prior to initiation of the research, the medical director and nurse manager for each unit were contacted. Medical, dietary and nursing staff in each unit were verbally informed of the requirements of the study. Recruitment flyers describing the study were placed in all of the hospital units with a pager number to contact the researcher for additional information (see Appendix C).

Participant Criteria and Sample Size

Potential subjects who met the study criteria were identified from the medical records. The ICU resident physician was contacted for permission to seek consent for patient enrollment in the study. The study details and informed consent were explained to the patient and/or legal next of kin, and written informed consent for study participation was obtained from the patient, when possible, or from the legal next of kin if the patient was unable to sign. A copy of the signed consent form was given to the consenting party.

The study sample consisted of ICU patients over 18 years of age who were intubated, mechanically ventilated, and receiving enteral nutrition support at the physician-prescribed goal rate. Potential patients were excluded if they were receiving parenteral or oral feedings. The original protocol required that all patients have energy expenditure measured by indirect calorimetry. However, after 9 months of data collection, more than half of the enrolled patients were no longer eligible due to investigator failure to obtain indirect calorimetry measurements. Reasons for this included (a) extubation before indirect calorimetry could be performed; (b) oxygen requirements greater than 65% Fraction of Inspired Oxygen ($FI0_2$); (c) unstable $FI0_2$; (d) tracheal cuff leaks; and (e) scheduling conflicts in obtaining the metabolic cart. All enrolled patients had estimated energy requirements documented by the ICU dietitian. To preserve the sample size, the protocol was revised during the data collection phase to include all enrolled patients with and without indirect calorimetry measurements.

Data were not available from previous research to calculate effect size of the variables analyzed in this study. Because the first three aims of the study were descriptive, the sample size requirements were based upon Aim 4, which sought to examine the influence of specific factors on the percentage of required enteral nutrition kilocalories actually received. Aim 4 was analyzed using multiple-regression techniques. The covariate was the number of minutes the feedings were held and the additional predictors, were gastric residual volume, episodes of diarrhea, episodes of vomiting, and tube placement/displacement episodes. The N-Query software program was used to calculate the sample size. For a multiple linear-regression model that already included four predictors with a squared multiple correlation of R^2 of 0.4, a sample size of 60 that presented 80% power to detect alpha at .050 and an increase in R^2 of .071 was required.

Measures

Instruments

Indirect Calorimetry

Indirect calorimetry measures oxygen consumption and carbon dioxide production. Steady state measures of these parameters are obtained while the patient is at rest (Weissman & Kemper, 1995). *Steady state* is defined as an interval where average oxygen consumption and carbon dioxide production change by less than 10%. This is usually achieved in a 20- to 30-minute testing period (McClave & Snider, 1992). The measured REE is calculated from these measures and expressed in kilocalories corresponding to daily caloric requirements. The accuracy and reliability of indirect calorimetry have been confirmed in previous research (Daly et al., 1985; Mullen, 1991). Measurement of REE by indirect calorimetry in mechanically ventilated patients is considered more accurate than predictive formulas (Flancbaum, Choban, Sambucco, Verducci, & Burge, 1999; McClave, McClain, & Snider, 2001) and is associated with reduced incidence of overfeeding and underfeeding, as well as decreased costs (McClave, 1997).

In this current study, REE was measured once when the patient was receiving enteral nutrition at the prescribed goal rate. The Vmax 29n Spectra metabolic cart (SensorMedics, Yorba Linda, CA) was used at both study sites. The pulmonary technologist employed by the Santa Clara Valley Medical Center performed the testing at the county hospital site. The investigator performed the indirect calorimetry measures at the Veterans Affairs hospital. In August 2001, the investigator received three sessions of supervised training from the pulmonary technologist at the Veterans Affairs site to ensure proper performance of the testing. Before each test, calibration of the gas analyzers was performed to reference tanks of known oxygen, nitrogen, and carbon dioxide concentrations according to the manufacturer's specifications. The endpoint of each test was the point at which steady state was achieved. For both sites, the results were based on a measurement period of 30 minutes; the first 5 minutes of measurement was discarded (McCarthy, 2000). An indirect calorimetry data report was printed out for all patients. If the measurement was unsuccessful, the reason was documented on the printout, and the test was aborted. According to the manufacturer, the Vmax29n metabolic cart, in the ventilator mode of application, is valid under the following test conditions: Inspired oxygen from room air to 80%, respiratory rate of 10-30 breaths per minute, tidal volume of 200-1000 ml, positive end expiratory pressure of up to 20 cmH_20, and flow-by of up to 20 liters per minute. Additional specifications are listed in Table 1.

Table 1

Flow / Volume and Gas Specifications for the Vmax 29n

Flow / Volume	0_2 Analyzer	$C0_2$ Analyzer
Type: Mass Flow Sensor Range: 0-16 liters/second Resolution: 0.003 liters/second from .20-16 liters/second Flow accuracy: ± 3% of reading or 0.25 liters/second, across the range of 0.2 to 14 liters/second Volume Accuracy: ± 3% of reading or 0.050 liters, whichever is greater Resistance: less than 1.5 cmH_20/liters/second at 12 liters/second	Type: Electrochemical fuel cell Range: 0-100% Resolution: 0.01% Accuracy: ± 0.02%	Type: Non-disperse infrared, themopile Range: 0-16% Resolution: 0.01% Accuracy: ± 0.02% $C0_2$ across range of 0-10%. There is no accuracy specification above 10% $C0_2$.

Harris-Benedict Equation and the Enteral Feeding Pump

The HBE is used to estimate BEE using calculations based upon height, weight, age and sex. This estimate is then multiplied by an additional stress factor to account for increases in energy expenditure resulting from injury or activity (McClave & Snider, 1992). Stress factors are used to attempt to increase the accuracy of the HBE by accounting for illness severity. The HBE alone often underestimates energy needs, whereas added stress factors tend to overestimate requirements (Makk et al., 1990). Comparison studies with indirect calorimetry have indicated reasonable accuracy in healthy control subjects. Although the HBE correctly predicts energy requirements in less than 50% of acutely ill patients (Daly et al., 1985; Weissman, Kemper, Askanazi et al., 1986), it is often used in clinical practice because it is less expensive and easy to use.

The same formula was applied by the dietary staff at both study sites to calculate BEE (men = 66 + [13.8 x W] + [5x H] – [6.8 x A]; women = 655 + [9.6 x W] + [1.7 x H] – [4.7 x A]; W = actual weight in kgs, H = height in cms, A = age in years). The BEE was multiplied by a stress factor selected by the ICU dietitian ranging from 1.3 to 1.5. The weight used to calculate the BEE was adjusted for patients who were more than 125% of their ideal body weight. Both study sites also applied the same formula to calculate adjusted body weight ([ABW – IBW x 0.25] + IBW = weight in kg for BEE and protein requirements, ABW = actual body weight, IBW = ideal body weight, 0.25 = 25% of body fat tissue that is metabolically active). Enteral feeding was infused using the Sherwood Kangaroo 324 enteral feeding pump (Sherwood Medical Industries) at both study sites. The manufacturer claims an accuracy rate of plus or minus10%.

Study Variables

The adequacy of nutritional intake was the dependent variable in this study. This variable determined whether a patient was underfed, overfed, or fed appropriately according to requirements. This concept is expressed as the ratio of kilocalories provided to the number required x 100 (McClave et al., 1998). The resulting percentage is used to define underfeeding as nutritional intake providing less than 90% of caloric requirements, appropriate feeding as intake providing plus or minus 10% of caloric requirements, and overfeeding as intake providing greater than 110% of caloric requirements (Makk et al., 1990; McClave et al., 1998).

GI dysfunction limits adequate enteral intake in ICU patients. Factors associated with gastric dysfunction include high gastric residuals, frequent diarrhea, and emesis (Montejo, 1999). Residual volumes were measured every 4 hours in this study and recorded in milliliters. Diarrhea was measured as the number of liquid stools charted per day. Emesis, defined as enteral formula ejected orally, was measured in episodes per day. Episodes of tube clogging or tube dislodgment were quantified, and the number of times feeding tubes were replaced was recorded on a daily basis. The duration of each feeding interruption in minutes was documented in minutes, also on a daily basis. Any interruption of duration of at least 15 minutes was recorded. The reason for each feeding interruption was also specified. The study concepts are displayed in Table 2.

Table 2

Study Concepts

Concept	Variable	Operational Definition	Measure
Adequacy of nutritional intake a) underfeeding b) appropriate feeding c) overfeeding	Energy and protein intake compared to requirements	Kilocalories provided / Kilocalories required x100 a) < 90% of required b) ± 10% required c) > 110% of required	Volume received according to intake and output records; Harris-Benedict Equation plus stress factors
Gastrointestinal factors	Gastrointestinal dysfunction	Residual volume	Gastric residual volumes
		Each charted loose stool	Number of episodes of diarrhea
		Formula ejected orally	Number of episodes of vomiting
Tube factors	Tube problems	Tube clogged or displaced	Number of times tube replaced
Intensive Care Unit factors	Interruptions for activities and procedures	All delays in continuous feeding	Number of minutes feedings withheld

Procedures

Data Collection

Demographic and nutritional data were recorded prospectively over a 3-day study period for each enrolled patient. Energy requirements, as estimated by the ICU dietitian using the HBE, as well as appropriate stress factors were documented in the medical record. Indirect calorimetry testing was performed at the beginning of the study period.

Daily enteral intake was recorded for three consecutive days beginning from the time of indirect calorimetry measurement or when enteral feeding goal rate was achieved. When the protocol was revised, data from enrolled patients who had previously been considered ineligible because indirect calorimetry data were lacking were collected retrospectively from the medical record using a decision rule. For these patients, the 3-day data collection period began at the point at which their goal rate was achieved. Propofol infusions during the study period were included as a calorie source.

Demographic information was recorded from the medical record using a data collection form (see Appendix D). Patient ID number, age, gender, hospital admission date, ICU admission date, type of feeding tube and date of insertion, date enteral feeding began and date goal rate was achieved, parenteral nutrition infusion date, primary diagnosis, surgical procedures, date mechanical ventilation was initiated, admission height and weight, admission albumin level, body mass index (BMI), and Simplified Acute Physiology Score II (SAPS II) were recorded. The BMI at the time of hospital admission was calculated by the admission height and weight. It is the ratio of weight in kilograms divided by height in square meters (August et al., 2002). It was included as a demographic variable to gauge nutritional status of patients upon admission.

Classification of BMI varies; however, current guidelines state that normal BMI for men and women is 19 to 25 kg/m^2, overweight is classified as BMI 25 to 29 kg/m^2, and underweight is classified as a BMI less than 18.5 kg/m^2 (NHLBI, 1998).

The SAPS II is a measure of illness severity. The scores for this system range from a minimum score of 0 to a maximum score of 160; the higher the scores, the greater the severity of illness (Le Gall, Lemeshow, & Saulnier, 1993). It is used to assess patients in the ICU and predict for risk of mortality using scores from 15 clinical variables. The SAPS II is a revision of the original instrument and has been validated in previous research (Castella, Artigas, Bion, & Kari, 1995). It was chosen as a variable in order to classify patients by severity of illness upon hospital admission.

Nutritional data were collected using a nutritional data form (see Appendix D). Caloric requirements as determined by indirect calorimetry, if available; caloric requirements as determined by the HBE; and vasoactive and analgesic medications received during indirect calorimetry measurement were all recorded. Daily enteral intake data were recorded using a data collection form (see Appendix D). Current weight, type and rate of prescribed enteral formula, total volume of enteral formula infused over 24 hours, total volume of water infused, number of minutes and reason for feeding interruption, gastric residual volume, number of episodes of diarrhea and emesis, number of times feeding tube was replaced, number of radiographs performed related to feeding tube placement, type and dosage of analgesic and infusion, propofol infusion, albumin level, and maximum temperature were all recorded. Daily calorie content was calculated from the volume and type of enteral nutrition received by the patient under study. The mean number of kilocalories received over the 3-day period was calculated.

Data Analysis

The Statistical Package for the Social Sciences, version 11.0, was the software used to analyze data. Descriptive statistics were determined for all variables. Primary Aim 1 was to determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by HBE. The mean enteral intake in kilocalories over the three-day study period was calculated. The HBE, as calculated by the ICU dietitian, represented the estimated REE. Descriptive statistics were used to report the mean and standard deviation of the estimated REE and the mean enteral intake in kilocalories. A two-tailed, paired Students *t*-test was used to determine if the mean estimated REE was different from the mean enteral intake. A p-value of $< .05$ was determined to be a critical value in terms of analyzing the significant difference between means.

Primary Aim 2 was to determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by indirect calorimetry. A subgroup of 25 patients was able to be measured by indirect calorimetry. This measurement represented the measured REE in kilocalories. Descriptive statistics were used to report the mean and standard deviation of the measured REE and the mean enteral intake in kilocalories for this subgroup. A two-tailed, paired Students *t*-test was used to determine if the mean measured REE differed from the mean enteral intake. A p-value of $< .05$ was determined to be a critical value in terms of analyzing the significant difference between means.

Primary Aim 3 was to determine the percentage of patients who received adequate enteral nutrition kilocalories, the percentage underfed, and the percentage overfed. The average enteral intake over 3 days was the numerator in a ratio with estimated REE as the denominator. The percentage of required kilocalories actually received by each patient was determined by multiplying this by 100. The following categories were determined: underfed (i.e., less than 90% of required kilocalories); adequately fed (i.e., plus or minus 10% of required kilocalories); and overfed (i.e., greater than 110% of required kilocalories). The patients were categorized into groups according to the percentage of enteral nutrition actually received. Frequencies were used to determine the number and percentage of patients within each group. The percentage of patients who were underfed, adequately fed, and overfed was thus determined.

Primary Aim 4 was to examine the influence of specific factors on the percentage of required enteral nutrition actually received. Multiple linear regression analysis was used to determine the effects of five specific predictors on the dependent variable of percentage of required enteral nutrition actually received over the 3-day study period. The predictor variables included the average number of episodes of emesis, the average number of episodes of diarrhea, the average amount of residual volume, the average number of times the feeding tube was replaced, and the average number of minutes enteral feeding was interrupted.

Secondary Aim 1 was to determine the difference between kilocalories determined necessary by indirect calorimetry compared to HBE in those patients with indirect calorimetry measurements. Raw difference scores were calculated between the kilocalories determined necessary by indirect calorimetry (i.e., measured REE) compared to HBE (i.e., estimated REE). A two-tailed, paired Students *t*-test was used to determine the difference between measured REE and estimated REE. A p-value of $< .05$ was determined to be a critical value in terms of analyzing the significant difference between means.

Secondary Aim 2 was to determine the differences in demographic variables between patients able to be measured by indirect calorimetry and those who were not. Patients were categorized into two groups those able to be measured by indirect calorimetry and those who were not. A chi-square test was performed to determine differences between the study groups on the categorical demographic variables, which included gender, race, whether the patient received parenteral nutrition, or whether the patient had undergone surgery. These variables were the dependent variables, and group membership was entered as the independent variable in the chi-square analysis.

An independent sample Students *t*-test was performed to determine differences between continuous variables and group membership. Group membership was entered as the independent variable and interval level demographic variables, including age, SAPS II, and BMI were entered as the dependent variables.

CHAPTER IV

RESULTS

Characteristics of the Study Sample

Seventy-nine patients were approached for participation in this study. Fifteen refused to participate primarily because the patient or family member was unable to cope with anything beyond the illness and treatment at that particular time. The mean age of patients who refused (*n* =15) was 65, *SD* = 15.9 years, 93% male, and 73% Caucasian. Sixty-four patients consented to participate in the study. Fifty-two of these were recruited from the MSICU at the Veterans Affairs hospital in northern California that served as the first study site from May 2001 through October 2002. Twelve patients were recruited from the coronary-care unit and the medical ICU at the county hospital in northern California that served as the second study site from August 2002 through October 2002. Four patients enrolled from the first study site withdrawn for failure to achieve their enteral nutrition goal rate before extubation (*n* = 2) or failure to advance from parenteral to enteral nutrition (*n* = 2). All four patients were male; two were Caucasian, and two were African-American. Admission diagnoses for those withdrawn from the study included respiratory (*n* = 2), GI surgery (*n* = 1), and sepsis (*n* = 1). Of these patients, three transferred out of the ICU and one expired.

The study sample included 60 mechanically ventilated patients receiving enteral nutrition support. The mean age of the total sample (*N* = 60) was 63.9, *SD* = 12.9 years, 86% were male, and 83% were Caucasian. Of this sample, 25 (41.7%) were surgical patients, with a mean SAPS II of 37, *SD* = 11.6, and mean BMI of 27.0, *SD* = 6.9. (see Table 3).

Table 3

Demographics of the Study Sample

Variables	Veterans Affairs	County Hospital	Total Sample
Total number of patients	48	12	60
Age in years (mean/*SD*)	65.6 / 11.3	56.7 / 16.5	63.9 / 12.9
Gender (male/female)	46 / 2	6 / 6	52 / 8
SAPS II score (mean/*SD*)	36.9 / 11.8	37.5 / 10.9	37.1 / 11.6
BMI (mean/*SD*)	27.4 / 6.7	24.8 / 7.5	26.9 / 6.9
Race (%)			
Caucasian	91.7	50.0	83.3
Black	4.2	8.3	5.0
Hispanic	4.2	25.0	8.3
Asian/Pacific Islander	0	16.7	3.3
Admitting diagnosis (%)			
Cardiac	35.4	8.3	30.0
Respiratory	33.3	25.0	31.7
Gastrointestinal	16.7	25.0	18.3
Neuro	2.1	16.7	5.0
Vascular	10.4	0	8.3
Renal	0	8.3	1.7
Sepsis	2.1	16.7	5.0
Medical (%)	52.1	83.3	58.3
Surgical (%)	47.9	16.7	41.7
Cardiac	20.8	0	16.7
Gastrointestinal	12.5	8.3	11.7
Vascular	10.4	0	8.3
Neurological	4.2	8.3	5.0

Note. SAPS = Simplified Acute Physiology Score; BMI = body mass index

Patients at each site were similar in age, SAPS II scores, and BMI. At the Veterans Affairs hospital site, the percentage of Caucasian patients was higher than at the county hospital site (91.7% vs. 50%, respectively). More patients were admitted for cardiac and respiratory disorders at the Veterans Affairs hospital (35.4% vs. 8.3% and 33.3% vs. 25%, respectively). Eighty-three percent of patients at the county hospital site were admitted for medical diagnoses versus 52.1% at the Veterans Affairs hospital. The majority of patients (66.7%) at this same hospital received enteral nutrition by nasoduodenal feeding tube. Eighty-three percent of patients at the county hospital were fed intragastrically. Nutritional data are provided in Table 4.

Table 4

Nutritional Data for the Study Sample

Nutritional Data	Veterans Affairs Hospital (*n* = 48)	County Hospital (*n* = 12)	Total Sample (*N* = 60)
Tube location			
Duodenal (# patients / percent)	32 / 66.7	2 / 16.7	34 / 56.7
Gastric	11 / 22.9	10 / 83.3	21 / 35
Jejunal	5 / 10.4	0	5 / 8.3
Days from feeding start to goal			
(Range/	0-31 days	0-9 days	0–31 days
mean / *SD*)	6.0 / 7.5	2.8 / 3.0	5.4 / 6.7

Primary Aim 1 was to determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by HBE. The normal distribution curve for the estimated REE over a 3-day period is displayed in Figure 2. For the total sample, mean estimated REE was 2,150, *SD* = 317 kcal. Mean kilocalories received were 1,410, *SD* = 731 kcal with a range of 213 to 2,630 kcal over the 3-day study period. A

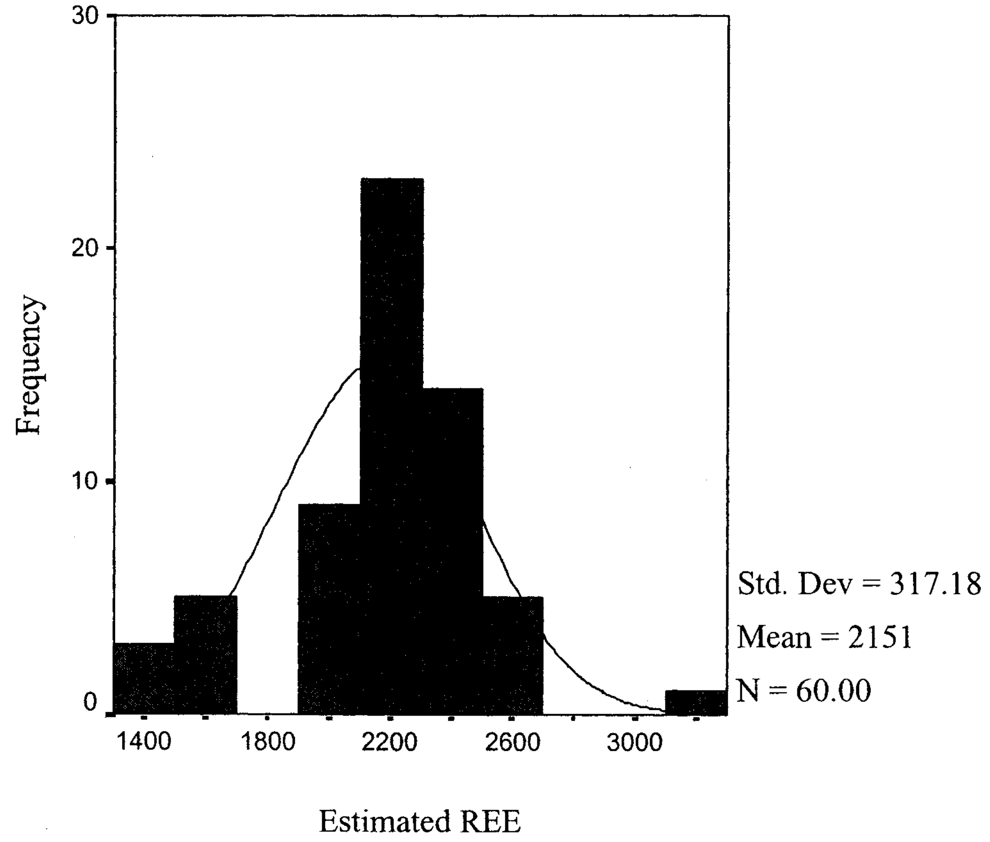

Figure 2: The histogram depicts the normal distribution curve for estimated resting energy expenditure (REE) as determined by the ICU dietitian for the study sample.

two-tailed, paired Students *t*-test found a statistically significant difference between the estimated REE and average kilocalories received (95% confidence interval [CI] 573-905, $p < .001$). Additionally, the amount of kilocalories actually received over the 3-day study period was found to be significantly less than the estimated amount of kilocalories required in this sample.

Primary Aim 2 was to determine the amount of enteral nutrition kilocalories received compared to the amount determined necessary by indirect calorimetry. The mean measured REE was 1,638, *SD* = 465 kcal, and the mean kilocalories received were 1,516, *SD* = 621 kcal. For this subgroup, kilocalories received ranged from 565 to 2385 kcal over the 3-day study period. A two-tailed, paired Students *t*-test indicated no significant difference between the measured REE and average kilocalories received ($p = .337$) (see Table 5). With the estimated means and a Cohen's d of .196 for a nondirectional correlated means *t*-test, a sample size of 207 would be required to detect a statistically significant difference with an alpha of .05 and a power of .80.

Table 5

Paired Samples *T*-Test Results

Variable	Mean (kcal)	*SD*	*t*	*p*	95% CI
EREE ($n = 60$)	2,150	317	8.911	< .001	573-905
Mean 3-day intake	1,410	731			
MREE ($n = 25$)	1,638	465	.980	.337	
Mean 3-day intake	1,516	621			

Note. EREE = estimated resting energy expenditure; MREE = measured resting energy expenditure.

Primary Aim 3 was to determine the percentage of patients who received adequate enteral nutrition kilocalories, the percentage underfed, and the percentage overfed. Patients were categorized into "adequacy groups" according to the percentage of enteral nutrition actually received. In the total sample of 60 patients, 41 (68.3%) were underfed, 18 (30%) were adequately fed, and 1 patient (1.7%) was overfed. Table 6 indicates the percentage of patients in each category based upon the percentage of required kilocalories received. Propofol is used routinely in the management of mechanically ventilated patients in the ICU. As an amnestic agent, it is administered in a lipid emulsion containing 1.1 kcal/ml, and is recognized as a source of calories (Vender, Cresci, & Lee, 2002). A total of seven patients received propofol infusions during the study period. The one patient who was overfed received propofol (528 kcal/day) in addition to enteral feeding at the goal rate.

Table 6

Nutritional Adequacy Categories

Adequacy group	Number of patients	Percentage
Underfed	41	68.3
Adequately fed	18	30.0
Overfed	1	1.7
Total	60	100.0

Upon further analysis, 23 out of the total sample of 60 patients (38.3%) received less than 50% of required calories. Ten patients out of 60 (16.6%) received less than 30% of required calories. Twenty-six patients (43.3%) received greater than or equal to 80% of required calories. The total number of patients who received greater than 90% of required calories was 19 (31.6%). This included one patient who received 113% of required calories due to continuous infusion of propofol.

Primary Aim 4 was to examine the influence of specific factors on the percentage of required enteral nutrition actually received. Multiple linear-regression analysis was used to examine this study aim. The dependent variable was the percent of required kilocalories received. Five quantitative predictor variables were entered into the model—average number of diarrhea episodes, average number of emesis episodes, average residual volume, average number of feeding tube replacements, and average number of minutes feeding was withheld. Due to missing data, the regression analysis was performed on 59 patients of the total sample. The correlation coefficients for this sample are displayed in Table 7.

Table 7

Correlations With Dependent Variable: Percent of Required Kilocalories Received

Predictor variable	*r*	*p*
Average number of diarrhea episodes	.257	.05
Average number of emesis episodes	-.202	.12
Average gastric residual volume	-.267	.04
Average number of tube replacements	-.364	.004
Average number of minutes feedings withheld	-.830	< .001

The results were significant in the overall model ($F_{5,53} = 25.335, p < .001, R^2$ .705). This finding revealed that over 70% of the variance in the percentage of required kilocalories received can be explained by the optimum combination of the five predictor variables in the model. The unique contribution of each variable controlling for the other four predictors is displayed in Table 8. The average number of minutes that feedings were withheld explained 45.3% of the variance in the dependent variable within the context of the four other predictor variables.

Table 8

Multiple Regression Summary Table

Source	R^2	beta	sr^2	*df*	*F*	*p*
Overall	.705			5,53	25.35	< .001
Predictor Variables						
number of diarrhea episodes		.027	.001	1,53	.114	.736
number of emesis episodes		-.083	.007	1,53	-2.186	.279
gastric residual volume		-.086	.007	1,53	-2.246	.266
number of tube replacements		.057	.002	1,53	.429	.515
number of minutes feedings withheld		-.818	.453	1,53	-18.03	.001

Data showed that, as the mean number of minutes that feedings were held increased, the percent of required kilocalories received dramatically decreased. This is clinically significant in that feedings were withheld an average of 422 plus or minus 351 minutes per day during the study period. Feedings were interrupted during this period for more than 15 documented reasons. Primary reasons with this sample population included nursing care activities (33% of patients), extubation or airway management procedures (30%), nothing per os (NPO) for surgery (23%), elevated gastric residual volume (21%), and bedside procedures including central or radial arterial line placement (15%). Enteral feeding was charted as "held" when the head of the bed was lowered to a flat position. The data indicated that these feedings were withheld for as briefly as 15 minutes to as long as 2 hours when patients were bathed or when dressings or linens were changed.

Secondary Aim 1 was to determine the difference between kilocalories determined necessary by indirect calorimetry compared to HBE in those patients with indirect calorimetry measurements. The comparison between estimates of energy requirements was posed as a secondary aim of this study. In the subgroup of 25 patients from whom indirect calorimetry measurements were successfully obtained, mean measured REE was 1,638, *SD* = 465 kcal. The mean estimated REE in this subgroup was 2,126, *SD* = 300 kcal. A two-tailed, paired samples Students *t*-test revealed a statistically significant difference between mean measured REE and mean estimated REE in this subgroup of patients (95% CI 299-678, $p < .001$). The mean difference score was 488.8 kcals with a standard error of 91.906 and a *t* value of 5.318. Results are displayed in Table 9 and Figure 3.

Table 9

Paired Sample *T*-Test Measured Versus Estimated Resting Energy Expenditure

Resting Energy Expenditure (kcal)	*n*	Mean	*SD*	*t*	*p*
Measured	25	1,638	300	5.318	< .001
Estimated	25	2,126	465		

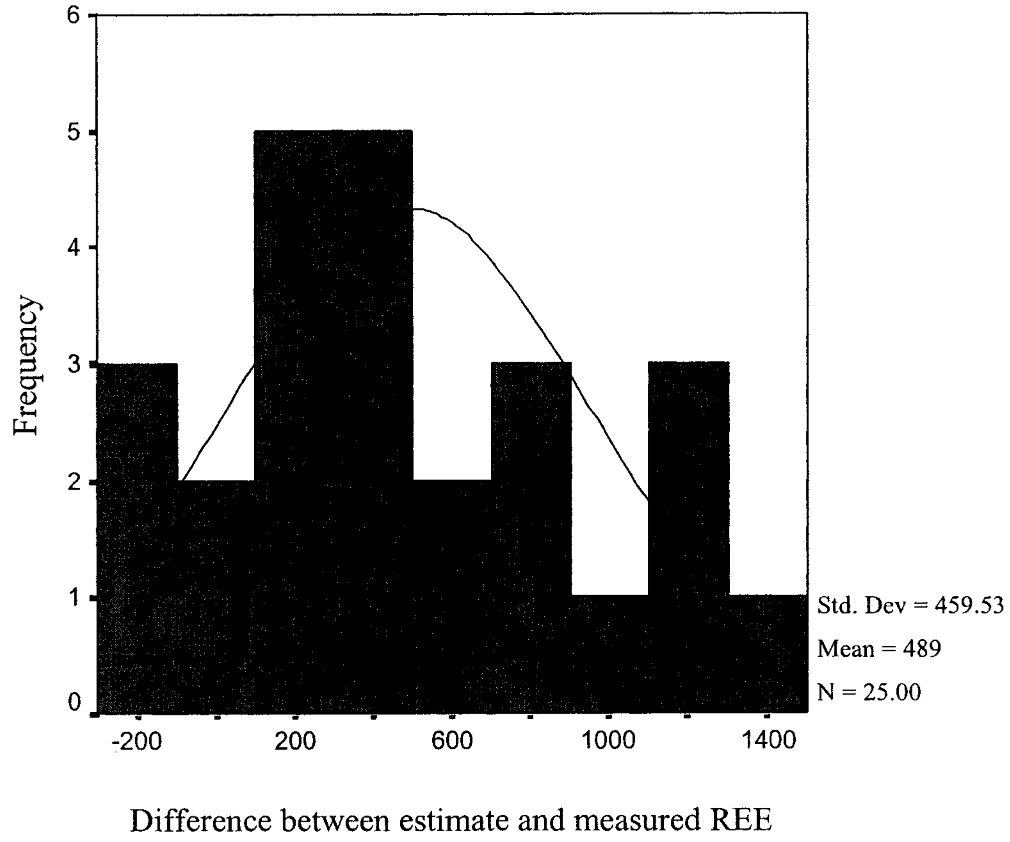

Figure 3: The histogram depicts the distribution of estimated REE minus measured REE for the subsample of patients with indirect calorimetry measurements.

Secondary Aim 2 was to determine the differences in demographic variables between patients able to be measured by indirect calorimetry and those who were not.

The logistics involved in managing indirect calorimetry measurements within the protocol requirements was the primary reason that measurements were not performed in 35 of the total 60 patients comprising the study sample. Over 58% of patients were unable to have indirect calorimetry performed. Reasons included unstable oxygen, technician unavailability, consent delays, and early removal from mechanical ventilation. Patients were categorized by whether or not indirect calorimetry was successfully completed. Group membership was selected as the independent variable and appropriate categorical variables were entered as dependent variables in a chi-square analysis. The categorical variables included gender, race, whether parenteral nutrition was received or surgery was performed, and the admitting diagnosis.

An independent sample Students *t*-test was used to determine differences in quantitative variables based upon group membership. The independent variable was group membership and selected quantitative variables (e.g., age, SAPS II, BMI, estimated REE, average kilocalories received, total days from feeding start to goal achievement, total residual volume, total dosage of opioids infused, and total number of minutes feedings were withheld) were entered as dependent variables. No significant differences were found between those patients measured by indirect calorimetry and those who were not. The categorical and quantitative variables are provided in Table 10.

Table 10

Chi-Square and *T*-Test Results

Variables	Patients measured by indirect calorimetry (n =25) (Mean / *SD*)	Patients not measured by indirect calorimetry (n = 35) (Mean / *SD*)	*p*
Categorical			
Gender			.304
Race			.351
Surgery			.452
Parenteral nutrition			.131
Admitting diagnosis			.142
Continuous			
Age (years)	64.5 / 12.0	63.4 / 13.6	.736
Simplified Acute Physiology Score II	36.7 / 14.1	37.3 / 9.6	.833
Body mass index	25.6 / 5.7	27.9 / 7.5	.190
Estimated resting energy expenditure (kcals)	2126 / 300	2167 / 331	.623
Average kilocalories received	1516 / 621	1335 / 800	.327
Total days from feeding start to goal	5.0 / 6.8	5.6 / 6.9	.732
Total residual volume (mls)	255 / 515	492 / 564	.099
Total dosage of narcotic infused (mcg/hr)	118 / 254	354 / 1026	.199
Total number of minutes feeding off	1023 / 856	1454 / 1170	.105

Summary of Results

The results indicate that enteral intake received was significantly less than requirements as determined by the HBE and stress factors. Thirty percent of patients received enteral nutrition within 10% of requirements, and 68.3% received less than 90% of requirements. There was no significant difference between enteral intake received and requirements as determined by indirect calorimetry. A statistically significant difference was observed between mean measured REE and mean estimated REE in the sample of 25 patients with indirect calorimetry measurements. There was no significant difference in the demographic variables between patients measured by indirect calorimetry and those who were not.

CHAPTER V

DISCUSSION

The purpose of this study was to examine the adequacy of enteral nutritional intake and the factors affecting its delivery in mechanically ventilated ICU patients. Sixty mechanically ventilated patients receiving enteral nutrition support were observed over a 3-day study period. Comparisons were made to determine whether patients received enteral nutrition in amounts matching requirements as determined by the HBE and indirect calorimetry, the latter whenever possible. The type and duration of all feeding interruptions during the study period were recorded.

Few nursing studies have examined the adequacy of enteral nutrition and the influence of factors related to feeding adequacy. This study was conducted to develop new nursing knowledge by determining whether mechanically ventilated patients in ICU settings receive adequate nutrition and what factors impact the adequacy of enteral intake. The research found that continuous enteral feeding infusions were interrupted multiple times, which resulted in inadequate intake in 68.3% of the patients under study. The relationship between enteral nutritional adequacy and GI factors, tube factors and ICU factors was examined as outlined in the conceptual model. Discussion of the study sample is presented, followed by the research findings, the study limitations, implications for nursing practice, and recommendations for future research.

The Study Sample

The study sample was comprised of 60 mechanically ventilated patients receiving enteral nutrition support at their feeding goal rate. Patients were enrolled in the research from two study sites. The majority of patients (*n* = 48) were enrolled from a Veterans

Affairs hospital in northern California. As a result, the majority of patients (86.7%) were male. The mean age of the sample was 63.9 years. A greater diversity was noted at the county hospital site (*n* = 12) with 50% being female patients and with a mean sample age of 56.7 years. BMI was included in order to classify patients according to nutritional status upon hospital admission. In general, anthropometric measures, including weight, are of limited use in determining nutritional status in critically ill patients. However, BMI has been used as an index of nutritional status in a variety of patients including the elderly (August et al., 2002; Saltzman et al., 2002). It has also been used as predictor of mortality in ICU patients with levels of 15 to 20 kg/m^2 associated with increased mortality (Engelman et al., 1999; Galanos et al., 1997). The mean BMI at hospital admission within the sample was 26.9 kg/m^2, *SD* = 6.9 with a range of 13.5 to 53.3 kg/m^2. The mean BMI was slightly above that considered normal weight, and the range reflects considerable variation. Although ICU mortality was not an outcome measure of this study, six (10%) of the patients under study were below 19 kg/m^2 and may have been at increased mortality risk. Sixteen (26%) of the patients had BMI greater than or equal to 30 kg/m^2, which is a BMI within the obesity range. Obesity has been associated with complications such as wound infection; however, it is not significantly related to mortality risk (Engelman et al., 1999; Galanos et al., 1997). In the current study, 19 (31%) of the total patient sample were within 19.1 to 25.2 kg/m^2, which is within the normal the normal weight range for BMI. There was no significant difference between the two study sites with regard to the BMI of the patients enrolled in the study.

The rationale for including the SAPS II as a variable in this study was primarily to rate illness severity of the patients in the sample. Patients with the greatest severity of illness require the most optimal nutritional support (McClave et al., 1998). The mean SAPS II upon admission in this study sample was 37, *SD* = 11 with a range between 18 and 65. This mean is lower than the mean SAPS IIs presented by Mentec and colleagues (2001). In their study, patients without GI complications had a mean SAPS II of 53 *SD* 16, and patients with GI complications had a mean score of 49, *SD* =16. Illness severity scoring systems have generally been used to predict mortality for large populations and are considered less useful for individual patients (Higgins, 2001). However, illness severity scoring systems allow clinical researchers the flexibility to categorize patients by severity of illness. There was no significant difference in SAPS IIs between patients from the Veterans Affairs hospital and the county hospital. The mean SAPS II of 37 indicated that illness severity was not elevated in this collective sample of mechanically ventilated ICU patients.

Critically ill surgical patients may experience delays in enteral feeding due to postoperative effects of anesthesia, ileus, or nausea (Montejo, 1999). In the total sample, 41.7% of the patients had surgery. The majority (52.1%) of patients at the Veterans Affairs hospital were surgical patients compared to only 16.7% at the county hospital. The majority (66.7%) of patients at the Veterans Affairs hospital received enteral nutrition by nasoduodenal methods versus 16.7% at the county hospital. Eighty-three percent of the patients at the county hospital received nasogastric feeding. Jejunal feeding was observed in five patients at the Veterans Affairs hospital and accounted for only 8.3% of the total sample under study. Enteral feeding into the stomach has been associated with decreased enteral intake in critically ill patients (Kearns et al., 2000). Although not examined as part of this research, inadequate intake is often related to delayed gastric emptying, high residual volume, and medications such as opioids and catecholamines (Mentec et al., 2001).

The Research Findings

Kilocalories Received

Use of the Harris-Benedict Equation

In the current study, the mean calorie intake for the study sample, according to the HBE, was 1,410 kcals compared to the mean estimated requirements of 2,150 kcals ($p < .001$). This is clinically important in that enteral nutrition received was significantly less than estimated requirements in this sample of mechanically ventilated ICU patients. Although requirements were based upon estimates using the HBE with stress factors and, as a result, may have overestimated requirements, the fact remains that, when using the most common method of calculating nutritional requirements (i.e., the HBE), enteral intake was significantly less than requirements. This finding confirms those reported by Stechmiller and colleagues (1994) that indicated that calories received compared to calories estimated by HBE was significantly less ($p = .001$) than requirements in the first 5 days of enteral feeding. Similar findings have been reported in other studies that used HBE to calculate requirements (Heyland et al., 1995; Makk et al., 1990). Inadequate enteral intake compared to requirements has also been found in studies that used other estimates to calculate requirements (Adam & Batson, 1997; Kemper et al., 1992; McClave, Sexton et al., 1999). In order to maximize the benefits of enteral support for mechanically ventilated ICU patients, the feeding must be prescribed and delivered in amounts that will improve nutritional status and avoid the complications associated with underfeeding and overfeeding (McClave, 1997). Inadequate nutritional intake puts patients at risk for complications related to malnutrition. As noted in previous research, complications may include respiratory muscle weakness and inefficient respiration resulting in increased minute ventilation and potential respiratory failure (McClave et al., 1998; Murciano et al., 1994).

Use of Indirect Calorimetry

In 25 of the patients (41.7%) in this study sample, REE was also measured by indirect calorimetry. These results indicated that the amount of enteral nutrition kilocalories received was not significantly different from the requirements determined by indirect calorimetry. This result conflicts with calculation of estimated needs when the HBE was used to determine nutritional requirements. One possibility for this result may be that the test was not adequately powered to reach statistical significance. A post hoc power analysis found that a sample of 207 patients would have been necessary for this test to reach statistical significance. From a clinical perspective, it seems that, for this group of patients, nutritional intake matched requirements as determined by indirect calorimetry.

In this sample of 25 patients whose REE was measured by indirect calorimetry, measured REE was 1,638, *SD* = 465 kcal with a range of 807 to 2414 kcals which reflects considerable variation. The mean 3-day intake was 1,516 kcals. Both means appear moderately low, and the difference between the two (i.e., 122 kcal) is relatively negligible. The clinical relevance of finding no significant difference between measured REE and mean enteral intake is difficult to determine. One quarter of the 25 patients had measured REE that was 1,218 kcals or less. These low measures may have skewed the mean measured REE to lower than expected. Response to critical illness can vary among patients, and some critically ill patients may have a hypometabolic response. This response is often viewed as abnormal and may signal a poor prognosis (McClave & Snider, 1994). Energy expenditure may be low as a result of advanced age or decreased fat-free mass (McClave & Snider, 1992). Medications, including sedatives, beta blockers, and anesthesia, lower energy expenditure (Weissman et al., 1984). Sepsis is also associated with a decrease in energy expenditure (McClave & Snider, 1994). Technical errors related to leaks, calibration problems, and unstable inspired oxygen levels are other possible reasons for low measures (McClave & Snider, 1992).

Critically ill patients demonstrate considerable variation in energy expenditure. One study showed that TEE may be as much as 10% lower to 23% higher than a single measured REE (Weissman, Kemper, Elwyn et al., 1986). To account for the variability in REE, researchers have endorsed the addition of 10% to 20% to the measured REE in determining energy requirements (Swinamer et al., 1987; Weissman et al., 1989). This practice is somewhat controversial and may lead to overfeeding (S. A. McClave, personal communication, May 24, 2002). A recent study evaluating indirect calorimetry and measures of steady state found that the addition of 10% above the measured REE was not necessary as long as criteria for steady state was met during the measurement (McClave et al., 2003).

Adequacy of Enteral Nutritional Intake

The exact amount of nutrition required to realize the benefits of enteral nutrition support is unknown (McClave, Sexton et al., 1999). Some clinicians have claimed that as little as 10 to 30 ml/hr, or "trickle feeds" are sufficient to maintain gut mucosal integrity. However, others have claimed that the benefits may be dose-dependent and that at least

50% to 60% of goal calories should be infused (McClave, Snider, & Ireton-Jones, 2002). Some clinicians advocate that at least 80% (DeBiasse & Wilmore, 1994) to 90% (Makk et al., 1990; McClave et al., 1998) of required nutrition must be received.

The reality is that many patients may not receive enteral nutrition in amounts adequate to meet body requirements. One of the most impressive findings in this study was that, according to HBE, 68.3% were underfed, 30% were adequately fed, and 1.7% was overfed. The findings are similar to other studies that examined enteral nutritional intake in critically ill patients (Kemper et al., 1992; McClave, Sexton et al., 1999; Stechmiller et al., 1994). Kemper et al. (1992) used indirect calorimetry plus 20% to determine requirements and found that 68% of mechanically ventilated, postoperative ICU patients who received enteral nutrition exclusively were underfed. This was attributed to slow advancement to goal rate, tube patency problems, slow gastric emptying, diarrhea, and delays for diagnostic tests. Patients who received parenteral nutrition, or a combination of enteral and parenteral support, received an average of 80% of requirements.

In a study conducted by Stechmiller and colleagues (1994), 80% of 52 mechanically ventilated, enterally fed neurosurgery and neurotrauma patients were underfed within the first 8 days following start of the feeding. As in the present study, the HBE was used to calculate energy requirements. It was not stated whether additional stress factors were applied. Stechmiller and colleagues found slow advancement to goal rate and multiple interruptions to be the major issues that limited intake. Thirteen (77%) patients did not meet their prescribed goal rate in the first 8 days. These researchers stated that, after day 12, enteral intake was "more stable" in these patients (p.236). Forty-one percent of the patients reached goal rate on at least 1 day. However, 59% of patients did not reach their prescribed goal rate during the entire study period. This is similar to another study of neurosurgical patients (*N* = 20) in which calorie intake was less than required, and patients did not reach enteral goal rate during the entire 10-day study period (Day et al., 2001). Slow advancement to goal rate due to GI intolerance is a common problem in critical care patients with neurological injuries (Norton et al., 1988; Rapp et al., 1983). In the current study, advancement to goal rate from start of feeding took an average of 6 days for patients at the Veterans Affairs hospital versus 2.8 days for the study group in the county hospital. Advancement to goal rate may have taken longer at the Veterans Affairs hospital because of the preference for nasoduodenal tube placement and the increased number of surgical patients. In both the Kemper et al. (1992) and Stechmiller et al. (1994) studies, data collection began upon the initiation of enteral feeding. Failure to reach goal rate, therefore, impacted the adequacy of enteral intake. This is in contrast to the current study in which data collection began when the enteral goal rate was achieved. From a methodological standpoint, this eliminated slow advancement as a confounding factor potentially impacting adequate intake; yet, 68% of the patient sample may have been underfed.

As in the current study, Stechmiller and colleagues (1994) also included propofol calories as a source of energy. However, it was not stated whether any patients were overfed as a result of propofol infusion. It is important to account for propofol calories in order to avoid complications related to overfeeding. Stechmiller did not state whether any patients received more than their required calories. Although the number of patients receiving propofol was not stated, it is possible that more patients would have been underfed if propofol had been excluded in the medical management protocol.

In the present study, 38.3% of the patients received less than 50% of their required kilocalories according to the HBE calculation. Over 16% of the patients received less than 30% of required kilocalories during the study period. The 3-day study period provided a brief snapshot of caloric intake in a sample of patients who had reached their enteral goal rate. These findings are clinically significant in that, even for a 3-day period, calorie intake was insufficient. Patients were thus rendered vulnerable to the risks associated with underfeeding. The present study was unique in that calories were determined using both indirect calorimetry and the HBE with additional stress factors. In the Kemper et al. (1992) study, indirect calorimetry was used exclusively to determine caloric requirements. The enterally fed patients received a mean of 1,227 ± 605 kcals. The mean measured REE was 1,864, *SD* = 282 kcals which included REE plus an additional 20%. Patients received 68% of calories based upon this value. The mean measured REE without the additional 20% was 1,553, *SD* = 235 kcals. The patients received 81% of calories when compared to this requirement. This showed that the additional calories (20%) that were added to the measured requirements made a difference in the results obtained. In the Stechmiller et al. (1994) study, calorie needs were based solely upon the HBE with no stress factors addressed in the documentation. The means and standard deviations were not explicitly stated, and the data were presented in graph form. The Kemper et al. and Stechmiller et al. studies used different methods to determine energy requirements. However, as in the current study, results indicated that enterally fed patients receive significantly less calories than required, regardless of the method used to determine requirements.

Influence of Specific Variables

Variables or predictors known to impact the adequacy of enteral nutrition received were derived from a review of the literature. The results indicated that the number of minutes feedings were withheld explained 45.3% of the variance in the dependent variable within the context of the four other predictor variables. A significant inverse correlation coefficient of -.830 revealed that, as the number of minutes feedings were withheld increased, the percentage of required calories received decreased. It is not particularly surprising that the length of time enteral feedings were withheld significantly decreased the amount of required kilocalories received. Frequent feeding interruption leading to inadequate intake has been found in other studies (Adam & Batson, 1997; Heyland et al., 1995; McClave, Sexton et al., 1999; Montejo, 1999; Stechmiller et al., 1994). The reasons for feeding interruption are similar, but vary somewhat across studies. In this current study, feedings were withheld an average of 7 hours per day during the study period, and several reasons for feeding interruption were observed in the medical record. For 33% of the patients, interruptions occurred as a result of nursing care activities. Although not an entirely universal practice, feedings were held when patients were bathed or when dressings or linens were changed. Enteral feeding was turned off when the patient was placed in a flat position, presumably to prevent pulmonary aspiration of enteral feeding. This finding was similar to that documented in the study conducted by McClave, Sexton, and colleagues (1999) in which feeding interruption due to nursing care occurred in 30% of the patient sample.

Pulmonary aspiration of gastric contents is a serious potential complication in enterally fed critically ill patients. Prevalence rates vary due to the variation in definitions of aspiration but are reported to be between 0% and 40% (Lazarus, Murphy, & Culpepper, 1990). In one study, mortality rates related to aspiration of enteral tube feeding varied between 1% and 33% (Mullan, Roubenoff, & Roubenoff, 1992). A great deal of nursing effort is aimed at preventing aspiration. Risk factors are many and include decreased level of consciousness, supine position, tracheal intubation, and advanced age (Metheny, 2002). Studies have shown that maintaining a semirecumbent position and preventing excessive periods of time in the supine position can limit the risk of aspiration and regurgitation (Ibanez et al., 1992; Orozco-Levi et al., 1995; Torres et al., 1992). Nursing recommendations support maintaining the patient in a semirecumbent position. It has also been suggested that enteral feedings be withheld whenever the patient is placed in the supine position for "long periods of time" (Davis, Arrington, Fields-Ryan, & Ortiz, 1995). Some clinicians have also recommended discontinuing enteral feeding for approximately 30 to 60 minutes prior to procedures that require the patient to be in a flat position (Bernard & Forlaw, 1984). However, no research-based data were found to support these recommendations. In the ICU, there are many situations that require the patient to be placed in a supine position, sometimes several times in a day (Metheny, 2002). It is impractical to turn feedings off each time the patient is placed in a supine position for brief periods. Although the supine position is known to increase risk for aspiration, it is doubtful whether turning the feeding off immediately prior to placing the patient flat prevents any clinically significant aspiration (Kirkland, 1999). Such practice may have a negative impact on the adequacy of enteral intake if it occurs often enough and long enough to limit adequate feeding.

Feeding interruption was related to gastric residual volume in 21.7% of the patient sample in this current study. Elevated residual volume and GI intolerance have been identified as factors related to inadequate intake in enterally fed critically ill patients (Adam & Batson, 1997; Heyland et al., 1995; McClave, Sexton et al., 1999; Mentec et al., 2001; Montejo, 1999). Elevated residual volumes are imprecise in monitoring for delayed gastric emptying and risk for aspiration. In this study, gastric residual volumes were aspirated approximately every 4 hours. Feedings were held based on volumes as ordered by the physician and ranged from 50 to 100 mls. Few studies have evaluated the relationship of gastric residual volume and risk of aspiration of gastric contents. One clinical study found that 200 mls was a more realistic volume to be used for cessation of feeding in patients fed into the stomach (McClave et al., 1992). Considerable controversy and variation in practice exists with regard to what volume represents a clinically relevant risk for aspiration. Given that gastric residual volume is a primary factor leading to enteral feeding interruption, continued clinical research is needed to minimize the negative impact on nutritional adequacy.

Practice patterns related to the delivery of enteral nutrition must be examined and evaluated using an evidence-based approach. Future recommendations may include the use of strict enteral protocols or determining hourly infusion rates based upon 20 hours instead of 24 hours to account for feeding interruptions (McClave, Sexton et al., 1999; Spain et al., 1999). As identified in this research study, it is important to explore variations in clinical practice and their relationship to outcomes. It is also incumbent upon health care providers to examine practice and implement evidence based procedures to ensure optimal results in patients receiving nutrition support.

Comparison of the Harris-Benedict Equation and Indirect Calorimetry Measurement

There was a significant difference between the HBE and the mean measured REE in the 25 patients measured by both HBE and indirect calorimetry in this study. The HBE overestimated caloric requirements by an average of approximately 488 kcals. This finding highlights the difference between estimates and measurement of energy expenditure. Several methods are used to determine energy expenditure in practice—measurement by indirect calorimetry, measurement by the Fick method, and estimates via the application of predictive equations such as HBE. Some researchers have compared predictive equations, such as the HBE, with indirect calorimetry in critically ill patients (Amato, Keating, Quercia, & Karbonic, 1995; Makk et al., 1990). Findings from the current study are similar to others that found the HBE with stress factors overestimated requirements when compared to indirect calorimetry (Makk et al., 1990; Mann, Westenskow, & Houtchens, 1985).

Although indirect calorimetry has been recognized as the "gold standard" for measurement of energy requirements, some studies have indicated that estimates using HBE may be suitable in some populations of critically ill patients (Donaldson-Andersen & Fitzsimmons, 1998; Hunter et al., 1988; Ireton-Jones & Jones, 2002; Swinamer et al., 1990; van Lanschot, Feenstra, Vermeij, & Bruining, 1986). Other equations that have been developed specifically from critically ill patient populations may be appropriate in the ICU. The Ireton-Jones equation was developed in patients receiving nutrition support. The equation accounts for diagnosis, presence of obesity, and ventilatory status in addition to age, gender, height, and weight. The Ireton-Jones equations are based on measured energy expenditure and have been closely correlated (r = .69) to measurement by indirect calorimetry (Ireton-Jones & Jones, 2002). Given the expense and accuracy limitations of indirect calorimetry, it has been recommended that appropriate estimates, coupled with close follow up of nutritional status, may represent a reasonable alternative (Campbell & Kudsk, 1988). Controversy continues between the use of indirect calorimetry and the use of predictive equations. Indirect calorimetry is labor intensive, expensive, and not available in all hospitals. Trained personnel are required for the measurement, and testing conditions must be stringently monitored to maintain accuracy (McCarthy, 2000).

Despite the known limitations, the accuracy provided by indirect calorimetry is extremely important for severely critically ill patients. Energy expenditure varies widely in these patients and, as a result, they require the most accurate nutrition assessment possible because they are unable to tolerate overfeeding and underfeeding (McClave, 1997; McClave et al., 1998). The benefit of indirect calorimetry is that it analyzes gas exchange and provides a real-time assessment of energy expenditure that can be used to guide nutritional requirements. Predictive equations with additional stress factors cannot account for the dynamic changes that occur during critical illness. Routine patients, or those who are less critically ill, can potentially tolerate calorie requirements based upon estimates; however, the most accurate technology is strongly preferred for the critically ill (McClave et al., 2002). New technology is currently being developed that may be more accessible and easier and less expensive to use. Critical care monitors with the capability to monitor oxygen consumption and energy expenditure are becoming available along with handheld calorimeters that can be used at the bedside (McClave et al., 2002). Regardless of the method used to assess energy requirements, the general consensus among clinicians is that the importance of monitoring the amount of nutrition support received cannot be overstated. The accuracy of determining energy needs is indeed meaningful; however, it will only help the patient if the required calories are actually given (Fung, 2000; Ireton-Jones, 2002).

Comparison of the HBE and indirect calorimetry was not a primary aim of this study. However, the findings indicated that the HBE with stress factors overestimated requirements by as much as 488 kcals on average. This finding poses questions about the validity of the methods used to determine nutritional requirements. If findings from HBE estimates were accurate, 68% of patients received less than 90% of requirements, and some patients received less than 50% and less than 30% of requirements. It is unknown whether overestimation of requirements by HBE resulted in overfeeding in this sample. Energy requirements can be determined from indirect calorimetry or estimates. These should be used only as guides and cannot replace the clinical judgment required to manage patients from acute illness to recovery. It is essential to monitor the adequacy of intake and whether the patient is meeting their individualized nutrition goals (Ireton-Jones, 2002). Further research should be conducted to determine accuracy rates between HBE and indirect calorimetry measurements and identify patient or ICU environment-related factors that influence accuracy.

Analysis of Subsamples

No significant differences were found in the demographics of indirect calorimetry patients and non—indirect calorimetry patients. An unknown element of systematic error may have been present which affected these results. There may have been a physiological reason why 35 patients were unable to be measured, and some of those reasons may have influenced the measurement accuracy as well as differences in results from the two methods of measuring requirements. For example, the 35 patients may or may not have been hypermetabolic but were unable to meet criteria for measurement by indirect calorimetry. Failure to account for these patients may have skewed the results. Theoretically, measurement via indirect calorimetry may not be possible in patients with greater illness severity because they may have clinical conditions outside the parameters for accurate measurement. Critically ill patients may be agitated, or have high oxygen or positive-end expiratory-pressure requirements, or they may require ventilatory modes that do not allow for accurate gas analysis (McClave & Snider, 1992). Differences in illness severity were considered as a possible reason why one group of patients could be measured via indirect calorimetry and the other was not. However, the admission SAPS II was not significantly different between the groups. Further analysis of other clinical and physiological variables may further emphasize differences between these two groups.

In this study, the main reasons for failure to obtain indirect calorimetry measurements were related to (a) the logistics in arranging for the measurement to be performed within the parameters outlined in the study protocol, and (b) unstable sources of inspired oxygen. As the technology for indirect calorimetry becomes more advanced, it may also become easier for nurses and other clinicians to monitor energy expenditure at the bedside. In this way, more patients may have access to this technology and benefit from more accurate measurement of energy requirements.

Limitations of the Study

Indirect calorimetry was initially proposed as the method by which calorie requirements would be based for this study. In the subgroup of 25 patients measured by indirect calorimetry, comparison between calories estimated by the HBE and calories measured by indirect calorimetry showed that, on average, the HBE with stress factors generally overestimated requirements. This study found that patients received significantly fewer ($p < .001$) calories than requirements estimated by the HBE. Given that indirect calorimetry is generally more accurate than estimates, the fact that calorie requirements were determined via application of the HBE may have limited the findings of this study. Although the findings from this study highlight the issues related to nutritional adequacy in ICU patients, it is difficult to draw clear conclusions from the results due to the discrepancy between measured and estimated requirements. The true requirements are not known definitively, and the subsequent percentage of calories received compared to required is difficult to determine. Results are similar to other studies that showed inadequate enteral intake compared to HBE estimates (Heyland et al., 1995; Stechmiller et al., 1994). No other studies have been found that used both HBE estimates and indirect calorimetry measurements. Future research is needed to clarify the accuracy of methods used to determine requirements. Regardless of the method used, enteral feedings were interrupted frequently and for prolonged periods in this study. It is therefore reasonable to presume that actual enteral intake was less than adequate in this sample. This study calls attention to the factors that may or may not be avoided in the delivery of enteral nutrition in mechanically ventilated ICU patients.

Additional limitations were daily enteral intake data were collected from the medical records, specifically the intake and output records. The inaccuracy of these data may have posed an additional limitation. Although staff nurses were educated on the charting requirements prior to and throughout the study, the true accuracy of the enteral intake information is unknown. Also, one investigator collected all data. Consequently, investigator bias may have influenced the study results.

Twenty patients were measured via indirect calorimetry at the Veterans Affairs hospital site and five at the county hospital. The same brand and model of metabolic cart was used at both sites, and efforts were made to ensure that the indirect calorimetry measurements were taken using identical techniques at each site. Urine collection for nitrogen is generally performed on the day of indirect calorimetry measurement as a means to evaluate substrate use and RQ (McCarthy, 2000; McClave & Snider, 1992). This study did not include such collection as part of the protocol, nor was measurement of RQ included in the data collection protocol. This was a limitation of the study in that measurement of RQ is often used to validate the accuracy of indirect calorimetry results (McClave & Snider, 1992). The protocol also did not include interpretation of the indirect calorimetry data by a physician or dietitian. This would have helped to further validate the measurements (Porter & Cohen, 1996).

This study used a prospective descriptive design and provided an account of either group or situational characteristics. Although this design has greater internal and external validity than a retrospective study, it does not establish sequence of events or inference to causation. A 3-day study period was selected to allow for adequate data collection and to minimize loss of patients. The study findings suggest that critically ill patients may not be adequately nourished and may be vulnerable to complications associated with malnutrition. However, the study cannot show a clear relationship between the nutritional intake over 3 days and the subsequent development of malnutrition. Therefore, this research is limited in that it highlights the nutritional outcome of the adequacy of enteral intake while it does not show a relationship to clinical outcomes such as ICU mortality, infectious morbidity, or other serious complications.

Implications and Recommendations

Daily monitoring of nutritional intake is an important aspect of the care management of mechanically ventilated ICU patients. It is a key element in preventing problems associated with underfeeding and overfeeding. This study demonstrated that enteral nutritional intake was significantly less than requirements, as determined by the HBE. It also highlighted some of the factors influencing the adequacy of enteral intake in mechanically ventilated ICU patients. However, findings generated questions about the relative accuracy of and differences between two common methods of estimating nutritional requirements that warrant further study.

Critical care practitioners must take a multidisciplinary approach in evaluating the effects of practice on nutritional outcomes. As noted by Flynn, Norton, and Fischer (1987), nutrition is often ignored in critical care because no single group of care providers has assumed responsibility for this aspect of patient care. Nursing may need to take the lead in exploring practice issues that promote improved nutritional outcomes in critically ill patients. Stechmiller (1994) stated the following similar viewpoint:

> It is within the scope of critical care nursing practice to calculate caloric requirements and analyze daily caloric delivery, advocate for early nutrition and minimize feeding interruptions through careful patient assessment and interruption analysis. Critical care nurses can assume this responsibility in collaboration with physicians and other health care professionals and can positively impact the outcome of patients with neurosurgical injury by promoting nutritional support. (p. 228)

This statement holds true for all clinicians who work to provide quality care for critically ill and injured patients. The nursing community must respond to this call and continue to develop research-based strategies related to enteral nutrition.

Nurse researchers have been involved with the science of nutrition support since its inception in the late 1960s. Nurse scientists published over 100 nutrition-related articles in the late 1970s and early 1980s (Moore, Guenter, & Bender, 1986). Although enteral nutrition support is primarily a medical treatment, the monitoring and delivery of this therapy is largely a function of nursing. Early research observed patient responses to parenteral and enteral nutrition support. Considerable progress has been made in this field as a result of advances in technology, and nurses continue to play a large role in contributing to the science of nutrition support (Heitkemper & Jarret, 1997).

Future research will continue to be framed around individual response to nutrition support and the study of factors that place patients at risk for complications. It will be important to examine the role and efficacy of nutrition support in particular disease states to enable generalization of findings to specific populations. It is also important to address the accuracy and utility of methods used to determine nutritional requirements in the clinical setting. Studies will be needed that look beyond to a wide variety of age groups and settings—from intensive care to home care. Future outcome studies could also include examination of such indicators as functional status and quality of life

(Heitkemper & Jarret, 1997). Nutrition support is a key component in the effective management of mechanically ventilated ICU patients. For these patients in particular, the goals of nutrition support are to provide nutrition that is adequate for individual requirements, avoid complications associated with its delivery, and improve clinical outcomes. Future research must continue to be framed from these scientific perspectives. It is important to further clarify the factors that influence nutritional adequacy. Once this is sufficiently accomplished, it will be necessary to establish the efficacy of nutrition support on outcomes including wound healing, immune function, functional status, and quality of life beyond the ICU.

References

Ackerman, M. H., Evans, N. J., & Ecklund, M. M. (1994). Systemic inflammatory response syndrome, sepsis, and nutritional support. *Critical Care Nursing Clinics of North America, 6*, 321-340.

Adam, S., & Batson, S. (1997). A study of problems associated with the delivery of enteral feed in critically ill patients in five ICUs in the UK. *Intensive Care Medicine, 23*, 261-266.

Amato, P., Keating, K. P., Quercia, R. A., & Karbonic, J. (1995). Formulaic methods of estimating calorie requirements in mechanically ventilated obese patients: A reappraisal. *Nutrition in Clinical Practice, 10*(6), 229-232.

Arora, N. S., & Rochester, D. F. (1982a). Effect of body weight and muscularity on human diaphragm muscle mass, thickness, and area. *Journal of Applied Physiology, 52*(1), 64-70.

Arora, N. S., & Rochester, D. F. (1982b). Respiratory muscle strength and maximal voluntary ventilation in undernourished patients. *American Review of Respiratory Disease, 126*, 5-8.

August, D., Teitelbaum, D., Albina, J., Guenter, P., Heitkemper, M., Ireton-Jones, C., et al. (2002). Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *Journal of Parenteral and Enteral Nutrition, 26*(1), 1SA-137SA.

Bartlett, R. H., Dechert, R. E., Mault, J. R., Ferguson, S. K., Kaiser, A. M., & Erlandson, E. E. (1982). Measurement of metabolism in multiple organ failure. *Surgery, 92*(4), 771-779.

Barton, R. G. (1994). Nutrition support in critical illness. *Nutrition in Clinical Practice, 9*(4), 127-139.

Bassili, H. R., & Deitel, M. (1981). Effect of nutritional support on weaning patients off mechanical ventilators. *Journal of Parenteral and Enteral Nutrition, 5*(2), 161-163.

Bernard, M., & Forlaw, L. (1984). Complications and their prevention In J. Rombeau & M. Caldwell (Eds.), *Clinical nutrition: Enteral and tube feeding.* (p. 534). Philadelphia: W. B. Saunders.

Bosscha, K., Nieuwenhuij, V. B., Vos, A., Samsom, M., Roelofs, J. M. M., & Akkermans, L. M. A. (1998). Gastrointestinal motility and gastric tube feeding in mechanically ventilated patients. *Critical Care Medicine, 26*(9), 1510-1517.

Brandi, L. S., Grana, M., Mazzanti, T., Giunta, F., Natali, A., & Ferrannini, E. (1992). Energy expenditure and gas exchange measurements in postoperative patients: thermodilution versus indirect calorimetry. *Critical Care Medicine, 20*(9), 1273-1283.

Branson, R. D., Hurst, J. M., Warner, B. W., Bower, R. H., & Arita, A. (1987). Measured versus predicted energy expenditure in mechanically ventilated patients with chronic obstructive pulmonary disease. *Respiratory Care, 32*(9), 748-752.

Branson, R. D., Lacy, J., & Berry, S. (1995). Indirect calorimetry In R. Levine & R. Fromme (Eds.), *Critical care monitoring.* (pp. 379-400). St. Louis, MO: Mosby.

Braun, N. M., Arora, N. S., & Rochester, D. F. (1983). Respiratory muscle and pulmonary function in polymyositis and other proximal myopathies. *Thorax, 38,* 616-623.

Braunschweig, C. L., Levy, P., Sheean, P. M., & Wang, X. (2001). Enteral compared with parenteral nutrition: A meta-analysis. *American Journal of Clinical Nutrition, 74*(4), 534-542.

Briggs, D. (1996). Nasogastric feeding practice in intensive care units: a study. *Nursing Standard, 10*(49), 42-45.

Buckley, S., & Kudsk, K. A. (1994). Metabolic response to critical illness and injury. *AACN Clinical Issues, 5*(4), 443-449.

Cahill, G. F. (1998). Survival in starvation. *American Journal of Clinical Nutrition, 68*, 1-2.

Campbell, R. S., Branson, R. D., Burke, W., & Covington, J. (1994). AARC clinical practice guideline: Metabolic measurement using indirect calorimetry during mechanical ventilation. *Respiratory Care, 39*(12), 1170-1175.

Campbell, S. M., & Kudsk, K. A. (1988). "High tech" metabolic measurements: Useful in daily clinical practice? *Journal of Parenteral and Enteral Nutrition, 12*(6), 610-612.

Castella, X., Artigas, A., Bion, J., & Kari, A. (1995). A comparison of severity of illness scoring systems for intensive care unit patients: Results of a multicenter, multinational study. *Critical Care Medicine, 23*(8), 1327-1335.

Cerra, F. B. (1987). Hypermetabolism, organ failure, and metabolic support. *Surgery, 101*(1), 1-14.

Cerra, F. B., Benitez, M. R., Blackburn, G. L., Irwin, R. S., Jeejeebhoy, K., Katz, D. P., et al. (1997). Applied nutrition in ICU patients: A consensus statement of the American College of Chest Physicians. *Chest, 111*(3), 769-778.

Chima, C. S., Barco, K., Dewitt, M. L. A., Maeda, M., Teran, J. C., & Mullen, K. (1997). Relationship of nutritional status to length of stay, hospital costs, and discharge status of patients hospitalized in the medicine service. *Journal of the American Dietetic Association, 97*(9), 975-978.

Chiolero, R., Mavrocordatos, P., Bracco, D., Schutz, Y., Cayeux, C., & Revelly, J. P. (1994). O2 consumption by the Fick method: Methodologic factors. *American Journal of Respiratory Care, 149*, 1118-1122.

Cohen, I. L., & Booth, F. V. (1994). Cost containment and mechanical ventilation in the United States. *New Horizons, 2*(3), 283-290.

Cunningham, K. F., Aeberhardt, L. E., Wiggs, B. R., & Phang, P. T. (1994). Appropriate interpretation of indirect calorimetry for determining energy expenditure of patients in intensive care units. *American Journal of Surgery, 167*, 547-549.

Cuthbertson, D. P. (1942). Post-shock metabolic response. *The Lancet, 1*, 433-437.

Daley, B. J., & Bistrian, B. R. (1994). Nutritional assessment. In G. Zaloga (Ed.), *Nutrition in critical care* (pp. 9-33). St. Louis, MO: Mosby-Year Book.

Daly, J. M., Heymsfield, S. B., Bell, S., Philstrom, J. B., Klein, G., Gottschlich, M., et al. (1993). Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *Journal of Parenteral and Enteral Nutrition, 17*(Suppl. 4), 5SA-28SA.

Daly, J. M., Heymsfield, S. B., Head, C. A., Harvey, L., Nixon, D. W., Katzeff, H., et al. (1985). Human energy requirements: Overestimation by widely used prediction equation. *American Journal of Clinical Nutrition, 42*, 1170-1174.

Davis, A. E., Arrington, K., Fields-Ryan, S., & Ortiz, J. (1995). Preventing feeding associated aspiration. *Medsurg Nursing, 4*(2), 111-119.

Day, L., Stotts, N. A., Frankfurt, A., Stralovich-Romani, A., Volz, M., Muswases, M., Fukuoka, Y., & O'Leary-Kelley, C. (2001). Gastric versus duodenal feeding in patients with neurological disease: A pilot study. *Journal of Neuroscience Nursing, 33*(3), 148-159.

DeBiasse, M. A., & Wilmore, D. W. (1994). What is optimal nutrition support? *New Horizons, 2*(2), 122-130.

De Jonghe, B., Appere-De-Vechi, C., Fournier, M., Tran, B., Merrer, J., Melchior, J. C., & Outin, H. (2001). A prospective survey of nutritional support practices in intensive care unit patients: what is prescribed? What is delivered? *Critical Care Medicine, 29*(1), 8-12.

Doekel, R. C., Zwillich, C. W., Scoggin, C. H., Kryger, M., & Weil, J. V. (1976). Clinical semi-starvation: Depression of hypoxic ventilatory response. *New England Journal of Medicine, 295*(7), 358-361.

Donaldson-Andersen, J., & Fitzsimmons, L. (1998). Metabolic requirements of the critically ill, mechanically ventilated trauma patient: Measured versus predicted energy expenditure. *Nutrition in Clinical Practice, 13*(1), 25-31.

Driver, A. G., & LeBrun, M. (1980). Iatrogenic malnutrition in patients receiving ventilatory support. *Journal of the American Medical Association, 244*(19), 2195-2196.

Efthimiou, J., Fleming, J., Gomes, C., & Spiro, S. G. (1988). The effect of supplementary oral nutrition in poorly nourished patients with chronic obstructive pulmonary disease. *American Review of Respiratory Disease, 137*, 1075-1082.

Engelman, D. T., Adams, D. H., Byrne, J. G., Aranki, S. F., Collins, J. J., Coupe, G. S., et al. (1999). Impact of body mass index and albumin on morbidity and mortality after cardiac surgery. J*ournal of Thoracic Cardiovascular Surgery, 118*(5), 866-873.

Flancbaum, L., Choban, P. S., Sambucco, S., Verducci, J., & Burge, J. C. (1999). Comparison of indirect calorimetry, the Fick method, and prediction equations in estimating energy requirements of critically ill patients. *American Journal of Clinical Nutrition, 69*, 461-466.

Flynn, K., Norton, L., & Fisher, R. (1987). Enteral tube feeding: Indications, practices and outcomes. *IMAGE: Journal of Nursing Scholarship, 19*(1), 16-19.

Foster, G. D., Knox, L. S., Dempsey, D. T., & Mullen, J. L. (1987). Caloric requirements in total parenteral nutrition. *Journal of the American College of Nutrition, 6*(3), 231-253.

Frankenfield, D. C., Muth, E. R., & Rowe, W. A. (1998). The Harris-Benedict studies of human basal metabolism: History and limitations. *Journal of the American Dietetic Association, 98*, 439-445.

Frankenfield, D. C., Sarson, Y. G., Blosser, S. A., Cooney, R. N., & Smith, J. S. (1996). Validation of a 5-minute steady state indirect calorimetry protocol for resting energy expenditure in critically ill patients. *Journal of the American College of Nutrition, 15*(4), 397-402.

Fuerer, I., & Mullen, J. L. (1986). Bedside measurement of resting energy expenditure and respiratory quotient via indirect calorimetry. *Nutrition in Clinical Practice, 1*(1), 43-49.

Fuhrman, M. P. (1999). Diarrhea and tube feeding. *Nutrition in Clinical Practice, 14*(2), 83-84.

Fung, E. B. (2000). Estimating energy expenditure in critically ill adults and children. *AACN Clinical Issues, 11*(4), 480-497.

Galanos, A. N., Pieper, C. F., Kussin, P. S., Winchell, M. T., Fulkerson, W. J., Harrell, F. E., et al. (1997). Relationship of body mass index to subsequent mortality among seriously ill hospitalized patients. *Critical Care Medicine, 25*(12), 1962-1968.

Giner, M., Laviano, A., Meguid, M. M., & Gleason, J. R. (1996). In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. *Nutrition, 12*(1), 23-29.

Grant, J. P. (1994). Nutrition care of patients with acute and chronic respiratory failure. *Nutrition in Clinical Practice, 9*(1), 11-17.

Guenst, J. M., & Nelson, L. D. (1994). Predictors of total parenteral nutrition-induced lipogenesis. *Chest, 105*(2), 553-559.

Harris, J. A., & Benedict, F. (1919). *Standard basal metabolism constants for physiologists and clinicians: A biometric study of basal metabolism in man.* Philadelphia: J. B. Lippincott.

Heitkemper, M., & Jarret, M. (1997). Research issues in nutrition support. *Nursing Clinics of North America, 32*(4), 755-768.

Herrmann, V. M. (1995). Nutritional assessment. In M. H. Torosian (Ed.), *Nutrition for the hospitalized patient* (pp. 233-253). New York: Marcel Dekker.

Heyland, D., Cook, D. J., Winder, B., Brylowski, L., Van deMark, H., & Guyatt, G. (1995). Enteral nutrition in the critically ill patient: A prospective survey. *Critical Care Medicine, 23*(6), 1055-1060.

Heyland, D. K. (1998). Nutritional support of the critically ill patient: A critical review of the evidence. *Critical Care Clinics, 14*(3), 423-440.

Higgins, T. L. (2001). Daily versus admission mortality estimates: Is admission severity yesterday's news? *Critical Care Medicine, 29*(1), 208-210.

Hunter, D. C., Jaksic, T., Lewis, D., Benotti, P. N., Blackburn, G. L., & Bistrian, B. R. (1988). Resting energy expenditure in the critically ill: Estimations versus measurement. *British Journal of Surgery, 75*, 875-878.

Ibanez, J., Penafiel, A., Raurich, J. M., Marse, P., Jorda, R., & Mata, F. (1992). Gastroesophageal reflux in intubated patients receiving enteral nutrition: Effect of supine and semirecumbent positions. *Journal of Parenteral and Enteral Nutrition, 16*(5), 419-422.

Ireton-Jones, C., & Jones, J. D. (2002). Improved equations for predicting energy expenditure in patients: The Ireton-Jones equations. *Nutrition in Clinical Practice, 17*(1), 29-31.

Ireton-Jones, C. S. (Ed.). (2002). Estimating energy requirements. In S. Shikora, R. Martindale, & S. Schwaitzberg (Eds.). *Nutritional considerations in the intensive care unit: Science, rationale, and practice* (pp. 31-37). Dubuque, IA: Kendall/Hunt.

Ireton-Jones, C. S., Turner, W. W., Liepa, G. U., & Baxter, C. R. (1992). Equations for the estimation of energy expenditure in patients with burns with special reference to ventilatory status. *Journal of Burn Care and Rehabilitation, 13*(3), 330-333.

Isbell, T. R., Klesges, R. C., Meyers, A. W., & Klesges, L. M. (1991). Measurement reliability and reactivity using repeated measurements of resting energy expenditure with a face mask, mouthpiece, and ventilated canopy. *Journal of Parenteral and Enteral Nutrition, 15*(2), 165-168.

Johnson, M. M., Chin, R., & Haponik, E. F. (Eds.). (1999). *Nutrition, respiratory function,and disease* (9th ed.). Baltimore: Williams & Wilkins.

Kay, S. P., Moreland, J. R., & Schmitter, E. (1987). Nutritional status and wound healing in lower extremity amputation. *Clinical Orthopedics, 217*, 253-256.

Kearns, P. J., Chin, D., Meuller, L., Wallace, K., Jensen, W. A., & Kirsch, C. M. (2000). The incidence of ventilator-associated pneumonia and success in nutrient delivery with gastric versus small intestinal feeding: A randomized clinical trial. *Critical Care Medicine, 28*(6), 1742-1746.

Kelly, S. M., Rosa, A., Field, S., Coughlin, M., Shizgal, H. M., & Macklem, P. T. (1984). Inspiratory muscle strength and body composition in patients receiving total parenteral nutrition therapy. *American Review of Respiratory Disease, 130*, 33-37.

Kelsen, S. G., Ference, M., & Kapoor, S. (1985). Effects of prolonged undernutrition on structure and function of the diaphragm. *Journal of Applied Physiology, 58*(4), 1354-1359.

Kemper, M., Weissman, C., & Hyman, A. I. (1992). Caloric requirements and supply in critically ill surgical patients. *Critical Care Medicine, 20*(3), 344-348.

Kirkland, L. L. (1999). Factors impeding enteral tube feedings. *Critical Care Medicine, 27*(7), 1383-1384.

Klein, C. J., Stanek, G. S., & Wiles, C. E. (1998). Overfeeding macronutrients to critically ill adults: Metabolic complications. *Journal of the American Dietetic Association, 98*, 795-806.

Klein, S., Kinney, J., Jeejeebhoy, K., Alpers, D., Hellerstein, M., Murray, M., et al. (1997). Nutrition support in clinical practice: Review of published data and recommendations for future research directions. *Journal of Parenteral and Enteral Nutrition, 21*(3), 133-156.

Knebel, A. R. (1992). When weaning from mechanical ventilation fails. *American Journal of Critical Care, 1*(3), 19-29.

Koretz, R. L. (1995). Nutritional supplementation in the ICU: How critical is nutrition for the critically ill. *American Journal of Respiratory Critical Care Medicine, 151*, 570-573.

Kresowick, T. F., Dechert, R. E., Mault, J. R., Arnoldi, D. K., Whitehouse, W. M., & Bartlett, R. H. (1984). Does nutritional support affect survival in critically ill patients? *Surgical Forum, 1*, 108-109.

Kudsk, K. A., Croce, M. A., Fabian, T. C., Minard, G., Tolley, E. A., Poret, H. A., et al. (1992). Enteral versus parenteral feeding: Effects on septic morbidity after blunt and penetrating abdominal trauma. *Annals of Surgery, 215*(5), 503-511.

Laaban, J. P., Kouchakji, B., Dore, M. F., Orvoen-Frija, E., David, P., & Rochemaure, J. (1993). Nutritional status of patients with chronic obstructive pulmonary disease and acute respiratory failure. *Chest, 103*(5), 1362-1368.

Larca, L., & Greenbaum, D. M. (1982). Effectiveness of intensive nutritional regimes in patients who fail to wean from mechanical ventilation. *Critical Care Medicine, 10*(5), 297-300.

Lazarus, B. A., Murphy, J. B., & Culpepper, L. (1990). Aspiration associated with long-term gastric versus jejunal feeding: A critical analysis of the literature. *Archives of Physical Medical Rehabilitation, 71*, 46-53.

Leff, M. L., Hill, J. O., Yates, A. A., Cotsonis, G. A., & Heymsfield, S. B. (1987). Resting metabolic rate: Measurement reliability. *Journal of Parenteral and Enteral Nutrition, 11*(4), 354-359.

Le Gall, J.-R., Lemeshow, S., & Saulnier, F. (1993). A new Simplified Acute Physiology Score (SAPS II) based on a European/North American Multicenter Study. *Journal of the American Medical Association, 270*(24), 2957-2963.

Leupold-DiCicco, C., & Monturo, C. A. (Eds.). (1996). *Stress states: Trauma, burns, and sepsis.* Silver Springs, MD: American Society for Parenteral and Enteral Nutrition.

Lewis, M. I., & Belman, M. J. (1988). Nutrition and the respiratory muscles. *Clinics in Chest Medicine, 9*(2), 337-348.

Lindquist, R., Banasik, J., Barnsteiner, J., Beecroft, P. C., Prevost, S., Reigel, B., et al. (1993). Determining AACN's research priorities for the 90s. *American Journal of Critical Care, 2*(2), 110-117.

Long, J. M., & Long, C. L. (1994). Fuel metabolism. In G. Zaloga (Ed.), *Nutrition in critical care* (pp. 35-53). St. Louis, MO: Mosby.

Long, C. L., Schaffel, N., Geiger, J. W., Schiller, W. R., & Blakemore, W. S. (1979). Metabolic response to injury and illness: estimation of energy and protein needs from indirect caloriemetry and nitrogen balance. *Journal of Parenteral and Enteral Nutrition, 3*(6), 452-456.

Makita, K., Nunn, J. F., & Royston, B. (1990). Evaluation of metabolic measuring instruments for use in critically ill patients. *Critical Care Medicine, 18*(6), 638-644.

Makk, L. J., McClave, S. A., Creech, P. W., Johnson, D. R., Short, A. F., Whitlow, N. L., et al. (1990). Clinical application of the metabolic cart to the delivery of total parenteral nutrition. *Critical Care Medicine, 18*(12), 1320-1327.

Mann, S., Westenskow, D. R., & Houtchens, B. A. (1985). Measured and predicted caloric expenditure in the acutely ill. *Critical Care Medicine, 13*(3), 173-177.

Marino, P. L. (1998). *The ICU book* (2nd ed.). Baltimore: Williams & Wilkins.

Martindale, R. G., Shikora, S. A., Nishikawa, R., & Siepler, J. K (2002). The metabolic response to stress and alterations in nutrient metabolism. In S. Shikora, R. Martindale, & S. Schwaitzberg (Eds.), *Nutritional considerations in intensive care: Science, rationale and practice* (pp. 11-19). Dubuque, IA: Kendall/Hunt.

McCarthy, M. S. (2000). Use of indirect calorimetry to optimize nutrition support and assess physiologic dead space in the mechanically ventilated ICU patient: A case study approach. *AACN Clinical Issues, 11*(4), 619-630.

McCarthy, M. S., & Deal, L. E. (2002). Nutrition support in respiratory failure. In S. Shikora, R. Martindale & S. Schwaitzberg (Eds.), *Nutritional considerations in intensive care: Science, rationale and practice* (pp. 187-197). Dubuque, IA: Kendall/Hunt.

McClave, S. A. (1997). The consequences of overfeeding and underfeeding. *RT: The Journal for Respiratory Care Practitioners, 10*(3), 57-64.

McClave, S. A., Lowen, C. C., Kleber, M. J., Nicholson, J. F., Jimmerson, S. C., McConnell, J. W., et al. (1998). Are patients fed appropriately according to their caloric requirements? *Journal of Parenteral and Enteral Nutrition, 22*(6), 375-381.

McClave, S. A., McClain, C. J., & Snider, H. L. (2001). Should indirect calorimetry be used as part of nutritional assessment? *J Clin Gastroenterol, 33*(1), 14-19.

McClave, S. A., Sexton, L. K., Spain, D. A., Adams, J. L., Owens, N. A., Sullins, M. B., et al. (1999). Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Critical Care Medicine, 27*(7), 1252-1256.

McClave, S. A., & Snider, H. L. (1992). Use of indirect calorimetry in clinical nutrition. *Journal of Parenteral and Enteral Nutrition, 7*(5), 207-221.

McClave, S. A., & Snider, H. L. (1994). Understanding the metabolic response to critical illness: Factors that cause patients to deviate from the expected pattern of hypermetabolism. *New Horizons, 2*(2), 139-146.

McClave, S. A., Snider, H. L., & Ireton-Jones, C. (2002). Can we justify continued interest in indirect calorimetry? *Nutrition in Clinical Practice, 17*(3), 133-136.

McClave, S. A., Snider, H. L., Lowen, C. C., McLaughlin, A. J., Greene, L. M., McCombs, R. J., et al. (1992). Use of residual volume as a marker for enteral feeding intolerance: prospective blinded comparison with physical examination and radiographic findings. *Journal of Parenteral and Enteral Nutrition, 16*(2), 99-105.

McClave, S. A., Spain, D. A., Skolnick, J. L., Lowen, C. C., Kleber, M. J., Wickerman, P. S., et al. (2003). Achievement of steady state optimizes results when performing indirect calorimetry. *Journal of Parenteral and Enteral Nutrition, 27*(1), 16-20.

McWhirter, J. P., & Pennington, C. R. (1994). Incidence and recognition of malnutrition in hospital. *British Medical Journal, 308*, 945-948.

Meijer, C., Muller, M. G., & Leeuwen, P. A. M van. (1996). The liver in the induction and regulation of the acute stress response. In A. Revhaug (Ed.), *Acute catabolic state* (pp. 129-140) Berlin, Germany: Springer-Verlag.

Mentec, H., Dupont, H., Bocchetti, M., Cani, P., Ponche, F., & Bleichner, G. (2001). Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Critical Care Medicine, 29*(10), 1955-1961.

Metheny, N. (2002). Risk factors for aspiration. *Journal of Parenteral and Enteral Nutrition, 26*(6), S26-S31.

Montejo, J. C. (1999). Enteral nutrition-related gastrointestinal complications in critically ill patients: A multicenter study. *Critical Care Medicine, 27*(8), 1447-1453.

Moore, F. A., Moore, E. E., Jones, T. N., McCroskey, B. L., & Peterson, V. M. (1989). TEN versus TPN following major abdominal trauma: Reduced septic morbidity. *Journal of Trauma, 29*(7), 916-923.

Moore, J. A., & Angelillo, V. A. (1988). Equations for the prediction of resting energy expenditure in chronic obstructive lung disease. *Chest, 94*(6), 1260-1263.

Moore, M. C., Guenter, P. A., & Bender, J. H. (1986). Nutrition-related nursing research. *IMAGE: Journal of Nursing Scholarship, 18*(1), 18-21.

Mullan, H., Roubenoff, R. A., & Roubenoff, R. (1992). Risk of pulmonary aspiration among patients receiving enteral nutrition support. *Journal of Parenteral Enteral Nutrition, 16*(2), 160-164.

Mullen, J. L. (1991). Indirect calorimetry in critical care. *Proceedings of the Nutrition Society, 50*, 239-244.

Murciano, D., Rigaud, D., Pingleton, S., Armengaud, M. H., Melchior, J. C., & Aubier, M. (1994). Diaphragmatic function in severely malnourished patients with anorexia nervosa. *American Journal of Respiratory Critical Care Medicine, 150*, 1569-1574.

Murray, J. F., & Nadel, J. A. (1994). *Textbook of respiratory medicine* (2nd ed.). Philadelphia: Saunders.

Myers, S. A., Takaguchi, S., Slavish, S., & Rose, C. L. (1990). Consistent wound care and nutritional support in treatment. *Decubitus, 3*(3), 307-314.

Naber, T. H. J., Schermer, T., de Bree, A., Nusteling, K., Eggins, L., Kruimel, J. W., et al. (1997). Prevalence of malnutrition in nonsurgical hospitalized patients and its association with disease complications. *American Journal of Clinical Nutrition, 66*, 1232-1239.

Nadeau, S., & Noble, W. H. (1986). Limitations of cardiac output by thermodilution. *Canadian Anaesthetists Society Journal, 33*(6), 780-784.

National Heart Lung and Blood Institute (NHLBI). (1998). Obesity Education Initiative Expert Panel on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Clinical guidelines on the indentification, evaluation, and treatment of overweight and obesity in adults: The evidence report. *Obesity Research, 6*(Suppl. 2), 51S-209S.

Niederman, M. S., Merrill, W. W., Ferranti, R. D., Pagano, K. M., Palmer, L. B., & Reynolds, H. Y. (1984). Nutritional status and bacterial binding in the lower respiratory tract in patients with chronic tracheostomy. *Annals of Internal Medicine, 100*, 795-800.

Norton, J. A., Ott, L. G., McClain, C., Adams, L., Dempsey, R. J., Haack, D., et al. (1988). Intolerance to enteral feeding in the brain-injured patient. *Journal of Neurosurgery, 68*(1), 62-66.

Orozco-Levi, M., Torres, A., Ferrer, M., Piera, C., El-Ebiary, M., Puig de la Bellacasa, J., et al. (1995). Semirecumbent position protects from pulmonary aspiration but not completely from gastroesophageal reflux in mechanically ventilated patients. *American Journal of Respiratory Care, 152*, 1387-1390.

Ott, L., Annis, K., Hatton, J., McClain, M., & Young, B. (1999). Postpyloric enteral feeding costs for patients with severe head injury: blind placement, endoscopy, and PEG/J versus TPN. *Journal of Neurotrauma, 16*(3), 233-242.

Pezza, M., Iermano, C., & Tufano, R. (1994). Nutritional support for the patient with chronic obstructive pulmonary disease. *Monaldi Archives of Chest Disease, 49*(3), 33-39.

Pinard, B., & Geller, E. (1995). Nutritional support during pulmonary failure. *Critical Care Clinics, 11*(3), 705-715.

Pingleton, S. K. (1996). Enteral nutrition in patients with respiratory disease. *European Respiratory Journal, 9*, 364-370.

Piquette, C. A., Rennard, S. I., & Snider, G. L. (Eds.). (2000). *Chronic bronchitis and emphysema* (3rd ed., Vol. 2). Philadelphia: W. B. Saunders.

Porter, C., & Cohen, N. H. (1996). Indirect calorimetry in critically ill patients: Role of the clinical dietitian in interpreting results. *Journal of the American Dietetic Association, 96*(1), 49-54,57.

Posa, P. (1994). Nutritional support of the critically ill patient. *Critical Care Nursing Quarterly, 16*(4), 61-79.

Potter, J., Langhorne, P., & Roberts, M. (1998). Routine protein energy supplementation in adults: Systematic review. *British Medical Journal, 317*, 495-501.

Rapp, R. P., Young, B., Twyman, D., Bivins, B. A., Haack, D., Tibbs, P. A., et al. (1983). The favorable effect of early parenteral feeding on survival in head-injured patients. *Journal of Neurosurgery, 58*(6), 906-912.

Reilly, J. J., Hull, S. F., Alpert, N., Waller, A., & Bringardener, S. (1988). Economic impact of malnutrition: A model system of hospitalized patients. *Journal of Parenteral and Enteral Nutrition, 12*(4), 371-376.

Robinson, G., Goldstein, M., & Levine, G. M. (1987). Impact of nutritional status on DRG length of stay. *Journal of Parenteral and Enteral Nutrition, 11*(1), 49-51.

Rochester, D. F. (1986a). Body weight and respiratory muscle function in chronic obstructive pulmonary disease. *American Review of Respiratory Disease, 134*, 646-647.

Rochester, D. F. (1986b). Malnutrition and the respiratory muscles. *Clinics in Chest Medicine, 7*(1), 91-99.

Rothkopf, M. M., Stanislaus, G., Haverstick, L., Kvetan, V., & Askanazi, J. (1989). Nutritional support in respiratory failure. *Nutrition in Clinical Practice, 4*, 166-172.

Rumpler, W. V., Seale, J. L., Conway, J. M., & Moe, P. W. (1990). Repeatability of 24-hour energy expenditure measures in human indirect calorimetry. *American Journal of Clinical Nutrition, 51*, 147-152.

Saltzman, E., Mogensen, K. M., & Hassoun, P. M. (2002). Malnutrition in the intensive care unit. In S. Shikora, R. Martindale, & S. Schwaitzberg (Eds.), *Nutritional considerations in the intensive care unit: Science, rationale and practice* (pp. 1-10). Dubuque, IA: Kendall/Hunt.

Sherman, M. S. (1994). A predictive equation for determination of resting energy expenditure in mechanically ventilated patients. *Chest, 105*(2), 544-549.

Shikora, S. A., & Benotti, P. N. (1997). Nutritional support of the mechanically ventilated patient. *Respiratory Care Clinics of North America, 3*(1), 69-90.

Spain, D. A., McClave, S. A., Sexton, L. K., Adams, J. L., Blanford, B. S., Sullins, M. E., et al. (1999). Infusion protocol improves delivery of enteral tube feeding in the critical care unit. *Journal of Parenteral and Enteral Nutrition, 23*(5), 288-292.

Spiekerman, M. A. (1995). Nutritional assessment: Protein nutriture. *Analytical Chemistry, 67*(12), 429R-436R.

Stechmiller, J., Treloar, D. M., Derrico, D., Yarandi, H., & Guin, P. (1994). Interruption of enteral feedings in head injured patients. *Journal of Neuroscience Nursing, 26*(4), 224-229.

Stryer, L. (1995). *Biochemistry* (4th ed.). New York: W. H. Freeman.

Sullivan, D. H., & Walls, R. C. (1994). Impact of nutritional status on morbidity in a population of geriatric rehabilitation patients. *Journal of the American Geriatrics Society, 42*(5), 471-477.

Swinamer, D. L., Grace, M. G., Hamilton, S. M., Jones, R. L., Roberts, P., & King, E. G. (1990). Predictive equation for assessing energy expenditure in mechanically ventilated critically ill patients. *Critical Care Medicine, 18*(6), 657-661.

Swinamer, D. L., Phang, P. T., Jones, R. L., Grace, M., & King, E. G. (1987). Twenty-four hour energy expenditure in critically ill patients. *Critical Care Medicine, 15*(7), 637-643.

Swinamer, D. L., Phang, P. T., Jones, R. L., Grace, M., & King, E. G. (1988). Effect of routine administration of analgesia on energy expenditure in critically ill patients. *Chest, 93*(1), 4-10.

Takahashi, I., & Kiyono, H. (1999). Gut as the largest immunologic tissue. *Journal of Parenteral and Enteral Nutrition, 23* (Suppl. 5), S7-S12.

Talpers, S. S., Romberger, D. J., Bunce, S. B., & Pingleton, S. K. (1992). Nutritionally associated increased carbon dioxide production: Excess total calories vs high proportion of carbohydrate calories. *Chest, 102*(2), 551-555.

Thys, D. M. (1988). Cardiac output. *Anesthesiology Clinics of North America, 6*, 803-824.

Torres, A., Serra-Batlles, J., Ros, E., Piera, C., Puig de la Bellacasa, J., Cobos, A., et al. (1992). Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: The effect of body position. *Annals of Internal Medicine, 116*(7), 540-543.

van Lanschot, J. J., Feenstra, B. W., Vermeij, C. G., & Bruining, H. A. (1986). Calculation versus measurement of total energy expenditure. *Critical Care Medicine, 14*(11), 981-985.

Van Way, C. W. (1999). Appendix I: Nutrition-related formulas and calculations. In C. V. Way (Ed.), *Nutrition secrets* (pp. 245-247). Philadelphia: Hanley and Belfus.

Vender, J. R., Cresci, G. A., & Lee, M. R. (2002). Nutritional considerations in severe brain injury. In S. Shikora, R. Martindale, & S. Schwaitzberg (Eds.), *Nutritional considerations in the intensive care unit: Science, rationale and practice* (pp. 259-267). Dubuque, IA: Kendall/Hunt.

Weinsier, R. L., & Heimburger, D. C. (1997). Distinguishing malnutrition from disease: The search goes on. *American Journal of Clinical Nutrition, 66*, 1063-1064.

Weir, J. B. d. (1949). New methods for calculating metabolic rate with special reference to protein metabolism. *Journal of Physiology, 109*, 1-9.

Weissman, C., & Kemper, M. (1995). Metabolic measurements in the critically ill. *Critical Care Clinics, 11*(1), 169-197.

Weissman, C., Kemper, M., Askanazi, J., Hyman, A. I., & Kinney, J. M. (1986). Resting metabolic rate of the critically ill patient: Measured versus predicted. *Anesthesiology, 64*(6), 673-679.

Weissman, C., Kemper, M., Damask, M. C., Askanazi, J., Hyman, A. I., & Kinney, J. M. (1984). Effect of routine intensive care interactions on metabolic rate. *Chest, 86*(6), 851-878.

Weissman, C., Kemper, M., Elwyn, D. H., Askanazi, J., Hyman, A. I., & Kinney, J. (1986). The energy expenditure of the mechanically ventilated critically ill patient: An analysis. *Chest, 89*(2), 254-259.

Weissman, C., Kemper, M., & Hyman, A. I. (1989). Variation in resting metabolic rate of mechanically ventilated critically ill patients. *Anesthesia Analog, 68*, 457-461.

Weissman, C., Sadar, A., & Kemper, M. (1994). An in vitro evaluation of an instrument designed to measure oxygen consumption and carbon dioxide production during mechanical ventilation. *Critical Care Medicine, 22*(12), 1995-2000.

Welborn, M. B., & Moldawer, L. L. (1995). Glucose metabolism. In J. Rombeau & R. Rolandelli (Eds.), *Clinical nutrition: Enteral and tube feeding* (pp. 61-80). Philadelphia: W.B. Saunders.

Williams, R. R., & Feunning, C. R. (1991). Circulatory indirect calorimetry in the critically ill. *Journal of Parenteral and Enteral Nutrition, 15*(5), 509-512.

Wilson, D. O., Rogers, R. M., & Hoffman, R. M. (1985). State of the art: Nutrition and chronic lung disease. *American Review of Respiratory Disease, 132*, 1347-1365.

Wilson, D. O., Rogers, R. M., & Openbrier, D. (1986). Nutritional aspects of chronic obstructive pulmonary disease. *Clinics in Chest Medicine, 7*(4), 643-656.

Windsor, A. C., Kanwar, S., Li, A. G., Barnes, E., Guthrie, J. A., Spark, J. I., et al.(1998) Compared with parenteral nutrition, enteral feeding attentuates the acute phase response and improves disease severity in acute pancreatitis. *Gut, 42*(3), 431-435.

Zaloga, G. P. (1999). Early enteral nutrition support improves outcome: Hypothesis or fact? *Critical Care Medicine, 27*(2), 259-261.

Zaloga, G. P., & Roberts, P. (1994). Permissive underfeeding. *New Horizons, 2*(2), 257-263.

APPENDIX A

COMMITTEE ON HUMAN RESEARCH APPROVAL LETTER

COMMITTEE ON HUMAN RESEARCH
OFFICE OF RESEARCH ADMINISTRATION, Box 0962
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
www.ucsf.edu/ora/chr

CHR APPROVAL LETTER

TO:	Kathleen A. Puntillo, R.N., D.N.Sc. Box 0610	Colleen O'Leary-Kelley, RN, M.S. Box 0610

RE: Factors that Affect Nutritional Adequacy in Mechanically Ventilated Patients Receiving Enteral Nutrition Support

The Committee on Human Research (CHR), the UCSF Institutional Review Board (IRB) holding Department of Health and Human Services Multiple Project Assurance #M-1169, has reviewed and approved this application to involve humans as research subjects. This included a review of all documents attached to the original copy of this letter.

APPROVAL NUMBER: H2280-18665-01 .This number is a UCSF CHR number and should be used on all correspondence, consent forms and patient charts as appropriate.

APPROVAL DATE: April 11, 2001. **Full Committee Review**

EXPIRATION DATE: April 11, 2002. If the project is to continue, it must be renewed *by the expiration date.* See reverse side for details.

ADVERSE EVENT REPORTING: All problems having to do with subject safety must be reported to the CHR within ten working days. All deaths, whether or not they are directly related to study procedures, must be reported. Please review Appendix A of the CHR *Guidelines* for additional examples of adverse events or incidents which must be reported.

MODIFICATIONS: Prior CHR approval is required before implementing any changes in the consent documents or any changes in the protocol which affect subjects.

QUESTIONS: Please contact the office of the Committee on Human Research at [redacted] or campus mail stop, Box 0962, or by electronic mail at [redacted].

Sincerely,

[redacted]

Jay H. Tureen, M.D.
Chair
Committee on Human Research

APPENDIX B

HUMAN SUBJECTS CONSENT FORM

FACTORS THAT AFFECT NUTRITIONAL ADEQUACY IN MECHANICALLY VENTILATED PATIENTS RECEIVING ENTERAL NUTRITION SUPPORT

INFORMED CONSENT

Are you participating in any other research studies? Yes_______ No_______

You are invited to participate in a research study of nutritional adequacy in mechanically ventilated patients receiving enteral nutrition support (nutritional formula fed through a tube placed into the stomach or small intestine). Forty-five participants will be enrolled in this study. We hope to learn more about the adequacy of nutritional intake specifically in those patients who require treatment with mechanical support from a ventilator. It is hoped that this information will build new knowledge to develop strategies that will promote optimal nutritional intake in mechanically ventilated ICU patients. You were selected as a possible participant in this study because you currently require enteral nutrition and mechanical support from a ventilator as part of your medical treatment. While you are on the ventilator your physician will order the amount of enteral nutritional support you will receive as part of your medical treatment.

The purpose of this study is to describe nutritional intake and whether it is appropriate for an individual patient's requirements. We also hope to learn more about the factors that affect the adequacy of daily nutritional intake. In this study, your metabolic rate (energy expenditure) will be measured using a device (machine) called an indirect calorimeter. This measurement is performed at the bedside to accurately determine how many calories your body needs. The machine that measures calories will be connected to your ventilator (breathing machine). This will not affect your ability to breathe on the ventilator.

Some patients experience discomfort during the short time when the two machines are connected. Once the indirect calorimeter has been connected, you will be asked to remain at rest for approximately 30 minutes. During this time, your metabolic rate will be measured and you will be continuously monitored by the nursing staff. The procedure will be discontinued if we notice changes in your blood oxygen level, heart rate or if you feel uncomfortable and wish to stop.

When the measurement is completed you will be disconnected from the indirect calorimeter. The investigator will record the amount of enteral nutrition (tube feeding) you actually receive for the next 3 days. Your ICU treatment will not differ in any way from the treatment you would receive if you were not in this study except that your metabolic rate (energy expenditure) will be measured by the indirect calorimeter.

____ __________________
Signature of Participant or Representative Date

FACTORS THAT AFFECT NUTRITIONAL ADEQUACY IN MECHANICALLY VENTILATED PATIENTS RECEIVING ENTERAL NUTRITION SUPPORT

You will be told if any new information is learned which may affect your condition or influence your willingness to continue participation in this study. While participating in this study, you should not take part in any other research project without approval from all of the investigators. This is to protect you from possible injury arising from such things as extra blood drawing, extra x-rays, interaction of research drugs, or similar hazards.

Possible risks or discomforts: It may be uncomfortable for you upon initial connection to the indirect calorimeter. You may choose not to continue to be measured. We will try to arrange another time for the measurement to be completed. If you think that you have experienced a research-related injury, call Dr. Marilyn Douglas at [redacted].

Benefits: You may benefit from participation in this study from the satisfaction of helping us learn more about the adequacy of nutritional intake in mechanically ventilated patients. WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.

The alternative is to not participate. You may choose not to participate in this research study, in which case you will receive your usual care, that is you will receive all of the treatments and care prescribed by your primary physician. Any data that may be published in scientific journals will not reveal the identity of the subjects. Patient information may be provided to Federal and regulatory agencies as required.

No payment will be provided for participation in this project. There will be no additional cost to you for participating in this study. The Department of Veterans Affairs is providing financial support and materials for this study.

Your decision whether or not to participate will not prejudice you or your medical care. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice to you or effect on your medical care.
At the discretion of the principal investigator, subjects may be taken out of this study due to unanticipated circumstances. Some reasons for withdrawing subjects from a study include: failure to obtain indirect calorimetry measurement, failure to follow instructions, the investigator decides that continuation could be harmful to you, you need treatment not allowed in this study, the study is cancelled, or other administrative reason.

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. Should you be injured as a result of participation in this research project which has been approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees, VA will provide you free medical care for those injuries pursuant to 38 C.F.F. 17.85. This section applies to both Veteran and non-veteran research subjects. You will not be afforded medical care for: (1) treatment for injuries due to noncompliance by you with study procedures, or (2) research conducted for VA under a contract with an individual or a non-VA institution.

Signature of Participant or Representative Date

If you are a Veteran, 38 U.S.C.A. § 1151 may provide you with dependency and indemnity compensation for a qualifying additional disability or a qualifying death in the same manner as if such additional disability or death were service-connected. A disability or death is a qualifying additional disability or qualifying death if the disability or death was not the result of you willful misconduct and was caused by hospital care, medical or surgical treatment, or examination furnished to you and the proximate cause of the disability or death was either: (a) carelessness, negligence, lack of proper skill, error in judgement, or similar instance of fault on the part of the Department in furnishing the hospital care, medical or surgical treatment, or examination; or (b) an event not reasonably foreseeable. For further information, contact the V.A. Regional Counsel at [redacted]. You do not waive any liability rights for personal injury by signing this form. If you feel that the above remedies for your injuries are not sufficient, and irrespective of your status as a Veteran or a non-veteran, the Federal Tort Claims Act, 28 U.S.C. §§ 1346(b) and 2671-2680, may provide an additional remedy if the VA is at fault for your injuries.

For further information, please call [redacted] or write the Administrative Panel on Human Subjects in Medical Research, Administrative Panels Office, Stanford University, Stanford, CA 94305-5401. In addition, if you are not satisfied with the manner in which this study is being conducted or if you have any questions concerning your rights as a study participant, please contact the Human Subjects Office at the same address and telephone number.
As a human subject you have the following rights. These rights include but are not limited to the subject's to:

1. be informed of the nature and purpose of the experiment.
2. be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
3. be given a description of any attendant discomforts and risks reasonable to be expected;
4. be given an explanation of any benefits to the subjects reasonable to be expected, if applicable;
5. be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
6. be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should rise;
7. be given an opportunity to ask questions concerning the experiment or the procedures involved;
8. be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
9. be given a copy of the signed and dated consent form;
10. and be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

Signature of Participant or Representative Date

FACTORS THAT AFFECT NUTRITIONAL ADEQUACY IN MECHANICALLY VENTILATED PATIENTS RECEIVING ENTERAL NUTRITION SUPPORT

YOUR SIGNATURE INDICATES THAT YOU HAVE READ AND UNDERSTOOD THE ABOVE INFORMATION, THAT YOU HAVE DISCUSSED THIS STUDY WITH THE PERSON OBTAINING CONSENT, THAT YOU HAVE DECIDED TO PARTICIPATE BASED ON THE INFORMATION PROVIDED, AND THAT A COPY OF THIS FORM HAS BEEN GIVEN TO YOU.

____
Printed name of Participant or Representative

____________________________________ ________________
Signature of Participant or Representative Date

Person Obtaining Consent

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied – that the participant has been provided with the Experimental Subject's Bill of Rights, if appropriate, that I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

____________________________________ ________________
Signature of Person Obtaining Consent Date

Approval Date: 1/08/02 Expiration Date: 1/07/03

APPENDIX C

STUDY RECRUITMENT FLYER

Enteral Nutrition Study

PURPOSE: Examine the adequacy of enteral nutritional intake and the associated factors in mechanically ventilated ICU patients

ELIGIBLE PATIENTS MUST BE:

- Intubated on mechanical ventilatory support
- Receiving enteral nutrition support exclusively
- Able to tolerate measurement by indirect calorimetry

FOR QUESTIONS OR TO ENROLL PATIENTS
PLEASE CONTACT
Colleen O'Leary-Kelley, RN
Pager [redacted]

Approved by the VA Nursing Research Council, Stanford Human Subjects Committee, VA Research and Development Committee, and UCSF Committee on Human Research
Primary Investigator: M. Douglas RN, DNSc
Co-Investigators: J. Barr, MD and C. O'Leary-Kelley, RN
This study is funded in part by a grant from the National Institute of Nursing Research, National Institutes of Health #1 F31 NR07707-01

APPENDIX D

DATA COLLECTION FORMS

DEMOGRAPHIC DATA COLLECTION

Subject ID number ___________

Age _______

Gender: 1. Female 2. Male

Date admitted to hospital ___________ Date admitted to ICU _________

Did patient receive parenteral nutrition support? Yes N o
If yes, date started __________

Date feeding tube inserted ________ Time _______Tube type/position______

Date enteral feeding started _______

Achieved target rate (Date/time)________________________

Primary diagnosis ___________________________________

Surgeries:

Date: ________ procedure _________________________

Date: ________ procedure _________________________

Date mechanical ventilation initiated_____________________

Time of intubation ___________________________________

Admission weight: _________kg Usual body weight _______kg

Admission height _________ cm Admission albumin
(if available) ________

SAPS II Score ___________

NUTRITIONAL DATA FORM

Subject ID number ___________

Caloric requirements measured by indirect calorimetry: ___________ kcal/day

Date performed: _______________ Time: ___________

Harris-Benedict Equation (HBE) estimated REE ______________ kcal/day

Date:___________ Time: __________

Degree of metabolism: (MREE / HBE predicted REE x 100)

_________ %

List medications received during or within one hour of indirect calorimetry measurement

_________________________ time _____________

_________________________ time _____________

_________________________ time _____________

_________________________ time _____________

_________________________ time _____________

_________________________ time _____________

24-hour UUN results (if available) _____________
Date performed ____________

DAILY DATA COLLECTION

Subject ID number __________ Study Day # ________

Current weight (measured q AM) ____________

Enteral formula ordered _________________________________

Prescribed goal rate __________________ ml/hr

Total volume of enteral formula received over 24 hours ___________ ml
Total volume of water instilled via feeding tube over 24 hours _______ ml

Was feeding held within last 24 hours? Yes No
(record # minutes)

_____________ Reason held / time 1:

_____________ Reason held / time 2:

_____________ Reason held / time 3:

_____________ Reason held / time 4:

Volume of gastric residuals in 24 hours:

Time 1 _______ volume _____ ml Time 4 _____ volume _____ ml

Time 2 _______ volume _______ ml Time 5 _____ volume ____ ml

Time 3 ________ volume ________ ml Time 6 _____ volume ____ ml

Number of episodes of diarrhea in 24 hours __________
Estimated volume of diarrhea in 24 hours __________ ml

Number of episodes of emesis in 24 hours __________
Estimated volume of emesis in 24 hours __________ ml
Was feeding tube replaced ? Yes No

Number of times tube replaced within the previous 24 hours _______
Number of xrays performed related to feeding tube placement ______

Narcotic or propofol gtt (dosage) ________________
Albumin ____________ Tmax ____________