THE USE OF HYPOCALORIC PARENTERAL NUTRITION
IN ACUTELY ILL OBESE PATIENTS

A Thesis

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by
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* * * * *

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CHAPTER I
INTRODUCTION

Background of Problem

Data from the Second National Health and Nutrition Examination Survey (NHANES II) indicated that 34 million American adults, 25.7% of the population, were overweight in the period 1976-1980 (1). Obesity is characterized by an excess amount of body fat (2). Being overweight is defined as having a body weight that is greater than national weight standards (2). A person may be overweight, yet not be obese (e.g. a professional football player may weigh more than the standard weight for his height because of an increased lean body mass, but have a normal amount of body fat). However, the terms obese and overweight are often used synonymously, for weighing greater than 120% of desirable body weight is usually associated with an excess amount of body fat and constitutes an established health hazard (3).

Having an excess amount of body fat frequently results in a significant impairment of health (3). Obesity impacts both morbidity and mortality. It is a significant independent risk factor for cardiovascular disease (4). The prevalence of hypertension is almost three times greater among
individuals weighing greater than 120% of desirable body weight than among individuals with normal body weight (3,5). Among young overweight persons, the prevalence of hypercholesterolemia (blood cholesterol greater than 250 mg/dL) is twice that found in young, normal-weight individuals (3). Adiposity increases the risk of non-insulin-dependent diabetes mellitus (6), with the prevalence of reported diabetes almost three times greater in overweight persons (3). The prevalence of osteoarthritis and gout are also increased in obese persons (6).

Obesity is also associated with decreased life expectancy. Males weighing greater than 120% of desirable body weight experience an excess mortality of almost 50% (7). Obese women have a slightly lower degree of excess mortality (7). As the degree of overweight increases, the excess death rate also increases, regardless of smoking status (3). Strauss and Wise concluded that this excess mortality is caused chiefly by cardiovascular disease, including cerebral hemorrhage and thrombosis (8). Increased mortality due to diabetes, cholelithiasis, cirrhosis, and malignant neoplasms also contributes to the excess mortality observed among obese individuals (8).

Surgeons have long blamed obesity for many postoperative complications (8). Obese patients demonstrate significantly higher rates of wound infection, disruption, and dehiscence (9-14). The rate of thrombophlebitis and
thromboembolism are not increased among obese surgical patients (15-17). Induction and maintenance of anesthesia may be more difficult and require greater caution in the obese patient (8). Obesity may also present technical difficulties for the surgeon (8). However, surgical mortality has not been shown to be greater among obese patients (15). The literature in this field indicates that surgery in the obese is not fraught with excessive risks.

The acutely ill obese patient poses a significant challenge to the nutrition support service. Little is known about the nutrient needs of metabolically-stressed obese patients (18). Standard nutrition care for the normal-weight stressed patient is to meet or exceed maintenance needs, in order to prevent depletion of body stores and to promote healing (19). Overfeeding the normal-weight stressed patient can result in fatty infiltration of the liver, hyperglycemia, and compromised respiratory status (20,21). These conditions often already exist in the obese patient; exacerbation of these conditions by the nutrition support regimen is undesirable (22).

The use of hypocaloric parenteral nutrition in acutely ill obese patients has recently been proposed. Dickerson, et al. demonstrated adequate nutrition support of thirteen obese patients receiving an average of 881 kcal/day and 2.13±0.59 gm protein/kg ideal body weight (IBW)/day (23). Others have also described the use of hypocaloric parenteral
nutrition in obese patients, though no further scientific studies have been published (19,24). It is not known if hypocaloric nutrition support is more advantageous than the standard isocaloric or hypercaloric nutrition support in obese patients.

**Significance of Problem**

The goal of nutrition support is to improve the nutritional status of the individual, thereby promoting healing and recuperation. Providing excessive nutrients to the acutely ill obese patient may actually prolong the recovery period. Based upon initial reports, hypocaloric regimens appear capable of providing adequate nutrients for healing, while still promoting weight loss. Further research is necessary to verify these findings and to determine if hypocaloric parenteral nutrition is more efficacious than isocaloric or hypercaloric parenteral nutrition in stressed obese patients.

**Objective**

The purpose of this research was to determine if hypocaloric parenteral nutrition is an adequate nutrition support regimen for acutely ill obese patients. The specific objective of this study is:
To determine if acutely ill obese patients receiving hypocaloric parenteral nutrition can achieve the same degree of improvement in nitrogen balance as can acutely ill obese patients receiving isocaloric parenteral nutrition.

**Hypothesis**

The null hypothesis of this study is:

There will be no difference in the ability to achieve nitrogen balance between stressed obese patients receiving hypocaloric parenteral nutrition and stressed obese patients receiving isocaloric parenteral nutrition.

The independent variable is the percentage of measured resting energy expenditure provided as nonprotein calories. The dependent variable is the ability to achieve nitrogen balance.

**Research Approach**

The posttest-only control group design (25) was used to address these objectives. Obese patients were randomly assigned to either the isocaloric control group, receiving 100% of the measured resting energy expenditure as nonprotein calories, or the hypocaloric experimental group, receiving 50% of the measured resting energy expenditure as nonprotein calories. The diets were isonitrogenous. Patients continued on the assigned diet for a maximum of two weeks. Nitrogen balance was monitored to determine if nitrogen balance could be achieved to the same degree in the experimental and control groups.
Definition of Terms

Indirect calorimetry - noninvasive method for determining an individual's energy expenditure and requirements, based upon gas exchange measurements.

Resting energy expenditure (REE) - energy expenditure of an individual who has rested in a supine position for greater than 30 minutes and has been without food for greater than two hours; can be measured by indirect calorimetry or estimated by the Harris-Benedict formula and activity and stress factors.

Hypocaloric parenteral nutrition - parenteral nonprotein caloric intake less than the measured resting energy expenditure; for this study, defined as 50% of measured resting energy expenditure.

Isocaloric parenteral nutrition - parenteral nonprotein caloric intake equal to the measured resting energy expenditure.

Assumptions of the Study

It is assumed that the acutely ill obese patients enrolled in this study are representative of all acutely ill obese patients. It is further assumed that the metabolic response to hypocaloric parenteral nutrition observed in these subjects would also be found in other similar obese subjects.
It is also assumed that any observed changes in nutritional status (i.e. improved serum proteins, nitrogen balance) are the result of the nutrition support provided, rather than other physiological changes in the subjects.

A third assumption is that any clinically significant differences between the two groups in the ability to achieve nitrogen balance will be apparent in the time frame of the study.

Limitations of the Study

Subjects enrolled in this study will be inpatients at The Ohio State University Hospitals. Though it is assumed that these obese patients are representative of all obese patients, it is possible that these subjects will be experiencing greater metabolic stress than those obese patients seen in smaller hospitals. Degree of metabolic stress will be documented for the study subjects, thereby controlling the effect of this limitation on the results of the study.

Threats to internal and external validity are controlled by the use of the posttest-only control group design (25).
CHAPTER II
REVIEW OF LITERATURE

Relatively little is known about the nutritional needs of acutely ill obese patients. This review of literature will focus upon energy metabolism in the obese and how starvation and stress alter their metabolism. The consequences of underfeeding and overfeeding the stressed obese patient will be explored, as well as current research on the use of hypocaloric nutrition support in these patients.

Energy expenditure in the obese

Basal metabolic rate (BMR) can be defined as the minimum energy needed to maintain vital bodily functions (26). It is measured in an awake person in a fasted state (12-18 hours after the last intake of food). The person should be resting quietly in a lying position, without any physical or psychological stress, in a thermoneutral environment (26, 27).

Since it is difficult to obtain true basal conditions in the clinical setting, the measurement of resting metabolic rate (RMR) (or resting energy expenditure (REE)) has
been proposed (28). REE is measured in a thermoneutral environment after the individual has rested in a supine position for greater than 30 minutes and has been without food for greater than two hours (27).

The landmark studies by Harris and Benedict resulted in the development of formulae to estimate BMR in males and females (29). These prediction equations result in an estimated basal energy expenditure (BEE) (29):

Women: BEE = 655.096 + 9.563(weight in kg) + 1.850(height in m) - 4.676(age in years) \hspace{1cm} (1)

Men: BEE = 66.473 + 13.752(weight in kg) + 5.003(height in m) - 6.755(age in years). \hspace{1cm} (2)

However, it must be recognized that these formulae were developed in the early 1900's in healthy normal males and females in situations that more closely resemble those required for measurement of RMR (30).

BMR is largely determined by the amount of lean body mass in an individual's body. Body composition analyses of obese individuals indicate that the excess weight accumulated is not pure fat. James, et al. found this excess weight to be 32-38% lean tissue and 62-68% fat (31), while Webster, et al. found it to consist of 22-30% lean and 70-78% fat (32). Forbes and Welle found that a mean of 29% of the excess weight in obese subjects is lean tissue (33). Therefore, as weight is gained, both lean and fat tissues increase quantitatively. However, when expressed as a percentage of body weight, lean tissue decreases and fat
increases in obesity (26).

Numerous studies have examined the RMR of obese persons and have compared them with the RMR of normal-weight individuals. Ravussin, et al. found that both resting metabolic rate and 24-hour energy expenditure were significantly greater in obese subjects than in normal-weight subjects when expressed as absolute values (34). However, when RMR and 24-hour energy expenditure were expressed as a function of lean body mass, there were no significant differences between normal-weight, overweight, and obese subjects (34). They concluded that the increased RMR was most closely related to the increased fat-free mass (lean body mass) found in the obese subjects (34). Franssila-Kallunki, et al. found basal energy expenditure was similar in anorectic, normal-weight control, and obese subjects, when expressed as kcal/kg lean body mass (35).

It appears that RMR correlates highly with lean body mass in obese and normal-weight individuals (34). Some researchers suggest that although fat tissue is known to be relatively metabolically inert, when it accounts for a significant portion of body weight, it may exert some influence on metabolic rate (26,36-38).

The efficacy of the Harris-Benedict equation in predicting REE among obese individuals has recently been questioned. Bernstein, et al. noted that many obese patients in their laboratory demonstrated lower measured metabolic rates
than predicted by the Harris-Benedict equations (36). Feurer, et al. examined the measured RMR in morbidly obese patients prior to gastric bypass surgery (30). Measured RMR was significantly greater than predicted RMR when ideal body weight was used in the Harris-Benedict equation and was significantly less than predicted RMR when actual body weight was used in the Harris-Benedict equation (30). Pavlou, et al. found similar results in moderately obese males (39). Pavlou concluded that obese individuals had a suppressed RMR when compared to persons of normal body weight and body composition (39). Obese persons appeared to require fewer kcal/kg of body weight for resting energy expenditure (than predicted from Harris-Benedict equations developed on normal weight persons), though these researchers did not explore RMR as a function of lean body mass (39).

These studies clearly demonstrate that the Harris-Benedict equations can not accurately estimate the resting metabolic rates of obese persons. Recent studies by Daly, et al. (40) and Clark and Hoffer (41) suggest that Harris-Benedict equations overestimate the resting metabolic rates of even normal-weight healthy subjects by 9-15%. Ireton-Jones has developed a prediction equation for resting energy expenditure for use with obese patients, taking into account sex, age, actual body weight, and ventilatory status (42). However, most researchers would recommend the use of indirect calorimetry to most accurately determine the RMR of
obese patients (18).

**Metabolic Changes in Starvation**

Starvation results in a series of adaptive changes that are designed to conserve energy, glucose, and protein (43). Under normal conditions, glucose is the preferential fuel of the brain, red blood cells, and renal medulla (44). Ketone bodies provide a very small percentage of the brain’s energy needs (44). A normal, 70-kg man has approximately 900 calories available as glycogen, 24,000 calories as muscle protein, and 141,000 calories as adipose tissue (45). Glycogen can provide only enough glucose for obligatory glucose tissues for 12-16 hours of fasting (46). During prolonged starvation, protein and fat must be metabolized to meet the body’s energy needs.

Alterations in the levels of glucocorticoids, catecholamines, glucagon, and insulin during starvation result in the metabolic changes observed. Glycogenolysis is initiated by increased levels of glucocorticoids and catecholamines (47). As hepatic glycogen is depleted, increased levels of glucagon stimulate gluconeogenesis (46). Initially, skeletal muscle protein is catabolized to provide glucogenic amino acids for gluconeogenesis in the liver (48). Approximately 75 g of protein are metabolized daily to maintain normal blood glucose levels in early starvation (45, 49). Urinary nitrogen excretion increases as body protein is catabolized.
Decreasing glucose and insulin levels allow fat to be mobilized as an energy source (44). Fat stores are catabolized to glycerol and free fatty acids (49). The glycerol is converted to glucose, while free fatty acids are used for energy and production of ketone bodies (acetoacetate, beta-hydroxybutyrate, and acetone) (49). Ketone bodies can then be utilized as fuel sources by certain tissues (49). Muscle and the liver greatly increase their utilization of free fatty acids for energy (44). Ketone bodies become the predominant fuel of the central nervous system, providing up to 70% of the brain's energy needs (44,49). As fat is mobilized for energy, less body protein is required for gluconeogenesis. Approximately 25 g of protein are used for energy during this adaptive phase of starvation (46,47,49). Therefore, urinary nitrogen excretion decreases (45,46).

The metabolic rate also declines during starvation, thereby reducing the energy requirements of the body (50,51). This acts as another mechanism to spare body protein from catabolism. The metabolic rate declines more rapidly than the loss of body weight or lean body mass, suggesting a true energy conservation (50,51).

Initial studies on starvation were conducted using lean individuals (50,51). Numerous starvation studies have also been done with non-stressed obese persons in the exploration for a treatment for obesity (52-56). These studies have confirmed that adipose tissue becomes the primary fuel
during starvation in the obese. Acetoacetate and beta-hydroxybutyrate become the brain's major energy sources (52), while free fatty acids account for 30-60% of the oxygen uptake of skeletal muscle (53). Klein, et al. in comparing the lipolytic rates of obese and lean subjects, concluded that adipose tissue can supply all of the daily energy needs of the obese person during starvation (54).

Some authors have concluded that obese subjects respond to starvation with the same metabolic changes observed in non-obese persons (52,55). Ketoacid and amino acid patterns in starvation appear similar in obese and lean individuals (52,55). However, other researchers have found evidence suggesting obese persons respond differently during starvation than do lean individuals (57-59). Forbes and Drenick reported slower relative rates of weight and nitrogen loss in obese subjects than in non-obese persons; however, estimates, rather than actual measurements, of lean body mass were used (57). These authors concluded that obese persons may be more efficient at conserving nitrogen during starvation (57,58). This decreased tendency to use protein as a fuel in starvation may possibly be due to greater ketone body production or greater sensitivity to ketone bodies (59).

The effects of providing exogenous substrates to the fasting obese person have also been studied. The provision of glucose, amino acids, or fat, individually or in
combination, acts to reduce the rate of gluconeogenesis and the mobilization of body fat and protein (44). Strang, et al. found that obese patients lost three to six grams of nitrogen/day in the first few weeks of severe caloric restriction, then reestablished nitrogen equilibrium (60,61). If the protein intake was maintained at one gm/kg IBW, the body could retain nitrogen even with intakes of only 250–450 kcal/day (60,61). Blackburn, et al. obtained similar results, finding that the net loss of nitrogen was significantly reduced with an intake of one gm protein/kg of body weight (62). Others have also reported similar findings with protein-supplemented fasts in the obese (63–65).

**Metabolism during Stress**

Physiological stress changes the body's priorities. Protein synthesis becomes the primary function, so healing can occur (66). However, adaptation to alternative fuel substrates does not occur in stress as it does during starvation; protein is not as readily spared during stress.

The normal stress response to injury can be separated into two phases. During the initial "ebb" phase, little response to injury is seen. Insulin is deficient and blood glucose and fats are elevated. The "flow" phase peaks in three to four days after initial injury and abates in five to seven days if no additional stress occurs (44).
Stress triggers a mediated-neurohormonal response that activates certain metabolic pathways to meet increased energy and biosynthetic demands (67). Increased levels of glucocorticoids, glucagon, catecholamines, and epinephrine are observed, resulting in glycogenolysis, lipolysis, and proteolysis (47,49,67). Blood glucose levels rise, though skeletal muscle is less able to utilize glucose due to peripheral insulin resistance (49,68). Insulin levels increase in response to the elevated glucose levels.

Keto-adaptation can not occur during stress as it does in starvation because insulin levels do not decrease (47). Skeletal muscle protein is degraded for energy and biosynthetic needs and urinary nitrogen excretion remains high (44,66,67).

Fat stores are not as readily mobilized as an energy source (66), though indirect calorimetry has shown that fat contributes approximately 63% of nonprotein energy by the third day after injury (69). Other researchers have found 75-90% of energy needs being met by utilization of body fat (70). Though it appears that fat is utilized during stress, fat metabolism may be abnormal compared to starvation (69).

The resting metabolic rate increases during stress in proportion to the severity of the injury (66). Most researchers agree that elective surgical procedures do not increase RMR significantly (66). Long, et al. found blunt and skeletal trauma to increase the RMR by 32-37%, while
sepsis increased RMR by 60% (71). Thermal injury increased RMR most significantly to levels 132% of those normally seen in healthy individuals (71). These increased energy needs do not allow the body to adapt as it does during starvation; protein must be used for energy production (66).

The provision of exogenous calories or amino acids during stress also do not have the same effect observed in starvation. With higher levels of stress, exogenous substrates are less able to suppress the proteolysis, gluconeogenesis, and lipolysis occurring (44). Providing an energy intake equivalent to estimated energy expenditure and amino acids in excess of amounts needed for protein homeostasis in healthy individuals can not entirely reverse the protein catabolic state of stress (66). Most researchers indicate that a goal of positive nitrogen balance (+4-6 gm/day) may not be realistic during the acute phases of stress; a value of -4 to +2 gm/day may be the best expected (20,72). Clearly, adequate nutrition support is much more difficult to achieve in stressed patients.

The body does eventually adapt to the stressed state as hormone levels return to more normal levels (e.g. insulin levels decrease, glucocorticoids return to normal values). Urinary nitrogen excretion decreases, and fat is mobilized for energy production (47,49). Fat stores can supply 80-85% of the body's energy needs during trauma (70).
Numerous studies have been conducted with normal-weight stressed patients to determine the metabolic response to stress and the resulting energy needs of these patients. Few researchers have explored the obese individual's metabolic response to stress. Upon examining seven obese and ten non-obese multiple trauma patients, Jeevanandam, et al. reported that the stressed obese patients mobilized relatively more protein and less fat than the non-obese stressed patients (73). They concluded that obese patients experienced a block in lipolysis and fat oxidation, thereby preventing them from using their most abundant fuel source (73). Significantly increased plasma C-peptide levels were seen, indicating higher insulin production (73). The increased levels of insulin may have contributed to the inability to utilize adipose tissue for energy (73). It must be noted that these researchers failed to measure the subjects' lean body mass, using instead estimations of body fat (73, 74). Since LBM differs between obese and non-obese individuals, errors from estimation of LBM may render the results meaningless (74). Therefore, the results must be viewed with some reservation.

**Effects of Under- and Overfeeding**

Patients weighing greater than 120% of ideal body weight are considered to be at high nutritional risk (48). Obese patients who are yo-yo dieters frequently have a
decreased lean body mass, making them more susceptible to the development of malnutrition when in a stressed condition (75). Iatrogenic malnutrition can potentially prolong and complicate the obese patient's hospital course. Providing adequate amounts of calories, protein, vitamins, and minerals can facilitate the recuperation of the stressed obese patient.

Overfeeding obese patients is equally detrimental to their health. Many obese patients are insulin resistant and glucose intolerant, conditions which are exacerbated by the stress response (19,22,24). Fatty liver infiltration is common in obese individuals, as well as compromised respiratory function (19). Overfeeding acutely ill obese patients may further increase glucose and insulin levels, limiting the body's ability to use fat stores for energy (22,24). Excess calories would be stored as fat, resulting in greater obesity. Hypoxemia and hypercarbia may result from overfeeding, lengthening the time of ventilator-dependence (76,77).

It is obvious that both extremes of caloric provision may be detrimental to the recovery of the acutely ill obese patient. However, it is not known what level of caloric intake is most appropriate for this patient population.

**Current Research on Hypocaloric Parenteral Nutrition**

The literature indicates that non-stressed obese individuals may use their lipid stores as a primary fuel source
during starvation (52, 53, 57), but may be unable to mobilize these stores during stress (62, 73). Therefore, during stress, lean body mass is degraded for energy. It would appear most appropriate to provide nutrition support that spares protein while allowing the body to mobilize its fat depots.

Foster, et al. propose that total parenteral nutrition (TPN) has three possible caloric goals: 1) creation of energy balance and preservation of fat calorie stores in well-nourished individuals, 2) creation of "negative" energy balance in the obese patients with over-abundant endogenous calorie stores, or 3) creation of "positive" energy balance in malnourished patients with depleted endogenous fat stores (78). Feurer and Mullen recommend nonprotein calories in the range of 50-100% of measured REE in the otherwise healthy obese individual with adequate protein stores and intake (27). Dickerson proposes that a gain in lean body mass with a loss of body fat mass is a desirable outcome from TPN in protein-depleted patients (79). Feeding nonprotein calories at a level less than the measured REE is recommended by Dickerson for unstressed depleted patients weighing greater than 120% of ideal body weight, with a protein intake of 2.0-2.5 gm/kg/day for stressed patients (79).

Dickerson, et al. demonstrated complete tissue healing and nitrogen balance in 13 mild to moderately stressed obese patients receiving an average of 881 nonprotein kcal/day and
2.13 gm protein/kg of ideal body weight (1.16 gm/kg ABW) (23). This hypocaloric parenteral nutrition formula provided approximately 51% of the patients' measured resting energy expenditure (23). Serum albumin and transferrin improved significantly over the course of 38-42 days; all patients achieved nitrogen balance in 24±9.7 days (23). Additionally, 2.3±2.7 kg/week of weight were lost over 47 days (23).

Others have described the use of similar hypocaloric formulas in stressed obese patients, though no other research studies were found in a search of the literature (19,24). Baxter and Bistrian recommend the provision of 300-500 calories less than the measured energy expenditure with protein at approximately 1.5 gm/kg IBW (24). Pasulka and Kohl provide a maximum of 25 kcal/kg with 1.5-1.7 gm protein/kg IBW (19).

Much more research is needed in this area. As to date, no one has replicated the work of Dickerson, et al. Their study did not include a control group, and therefore could not compare the efficacy of hypocaloric parenteral nutrition with that of isocaloric parenteral nutrition. This study is designed to address these issues.
CHAPTER III
DESCRIPTION OF THE STUDY

Introduction

Obesity is prevalent in the United States, affecting over 34 million adults (1). Weighing greater than 120% of desirable body weight represents a significant health hazard, as obesity increases both morbidity and mortality for certain diseases (3). Though many scientific studies have explored the use of clinical starvation or semi-starvation as a treatment for obesity in otherwise healthy obese individuals, little is known about the safety of hypocaloric parenteral nutrition in acutely ill obese patients.

Recent research has demonstrated the difficulty of predicting the energy requirements of obese patients. Harris-Benedict equations underestimate resting metabolic rate of obese individuals when ideal body weight is used and overestimate RMR when actual body weight is used in the equations (30,39). The use of indirect calorimetry for accurate identification of energy requirements is especially important in this population.
Clinical starvation has been used as a treatment for obesity. Adaptive changes during starvation allow fat depots to be utilized for energy, while sparing muscle protein from excessive catabolism. The administration of exogenous protein (approximately one g/kg IBW) results in nitrogen equilibrium or positive nitrogen balance (60–65).

During stress, high insulin levels prevent this adaptive mechanism from occurring. As a result, muscle protein is actively catabolized for energy. It appears that stressed obese patients are less able to mobilize fat for energy than stressed non-obese patients (73).

However, Dickerson, et al. demonstrated that nitrogen balance could be achieved in stressed obese patients receiving hypocaloric nutrition (23). They reported the use of hypocaloric parenteral nutrition in 13 mild to moderately stressed obese patients receiving approximately 51% of measured resting energy expenditure (23). Nonprotein caloric intake averaged 881 kcal/day, and protein intake was 2.13±0.59 g/kg IBW (23). All subjects attained nitrogen balance within 24±9.7 days (23). Serum albumin and total iron binding capacity improved significantly, while all had complete tissue healing (23).

Dickerson, et al. did not employ a true experimental study design in this study (23). Without a control group, it is unknown if hypocaloric parenteral nutrition is as efficacious as isocaloric parenteral nutrition (providing 100% of
REE as nonprotein calories) in stressed obese patients. The objective of this study was to determine if acutely ill obese patients receiving hypocaloric parenteral nutrition can achieve the same degree of nitrogen balance as can acutely ill obese patients receiving isocaloric parenteral nutrition.

Methods

Thirteen obese individuals were prospectively identified upon referral to the Nutrition Support Service of The Ohio State University Hospitals for total parenteral nutrition. Patients weighed 130% or greater of ideal body weight, according to the standards of Hamwi (80). Patients were excluded if they had pre-existing insulin-dependent diabetes mellitus, renal disease, or hepatic disease. Also excluded were prisoners, pregnant women, and those with mental or physical retardation. The study was described in detail to the subject or closest family member, and informed consent was obtained prior to enrollment in the study. The study was approved by the Biomedical Sciences Human Subjects Review Committee of The Ohio State University (Protocol No. 90H0123) (Appendix A).

Upon enrollment, indirect calorimetry using the MedGraphics Critical Care Monitor/Canopy Respiratory Pressure Monitor (Medical Graphics Corporation, St. Paul, Minnesota) was conducted to determine each subject's resting energy
expenditure. One subject's REE was measured by the Metabolic Gas Monitor 2 cart (Utah Medical Products, Midvale, Utah) due to the inavailability of the other metabolic cart. Each subject was resting in a supine position in bed for at least 30 minutes prior to measurement. None of the subjects were receiving prior nutrition support, though some did have intravenous fluids infusing. Repeat REE measurements were completed after seven and fourteen days when possible.

Subjects were randomized by Pharmacy personnel not involved in the study to receive either 100% or 50% of the measured REE as nonprotein calories. Investigators were blinded to the formula assignment. Patients randomized to the hypocaloric group (50% of the measured REE) received a parenteral solution of 75 g dextrose, 60 g crystalline amino acids (Travasol, Baxter Healthcare Corp., Deerfield, IL), and 20 g lipids (Intralipid, Baxter Healthcare Corp., Deerfield, IL) at a rate sufficient to provide the appropriate number of calories. Patients randomized to the isocaloric group (100% of measured REE) received a parenteral solution of 150 g dextrose, 60 g crystalline amino acids (Travasol, Baxter Healthcare Corp., Deerfield, IL), and 40 g lipids (Intralipid, Baxter Healthcare Corp., Deerfield, IL). Both solutions were supplemented with electrolytes, vitamins (MVI-12, Astra Pharmaceutical Products, Inc., Westboro, MA), and trace minerals (MulTE-Pak-4, Smith & Nephew SoloPak, Elk Grove Village, IL). Patients continued on the assigned
parenteral solution for a period of two weeks or until advanced to an enteral tube feeding or an oral diet, whichever occurred first.

Twenty-four hour urine collections were obtained daily for determination of urinary urea nitrogen (UUN) and calculation of nitrogen balance. Serum albumin and total-iron-binding capacity (TIBC) were obtained upon enrollment and on a weekly basis in accordance with current Nutrition Support Service protocol. Blood urea nitrogen (BUN) was monitored daily. Electrolytes were monitored daily by the Nutrition Support Service and adjustments made as necessary. Each patient's body weight and peak body temperature were obtained daily from the Nursing service.

Serum albumin was determined by a dye-binding procedure with bromcresol green on an Ektachem 700 Analyzer (Eastman Kodak, Rochester, New York) (81). Serum TIBC was determined colorimetrically on the Cobas Mira Chemical System (Roche Diagnostic Systems, Nutley, New Jersey) (82, 83). Blood and urinary urea nitrogen were determined by the enzymatic conductivity rate method on the Beckman Astra 8 Analyzer (Beckman Instruments, Inc., Brea, CA) (84).

Nitrogen balance was determined using the methods of Wilmore (86):

\[
\text{Nitrogen balance} = \text{Nitrogen intake} - \frac{(\text{UUN} + 0.2(\text{UUN}) + 2)}{100}. \tag{3}
\]

Missing data points were common due to errors in 24-hour urine collection or failure to complete daily 24-hour
collections. However, each subject had a minimum of four complete collections.

The occurrence of any metabolic complications or mortality was documented. Patients were discontinued from the study if surgery or reoperation was deemed necessary.

All values were expressed as the mean ± standard deviation. Mean values were compared between groups using a non-paired two-tailed t-test. Regression analysis was used to identify trends in nitrogen balance for subjects on the hypocaloric and the isocaloric parenteral formulas. Fisher's exact test was used to analyze the proportion of subjects in each group to achieve improvement in serum albumin and TIBC. The alpha level was set at ≤0.05 a priori.

Results

Thirteen obese stressed patients participated in the study. The subjects weighed an average of 97.0±18.3 kg, which was 164% (range 130-210%) of ideal body weight. Eleven were postoperative from primarily abdominal procedures, while two were recovering from pancreatitis with pseudocysts. One subject (subject 5) died during the course of the study from multisystem failure and sepsis (Table 1).

Initial measured resting energy expenditures (MREE) and respiratory quotients (RQ) were not significantly different between the hypocaloric (MREE=1803±535 kcal, RQ=0.75±0.11) and the isocaloric group (MREE=1997±280 kcal, p=0.42;
<table>
<thead>
<tr>
<th>Patient #</th>
<th>Age yr.</th>
<th>Sex</th>
<th>Body Weight kg</th>
<th>% IBW</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPOCALORIC GROUP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>41</td>
<td>M</td>
<td>97.7</td>
<td>130</td>
<td>acute pancreatitis with multiple pseudocysts</td>
</tr>
<tr>
<td>2</td>
<td>86</td>
<td>F</td>
<td>87.9</td>
<td>164</td>
<td>total abdominal hysterectomy- endometrial cancer</td>
</tr>
<tr>
<td>5</td>
<td>58</td>
<td>F</td>
<td>85.4</td>
<td>179</td>
<td>re-operation for A-V bypass graft</td>
</tr>
<tr>
<td>7</td>
<td>38</td>
<td>F</td>
<td>78.2</td>
<td>138</td>
<td>pancreatitis, ARDS</td>
</tr>
<tr>
<td>9</td>
<td>61</td>
<td>F</td>
<td>77.0</td>
<td>178</td>
<td>adrenalectomy, sigmoid colectomy</td>
</tr>
<tr>
<td>11</td>
<td>62</td>
<td>M</td>
<td>114.0</td>
<td>151</td>
<td>laparotomy, splenectomy- MVA</td>
</tr>
<tr>
<td>ISOCALORIC GROUP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>F</td>
<td>101.5</td>
<td>172</td>
<td>hemicolecetomy, jejunal resection- desmoid tumor</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>F</td>
<td>71.1</td>
<td>142</td>
<td>exploratory laparotomy- necrotic small bowel and fistula</td>
</tr>
<tr>
<td>6</td>
<td>29</td>
<td>M</td>
<td>136.0</td>
<td>168</td>
<td>multiple trauma, closed head injury- MVA</td>
</tr>
<tr>
<td>8</td>
<td>67</td>
<td>F</td>
<td>119.5</td>
<td>210</td>
<td>total abdominal hysterectomy, bowel resection- ovarian CA</td>
</tr>
<tr>
<td>10</td>
<td>58</td>
<td>F</td>
<td>92.5</td>
<td>170</td>
<td>hemicolecetomy- ovarian CA</td>
</tr>
<tr>
<td>12</td>
<td>30</td>
<td>F</td>
<td>99.5</td>
<td>190</td>
<td>pancreatitis with pseudocyst</td>
</tr>
<tr>
<td>13</td>
<td>78</td>
<td>M</td>
<td>100.7</td>
<td>138</td>
<td>acute/chronic respiratory failure, congestive heart failure</td>
</tr>
</tbody>
</table>
RQ=0.68±0.10, p=0.29). Data for subjects with repeat measures of MREE and RQ are shown in Table 2. The hypocaloric subjects had final RQ values consistent with fasting, while isocaloric subjects had final RQ values consistent with mixed fuel consumption. The MREE tended to decline over time in both groups with the exception of two patients whose clinical status failed to improve or worsened during the study period.

Table 2: Measured Resting Energy Expenditures and Respiratory Quotients, Initial and Final Measures

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Initial MREE</th>
<th>RQ</th>
<th>Final MREE</th>
<th>RQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPOCALORIC GROUP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1090</td>
<td>0.77</td>
<td>1269</td>
<td>0.71</td>
</tr>
<tr>
<td>7</td>
<td>2270</td>
<td>0.73</td>
<td>3463a</td>
<td>0.85a</td>
</tr>
<tr>
<td>11</td>
<td>2552</td>
<td>0.55</td>
<td>2211</td>
<td>0.58</td>
</tr>
<tr>
<td>ISOCALORIC GROUP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2236</td>
<td>0.68</td>
<td>585</td>
<td>0.79</td>
</tr>
<tr>
<td>4</td>
<td>1772</td>
<td>0.61</td>
<td>578</td>
<td>0.81</td>
</tr>
<tr>
<td>6</td>
<td>2238</td>
<td>0.79</td>
<td>3653b</td>
<td>0.82</td>
</tr>
<tr>
<td>8</td>
<td>1750</td>
<td>0.83</td>
<td>1565</td>
<td>0.92</td>
</tr>
<tr>
<td>12</td>
<td>2345</td>
<td>0.64</td>
<td>744</td>
<td>0.68</td>
</tr>
<tr>
<td>13</td>
<td>1992</td>
<td>0.64</td>
<td>2270</td>
<td>0.78</td>
</tr>
</tbody>
</table>

a= Patient's medical condition deteriorated during study period.
b= Patient remained hypermetabolic throughout study period.
The measured resting energy expenditure (MREE) was greater than the predicted energy expenditure (using Harris-Benedict equations) in 62% of the subjects, while MREE was less than the Harris-Benedict predicted REE in 15% of the patients. Twenty-three percent of the subjects exhibited a MREE which was within ten percent of the predicted REE. The proportion of subjects who were hypermetabolic, hypometabolic, or within in the predicted range for energy expenditure did not differ between groups (Table 3).

Table 3: Comparison of Measured and Predicted Resting Energy Expenditure

<table>
<thead>
<tr>
<th></th>
<th>Hypocaloric</th>
<th>Isocaloric</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>MREE &gt; Predicted</td>
<td>4</td>
<td>4</td>
<td>8 (62%)</td>
</tr>
<tr>
<td>MREE &lt; Predicted</td>
<td>1</td>
<td>1</td>
<td>2 (15%)</td>
</tr>
<tr>
<td>MREE = Predicted</td>
<td>1</td>
<td>2</td>
<td>3 (23%)</td>
</tr>
</tbody>
</table>

Examination of initial UUN values, as a measure of metabolic stress, indicated no significant differences in stress level between the two groups (hypocaloric- 7.03±3.01 g UUN/day; isocaloric- 7.24±3.90 g UUN/day; t=0.11, p=0.92). Ten subjects had initial UUN values less than 10 g/day, while three (one in the hypocaloric group, two in the isocaloric group) had initial UUN values between 10 and 15 g/day.

Total parenteral nutrition support was provided for 9.6±3.0 d (range 5-15 d). The length of time on parenteral nutrition did not differ significantly between the
hypocaloric and the isocaloric groups. Nonprotein caloric intake averaged 936 kcal/day in the hypocaloric group, 54.2% of the measured REE. The isocaloric group received 1885 nonprotein kcal/d. Total caloric intake averaged 1440 kcal/day for the hypocaloric group and 2405 kcal/day for the isocaloric group. Protein intake did not differ significantly between groups. The hypocaloric subjects received 126 g protein (2.21 g/kg IBW) and the isocaloric group received 130 g protein (2.18 g/kg IBW). Table 4 summarizes the nonprotein caloric, protein, and total caloric intake for the experimental and control groups.

Regression analysis of the daily nitrogen balances revealed that nitrogen balance tended to decline over time in both the hypocaloric and the isocaloric groups, though only reaching statistical significance in four subjects (Table 5). Comparable numbers of subjects in both groups had mean nitrogen balances of less than -3 g/day (hypocaloric-2/6; isocaloric-2/7). The remainder of subjects had mean nitrogen balances in the range of -2 to +10 g/day. Mean nitrogen balance values were not significantly different between the hypocaloric and the isocaloric groups (Table 6).

Examination of changes in albumin and TIBC revealed no significant differences between the hypocaloric group and the isocaloric group. One of six hypocaloric subjects and three of seven isocaloric subjects achieved some improvement in serum albumin levels (p=0.34, one-tailed).
Table 4: Nutrient Intake

<table>
<thead>
<tr>
<th>Pt. #</th>
<th>Nonprotein calories</th>
<th>Protein</th>
<th>Total calories</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>total /kg IBW /kg ABW</td>
<td>g /kg IBW /kg ABW</td>
<td>total /kg IBW /kg ABW</td>
<td>days</td>
</tr>
<tr>
<td><strong>HYPOCALORIC GROUP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>730.8 9.7</td>
<td>7.3 100.8 1.34 1.03</td>
<td>1134.0 15.9</td>
<td>11.6</td>
</tr>
<tr>
<td>2</td>
<td>1148.4 21.4</td>
<td>13.1 158.4 2.96 1.80</td>
<td>1782.0 33.2</td>
<td>20.4</td>
</tr>
<tr>
<td>5</td>
<td>730.8 15.3</td>
<td>8.6 100.8 2.11 1.18</td>
<td>1134.0 23.8</td>
<td>13.3</td>
</tr>
<tr>
<td>7</td>
<td>1044.0 18.4</td>
<td>13.4 144.0 2.54 1.84</td>
<td>1620.0 28.5</td>
<td>20.7</td>
</tr>
<tr>
<td>9</td>
<td>812.0 18.8</td>
<td>10.5 94.6 2.19 1.29</td>
<td>1184.8 27.4</td>
<td>15.4</td>
</tr>
<tr>
<td>11</td>
<td>1148.4 15.2</td>
<td>10.1 158.4 2.10 1.39</td>
<td>1782.0 23.6</td>
<td>15.6</td>
</tr>
<tr>
<td>Mean</td>
<td>935.7 16.47</td>
<td>10.53 126.17 2.21 1.41</td>
<td>1439.47 25.25</td>
<td>16.17</td>
</tr>
<tr>
<td>S.D.</td>
<td>200.7 4.06</td>
<td>2.36 30.59 0.65 0.34</td>
<td>322.09 40.34</td>
<td>23.97</td>
</tr>
</tbody>
</table>

| **ISOCALORIC GROUP** | | | | |
| 3     | 2088.0 35.3 | 20.6 144.0 2.44 1.42 | 2664.0 45.1 | 25.2 | 14 |
| 4     | 1712.2 54.2 | 24.1 118.1 2.36 1.66 | 2184.5 43.7 | 30.7 | 11 |
| 6     | 2088.0 25.8 | 15.4 144.0 1.78 1.06 | 2664.0 32.9 | 13.6 | 7 |
| 8     | 1670.4 29.4 | 14.0 116.2 2.03 0.96 | 2131.2 37.5 | 17.8 | 11 |
| 10    | 1566.0 28.7 | 16.9 108.8 1.98 1.17 | 1998.0 36.7 | 21.6 | 5 |
| 12    | 2192.4 41.9 | 22.0 151.2 2.69 1.52 | 2797.2 53.3 | 28.1 | 15 |
| 13    | 1879.2 25.8 | 18.7 123.6 1.78 1.29 | 2397.6 33.0 | 23.8 | 12 |
| Mean  | 1885.2 31.59 | 18.81 130.01 2.18 1.30 | 2405.21 40.34 | 23.97 | 10.7 |
| S.D.  | 243.1 5.87 | 3.66 16.76 0.41 0.25 | 310.18 7.50 | 4.66 | 3.6 |

32
Table 5: Nitrogen Balance Regression Analysis

<table>
<thead>
<tr>
<th>Pt. #</th>
<th>Mean N2 balance&lt;sup&gt;a&lt;/sup&gt;</th>
<th>n</th>
<th>Duration days</th>
<th>r</th>
<th>p</th>
<th>Regression Equation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-0.39</td>
<td>7</td>
<td>8</td>
<td>-0.48</td>
<td>0.28</td>
<td>(-0.54)x + 1.77</td>
</tr>
<tr>
<td>2</td>
<td>2.34</td>
<td>6</td>
<td>9</td>
<td>-0.63</td>
<td>0.18</td>
<td>(-1.60)x + 9.79</td>
</tr>
<tr>
<td>5</td>
<td>8.35</td>
<td>8</td>
<td>10</td>
<td>-0.97</td>
<td>&lt;0.001</td>
<td>(-0.89)x + 12.93</td>
</tr>
<tr>
<td>7</td>
<td>-1.58</td>
<td>8</td>
<td>10</td>
<td>-0.74</td>
<td>0.04</td>
<td>(-0.84)x + 2.64</td>
</tr>
<tr>
<td>9</td>
<td>-3.70</td>
<td>4</td>
<td>7</td>
<td>-0.15</td>
<td>0.85</td>
<td>(-0.23)x - 2.90</td>
</tr>
<tr>
<td>11</td>
<td>-12.97</td>
<td>4</td>
<td>6</td>
<td>-0.94</td>
<td>0.06</td>
<td>(0.67)x - 3.21</td>
</tr>
</tbody>
</table>

**HYPOCALORIC GROUP**

**ISCALORIC GROUP**

| 3     | 0.46                         | 8 | 14            | -0.90 | 0.003 | (-1.91)x + 13.35             |
| 4     | 5.81                         | 4 | 11            | -0.41 | 0.59  | (-0.39)x + 7.74              |
| 6     | -17.39                       | 4 | 7             | 0.04  | 0.96  | (0.08)x - 17.76              |
| 8     | 9.95                         | 5 | 11            | -0.97 | 0.006 | (-1.27)x + 16.86             |
| 10    | -2.37                        | 4 | 5             | -0.61 | 0.39  | (-2.15)x + 4.62              |
| 12    | 8.89                         | 7 | 15            | -0.47 | 0.28  | (-0.47)x + 11.78             |
| 13    | -3.40                        | 11| 12            | 0.09  | 0.78  | (0.08)x - 3.96               |

<sup>a</sup> = calculated by summation of daily nitrogen balances, divided by n (number of data points)

n = number of data points
Table 6: Comparison of Hypocaloric and Isocaloric Groups

<table>
<thead>
<tr>
<th></th>
<th>HYPOCALORIC (mean±S.D.)</th>
<th>ISOCALORIC (mean±S.D.)</th>
<th>SIGNIFICANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57.7±17.3</td>
<td>57.9±20.4</td>
<td>NS (p=0.99)</td>
</tr>
<tr>
<td>Initial body weight, kg</td>
<td>90.0±13.9</td>
<td>103.0±20.5</td>
<td>NS (p=0.22)</td>
</tr>
<tr>
<td>% IBW</td>
<td>156.7±20.5</td>
<td>170.0±25.2</td>
<td>NS (p=0.32)</td>
</tr>
<tr>
<td>Initial UUN, g/day</td>
<td>7.03±3.01</td>
<td>7.24±3.90</td>
<td>NS (p=0.92)</td>
</tr>
<tr>
<td>Nonprotein calories</td>
<td>935.7±200.7</td>
<td>1885.2±243.1</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Nonprotein kcal/kg IBW</td>
<td>16.37±4.06</td>
<td>31.59±5.87</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Nonprotein kcal/kg ABW</td>
<td>10.53±2.36</td>
<td>18.81±3.65</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Protein, g</td>
<td>126.17±30.59</td>
<td>130.01±16.76</td>
<td>NS (p=0.78)</td>
</tr>
<tr>
<td>Protein g/kg IBW</td>
<td>2.21±0.54</td>
<td>2.18±0.40</td>
<td>NS (p=0.91)</td>
</tr>
<tr>
<td>Protein g/kg ABW</td>
<td>1.41±0.34</td>
<td>1.30±0.25</td>
<td>NS (p=0.52)</td>
</tr>
<tr>
<td>Total calories</td>
<td>1439.47±322.09</td>
<td>2405.21±310.18</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Total kcal/kg IBW</td>
<td>25.25±6.14</td>
<td>40.34±7.50</td>
<td>p=0.003</td>
</tr>
<tr>
<td>Total kcal/kg ABW</td>
<td>16.17±3.70</td>
<td>23.97±4.66</td>
<td>p=0.007</td>
</tr>
<tr>
<td>Duration, days</td>
<td>8.3±1.6</td>
<td>10.7±3.6</td>
<td>NS (p=0.16)</td>
</tr>
<tr>
<td>Weight lost, kg</td>
<td>5.48±6.38</td>
<td>9.60±8.49</td>
<td>NS (p=0.35)</td>
</tr>
<tr>
<td>Mean Nitrogen Balance, g/day</td>
<td>-1.33±7.06</td>
<td>0.28±9.41</td>
<td>NS (p=0.74)</td>
</tr>
</tbody>
</table>
Only one subject in each of the groups realized any improvement in serum TIBC (p=0.73, one-tailed).

Weight loss was not statistically different between the two groups. Subjects receiving the hypocaloric formula lost 5.5±6.4 kg, while those in the isocaloric group lost 9.6±8.5 kg (t=0.97, p=0.35). Two subjects (one in each group) failed to lose weight. Patient 7's clinical condition worsened and she experienced fluid overload; pt. 12's weight remained stable throughout the study period.

Table 6 summarizes the statistical analyses comparing the hypocaloric and isocaloric groups.

Discussion

Nitrogen balance remains the gold standard for measuring the adequacy of a nutrition support regimen (79). Nitrogen balance is the difference between nitrogen intake and nitrogen output. A positive nitrogen balance reflects anabolism of body tissues, while a negative nitrogen balance represents catabolism.

Several methods have been suggested in the literature for determining nitrogen output (85-89). All require an estimation of total urinary nitrogen (TUN) by using urinary urea nitrogen (UUN) plus a fudge factor to account for non-UUN nitrogen losses. Recent studies have indicated that the determination of TUN directly is a preferable method, for the underlying assumption that urea is approximately 80%
of nitrogen excretion is not always true in stressed patients (90,91). However, measurement of TUN is not available in many clinical settings, including the setting for this study. Therefore, the use of UUN values and fudge factors is still appropriate in these situations.

Shifts in body urea nitrogen (due to an inability to excrete urea) affect the determination of nitrogen balance. As a result of these shifts, corrections are suggested for patients with rapidly changing renal function. The method of Harvey et al. is recommended when BUN values change by more than 5 mg/dL during a collection period (92). This study excluded those with renal disease at the beginning of the study period. Patient 5 died of multisystem failure; her BUN values did change significantly during the study. Correction by Harvey's method was pursued; the resulting regression equation \((-1.73)x + 12.4, r=-0.95\) was very similar to the equation obtained using uncorrected nitrogen balance data \((-0.89)x + 12.93, r=-0.97\). The uncorrected equation was retained.

Nitrogen balance tended to decline in both groups, regardless of nonprotein caloric intake. Additionally, the mean nitrogen balance of both groups was very similar. This supports the hypothesis that obese patients can retain lean body mass while receiving hypocaloric, high-protein nutrition support.
A decline in nitrogen balance (toward equilibrium) would be expected in those patients who began the study in positive nitrogen balance as their metabolic stress decreased and their condition improved. However, the decline observed in those who began in negative nitrogen balance is more worrisome. This may indicate that these patients' condition did not improve over the study period; several patients did experience a deterioration in medical status during the study, though they did improve subsequently. It must be emphasized that few of the regression analyses were statistically significant; several contained only four data points, making any conclusions weak at best.

The protein intake of these subjects was similar to published recommendations for stressed obese patients. Pasulka and Kohl recommend an intake of 1.5–1.7 g protein/kg IBW (19). Baxter and Bistrian also suggest 1.5 g protein/kg IBW (24). Dickerson recommends an intake of 2.0–2.5 g protein/kg for stressed patients (79). Dickerson, et al. fed 2.13 g protein/kg IBW (1.16 g/kg actual body weight (ABW)) to the obese patients in their study (23). Hypocaloric subjects in this study received 2.21 g protein/kg IBW (1.41 g/kg ABW).

Published recommendations for nonprotein caloric intake vary more widely. A maximum of 25 kcal/kg is recommended by Pasulka and Kohl, though it is not indicated if this suggestion is for nonprotein or total calories (19). Dickerson
recommends a nonprotein caloric intake that is less than the measured REE for unstressed patients weighing greater than 120% IBW (79). Baxter and Bistrian recommend feeding 300-500 calories less than the measured or estimated REE, up to a maximum of 2000 kcal/day (24). Dickerson, et al. fed an average of 880 nonprotein kcal to the obese subjects in their study, providing approximately 14 kcal/kg IBW or 7 kcal/kg ABW (23). Subjects receiving hypocaloric parenteral nutrition in this study received 16.5 kcal/kg IBW (10.5 kcal/kg ABW).

Greater than 75% of the obese subjects in this study had initial measured resting metabolic rates that were more than ten percent different than their predicted RMR (by Harris-Benedict equations). These results agree with the findings of other researchers (30,39). The observed difference in measured and predicted RMR supports the need for indirect calorimetry in the obese population. Repeat of RMR tended to fall, indicating the resolution of the initial stress.

Examination of repeat RQ measures revealed the hypocaloric subjects tended to have values indicative of fasting. This is consistent with catabolism of endogenous fat for energy. The isocaloric group demonstrated RQ values more consistent with mixed fuel consumption.

The stress level of the patients in this study are very similar to those studied by Dickerson, et al. Ten of the
thirteen patients in this study had initial UUN values less than 10 g/day, while three had initial UUN values between 10 and 15 g/day. These patients would be classified as mildly to moderately stressed (67). Dickerson, et al. also reported their subjects as mildly to moderately stressed (23).

Dickerson, et al. observed patients receiving hypocaloric nutrition for a mean of 48 days (23). Over this time period, patients achieved positive nitrogen balance or nitrogen equilibrium, improvements in serum albumin and TIBC, and tissue healing (23). Given the similarity of their patients and the patients in this study, it is likely that similar results would have been realized in this study if the duration of hypocaloric feeding was longer.

Weight loss was not the primary goal of hypocaloric feeding in this study. The purpose was to achieve clinical improvement without contributing further to the individual's obesity. Comparable weight loss was observed in both the isocaloric and the hypocaloric groups. Weight loss is common in the acute period after illness or injury. Many of the subjects were postoperative; some of the weight loss could be attributed to the diuresis of fluids given during surgery. Another patient had suffered a closed head injury and was comatose; weight loss and muscle atrophy is not uncommon in this circumstance.

The null hypothesis of this study was accepted. Patients receiving hypocaloric parenteral nutrition were able
to achieve nitrogen balance to the same degree as those receiving isocaloric parenteral nutrition. Mean nitrogen balance values were not statistically different between groups. Additionally, nitrogen balance tended to decline over time in both groups without significant differences between groups.
CHAPTER IV
SUMMARY AND CONCLUSIONS

Summary

The use of hypocaloric parenteral nutrition in stressed obese patients has recently been suggested. It is unknown if hypocaloric parenteral nutrition support is as efficacious as providing acutely ill obese patients with their measured resting energy expenditure. The purpose of this study was to determine if acutely ill obese patients receiving hypocaloric parenteral nutrition can achieve nitrogen balance to the same degree as those obese patients receiving isocaloric parenteral nutrition.

Thirteen patients were randomly assigned to receive either 50% (n=6) or 100% (n=7) of their measured resting energy expenditure as nonprotein calories. The protein content of the two parenteral solutions was identical. Patients received the assigned diet for a maximum of fifteen days.

Daily 24-hour urine collections were obtained to determine urinary urea nitrogen excretion. Nitrogen balance was determined daily. Blood urea nitrogen and weight were also
monitored daily. Serum albumin and TIBC were obtained upon enrollment and on a weekly basis.

The hypocaloric and isocaloric groups were similar on age, initial body weight, % IBW, duration on TPN, initial UUN values, and protein intake. The hypocaloric group received 2.21±0.54 g protein/kg IBW, while the isocaloric group received 2.18±0.40 g protein/kg IBW (p=0.91). Nonprotein caloric intake averaged 936 kcal (16 kcal/kg IBW) in the hypocaloric group. The isocaloric group received 1885 kcal (32 kcal/kg IBW) (p<0.001).

No significant differences were found in the ability to achieve nitrogen balance between those receiving 50% and 100% of measured resting energy expenditures. Mean nitrogen balance was -1.33±7.06 gm/day in the hypocaloric group and 0.28±9.41 gm/day in the isocaloric group (p=0.74). Nitrogen balance tended to decline over time in both obese patients receiving hypocaloric and those receiving isocaloric parenteral nutrition, though only to a significant degree in four subjects (two in each group). No differences were seen between the two groups in the ability to improve serum albumin or TIBC.

Conclusions

The mildly to moderately stressed obese patients receiving hypocaloric parenteral nutrition in this study were able to achieve nitrogen balance to the same degree
as those obese patients receiving isocaloric parenteral nutrition. This confirms the results found by Dickerson et al (23) in a study of 13 obese patients. Though this study did not see the same degree of improvement in serum albumin or TIBC or the attainment of nitrogen balance as observed by Dickerson, et al., it is likely that similar results would have been obtained if the duration of this study was extended. These findings also support the recommendations of other clinicians (19, 24).

Considering these results and conclusion, the following recommendations are given:
1. Further scientific studies are needed to replicate these results. A multicenter study would be the most effective strategy to realize this need.
2. The use of hypocaloric feeding in severely stressed obese patients should be further explored. This study involved mildly to moderately stressed obese patients; these patients achieved nitrogen balance to the same degree when receiving 50% or 100% of the measured resting energy expenditure. It is unknown if severely stressed obese patients can achieve similar results while receiving hypocaloric nutrition.
3. Further study is needed to determine the most beneficial protein intake. Current recommendations for obese patients are 1.5-2.5 g protein/kg IBW (19,23,24). This study provided 2.2 g/kg IBW. Provision of protein in the
lower end of the recommended range may not achieve the same results.

4. Indirect calorimetry should become a part of standard nutrition support for obese patients. This study demonstrates the importance of indirect calorimetry for obese patients receiving nutrition support. Seventy-seven percent of these subjects had measured resting energy expenditures that varied more than ten percent from their predicted energy needs using Harris-Benedict equations.
APPENDIX A

Consent to Investigational Treatment or Procedure
THE OHIO STATE UNIVERSITY

CONSENT TO INVESTIGATIONAL TREATMENT OR PROCEDURE

I, ____________________________, hereby authorize or direct Drs. Louis J. Flanbaum and associated or assistants of their choosing, to perform the following treatment or procedure, (described in general terms), I will be given an intravenous diet containing a normal or reduced amount of calories in order to determine whether this dose is capable of meeting my nutritional needs, while minimizing complications. Neither I nor the investigators will know which solution is given and that it will be determined by random selection (similar to a flip of a coin).

upon ________________________________________________

(myself or name of subject)

The experimental (research) portion of the treatment or procedure is: One of two levels of (normal vs low) will be given to me as part of my intravenous nutrition to determine whether the lower level of calories is sufficient for patients with my condition. The normal level of calories is that which is usually given to patients in the surgical intensive care unit. Collection of urine, daily weight measurements, daily fluid intake and output and weekly measurement of my energy (calorie) needs will occur.

This is done as part of an investigation entitled: Use of Hypocaloric feedings in Acutely Ill Obese Patients

1. Purpose of the procedure or treatment: Understanding the amount of calories which is needed by patients with my condition will provide an improvement in treatment of sick obese patients; that is, lowering the amount of calories fed may be beneficial in sick obese patients.

2. Possible appropriate alternative procedures of treatment (not to participate in the study is always an option). I understand that I may not participate in this study and in this event, there will be no change in the way I am treated.

3. Discomforts and risks reasonably to be expected: I understand that the only addition to my standard treatment is collection of blood (approximately 2 tablespoons) and measurement of my energy requirements. The blood will be drawn from my catheter and the test for energy requirements will analyze air that I breathe, either directly from my breathing machine or using a mask on my face for about 30 minutes. I understand that it may take longer for me to achieve a positive nitrogen balance if I am given fewer calories.

4. Possible benefits for subjects/society: Information concerning the most appropriate amount of calories needed in the diet of patients with my problem will be determined.

5. Anticipated duration of subject's participation (including number of visits): This study will be continued while I am a patient at the Ohio State University Hospital and require total nutrition support. I will be seen daily by the nutrition support service.

I hereby acknowledge that __________________________ has provided information about the procedure described above, about my rights as a subject, and he/she answered all questions to my satisfaction. I understand that I may contact his/her at Phone No. __________ should I have additional questions. He/She has explained the risks described above and I understand them; he/she has also offered to explain all possible risks or complications.
I understand that, where appropriate, the U.S. Food and Drug Administration may inspect records pertaining to this study. I understand further that records obtained during my participation in this study that may contain my name or other personal identifiers may be made available to the sponsor of this study. Beyond this, I understand that my participation will remain confidential.

I understand that I am free to withdraw my consent and participation in this project at any time after notifying the project direct without prejudicing future care. No guarantee has been given to me concerning this treatment or procedure.

In the unlikely event of injury resulting from participation in this study, I understand that immediate medical treatment is available at University Hospital of The Ohio State University. I also understand that the costs of such treatment will be at my expense and that financial compensation is not available. Questions about this should be directed to the Human Subjects Review Office at 292-9046.

I have read and fully understand the consent form. I sign it freely and voluntarily. A copy has been given to me.

Date: ____________ Time ____________ PM Signed______________

Subject

Witness(es) ____________

(Person Authorized to
Consent for Subject If Required)

Required

I certify that I have personally completed all blanks in this form and explained them to the subject or his/her representative before requesting the subject or his/her representative to sign it.

Signed __________________

(Signature of Project Director or his/her
Representative)

Authorized

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LIST OF REFERENCES


