CALORIC NEEDS OF LESS THAN 1250 GRAM INFANTS IMMEDIATELY AFTER EXTUBATION

by

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ABSTRACT

CALORIC NEEDS OF LESS THAN 1250 GRAM INFANTS IMMEDIATELY AFTER EXTUBATION

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The purpose of this study was to retrospectively investigate the effect of mechanical ventilator support, via an endotracheal tube, on the nutritional intake and weight gain patterns of infants weighing less than 1250 grams at birth. The hypothesis was that preterm infants who have recently been extubated (PV) require more calories than they did immediately prior to extubation (V) in order to continue the same rate of growth once full respiratory support via an endotracheal tube and mechanical ventilator has been discontinued.

An initial assessment of 15 patients revealed a non-significant trend towards improved weight gain (g/kg/day) post-extubation. Energy utilization (Cal/g) remained unchanged. Six of the initial 15 patients continued to receive supplemental oxygen at 2 months of age; they were matched, by birth weight and gestational age, to 6 patients (from the same initial sample) who did not receive supplemental oxygen at 2 months of age (no O_2 at 2 mo). Upon comparison of the two sub-groups, it was noted that extubation took place at a significantly earlier age and

lower weight for the patients not on O_2 at 2 mo. While weight gain was unchanged from V to PV for patients on O_2 at 2 mo, it increased significantly for infants not on O_2 at 2 mo. Similarly, energy utilization per gram of weight gain (Cal/g) increased for patients on O_2 at 2 mo, yet for patients not on O_2 at 2 mo, it decreased, showing improved energy efficiency. All comparisons were made by paired 2-tailed t test. The two matched sub-groups seem to represent two different types of infants in regard to weight gain and energy utilization; the results are most likely related to degree of morbidity. Recommendations are provided as to how this study can be expanded and therefore become applicable to the increasing population of less than 1250 gram infants. If efficiency of energy utilization is indeed significantly less in certain sub-groups of VLBW infants, then more attention must be paid to the provision of adequate calories for these individuals.

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CHAPTER 1

THE PROBLEM AND ITS SETTING

Introduction

In recent years, medical science has made great advances. It is now possible to provide the types and amounts of nutrients necessary to sustain many small and/or sick infants who previously would not have survived past the first days or weeks of life. One of the reasons for this drastic improvement is the discovery of parenteral nutrition as a viable feeding regimen. In addition, neonates who are able to tolerate enteral feedings are now fed infant formulas that have been refined to meet the needs of premature infants. Other major medical strides relating to the care of the high risk infant revolve around the technological developments which have occurred. Advances in the area of respiratory care have greatly improved the chances for premature infants to survive the arrival to extrauterine life with immature lungs. Respiratory and nutritional support can now decrease neonatal morbidity and mortality in ways that were not possible only a few short years ago.

The Statement of the Problem

The purpose of this study was to investigate the rate of growth of pre-term infants during intubation and immediately after extubation in order to see how respiratory support affects nutritional needs and growth patterns.

The Hypothesis

The hypothesis was that pre-term infants who have recently been extubated require more calories than they did during intubation in order to continue the same rate of growth once full respiratory support via a ventilator and an endotracheal tube has been discontinued.

The Delimitations

This study did not include full-term infants or infants with birth weights greater than 1250 grams.

This study was not limited solely to patients who were fed by the parenteral route since it is not ethical to withhold enteral feedings simply for study purposes. Therefore, patients were fed parenterally or enterally, or with a combination of parenteral and enteral feedings.

Definition of Terms

Appropriate-for-gestational age Appropriate-for-gestational age refers to a birth weight that is between the 10th and 90th percentiles for a given gestational age.

<u>Enteral nutrition</u> Enteral nutrition is a term that is used to describe a route of feeding whereby nutrients enter the body through the gastrointestinal tract in contrast to going directly through the veins into the bloodstream.

<u>Extubation</u> Extubation means the removal of an endotracheal tube which attaches a patient to the respirator.

<u>Full-term</u> A full-term or term infant is one who is born at or after 37 weeks' gestation.

<u>Gestational age</u> Gestational age is the duration of gestation as measured from the first day of the last menstrual period. It is usually expressed in days or weeks.

<u>High-risk neonate</u> The term high-risk neonate, as used in this paper, refers to an infant who is predisposed to developing physical problems because it is premature and/or of low birth weight (LBW), or one who is experiencing medical or surgical complications due to a congenital condition or to difficulties arising during the first 28 days of life.

<u>Intubation</u> Intubation is the insertion of an endotracheal tube into the larynx through the glottis for entrance of air via a respirator.

<u>Large-for-gestational age</u> Large-for-gestational age refers to a birth weight that is above the 90th percentile for a given gestational age.

<u>Low birth weight</u> A low birth weight infant is one who weighs less than 2500 grams at birth.

Neonatal The neonatal period is the time from birth through 28 days of life.

Parenteral nutrition Parenteral nutrition is a term that is used to describe a route of feeding whereby nutrients are placed directly into the veins rather than into the gastrointestinal tract (as with enteral alimentation). Standard parenteral nutrition solutions contain protein, carbohydrate, vitamins and minerals. Lipids (fat) may also be provided parenterally.

Premature or pre-term A premature or pre-term infant is one who is born before 37 weeks' gestation.

Respirator A respirator is a machine which is used to provide prolonged artificial respiration. It is sometimes referred to as a mechanical ventilator. A patient may be attached to a respirator by an endotracheal (ET) tube, a mask or nasal prongs.

Specific dynamic effect The specific dynamic effect is the heat or energy produced in excess of basal metabolism as the result of the ingestion of nutrients in food. (Also called specific dynamic action, the thermic effect of food, the calorigenic effect or diet-induced thermogenesis).

Small-for-gestational age Small-for-gestational age refers to a birth weight that is below the 10th percentile for a given gestational age.

Total parenteral nutrition The term total parenteral nutrition is used to refer to an intravenous solution that provides a complete diet (protein, carbohydrate, fat, vitamins and minerals).

<u>Very low birth weight</u> A very low birth weight infant is one who weighs less than 1500 grams at birth.

<u>Abbreviations</u>

<u>AGA</u> is the abbreviation for appropriate-for-gestational age.

<u>BPD</u> is the abbreviation for bronchopulmonary dysplasia.

<u>CLD</u> is the abbreviation for chronic lung disease.

<u>ET</u> is the abbreviation for endotracheal (as in endotracheal tube).

<u>GA</u> is the abbreviation for gestational age.

<u>GI</u> is the abbreviation for gastrointestinal.

<u>HMD</u> is the abbreviation for hyaline membrane disease.

<u>IUGR</u> is the abbreviation for intrauterine growth retardation.

<u>IVH</u> is the abbreviation for intraventricular hemorrhage.

<u>LBW</u> is the abbreviation for low birth weight.

<u>LGA</u> is the abbreviation for large-for-gestational age.

<u>NEC</u> is the abbreviation for necrotizing enterocolitis.

<u>NICU</u> is the abbreviation for neonatal intensive care unit.

<u>OFC</u> is the abbreviation for occipital-frontal circumference.

<u>PDA</u> is the abbreviation for patent ductus arteriosus.

<u>PN</u> is the abbreviation for parenteral nutrition.

RDS is the abbreviation for respiratory distress syndrome.

SDE is the abbreviation for specific dynamic effect.

SGA is the abbreviation for small-for-gestational age.

TPN is the abbreviation for total parenteral nutrition.

VLBW is the abbreviation for very low birth weight.

Assumptions

The first assumption The first assumption is that in order to be able to compare growth during and post respiratory support, the "normal" growth rate for the entire period of time must be constant.

The second assumption The second assumption is that certain abnormal physical or medical conditions (which are not experienced by all premature infants) may influence growth adversely. Infants with these conditions must be addressed separately.

The third assumption The third assumption is that once preterm infants regain their birth weight, they will grow at a steady rate (at least until approximately 40 weeks' post-conceptual age) as long as they receive adequate nutritional support and do not experience major medical complications or setbacks.

The fourth assumption The fourth assumption is that nutritional needs of premature infants are different during periods of respiratory support in comparison to the time immediately following discontinuation of ventilator support.

The fifth assumption The fifth assumption is that enteral calories can theoretically be equated to parenteral calories by subtracting a factor (% of enteral calories) that accounts for the caloric expenditure of the specific dynamic effect of enteral feedings, as well as energy losses through the stool. That is, parenteral calories are apparently somewhat more efficient (less wasteful) than enteral calories with regard to absorption. It is a generally accepted fact that it takes more enteral calories, as compared to parenteral, to produce equivalent weight gain in infants.

The sixth assumption The sixth assumption is that the margin of error in calculating nutritional intake and in measuring body weight is low and is uniform among all study patients.

CHAPTER 2

REVIEW OF RELATED RESEARCH AND LITERATURE

Introduction

Definition of Prematurity and Low Birth Weight

Tiny infants have been described as pre-term, term and post-term, as well as low birth weight. Strict definitions of these and other related terms have been published (Dunn 1985) in hopes that all infants could be neatly classified at birth. In reality, though, there are no sharp dividing lines between mature and premature babies. Not all so-called "premature" infants (those who are born at less than 37 weeks' gestation), for example, are low birth weight (less than 2500 grams at birth). Likewise, not all low birth weight infants are premature. While premature infants generally are expected to be confronted with certain medical complications, not all pre-term neonates face all of the same problems to the same degree. Not all premature infants grow or fail to grow to the same extent. All of these factors tend to make the job of caring for infants who spend their first weeks or months in an intensive care nursery both difficult and confusing. In an attempt to approach the care of these infants in an orderly manner, strict definitions in regard to the birth age and size of small infants continue to be applied.

Incidence of Prematurity and Low Birth Weight

Premature infants are classified into several groups by birth weight when morbidity and mortality are discussed. For example, while infants who weigh up to 2500 grams at birth are called low birth weight (LBW), those who weigh up to 1500 grams at birth are classified as very low birth weight (VLBW). Low birth weight infants are usually the result of premature birth or intrauterine growth retardation (IUGR); LBW infants are 40 times more likely to die during the neonatal period than normal birth weight infants (Behrman 1987). However, VLBW infants are 200 times more likely to die during this period according to Behrman (1987). In 1981, the incidence of very low birth weight deliveries in the United States was 12 per 1000. Survival is directly related to birth weight. Approximately 2% of 501 to 600 gram infants survive; however, 85% to 95% of 1250 to 1500 gram infants survive (Behrman 1987).

Growth of Premature Infants

Normal Growth Patterns in Premature Infants

This study focused on infants who fall into the categories of premature or pre-term and very low birth weight. Basically, all VLBW infants are premature. For these neonates, there are two general goals during hospitalization: to allow normal growth to occur and to discharge healthy (or nearly healthy) infants. With regard to the overall health status of the babies, each medical problem, including growth, must be addressed in relation to the patient's total health or disease status. Currently accepted treatment modalities are applied with hopes that the result will be positive; that is, that diseases and deficiencies will be eliminated. The goal of allowing for normal growth to occur is not as clearly defined, however. All premature infants are, by definition, abnormal. Therefore, what is "normal" growth for these "abnormal" patients? Keen and Pearse (1985) touched on the problem when they asked the question: ". . . is normality a description of the entire population or is it to be defined with reference to some ideal standard?" For lack of a better goal, neonatal health care providers seek to support growth rates that approximate those of the third trimester of intrauterine life (Heird 1979).

Intrauterine weight gain Many researchers have compiled growth curves for premature infants in an attempt to describe normal intrauterine growth patterns. One of the most commonly used intrauterine growth curves, that of Lubchenco, et al. (1963), is based on the birth weights of more than 5000 live-born infants. As a result of the work of Lubchenco, et al., it can be shown, as stated by Shaw

(1982), that "between 24 and 26 weeks gestation a fetus growing along the 50th percentile is gaining 14.5 g/kg/day."

Extrauterine weight gain Longitudinal research conducted by Grausz and Bamberger (1985) focused on weight gain of 290 infants who weighed less than 1750 grams at birth. Study criteria were that participants grew for 2 or more weeks after regaining their birth weight, were discharged alive, and did not suffer from chronic respiratory, gastrointestinal (necrotizing enterocolitis) or neurological disease. Weight gain, from the time the patient regained birth weight, was recorded weekly until discharge. Mean daily weight gain was analyzed for all patients. Patients were grouped by gestational age and by birth weight (based on 250 gram increments from 500 to 1750 grams). There was no significant correlation between mean daily weight gain (g/kg/day) and gestational age, birth weight, percent weight loss after birth, or the number of days needed to regain birth weight after the initial weight loss. A significant difference in weight gain was seen between appropriate-for-gestational age (AGA) and small-for-gestational age (SGA) infants. The AGA infants gained 15.9 g/kg/day from the time they regained their birth weight until the time they were discharged from the hospital. The SGA infants gained 16.8 g/kg/day during the same period. Ten to fifteen percent of the 290 infants studied exhibited slightly lower rates of weight gain during the first one to two weeks after regaining their birth weight, in comparison to the subsequent nursery course. Surprisingly, there was a lack of significant difference in mean daily weight gain for the patients studied, in relationship to both birth weight and gestational age. There was also no evidence of a diminished rate of weight gain (at least up to the time when most babies left the nursery). In general, patients were discharged at a weight of 2000 to 2100 grams. Though babies did not gain weight at a steady daily rate each and every day (periods of rapid weight gain were interspersed with days of slow gain and even losses), a steady average daily weight gain was documented.

The work of Grausz and Bamberger (1985) revealed that certain normal events in the hospital course of LBW infants played predictable roles in regard to weight gain. For example, changing from mixed enteral-parenteral intake to 100% enteral feeding or extending intervals between feedings from 2 to 3 hours resulted in a transient decrease in caloric intake, and thus decreased weight gain.

<u>Aberrant Intrauterine Growth Patterns in Premature Infants</u>

In addition to the "normal" events which can affect weight gain in neonates, there are a number of medical conditions which can have profound effects on weight gain and growth. Aberrant growth patterns can actually begin during intrauterine life.

<u>Large-for-gestational age</u> Large-for-gestational age (LGA) premature infants are typically infants of diabetic

mothers. These infants have hyperinsulinemia. It is not known whether or not the excessive growth is the result of the hyperinsulinemia or whether other growth parameters are affected by the increase in insulin (Lubchenco and Koops 1987). These infants are rarely a problem with regard to future growth.

Small-for-gestational age By far, the group of premature infants who begin life with the greatest disadvantage in relation to growth is the group labeled small-for-gestational age. Conditions related to intrauterine growth retardation (IUGR) are much more common than those leading to excessive intrauterine growth (Lubchenco and Koops 1987). The incidence of congenital anomalies in SGA infants is high. In general, malformed fetuses experience decreased intrauterine growth. Chronic intrauterine infections, such as those caused by rubella virus, cytomegalovirus and Toxoplasma, usually inhibit growth. Fetal undernutrition, whether related to inability of nutrients to reach the fetus or to maternal starvation or nutrient deficiencies, is responsible for the majority of SGA infants. Low socioeconomic status, twins, toxemia, hypertensive cardiovascular disease and small or diseased placenta, as well as smoking and the abuse of alcohol and drugs, can all lead to the birth of an infant with IUGR (Lubchenco and Koops 1987).

Aberrant Extrauterine Growth Patterns in Premature Infants

Intrauterine growth retardation must be discussed any time that the topic of extrauterine growth is addressed because certain intrauterine conditions, namely IUGR, are clinically significant in SGA infants. Small-for-gestational age infants have an inability to conserve heat; therefore, they have an increased need for energy (caloric intake). They have been unable to build up large stores of glycogen or fat reserves during intrauterine life. This frequently results in hypoglycemia (Lubchenco and Koops 1987). Such infants also appear to run a higher risk of developing necrotizing enterocolitis (a gastrointestinal condition which usually leads to growth retardation). The prognosis for catch-up growth (i.e., growth rates in excess of those found <u>in utero</u>) depends partly on the initial cause of the growth retardation. A head circumference less than the tenth percentile at birth is associated, in part, with poor growth (Behrman 1987).

<u>Medical problems</u> There are two major causes of extrauterine growth failure in LBW infants: intrauterine growth retardation and failure of an infant to grow because of severe illness or inadequate nutrition during extrauterine life (Fitzhardinge 1987). A number of problems typically occurring among LBW infants and causing poor weight gain, relate to severe illness or inadequate nutrition. Medical problems will be addressed first. The

condition of small-for-gestational age has already been discussed. As long as adequate calories are provided, infants who are SGA tend to exhibit a higher rate of weight gain than those who are AGA (Grausz and Bamberger 1985).

The extremely premature infant, on the other hand, fails to gain weight or gains very slowly because he/she is very ill and unable to tolerate adequate enteral or parenteral nutrition (Fitzhardinge 1987). Patent ductus arteriosus (PDA), for example, may lead to growth failure because caloric intake is limited due to fluid restriction. Another cardiac problem, congestive heart failure, is almost always associated with growth failure due to periods of acute illness. Congenital gastrointestinal anomalies nearly always require surgical repair and special attention to possible nutritional complications. Necrotizing enterocolitis, primarily a disease of LBW infants, can result in severe bowel injury and subsequent malnutrition and growth failure. Bronchopulmonary dysplasia (BPD), a chronic lung disorder that develops in some newborn infants following respiratory distress syndrome (RDS) or mechanical ventilation, often results in growth failure (Ohio Neonatal Nutritionists 1985a). Patients with chronic central nervous system abnormalities, such as those related to an intraventricular hemorrhage, are also likely to exhibit poor weight gain (Grausz and Bamberger 1985). Thus, there are many medical problems which can contribute to poor weight gain in VLBW infants.

Mechanical feeding difficulties Along with medical conditions or disease states that put VLBW infants at risk for poor weight gain, clinical experience of this researcher indicates that a second set of problems has to do with mechanical difficulties which interfere with caloric intake and, ultimately, with growth. For the infant who is fed parenterally, there may be difficulties with venous access. Long periods of intravenous nutrient administration through the peripheral veins and/or the continuous use of 12% to 13% peripheral dextrose solutions tend to cause the peripheral veins to break down. This severely limits the concentration of nutrients that can be infused into a patient. While the use of a central venous line may eliminate these two problems, it does greatly increase the infant's risk of infection. Infection could then lead to poor growth. For patients who are fed enterally, feeding difficulties usually revolve around feeding intolerance (the presence of significant gastric residuals, vomiting, diarrhea, malabsorption, constipation) or, for nipple-fed infants, poor sucking ability. Inefficient sucking motions can tire a baby during feedings, thus wasting calories that could otherwise be available for growth. Other mechanical feeding problems may also exist.

Iatrogenic malnutrition There may be a third major cause of extrauterine growth failure, in addition to diseases and/or mechanical difficulties. Iatrogenic malnutrition cannot be overlooked. At times, malnutrition, which can then cause growth retardation, may be the result of an inappropriate feeding choice by the physician, inadequate provision of nutrients (i.e., low volume of feeding or low concentration of nutrients in the feeding), or frank inability to provide adequate nutrition due to an unstable medical condition or unacceptable laboratory values. It is clear that there are a number of conditions, many of which are beyond the physician's control, which can lead to aberrant extrauterine growth patterns.

Feeding of Premature Infants

General Goals

If aberrant extrauterine growth is to be avoided, adequate nutrition is crucial for premature infants. The 3 primary goals of feeding such patients are: 1) to maintain good physical growth, 2) to provide sufficient energy for respiration, and 3) to permit the rapid brain growth that would normally occur during the last trimester of fetal life and beginning of infancy.

<u>Weight stabilization followed by overall growth</u> Maintaining good physical growth is easier said than done. The relative inability of VLBW infants in the neonatal intensive care unit (NICU) to metabolize nutrients and to excrete waste products and water, in the words of Usher (1987), "presents a formidable nutritional challenge to the therapist." After birth, there is, according to Usher (1987), an "obligatory" weight loss of about 13% in VLBW

infants weighing 500 to 1000 grams and about 10% in those weighing between 1000 and 1500 grams. This weight loss is the result of stress, respiratory failure, acidosis and infection which combine to create a catabolic state. After approximately 3 days of tissue loss, which Usher notes is not due to dehydration, there is a 2- to 3-day period of weight stabilization once nutritional intake rises enough to meet maintenance needs. As caloric intake is increased above maintenance needs, weight gain begins between days 4 and 7. Small VLBW infants usually regain their birth weight by about 17 days of age while larger ones usually do so at 10 days of age (Usher 1987). If infants are to "catch up" after experiencing the growth retardation that takes place both before birth (IUGR) and after birth as a result of initial weight loss, extrauterine growth rates must exceed intrauterine growth rates (Usher 1987).

Lung development and brain growth While the maintenance of good physical growth in general is dependent upon adequate nutrition, proper nutrient intake is also required for specific organ systems. Most importantly, sufficient nutrients are needed to provide energy for respiration and to allow rapid brain growth to occur. Usher (1987) indicates that undernutrition during neonatal life may result in apneic spells and mental retardation.

Nutrient Intake

Nutrients are provided to pre-term infants either through parenteral (peripheral or central venous) alimentation or via enteral feedings.

Calories To produce the intrauterine rate of growth, 85 to 90 Calories/kg/day are required for parenterally fed infants. Enterally fed premature infants typically require 100 to 120 Calories/kg/day (Usher 1987). However, some intravenously fed babies may fail to gain on 120 Cal/kg/day. Montgomery (1962) has shown that requirements may range as high as 160 to 185 Cal/kg/day to achieve catch-up growth in a cachexic infant. Actual requirements may differ greatly from one individual to another, depending on activity level, degree of illness and environmental conditions.

An attempt to give adequate calories for catch-up growth in a VLBW infant is frequently blocked by the fact that "The smallest and sickest infants who are in greatest need of adequate nutrition are least capable of handling it" (Usher 1987).

Protein Renal excretory capacity is the determining factor when it comes to protein, water and electrolyte capacity. For parenterally fed premature infants, protein intake is usually started at 1 g of amino acids per kg per day and increased to 3 g/kg/day, provided that renal function is adequate (Usher 1987).

Other nutrients Glucose intake is advanced to between 10 and 12 g/kg/day, while the lipid dose begins at 0.5 to 1 g/kg/day and is increased to 3 to 3.5 g/kg/day (Usher 1987). Adequate vitamins and minerals are also provided parenterally. Without parenteral nutrition, many VLBW infants would have little or no chance of receiving adequate caloric intake during the first weeks of life.

Feeding Route and Its Relationship to Energy Expenditure

Parenteral feedings The limited ability of the VLBW infant to digest, absorb and metabolize enteral feedings makes the use of parenteral feedings quite desirable. Kerner (1988) lists the following indications for parenteral nutrition in neonates: surgical gastrointestinal disorders, short bowel syndrome, serious acute alimentary diseases (NEC), acute renal failure, meconium ileus, respiratory distress syndrome, intensive care of LBW infants, neonatal asphyxia and other abnormal disorders. When deciding on the route of administration of parenteral nutrition, Ziegler, et al. (1980) suggest that caloric need should be the primary determining factor for selecting the route. Peripheral vein parenteral nutrition solutions are less calorically dense and, therefore, provide fewer calories in the end than central vein solutions. In addition, infusing parenteral nutrition solutions centrally, or through the superior vena cava, prevents the phlebitis and thrombosis which frequently occur with peripheral lines (Kerner 1988).

Enteral feedings Though parenteral nutrition solutions are very crucial to the growth and recovery of most VLBW infants, clinical experience of the author indicates that enteral feedings are the most desirable for infants who can tolerate this route. Enteral feedings are much more simple to administer, more "physiologic" in nature, and eliminate the risks that go along with intravenous feedings. Caloric requirements for growth are higher for enterally fed infants in comparison to parenterally fed infants (Avery and Fletcher 1987). Though a review of the literature did not reveal specific information as to the absolute calorie difference between what is needed to generate equivalent growth of enterally and parenterally fed infants, and precisely what contributes to this difference, several facts need to be considered.

Specific dynamic effect (SDE) and energy loss All infants, whether fed enterally or parenterally, expend energy for basal metabolism, activity and tissue synthesis. In addition, if caloric intake is adequate, energy may be stored and/or used for growth (Butte 1988). When energy requirements during infancy are partitioned, there seem to be two major places where calories are "wasted" during enteral feeding as compared to parenteral feeding: thermic effect of feeding and energy excretion (principally through the stool). The thermic effect of feeding (TEF), also called the calorigenic effect, diet induced thermogenesis (DIT), or specific dynamic action or effect (SDA or SDE), is the energy expended or heat produced above basal metabolism in response to feeding or to the ingestion of nutrients in food. It is thought that the increased oxygen consumption and carbon dioxide production which occur following ingestion of food, represent energy that is mobilized to digest, absorb, distribute, modify and store digestible nutrients (Linder 1985). The metabolic cost of substrate storage is listed as 15 to 25% for ingested protein calories, 6 to 7% for carbohydrate calories, and 2 to 4% for fat calories. A mixed diet is thought to increase heat production by 6 to 10%, though 10% is the figure that is usually used (Alpers, et al. 1983; Linder 1985; Butte 1988). Alpers, et al. (1983) indicate that the calorigenic effect is present even after intravenous feeding, but that the figure for calculating additional energy requirements for hypermetabolic or infected febrile patients should be 5% rather than 10% since the SDE of food is lower than normal because of already increased heat production. In pre-term infants, the thermic effect of feeding has been shown to be proportional to the rate of weight gain (Reichmen, et al. 1982). It is thought that increased energy expenditure is due to the metabolic cost of tissue synthesis (Butte 1988). There is clearly some amount of energy that is used to process food after ingestion.

Not all foods eaten enterally are digestible. Fiber is the best known non-digestible food. Linder (1985) suggests that 1 to 9% of food energy is non-digestible energy which is lost in feces or used by intestinal bacteria. Though studies have calculated heat production associated with food intake, it is still unclear as to exactly what variation takes place in stool energy loss and specific dynamic effect of food when comparing enteral feeding to parenteral.

O'Leary (1985) states that parenterally fed LBW infants usually have decreased energy needs, as compared to enterally fed, "because absorptive loss does not occur when nutritional intake bypasses the intestinal tract."

According to Avery and Fletcher (1987),

> The figure of 120 cal/kg/day provides a rough rule of thumb that is sufficient for growth in most term newborns and prematures on oral feedings. By the intravenous route, 85 to 95 calories are normally sufficient.

In other words, 21 to 29% fewer calories are needed if a premature infant is fed parenterally rather than enterally.

Avery and Fletcher (1987) further indicate that 20 to 38 Cal/kg/day (16.7 to 20.9%) of a total intake of between 120 and 182 Cal/kg/day are lost in the stool when an infant is on oral feedings. The authors indicate that this loss is due mostly to fat malabsorption. Reichmen, et al. (1982) found stool losses to be about 17.5 Cal/kg/day (11.8%) out of 148.6 Cal/kg/day.

While stool loss is much less for parenterally fed (vs. enterally fed) infants, some loss does occur due to routine epithelial cell sloughing from the gut. To summarize the information on energy loss related to feeding route, it seems reasonable that between 1 and 20%, maybe 10%, of enteral calories are lost through the stool (Linder 1985; Avery and Fletcher 1987) and that possibly as much as 5 to 10%, probably 5%, of enteral calories are utilized for SDE (Linder 1985; Alpers, et al. 1983).

Respiratory Support of Premature Infants

Premature infants need to fight many battles if they are to survive past the neonatal period. Along with the so-called "formidable nutritional challenge" (Usher 1987) presented to those who care for low birth weight infants, practitioners must often deal with respiratory problems.

Common Respiratory Diseases

There are two pulmonary diseases which often afflict premature infants.

Hyaline membrane disease Hyaline membrane disease (HMD), also called respiratory distress syndrome (RDS), is of major clinical significance after premature birth. Hyaline membrane disease is the most common cause of acute lung injury in the newborn (O'Brodovich and Mellins 1985). It is defined clinically, by Toce, et al. (1984), as

> persistent respiratory distress manifested by tachypnea, grunting, nasal flaring, retractions (...), cyanosis, requirement for supplemental oxygen for more than 24 hours, and characteristic chest roentgenograms.

Since the mid- to late 1970's, the use of mechanical ventilation has lead to an obvious reduction in the mortality and morbidity of infants, particularly infants weighing less than 1500 g at birth. Hyaline membrane disease remains the most common condition for which infants receive mechanical ventilation (Saigal and O'Brodovich 1987). It is believed to be related to a deficiency of surfactant. These infants may lack energy to suck and swallow effectively. They typically have poor gastric motility and they may be ventilated via an endotracheal tube which prevents sucking and swallowing (Ohio Neonatal Nutritionists 1985b).

Bronchopulmonary dysplasia The term bronchopulmonary dysplasia (BPD) refers to a chronic pulmonary disorder experienced by some newborn infants following hyaline membrane disease, or other acute lung injury, or mechanical ventilation (Northway, et al. 1967; O'Brodovich and Mellins 1985). Several sets of criteria have been used in the diagnosis of BPD. A simplified approach looks at the need for mechanical ventilation and/or the requirement for supplemental oxygen for at least 21 days of life (Kurzner, et al. 1988). Alternatively, BPD has also been diagnosed with a more extensive list of criteria including: "tachypnea, dyspnea as manifested by chest retractions, requirement for supplemental oxygen, and hypercapnia" (Toce, et al. 1984). Greer and McCormick (1987) utilized three criteria in order to diagnose their patients with BPD:

> (1) initial diagnosis of respiratory distress syndrome, (2) supplemental oxygen requirement for more than 30 days, and (3) chest roentgenographic evidence of BPD (eg, hyperexpansion, interstitial densities, and focal emphysema).

BPD is classified or staged according to degree of severity. Stage I, a period of acute hyaline membrane disease, presents during day 2 or 3 of life. Stage II, during days 4 to 10, is a period of regeneration and proliferation of bronchial epithelium. Stage III, during days 10 to 20, is a period of transition to chronic disease, while Stage IV, beyond 1 month, is a period of chronic disease (Hodgman 1987).

Other researchers have avoided the problem of choosing a definition of BPD and analyzing radiographic changes by setting up criteria for the diagnosis of chronic lung disease. Avery, et al. (1987) arbitrarily defined chronic lung disease of prematurity as "an oxygen requirement greater than room air at 28 days of age." Additionally, they determined the number of infants with severe lung disease as indicated by oxygen dependency at 3 months.

A discussion of a disease is rarely complete without some mention of incidence. According to Saigal and O'Brodovich (1987), prevalence and sequelae of BPD cannot easily be summarized, since the definition of BPD itself has been questioned and modified repeatedly. In their article, entitled, "Long-Term Outcome of Preterm Infants with Respiratory Disease," they state:

> The incidence of BPD has been variously reported as unchanged, increased or decreased, with a range of 5 to 70 percent. The reasons for these discrepancies in the population under study include inconsistency in the denominator used to express the population at risk, lack of consensus in the definition of BPD, disagreement in roentgenographic interpretation and small sample size spread over a long time span. The problems are further compounded by recent changes in survival of very tiny infants and the use of therapeutic interventions designed to ameliorate BPD (...), resulting in a different breed of infants with BPD who would not have survived a few years ago.

No matter how BPD is defined, nutritional management is an important part in the care of patients with bronchopulmonary dysplasia. Like patients with RDS, those with Stage IV BPD frequently have feeding problems. According to the Ohio Neonatal Nutritionists (1985a), they may exhibit a decreased ability to suck and swallow efficiently. As they grow older, they may have an impaired ability to tolerate spoon feedings and to initiate self-feeding behaviors. Inadequate intake may, according to Koops et al. (1984), be related to fussiness that results from stress or hypoxia that occurs with feedings.

Respiratory Status as It Relates to Growth

In recent years, researchers have noted that premature infants with BPD or chronic lung disease generally grow poorly as compared to those without pulmonary disease (Greer and McCormick 1987).

Growth failure in BPD Weinstein and Oh (1981) suggested that the cause of growth failure in infants with bronchopulmonary dysplasia is elevated metabolic expenditure, since oxygen consumption is increased in these neonates. To look further into the question of metabolic expenditure, a study by Kurzner, et al. (1988) attempted to answer two questions:

> (1) Is growth failure in infants with bronchopulmonary dysplasia caused by poor nutritional intake or excessive gastrointestinal losses? (2) What is the resting metabolic expenditure of infants with growth failure, and how does it compare with that of normally growing infants?

The researchers found that infants with BPD and growth failure had an elevated resting metabolic expenditure which was inversely correlated with body weight. They concluded that such infants have increased metabolic demands and that the existence of decreased prealbumin values in infants with BPD and growth failure suggests a relative state of protein-calorie malnutrition.

Greer and McCormick (1987) also studied growth in VLBW infants with BPD. In contrast to other studies, they carefully controlled for birth weight and gestational age. According to their data, "factors in VLBW infants other than the presence or absence of BPD are associated with growth retardation."

Improvement of growth Though the diagnosis of BPD may be based on either conservative or liberal criteria, the most critical feature in the management of infants with BPD is adequate oxygenation. Studies have shown that adequate oxygenation, via home oxygen therapy for example, improves weight gain in infants with BPD (Groothuis and Rosenberg 1987). The result is decreased work of breathing and diminished overall caloric expenditure. Groothuis and Rosenberg (1987) suggested, based on their data, that improved NICU weight gain (due to proper oxygen support) may be negated by discontinuing oxygen therapy after discharge.

In general, as reported by Markestad and Fitzhardinge (1981), "catch-up growth" is seen with improved respiratory function. Likewise, growth retardation is associated with prolonged respiratory problems.

Increased oxygen consumption may be only one of several explanations for the growth failure seen in infants with

BPD. Poor caloric intake, due to respiratory distress, anorexia, or iatrogenic fluid limitation, as well as impaired gastrointestinal absorption, may also be responsible. Kurzner, et al. (1987) have stated that work of breathing does not totally explain poor growth in BPD infants with increased oxygen consumption.

An article by Saigal and O'Brodovich (1987) listed several important ideas in relation to growth problems in infants with BPD. At the time of their study, no research findings had been published on nutritional management designed specifically to promote improvement in weight gain and growth in length and head circumference. This author is still not aware of any such studies. Saigal and O'Brodovich (1987) suggested that efforts "should be directed toward providing higher caloric intake and minimizing energy expenditure." Furthermore, the use of low-flow home oxygen therapy in order to provide for adequate oxygenation during the convalescent stage may be warranted, if appropriate weight gain and growth velocity are to occur.

Summary

Caring for VLBW infants is clearly a complicated task. Such infants begin life with a disadvantage in that they have not had the opportunity to complete the maturing process of intrauterine life and to accrue all of the nutrients that are necessary at the beginning of postnatal life. Additionally, those who experience intrauterine growth retardation are even further behind than normal premature infants with regard to growth. Numerous medical problems can potentially complicate the care and growth of these infants.

The provision of proper nutritional support to small neonates requires a great deal of knowledge and skill. While many options are open to the practitioner, frequently few, and sometimes none, work well. Growth failure or inadequate growth are common problems. Ventilatory and nutritional support are critical to the survival of the very immature infant. Immaturity of organ systems, particularly the lungs and kidneys, continues to make nutritional support of these infants a challenging task. Respiratory complications have been clearly implicated as one cause of poor growth in small premature infants. Unfortunately, the exact relationship between poor growth and respiratory disease has still not been determined.

CHAPTER 3

METHODS

Many premature infants are routinely supported by mechanical ventilators today. The purpose of this study was to retrospectively look at the effect of mechanical ventilation, via an endotracheal tube, on nutritional intake and growth patterns of these very small babies.

Subjects

A retrospective review was conducted of all infants who were admitted to the Neonatal Intensive Care Unit at the Milwaukee County Medical Complex (MCMC), Milwaukee, WI, during 1987 and 1988 with a birth weight of less than 1251 grams. Initial criteria for entrance into the study included: 1) birth weight less than or equal to 1250 grams, 2) intubated and supported by a mechanical ventilator for at least 14 consecutive days before final extubation, 3) weight gain and nutritional intake data available for at least 14 consecutive days prior to extubation and 14 consecutive days immediately after extubation (that is, before discharge from the hospital), 4) discharged alive. Growth during intubation, that is, while the infant was supported by a mechanical ventilator (V), was compared to growth post-extubation (PV), or immediately following discontinuation of mechanical ventilator support via an endotracheal tube. Each patient served as his or her own control. This was important because of the considerable variation in birth weight and gestational age. If a patient was intubated more than once during the hospital stay, the last 28 days that met these criteria were utilized. All patients remained in closed isolettes throughout the study period. All patients were fed according to standard nursery protocol (Appendix A).

During 1987 and 1988, there were 50 patients with birth weights less than 1251 grams who were discharged alive from the MCMC neonatal intensive care unit. Fifteen neonates, or 30% of the original target population of 50 infants, met the initial criteria for entrance into the study. All fifteen infants, or 100% of those meeting the initial criteria for entrance into the study, were included in the project. Due to the limited number of patients fitting the study criteria over two years, patients were not eliminated from the sample on the basis of diagnoses, such as sepsis or NEC.

Collection of Data

The following demographic data were collected for each patient: 1) gestational age (weeks), 2) birth weight (g), 3) sex, 4) appropriateness of weight for gestational age (SGA or AGA), 5) birth length (cm), 6) birth occipital-frontal circumference (cm), 7) age (days) at which the lowest weight was reached before regaining birth weight, 8) age (days) at final extubation, 9) weight (g) at final extubation, 10) presence or absence of growth failure at the time of extubation, 11) incidence of the provision of supplemental oxygen (>21%) at 28 days of age and 2 months of age, and 12) diagnoses. Study data included: 1) mean daily caloric intake (Cal/kg/day), total and enteral, during the 14 days prior to extubation and during the 14 days immediately following extubation, 2) mean daily fluid intake and urine output (cc/kg/day) during the 14 days prior to extubation and during the 14 days immediately following extubation, and 3) mean daily weight gain (g/kg/day) during the 14 days prior to extubation and during the 14 days immediately following extubation.

Nutrient intake data were collected, per nursery protocol, in 24 hour blocks from 6:00 a.m. to 6:00 a.m. Thus, nutrient intake for the day of extubation was included in the 14 days prior to extubation if extubation took place after 6:00 p.m., or more than half way through the 24 hour block. If extubation occurred before 6:00 p.m., or less than half way through the 24 hour period, nutrient intake for the day of extubation was included in the 14 days past extubation. Nutritional calculations were run on the Milwaukee County Medical Complex Nursery Data System Nutritional Analysis software. Patients were weighed on a NARCO Isolette neonatal scale; measurements were recorded to the nearest 5 grams. A paper tape was used to measure length and OFC to the nearest tenth of a centimeter. Nurses determined urine volume by subtracting the weight of a dry diaper from the weight of the soiled diaper; grams of urine were equated to milliliters (cc's) of urine. Stool weight was estimated to the nearest gram by nursing staff.

Transformation of Data

After the above pieces of data were collected for each patient, a series of calculated values was generated for each patient for the 14 day period prior to extubation as well as for the 14 day period immediately following extubation. These values included: 1) adjusted Calories/kg/day, 2) energy intake (Cal/kg/day) divided by weight gain (g/kg/day), or Cal/g, 3) adjusted Calories/kg/day divided by weight gain (g/kg/day), or Adj Cal/g, and 4) percentage of calories provided enterally, or %PO Cal.

Additional Data

Finally, due to questions that emerged during the analysis of the data, additional pieces of data were collected after the initial data collection, since the raw data were readily available in either the medical record or the dietitian's record for the appropriate time periods. These items included: 1) stool output (g/kg/day), and 2) sodium intake (mEq of sodium/kg/day). In addition, as the data were analyzed, it became apparent that separating the existing sample into two sub-groups for comparison of the same parameters might provide information that could help explain the initial results. Therefore, all six patients who were receiving supplemental oxygen at 2 months of age were compared to six patients, matched by birth weight and gestational age, who were not receiving supplemental oxygen at 2 months of age (Appendix B).

Adjusted Calories

Infants included in this retrospective study were on a variety of feeding regimens, depending on age, maturity and level of tolerance, though all patients were fed according to a standard nursery protocol which calls for a typical progression from parenteral to enteral feedings. The calculation of calorie per gram (Cal/g) was based on the assumption that all calories are utilized equally as well for growth. Several authors have commented, however, on the idea that, in order to elicit equivalent growth, energy needs of LBW infants differ depending on whether they are fed enterally or parenterally. This issue was discussed in the "Review of Related Research and Literature," under the sub-heading "Specific dynamic effect (SDE) and energy loss" (page 21). Based on the information contained in that discussion, "adjusted calories" were calculated in this study. Adjusted calories were defined as the sum of 100% of the parenteral calories and 85% of enteral calories, or:

Adj Cal = 100% of IV Cal + 85% of PO Cal,

where Adj Cal represents adjusted caloric intake/kg/day; and IV Cal and PO Cal represent intravenous caloric intake and enteral caloric intake/kg/day, respectively. Thus, 15% of enteral calories were subtracted to allow for stool energy losses (1-21% of enteral calories) and specific dynamic effect (5-10% of enteral calories) associated with enteral feeding.

Though the use of such an "adjusted calories" approach has not been documented in the literature, to this author's knowledge, except in an abstract written in part by this author (Heimler, et al. 1988), the idea is supported in theory by research results and published feeding recommendations.

Statistical Evaluation

Two-tailed paired t-tests were performed on each series of data collected. In each case, data collected during the 14 days prior to extubation (V) were compared to data collected during the 14 days immediately following extubation (PV). "PC STATISTICIAN Version 1.1 The Statistical Report Program," a statistical software program requiring an IBM or IBM compatible personal computer was used by the author to calculate means, standard deviations, and t-test values (Human Systems Dynamics 1983). Results were considered to be significant at the 5% level.

CHAPTER 4

RESULTS AND DISCUSSION

Results

The courses of 15 VLBW infants supported by mechanical ventilation were analyzed retrospectively over a four week period which included the two weeks prior to removal of the endotracheal tube (V) and the two weeks immediately following removal of the endotracheal tube (PV). Extubation took place on day 42 ± 13 (mean ± S.D.) of life. Table 1 includes demographic data describing the 15 infants studied. The mean birth weight was 799 ± 191 g while the mean gestational age was 26.3 ± 1.5 weeks. Ten patients were female; five were male. Fourteen patients (93%) were diagnosed with bronchopulmonary dysplasia, based on the criteria of Greer and McCormick (1987); see page 25. Nine infants (60%) had laboratory evidence of septicemia at some point during the hospital stay. Seven infants (47%) had an intraventricular hemorrhage; three were classified as Grade IV while four were classified as Grade I. No patients were known to have congenital malformations. Only one patient experienced necrotizing enterocolitis.

Table 2 compares a number of nutritional and growth parameters during the ventilator and post-ventilator

TABLE 1

DEMOGRAPHIC DATA OF 15 PATIENTS

Neonatal Variables	Mean	S.D.	Range	No.	%
Gestational age (wks)	26.3	1.5	24-29		
Birth weight (g)	799	191	560-1150		
Birth length (cm)	33.6	2.5	30-38		
Birth OFC*(cm)	24.2	2.1	20.5-28.0		
Low weight age (days)	10.5	6.2	4-26		
Extubation age (days)	41.9	13.3	20-62		
Extubation weight (g)	1094	288	760-1780		
# of patients in growth failure at extubation				10	67
Number of patients with+ :					
Bronchopulmonary dysplasia				14	93
Respiratory distress syndrome				11	73
Previous sepsis				9	60
Previous patent ductus arteriosus				8	53
Intraventricular hemorrhage				7	47
Seizures				2	13
Previous necrotizing enterocolitis				1	7

*Abbreviation used: OFC, occipital-frontal circumference
+Patients had more than one complication.

periods. Energy intake calculated as Cal/kg/day increased significantly from a mean (± S.D.) of 92.7 (± 14.5) during ventilator support to 100.5 (± 8.0) post-ventilator support ($p = .015$). Adjusted caloric intake also rose (84.3 ± 12.2 to 89.0 ± 5.9), but not significantly (Figure 1). The percentage of calories provided via enteral nutrition, in contrast to parenteral nutrition, increased significantly from a mean (± S.D.) of 56.5 (± 35.2)% to 73.9 (± 28.2)%. Sodium intake remained stable, as did fluid intake. Urine output, however, decreased significantly from 83.9 ± 10.4

TABLE 2

A COMPARISON OF CLINICAL CHARACTERISTICS OF 15 PATIENTS DURING MECHANICAL VENTILATION (V) AND POST-MECHANICAL VENTILATION (PV) VIA AN ENDOTRACHEAL TUBE

	V	PV	
	Mean ± S.D.	Mean ± S.D.	P*
Calories/kg/day	92.7 ± 14.5	100.5 ± 8.0	.015
Adjusted Cal/kg/day+	84.3 ± 12.2	89.0 ± 5.9	NS
%PO Calories++	56.5 ± 35.2	73.9 ± 28.2	.007
Sodium Intake (mEq/kg/d)	3.6 ± 1.4	3.6 ± 1.2	NS
Fluid Intake (cc/kg/d)	139.0 ± 8.9	134.8 ± 6.8	NS
Urine Output (cc/kg/d)	83.9 ± 10.4	72.1 ± 12.4	.001
Stool Output (g/kg/d)	7.1 ± 3.5	7.0 ± 3.9	NS
Weight Gain (g/kg/day)	12.3 ± 2.0	14.3 ± 3.9	.098
Calorie/g wt gain	7.7 ± 1.7	7.6 ± 2.4	NS
Adjusted Cal/g wt gain	7.0 ± 1.3	6.7 ± 2.0	NS

* Significance by paired 2-tailed t tests.
\+ Adjusted Cal = 100% IV Cal + 85% PO Cal
++%PO Calories = % of total caloric intake obtained via enteral calories (rather than parenteral)

cc/kg/day to 72.1 ± 12.4 cc/kg/day. Stool output did not fluctuate (Figure 2); however, it was an estimate.

Though the caloric intake increased significantly during the period immediately after extubation, and weight gain rose, the increase in mean weight gain was significant only at a level of $p = .098$, based on a paired 2-tailed t test. Weight gain during the two weeks prior to extubation was 12.3 ± 2.0 g/kg/day (mean ± S.D.). During the two weeks

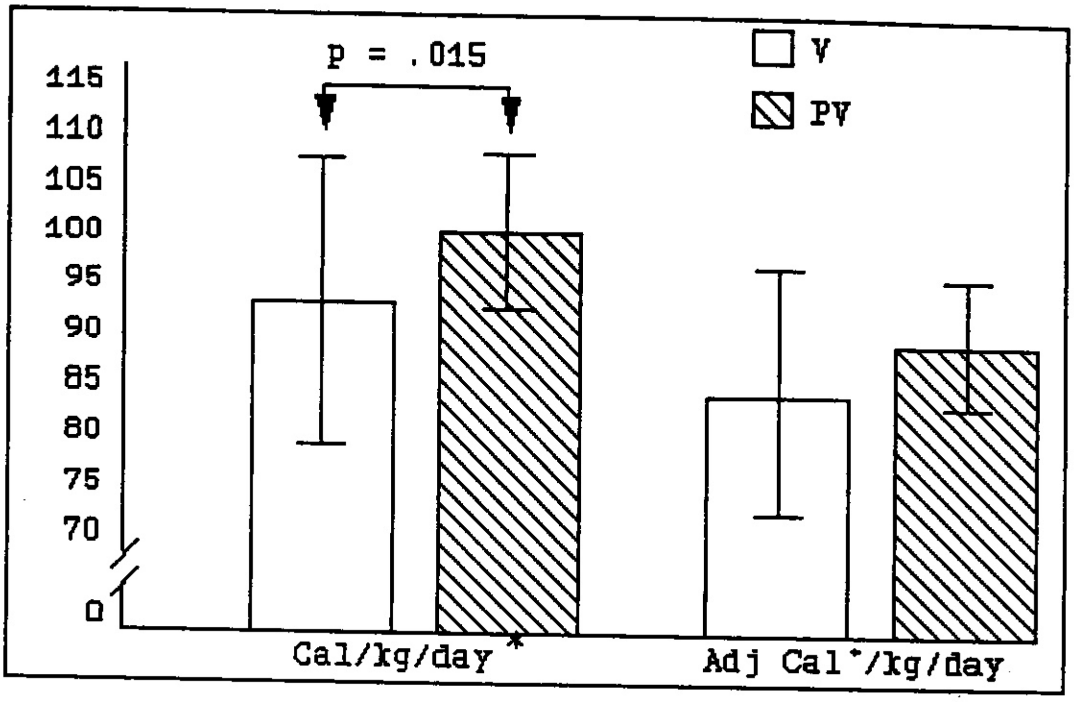

FIGURE 1

ENERGY INTAKE OF 15 PATIENTS DURING VENTILATOR SUPPORT (V)
AND POST-VENTILATOR SUPPORT (PV)
*Significance by paired 2-tailed t test.
+Adj Cal = 100% IV Cal + 85% PO Cal

immediately following extubation, weight gain was 14.3 ± 3.9 g/kg/day (Figure 3). Energy intake per gram of weight gain did not change significantly from V to PV, as evidenced by either Cal/g or Adj Cal/g (Table 2).

Six patients out of the initial sample of 15 infants continued to receive supplemental oxygen at 2 months of age. These 6 infants (O_2 at 2 mo) were compared to 6 infants, matched retrospectively by birth weight and gestational age, who did not receive supplemental oxygen at 2 months of age (No O_2 at 2 mo). Table 3 contains a brief clinical profile of these 6 matched pairs. Birth weight, gestational age, birth length and age at which low weight was reached did not

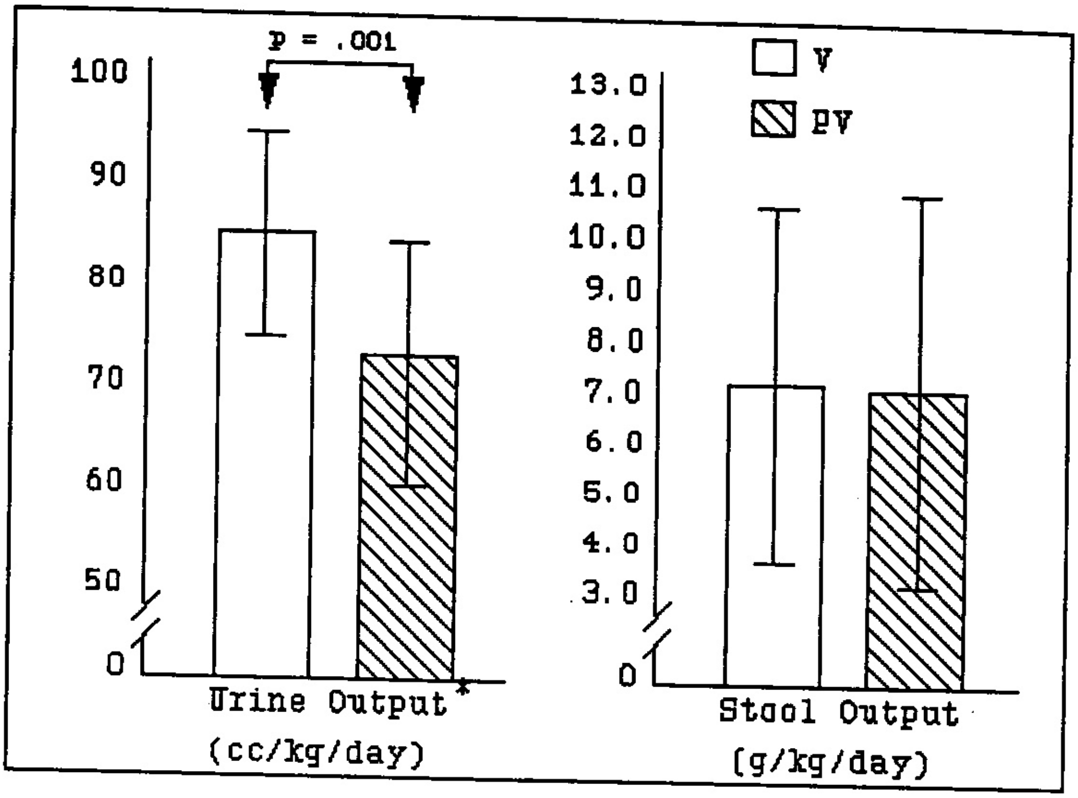

FIGURE 2

MEAN URINE AND STOOL OUTPUT OF 15 INFANTS
DURING VENTILATOR SUPPORT (V) AND
POST-VENTILATOR SUPPORT (PV)
*Significance by paired 2-tailed t test.

differ between the two sub-groups. The patients who were not on O_2 at 2 mo had a smaller mean (± S.D.) OFC at birth (23.1 ± 2.2 cm) than those who were on O_2 at 2 mo (25.3 ± 2.0 cm). The difference was significant only at a level of less than 10% (p = .064). Both the age at extubation and the weight at extubation were significantly lower for the patients who received no oxygen supplement at 2 months of age, as compared to those who did receive oxygen at 2 months of age. The mean (± S.D.) values were 29.3 ± 7.5 days and 923 ± 134 grams as compared to 54.3 ± 7.9 and 1246 ± 352,

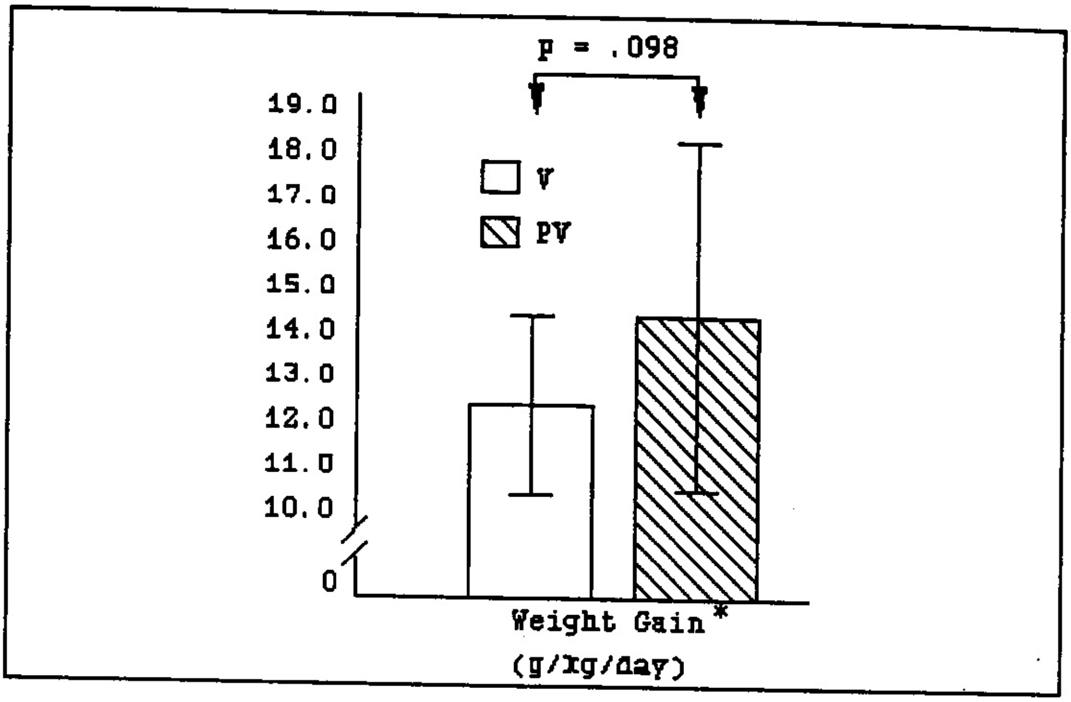

FIGURE 3

MEAN WEIGHT GAIN OF 15 INFANTS DURING VENTILATOR SUPPORT (V) AND POST-VENTILATOR SUPPORT (PV)
* Significance by paired 2-tailed t test.

respectively.

Mean nutritional and weight gain values during ventilator support and post-extubation were calculated for the two sub-groups, O_2 at 2 mo and No O_2 at 2 mo (Table 4). In contrast to the initial 15 patient sample results where weight gain rose slightly but not significantly from V to PV, weight gain remained stable for those on O_2 at 2 mo (12.6 $\pm$ 2.4 g/kg/day (V) and 12.3 $\pm$ 3.6 g/kg/day (PV)), but went up significantly for those not on O_2 at 2 mo (12.4 $\pm$ 1.1 g/kg/day (V) and 16.6 $\pm$ 3.0 g/kg/day (PV)). This increase was significant at $p = .025$, based on a paired 2-tailed t test. The difference in mean weight

TABLE 3

CLINICAL PROFILE OF 6 MATCHED PAIRS OF INFANTS*,+

Characteristic	O_2 at 2 mo (n = 6)	No O_2 at 2 mo (n = 6)	p
Gestational age (wks)	26.3 ± 1.0	26.0 ± 1.4	NS
Birth weight (g)	776 ± 184	768 ± 172	NS
Birth length (cm)	33.4 ± 2.3	33.7 ± 2.8	NS
Birth OFC (cm)	25.3 ± 2.0	23.1 ± 2.2	.064
Low weight age (days)	11.8 ± 7.6	10.0 ± 6.8	NS
Extubation age (days)	54.3 ± 7.9	29.3 ± 7.5	.003
Extubation weight (g)	1246 ± 352	923 ± 134	.027

* Values are mean ± S.D.; comparisons are paired 2-tailed t test.
+ Abbreviations: O_2 at 2 mo, infants receiving supplemental oxygen at 2 months of age; No O_2 at 2 mo, infants receiving no supplemental oxygen at 2 months of age; OFC, occipital-frontal circumference.

gain PV values between the O_2 at 2 mo and No O_2 at 2 mo groups was also significant ($p = .046$) (Figure 4).

Once again, there was a decrease in urine output from V to PV, though the decrease was only significant for the group that was on O_2 at 2 months of age. The most notable difference between the 15 patient sample and the two 6-patient subgroups, however, was in the values that reflect utilization of energy per gram of weight gain (Figure 5). While Cal/g and Adj Cal/g increased for the patients on supplemental oxygen at 2 months of age from V to PV, they decreased from V to PV for infants who received no supplemental oxygen at 2 months of age. The difference

TABLE 4

CLINICAL CHARACTERISTICS OF 6 INFANTS RECEIVING SUPPLEMENTAL OXYGEN AT 2 MONTHS OF AGE (O_2 at 2 Mo) MATCHED TO 6 INFANTS NOT RECEIVING SUPPLEMENTAL OXYGEN AT 2 MONTHS OF AGE (NO O_2 at 2 Mo)

		O_2 at 2 mo	No O_2 at 2 mo	
		Mean ± S.D.	Mean ± S.D.	P
Calories/kg/day	V*	90.3 ± 10.9[a]	90.7 ± 18.8	NS
	PV+	97.7 ± 8.3[a]	100.8 ± 6.2	NS
Adj Cal**/kg/day	V	84.0 ± 10.0	81.0 ± 13.6	NS
	PV	89.0 ± 7.7	88.5 ± 2.6	NS
%PO Calories++	V	45.5 ± 38.1	63.2 ± 40.2	NS
	PV	57.7 ± 32.6	79.3 ± 22.8	NS
Fluid Intake (cc/kg/day)	V	137.7 ± 7.4	137.0 ± 9.3	NS
	PV	131.3 ± 9.2	136.2 ± 3.4	NS
Urine Output (cc/kg/day)	V	87.7 ± 15.8[b]	83.5 ± 12.0[c]	NS
	PV	69.7 ± 13.2[b]	74.8 ± 14.4[c]	NS
Weight Gain (g/kg/day)	V	12.6 ± 2.4	12.4 ± 1.1[d]	NS
	PV	12.3 ± 3.6	16.6 + 3.0[d]	.046
Calorie/g wt gain	V	7.3 ± 1.4	7.4 ± 1.8[e]	NS
	PV	8.4 ± 2.3	6.2 ± 1.0[e]	.050
Adj Cal**/g wt gain	V	6.8 ± 1.0	6.9 ± 1.5[f]	NS
	PV	7.6 ± 1.9	5.4 ± 0.9[f]	.029

* V = During mechanical ventilation
\+ PV = Post mechanical ventilator support via an endotracheal tube
** Adj Cal = 100% IV Cal + 85% PO Cal
++ %PO Calories = % of total caloric intake obtained via enteral calories (rather than parenteral)
All comparisons by paired 2-tailed t test.
[a] p = .098 [b] p = .016 [c] p = .125
[d] p = .025 [e] p = .261 [f] p = .087

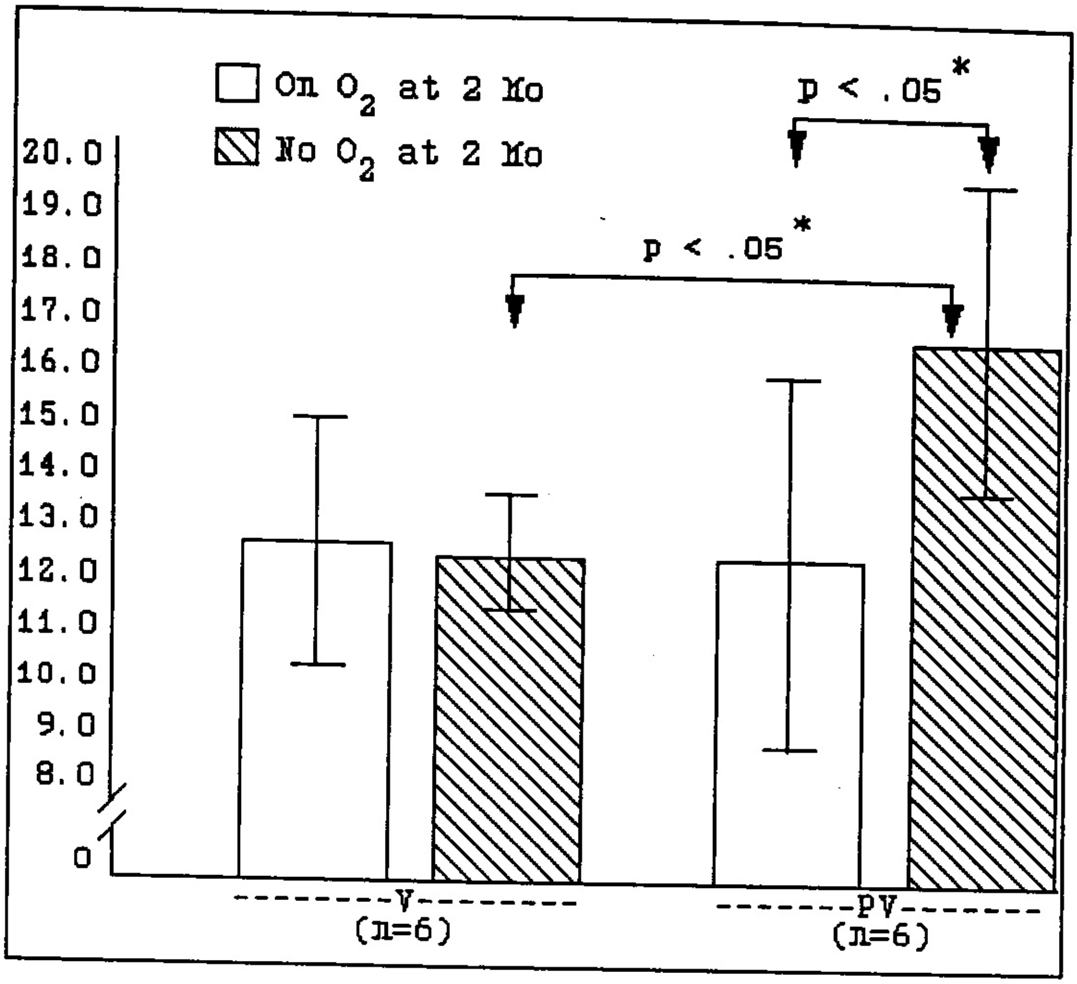

FIGURE 4

WEIGHT GAIN (g/kg/day) OF INFANTS DURING VENTILATOR SUPPORT (V) AND POST-VENTILATOR SUPPORT (PV)
* Significance by paired 2-tailed t test.

was not significant within the sub-groups, but the PV value was significantly different between the sub-groups (p=.05) (Figures 6 and 7).

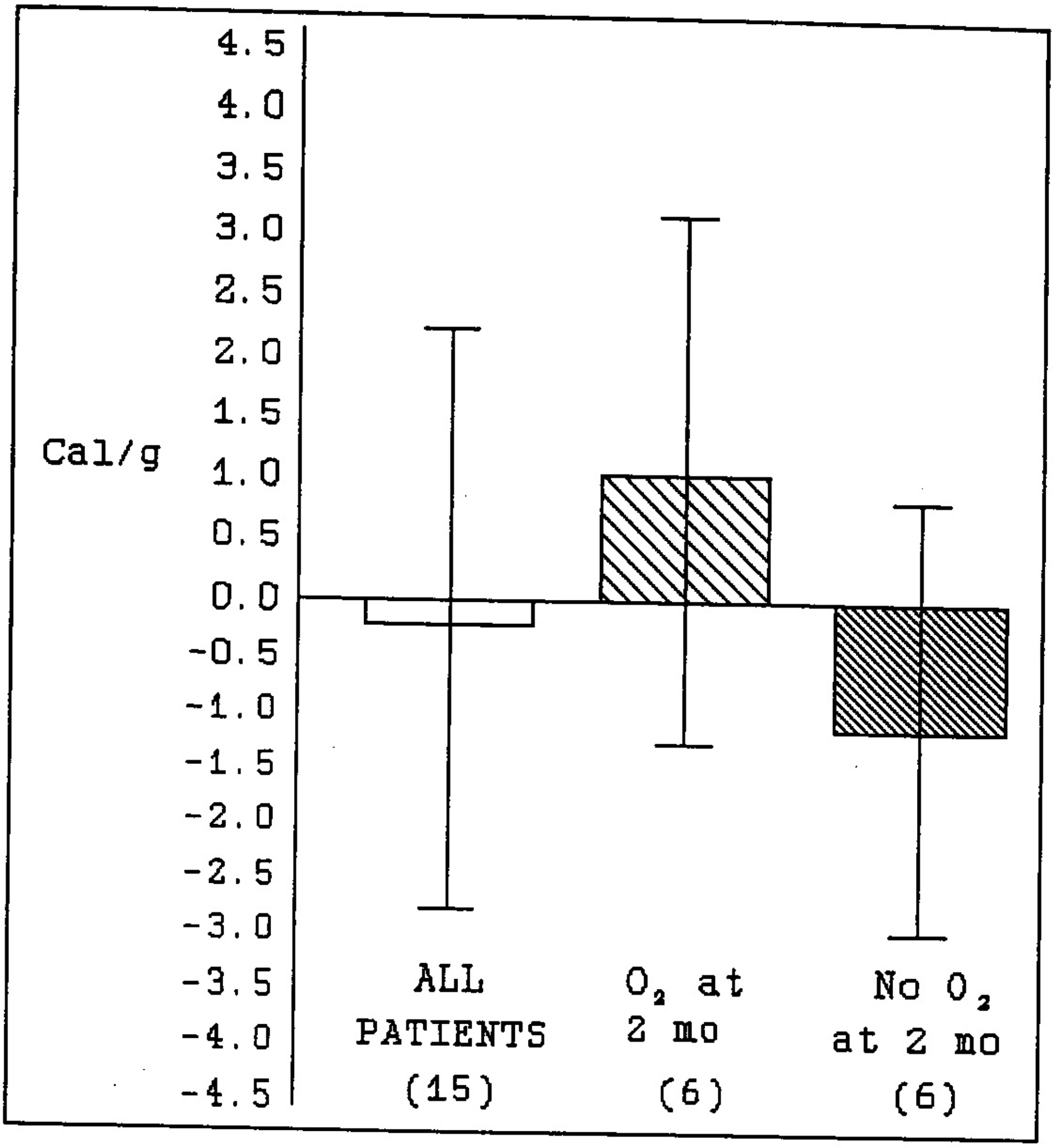

FIGURE 5

MEAN CHANGE IN Adj Cal/g FROM THE PERIOD DURING VENTILATOR SUPPORT TO THE PERIOD POST-VENTILATOR SUPPORT

DISCUSSION

According to the initial results of this study, there was no significant change in energy utilization by VLBW infants, as reflected by comparing caloric intake to growth in weight, and also by the Cal/g parameter, between the

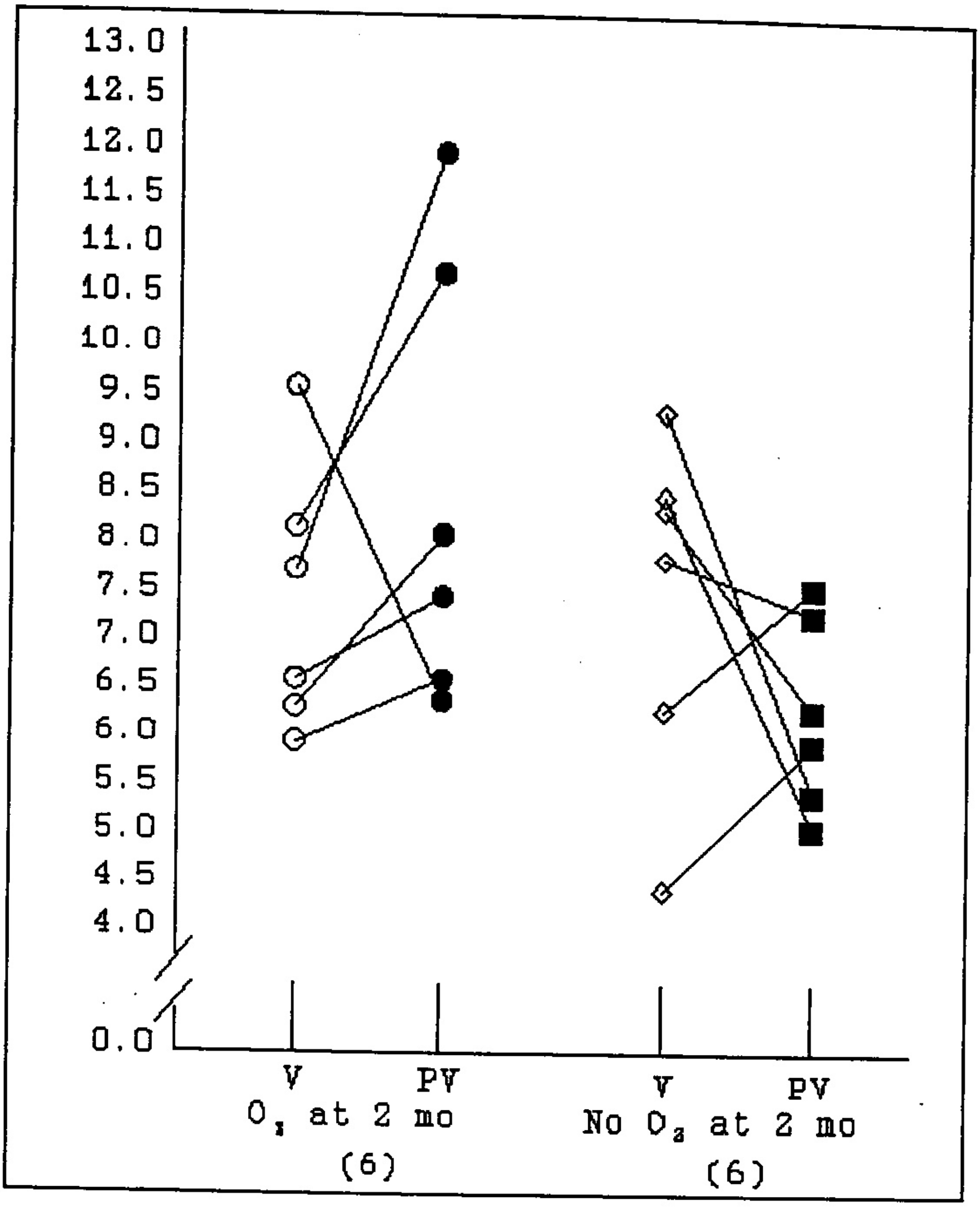

FIGURE 6

CHANGE IN ENERGY INTAKE PER GRAM OF WEIGHT GAIN (Cal/g)
O_2 and No O_2 status at 2 mo reflects retrospective division of patients by severeness of morbidity.

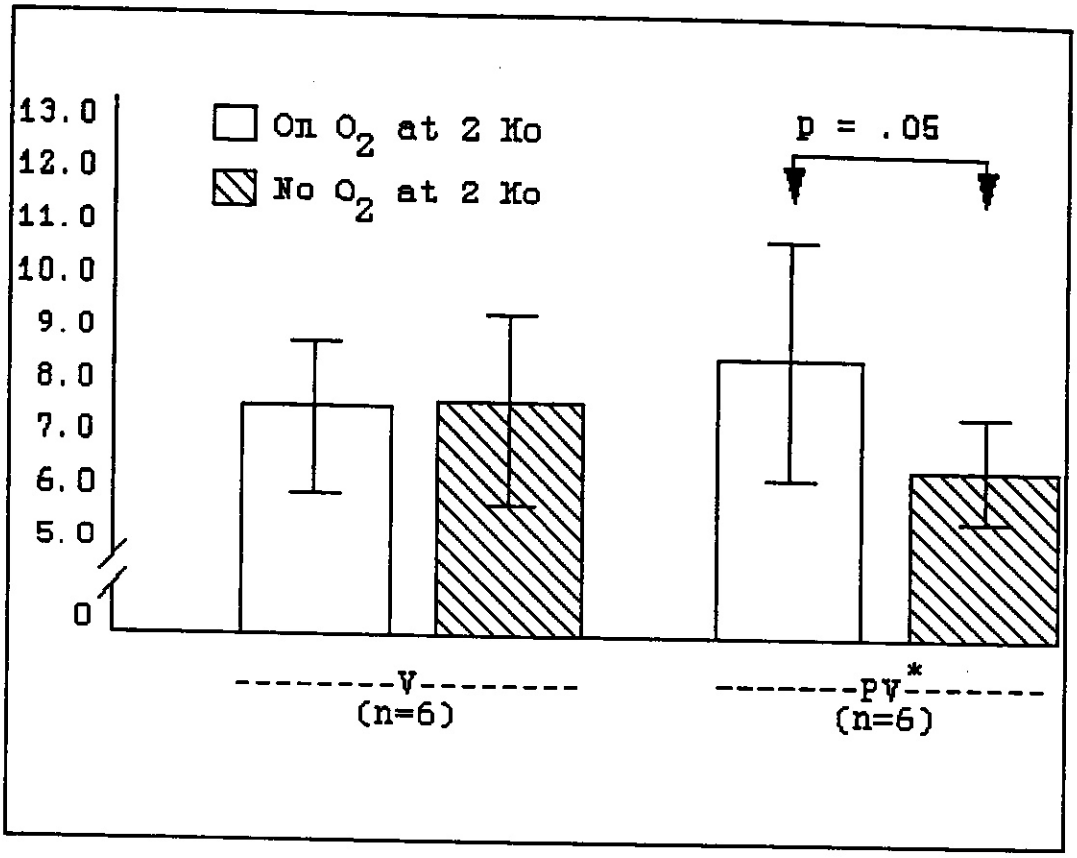

FIGURE 7

MEAN CALORIC INTAKE PER GRAM OF WEIGHT GAIN FOR INFANTS DURING VENTILATOR SUPPORT (V) AND POST-VENTILATOR SUPPORT (PV)
* Significance by paired 2-tailed t test.

period when the infants were supported by a mechanical ventilator (via an endotracheal tube) and the period immediately after extubation. A rise in caloric intake is typically accompanied by improved weight gain in VLBW infants. Though Caloric intake/kg/day rose significantly from V to PV, adjusted Calories/kg/day did not rise significantly, since there was a significant increase in the percentage of total calories provided enterally rather than parenterally. (See page 34 for the definition of "Adjusted

calories.") Actual weight gain increased, but only at the 10% level of significance (by paired 2-tailed t test). This slight increase in weight gain could have been due to one of three factors. First, the weight gain seen in this sample could have been due to chance. Second, the weight gain could have been related to the slight rise in caloric intake from V to PV. Finally, fluid retention may have been responsible for the increased weight gain since urine output decreased from V to PV while fluid intake and estimated stool output remained unchanged. Since each infant served as his or her own control, sex and age could not have been responsible for the difference or lack of difference between V and PV values in this 15 patient sample.

The actual reason for the decreased urine output is not discernible given the retrospective nature of the study. Since diuretics (that is, medications which stimulate urination) are used from time to time during the hospital course of patients with bronchopulmonary dysplasia, a significant decrease in diuretic usage from V to PV could have contributed to a drop in PV urine output. The use of such medications was not assessed in this study. However, typical management of BPD patients in the MCMC Neonatal Intensive Care Unit does not suggest this to be the case. Increased sodium intake was also not responsible for decreased urine output, fluid retention, since sodium intake remained unchanged from V to PV. A change in fluid content of the stool cannot be ruled out.

One way of assessing weight gain in relation to energy intake is to look at calories ingested per gram of weight gained (Cal/g). Though this does not eliminate the fluid variable and its confounding effect on weight gain, it does directly relate calories to weight gain so that weight gain can be compared from one group to another regardless of varying energy intake. When the results of the initial 15 patient study sample were compiled, Cal/g did not change from V to PV. Though Adj Cal/g decreased slightly from V to PV for this group, the change was not significant.

The division of the initial 15 patients into 2 matched sub-groups, each with 6 patients, provided some explanation for the initial findings. First, it should be noted that though the matching was done retrospectively, the mean gestational ages, birth weights and birth lengths of the two sub-groups were nearly identical. The mean occipital-frontal circumference of the patients on O_2 at or past 2 mo was higher than that of the infants who did not receive supplemental oxygen at 2 months. The difference was significant at $p>.05$, however. Both groups reached their lowest weight at a similar age.

Demographic differences did exist between the patients who received O_2 at 2 mo and those who did not. The age at extubation and the weight at extubation were considerably different between the two sub-groups. The infants who remained on O_2 at or past 2 months of age were intubated nearly 2 times as long as the patients who were not on O_2 at

2 months. While all 12 patients had BPD and a sporadic assortment of other complications (see Appendix B), the 6 patients on O_2 at 2 mo tended to have worse BPD, by clinical assessment, by results of chest x-rays and by the fact that they still required supplemental oxygen at age 2 months, than those not on O_2 at 2 mo. The retrospective grouping of patients according to the incidence of oxygen supplementation at 2 months of age is accepted as a reasonable measure of general morbidity of patients in the initial sample group. Interestingly, the patients not on O_2 at 2 mo were extubated at a much lower mean weight (1246 g vs. 923 g) than those who continued to receive supplemental oxygen at 2 months of age.

The energy intake for both sub-groups increased from V to PV, though the increase was not significant as it had been for the initial 15 patient sample. The proportion of calories provided enterally rose for both the O_2 at 2 mo and No O_2 at 2 mo sub-groups, though the rise was not significant. Adj Cal/kg/day increased from V to PV, but not significantly. The energy intake, by either parameter, was similar for both sub-groups. Fluid intake both from V to PV within the sub-groups, and for V and PV from one sub-group to the next, was not significantly different. Urine output for V and PV was not different between sub-groups; however, urine output dropped significantly from V to PV for the patients on O_2 at 2 mo. This change may have been the result of a change in stool water loss or the use of diuretics, the existence of some amount of congestive heart failure or pulmonary hypertension, or it may have been related to the decrease, though statistically not significant, in fluid intake (see Table 4). Thus, despite decreased urine output, Cal/g increased for the infants on O_2 at 2 mo while weight gain per kg did not change.

The most enlightening results of this study are the numbers associated with weight gain and energy intake per gram of weight gain for the two sub-groups. Weight gain (g/kg/day) during intubation (V) was similar for both sub-groups. However, while weight gain remained unchanged from V to PV for the infants on O_2 at 2 mo, it increased significantly from V to PV for those not on O_2 at 2 mo. The PV value was also significantly different between sub-groups. With regard to energy intake per gram of weight gain, there was no difference in V Cal/g or V Adj Cal/g between the sub-groups. There was a significant difference in both PV Cal/g and PV Adj Cal/g, however, between the O_2 at 2 mo and No O_2 at 2 mo sub-groups. Most importantly, the change from V to PV for patients on O_2 at 2 mo was opposite the change from V to PV for patients not on O_2 at 2 mo. While energy intake per gram of weight gain rose from V to PV for infants on O_2 at 2 mo, it decreased from V to PV for those not on O_2 at 2 mo. The differences were not statistically significant, except for the borderline significant difference between Adj Cal/g from V to PV for patients not on O_2 at 2 mo ($p = .087$). However, such differences do show a definite trend toward improved energy efficiency in patients on O_2 at 2 mo during the period immediately following extubation, as compared to the period during intubation. Thus, while all patient sub-groups gained weight, only the infants not on O_2 at 2 mo, and then only during the PV period, gained the amount of weight (g/kg/day) that might normally be expected of typical premature infants, as noted by Grausz and Bamberger (1985).

For the patients on O_2 at 2 mo (or 60 days of age), extubation took place at between 45 and 62 days of life. Thus, most if not all of these infants received supplemental oxygen during part or all of the PV period. Oxygen supplementation has been shown to improve weight gain in patients with bronchopulmonary dysplasia (Groothuis and Rosenberg 1987). Despite oxygen supplementation, weight gain did not increase in the period post-ventilator support (PV) in the patients studied. Possibly these patients spent more energy doing the work of breathing during PV, than they had during V when the ventilator assisted with the breathing efforts, or even provided total breathing support. If this assumption is true, then the original hypothesis, that is, that pre-term infants require more calories post-extubation than during intubation in order to continue the same rate of growth, may be true. Possibly, the energy saved by oxygen supplementation during PV, for the patients on O_2 as 2 mo, compensated for the additional energy expended for the increased work of breathing during PV, thus causing weight gain to remain unchanged.

While patients not on O_2 at 2 mo were extubated at between 20 and 41 days of life, the fact that they did not receive oxygen supplementation at 2 months (60 days) does not indicate when oxygen supplementation ceased, or how far prior to 2 months of age. In fact, this group might also have received supplemental oxygen during PV. If so, oxygen supplementation may not offer any explanation for either the improved or unchanged weight gain seen in this study, except that those infants still on supplemental oxygen at 2 months of age were obviously less "healthy" than those not on supplemental oxygen at 2 months. When the less healthy, or sick, infants were extubated, they gained less weight on the same amount of calories, most likely because of an increase in the work of breathing post-extubation. In relatively healthy babies, the endotracheal tube may disturb technical provision of nutrients, and may even interfere with respiration in such a way that work of breathing diminishes when the tube is removed. For healthy premature infants, extubation is a benefit. Conversely, extubation may place sick premature babies at greater risk for complications related to feeding and growth.

CHAPTER 5

CONCLUSIONS, RECOMMENDATIONS AND SUMMARY

The purpose of this study was to retrospectively investigate the effect of mechanical ventilation via an endotracheal tube, on the nutritional intake and growth patterns of infants who weighed less than 1250 grams at birth. The hypothesis was that pre-term infants who have recently been extubated require more calories (i.e., more calories per gram of weight gain) than they did during intubation in order to continue the same rate of growth once full respiratory support via a ventilator and endotracheal tube has been discontinued.

Conclusions

The initial results of this study, based on a 15 patient sample of infants weighing less than 1250 grams at birth, showed a trend towards improved weight gain post-extubation. This increase was not significant, however. In addition, it was not supported by improvement in energy utilization as evidenced by Cal/g or Adj Cal/g.

In order to investigate the situation further, the characteristics of the 15 patients were scrutinized in an attempt to see whether there were any significant differences within the group itself. Of the demographic data collected, the one item which appeared to divide the initial sample into two sub-groups, was the presence or absence of oxygen supplementation at 2 months of age. Therefore, all 6 patients who received supplemental oxygen at 2 months were matched by gestational age and birth weight to 6 patients who did not receive supplemental oxygen at 2 months. This procedure made it possible to compare the parameters by paired 2-tailed t test.

The most significant findings of the latter part of the study, or the comparison of patients who received O_2 at 2 months to those who did not, were that Cal/g and Adj Cal/g increased from V to PV for patients on O_2 at 2 months, showing a decrease in efficiency of energy utilization, even though weight gain (g/kg/day) did not decrease as hypothesized. For this sub-group which received O_2 at 2 months, more energy was needed to elicit a similar weight gain when the V and PV periods were compared. In fact, while mean Adj Cal/g went up by 0.8 Cal/g from V to PV for infants on O_2 at 2 mo, it went down by twice as much, or 1.5 Cal/g for those not on O_2 at 2 mo.

The results of this retrospective study, based on patients cared for in the NICU at the Milwaukee County Medical Complex, indicate that energy efficiency of healthy VLBW infants (i.e., the infants in this study who were not on O_2 at 2 months of age) improved during the 2 weeks after extubation, as compared to the 2 weeks immediately prior to extubation. Similarly, the reverse trend was seen in VLBW infants who continued to receive supplemental oxygen at 2 months of age.

Actual weight gain (g/kg/day) in 11 of the 15 sample patients increased from V to PV. This seems to indicate that all or nearly all of the patients were physically ready to be extubated when the extubation occurred. The 4 patients who did not show improved weight gain, did however continue to gain weight, though at a lower rate. Weight gain during PV, for the patients on O_2 at 2 months, might have increased if more calories had been provided.

Recommendations

A number of recommendations can be made in order to explore this topic of weight gain during and after mechanical ventilator support via an endotracheal tube.

First, a larger patient sample should be studied in order to determine if the results of this study are at all universal. Second, the study should be prospective in nature to eliminate variables related to medical management. Medical management should be as similar as possible between patients with regard to type of feeding, fluid intake (cc/kg/day), type and amount of diuretics (if required), and the type of isolette or radiant warmer in which the child is maintained. Third, if possible the length of time for periods V and PV should be expanded. If the length of time is expanded, occipital-frontal circumference and body length should be carefully measured and recorded weekly during the study periods to allow for further assessment of growth. Skin-fold measurements could be included as well. Fourth, the age at which oxygen supplementation was stopped should be recorded so that it can be determined if and how long infants received supplemental oxygen during the PV period. This would aid in deciding whether oxygen supplementation itself was at all related to the results of this study, or if the presence of supplemental oxygen at 2 months of age was simply a marker of the severity of morbidity. Fifth, the most accurate way to assess the implications of this study is to utilize a metabolic gas monitor and couple the results (namely oxygen consumption) with the results of a metabolic balance study of patients during intubation and post-extubation. In this way the actual amount of energy utilized could be determined. Finally, a modification of this study might entail looking at the same parameters for patients before and after oxygen supplementation and/or before and after all respiratory support (endotracheal tube, mask and prongs). Another complex study which could aid in conducting research such as this, would be to determine if it is indeed possible to arrive at an adjustment factor that can be applied to enteral calories, as was done in this study, to equate them to parenteral calories as utilized by VLBW premature infants.

Summary

The purpose of this study was to retrospectively investigate the effect of mechanical ventilator support, via an endotracheal tube, on the nutritional intake and weight gain patterns of infants weighing less than 1250 grams at birth. The hypothesis was that preterm infants who have recently been extubated (PV) require more calories than they did immediately prior to extubation (V) in order to continue the same rate of growth once full respiratory support via an endotracheal tube and mechanical ventilator has been discontinued.

An initial assessment of 15 patients revealed a non-significant trend towards improved weight gain (g/kg/day) post-extubation. Energy utilization (Cal/g) remained unchanged. Six of the initial 15 patients continued to receive supplemental oxygen at 2 months of age; they were matched, by birth weight and gestational age, to 6 patients (from the same initial sample) who did not receive supplemental oxygen at 2 months of age (No O_2 at 2 mo). Upon comparison of the two sub-groups, it was noted that extubation took place at a significantly earlier age and lower weight for the patients not on O_2 at 2 mo. While weight gain was unchanged from V to PV for patients on O_2 at 2 mo, it increased significantly for infants not on O_2 at 2 mo. Similarly, energy utilization per gram of weight gain (Cal/g) increased for patients on O_2 at 2 mo, yet for

patients not on O_2 at 2 mo, it decreased, showing improved energy efficiency. All comparisons were made by paired 2-tailed t test. The two matched sub-groups seem to represent two different types of infants in regard to weight gain and energy utilization; the results are most likely related to degree of morbidity. Recommendations are provided as to how this study can be expanded and therefore become applicable to the increasing population of less than 1250 gram infants. If efficiency of energy utilization is indeed significantly less in certain sub-groups of VLBW infants, then more attention must be paid to the provision of adequate calories for these individuals.

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APPENDIX A

NEONATAL INTENSIVE CARE NURSERY FEEDING PROTOCOL (In Part)

From: <u>The Milwaukee County Medical Complex Neonatal Intensive Care Nursery Resident's Manual</u>
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1988

<u>Composition of Parenteral Nutrition Solution</u>

Carbohydrate	Start	6-9 g/kg/day (5-10% glucose)
	Then	7.2-11.5 g/kg/day
	Finally	17.8-21.6 g/kg/day peripherally
	or	20-25 g/kg/day centrally
Protein	Start	1.0 g/kg/day of IV amino acids
	Then	Increase by 0.5-1.0 g/kg daily to a maximum of 2.5 g/kg/day
	Provide	8-15% of total calories as protein
Fat	Start	1.0 g/kg/day (0.5 g/kg/day for infants <1250 g birth weight) Administer over 24 hours at an infusion rate at or below 0.15 g/kg/hr.
	Then	Gradually increase 2-3 times a week by 0.5 g/kg/day increments until optimal calories are reached. Do not exceed 3.0-3.5 g/kg/day of fat by IV.

1. PARENTERAL NUTRITION (PN)

a. Introduction

As stated by the Committee on Nutrition of the American Academy of Pediatrics, nutritional care must be a major component of medical care.[1]

> Clinical experience has demonstrated the value of optimal nutritional status in resisting the effects of trauma and disease as well as in improving response to medical and surgical therapy. The metabolic demands of rapid growth and the low nutritional reserves in infancy make the potential benefit of good nutrition to critically ill pediatric patients even greater.

Parenteral nutrition, the intravenous provision of partial or total nutrition (TPN) which supplies energy, protein, fat, carbohydrate, and other essential nutrients, is instituted to adequately support tissue maintenance and repair, as well as growth and development, when enteral feedings are either impossible, impractical or inadequate.[2,3]

b. Goals of Parenteral Nutrition

The nutritional requirements (fluids, calories, minerals and vitamins) of basal metabolism and growth can be provided either partially or completely through parenteral nutrition when an infant is incapable of tolerating them enterally. Since adequate calories and positive nutrient balance are essential in the newborn period, no infant should go longer than 3 days without a protein source and basal calories.

Nutritional goals must be assessed with the state of health of the infant in mind. The ultimate goal in relation to the nutritional care of preterm infants is to "achieve a postnatal growth which approximates the growth in utero normal fetus at the same postconception age".[4] According to the Committee on Nutrition of the American Academy of Pediatrics, it is believed that this approach will provide the best possible conditions for subsequent normal growth and development. The goals for monitoring PN patients in the Neonatal Intensive Care Nursery at MCMC include:

1) to obtain and maintain acceptable growth and an optimal nutritional status,
2) to avoid metabolic complications of both short and long term PN,
3) to standardize care plans and treatment for metabolic complications of patients on PN.

<u>NOTE</u>
PN solutions at MCMC are ordered daily (by 12:00 noon, preferably) from the Pharmacy. Each solution is tailor-made according to the patient's needs. Orders are written via the NICU computer system which aids the physician in ordering a solution of proper composition.

During the first 24 hours of life, a <u>5-10% Dextrose</u> solution may be used to provide fluid requirements. Electrolytes are usually not needed during the first 24 hrs. Electrolytes and calcium gluconate may be added depending on the results.

<u>D5E48</u> is a good maintenance solution which provides 25 mEq Na, 20 mEq K, 24 mEq Cl, 20 mg P,and 37 mg Mg/liter. In order to make it 10% Dextrose, 10cc D50% are added to 90cc D5E48.

c. <u>Indications for Use</u>
Indications for total or supplemented parenteral nutrition include:

1) the postsurgical infant or any infant unable to feed enterally for an extended period of time (at least 3-4 days),
2) the preterm infant unable to tolerate enteral feedings, or unable to tolerate adequate enteral nutrition, (fluids and/or calories)
3) the SGA infant unable to tolerate enteral feedings within 24 hrs,
4) acquired GI tract anomalies (e.g., necrotizing enterocolitis, volvulus, short bowel syndrome, intestinal perforation),
5) excessive metabolic stress (e.g., respiratory distress syndrome, meconium aspiration syndrome, chronic diarrhea),
6) congenital gastrointestinal anomalies preventing the use of enteral feedings (e.g., gastroschisis, omphalocele, tracheoesophageal atresia), and
7) inborn errors in metabolism.

Although the list of indications for parenteral nutrition is long, there are circumstances which prohibit the use of PN.

Contraindications to PN include:
1) when adequate patient management can be accomplished via the enteral route,
2) when only short term support is required in a patient who has been in good nutritional status.

Abuses of PN include:
1) either one of the above situations,
2) disregard or ignorance of the established principles or techniques for safe long term PN,
3) lack of requisite knowledge of nutrition, metabolism, metabolic responses to surgery, trauma, sepsis and malnutrition,
4) lack of meticulous attention to asepsis in insertion of catheters, maintenance of catheter and in formulating solution,
5) lack of adequate monitoring for normal requirements and toxicity,
6) errors in formulation of solutions, i.e. lack of knowledge of composition of solutions used, incompatibilities, routine use of prophylactic antibiotics, making solution too far in advance, inadequate storage,
7) improper administration over a few hours rather than 24 hours.

d. Route - Peripheral vs. Central

Total or partial parenteral nutrition may be done by either the peripheral or central route. There are, however, indications for using one route rather than the other.

Peripheral Vein

The peripheral route is usually used when it supplements oral feedings, or when nutritional support is expected to be required for a relatively short time, usually less than two weeks. Standard peripheral solutions have an osmolarity of 300-900 mOsm/L.[1]

Peripheral nutrition solutions used in neonates at maintenance fluid rates generally provide a maximum of 80-90 Cal/kg/day; this level of intake can prevent weight loss but it generally does not promote adequate growth. When providing peripheral solutions, dextrose is limited to a 10-12% concentration in order to avoid skin sloughs. Intravenous fat is necessary to achieve adequate calories because of this limitation in glucose intake. Fat should be administered at a maximum rate of 3-3.5 gm/kg/day. Peripheral alimentation is commonly used to supplement feedings to low birth weight infants. When doing so, it is important to closely monitor the volume and caloric density of the nutrients.[5]

Intravenous nutrition solutions should be continued until maintenance fluid volumes (100-120 cc/kg/day) and 75% of the caloric requirements are being provided by enteral feedings. IV feedings may be discontinued at this point if it is anticipated that the infant will be receiving adequate calories within a few days. During this weaning process a careful plan for modifying the volumes of the nutrients received by both parenteral and enteral routes is important in order to avoid inadequate caloric intake. A major nursing responsibility includes close observation of the rate of the solutions infused by a volumetric pump and of the peripheral vein site for signs of fluid infiltration or phlebitis.

Central Vein

Indications for the delivery of TPN solutions by central vein catheters include the following conditions:

1) the duration of nutritional therapy is expected to be for periods greater than two weeks,
2) accessibility to peripheral veins is difficult,
3) the neonate is fluid restricted and requires TPN,
4) intravenous caloric requirements exceed 100 Cal/kg/day,
5) the osmolarity of the solution is > 900 mOsm/l.

A central venous catheter is valuable because it is placed at the junction of the superior vena cava and the right atrium, a region where high blood flow allows rapid dilution of the hypertonic infusates thus preventing venous inflammation and thrombosis.[5] Some flexible catheters can be introduced percutaneously into the subclavian vein.[1] CBC's should be monitored for these patients (r/o infection).

e. Composition of Parenteral Nutrition Solutions

1) Fluids

The daily maintenance water requirement for the term and low-birth weight infant includes insensible water loss, urinary output, and stool losses. In addition, approximately 0.85 cc of water per gram of weight gain are needed for new tissue synthesis.[6] Preterm infants experience a greater percentage of weight loss compared to that of term infants, mostly because they have a large fluid component (up to 85% of body weight) which exists primarily as extracellular water.[7]

Table 1 lists approximations of daily fluid requirements. Low volume fluid infusions are usually given during the first postnatal days because of lower basal metabolic rates, decreased activity, and allowance for the normal contraction of extracellular fluid volume. (The patient also requires less calories because of the low metabolic rate and activity level.)

Table 1. Estimated Basic Maintenance Fluid Requirements for Newborns i
Isolettes (cc/kg/day)

Wt (gms)	500-750*	751-1000	1001-1250	1251-1500	1501-1750	1751-2
Day 1	100-120	105	100	90	80	80
Day 2	100-120	105	100	90-100	80	80
Day 3	120-150	120-140	130	100-130	100-120	100-12
Day 4	120-150	120-150	130	130	130	130
Day 5	120-150	120-150	130	130	130	130
Day 6-30	120-150	120-150	130	130	130	130

* Adapted from data of Bell,[8], and Fanaroff and Martin[9].
Very low birthweight (VLBW) infants who have very immature skin and a
unstable temperature, thus necessitating the use of a radiant warmer, may require more fluids during the first days of life.

12) WEANING FROM TPN

When oral feedings are begun, parenteral nutrition must not be stopped abruptly. If at all possible, the baby should be maintained on adequate calories (at least 100 Cal/kg/day) via both routes. Parenteral nutrition may be discontinued when approximately 75% of desired caloric intake is provided by formula, with a minimum maintenance volume of 100-120 cc/kg/day. When intake is approaching this level, or the PN solution is infusing at about 1 cc/hr, the PN may be replaced with a 10% dextrose solution. IV lipid may be continued (with or without $D_{10}W$) in malnourished infants. (The cost-nutritional benefit ratio of using small volumes of PN solution is generally prohibitive; a dextrose solution is a more reasonable choice in this circumstance.) The IV may be dropped entirely when a maintenance oral fluid level of 100 cc/kg/day (full-strength formula) is reached, if it is expected that the infant will be receiving adequate oral intake within several days. Feedings for sick or VLBW infants may need to be handled somewhat differently if dilute formula is utilized for more than a short period of time.

When a baby is being weaned from parenteral to oral feedings, it is necessary to simultaneously increase the volume of oral feeds and decrease the volume of the IV (PN) solution. During this period of adjustment, it is important to keep the nutrient concentration of the PN solution within an acceptable range; this is important at any point in time. The osmolarity of a peripheral parenteral nutrition solution should not go above 1000 mOsm/L. As the volume of the PN solution decreases (while the volume of the enteral feedings increases), it is important to avoid overconcentrating the PN. Keep the concentration of the nutrients in the PN (in units/dl) constant or decrease the concentration. Do not attempt to put the same amount of nutrients that were provided by a large volume of solution into a small volume of solution. As a general rule, the PN solution during this time of weaning should not contain more than 2.5% amino acids, 10-12% dextrose (more is allowed if it is a central line solution), 3-4 mEq of NaCL/100 cc, and 3 mEq of KCL/100 cc. Calcium and phosphorus may still be provided at a level of 40 and 25 mg/kg/day, respectively, provided that the concentration does not exceed precipitation limits.

Choice of infant formula should be based on the infant's individual situation (initial problem, course of illness, current state of health, tolerance). The following factors are important to remember:

1. Attempts should be made to maintain adequate total calories throughout the period of initial feeding or refeeding.
2. The concentration of formula and the volume should not be increased at the same time.
3. Each change, whether in concentration or volume, should be given an adequate trial period before the next change.
4. Caloric monitoring of tolerance and nutritional status should be performed; response to problems should be immediate.

e. <u>GUIDELINES FOR INITIATING ENTERAL FEEDING FOR PREMATURE INFANTS</u>

As suggested by Avery and Fletcher,[18] the following guidelines should be considered when choosing the appropriate feeding for an infant:

1) The diet should contain adequate calories (90-150 Cal/kg/day) and essential nutrients.
2) The diet should be digestible, especially in the light of the infant's particular medical status and history.
3) Reasonable distribution of calories should be achieved
(i.e., protein 7%-16%, carbohydrate 35%-65%, fat 35% -55%).
4) The diet should be chosen so that potential problems suspected from a family history are avoided.

With regard to feeding, premature infants are known to face many problems.[18] Such problems generally include: poor sucking and swallowing reflexes, poor gag reflexes (leading to aspiraton), relatively high caloric requirements (with a small stomach capacity), an incompetent esophageal cardiac sphincter, decreased absorption of essential nutrients, and decreased gastrointestinal hormone response.

Keeping the above information in mind, the following <u>general recommendations</u> may be <u>used when initiating enteral feedings</u> for premature infants.

<u>Birth weight < 1250 g</u> - Start 1-3 cc of 1/2 strength or full-strength term infant formula (Enfamil 10 or 20 cal/oz) q 2 hr. If using continuous orogastric or transpyloric feedings, begin with 1/2 to 1 cc q hr. Advance by 1 cc/day as tolerated (to 10-15 cc q 2 hrs).

Birth weight 1251-1500 g Start 2-6 cc of Full Strength Enfamil 20 cal/oz q 2 hrs. Advance by 1-2 cc/day as tolerated to 20-28 cc q 2-3 hrs).

Birth weight 1501-2000 g Start 5-10 cc of Full Strength Enfamil 20 cal/oz q 2-3 hrs. Advance by 5-10 cc/day as tolerated to 28-37 cc q 3 hrs.

Birth weight > 2000 g - Start 10-20 cc/day q 3-4 hrs of Full Strength term infant (20 cal/oz). Advance as tolerated to 37-50 cc q 3-4 hrs.

Additional Guidelines:

- For infants weighing < 1900 g, premature formula should be utilized after an initial stabilization period on term infant formula. Infants weighing >1900 g may be fed term formula.
- Infants weighing < 1500 g should not be given 24 cal/oz formula during the first 2 weeks of feedings.
- In cases of short gut syndrome, post NEC or post -asphyxia, start with dilute formula if infants weight < 1250 g.
- Do not increase both strength and volume at the same time.
- If a baby appears to be intolerant (residuals, abdominal distention, vomiting), several options exist:
  1) Do not increase feeding volume until infant appears stable
  2) Decrease feeding volume
  3) Change interval of feeding (decrease if hypoglycemic)
  4) Change formula
  5) Change feeding method
  6) NPO if NEC is suspected. Always check stool hemotest and clinitest.

(References are available in the complete document.)

APPENDIX B

COMPUTER FILE OF PATIENT DATA

File name: ventgro

	NAME	GA	BWt	SEX	1S2AGA	BHt	Bofc	LWt d	EXTB d	EXTB wt	FAILgr	BPD1-3	Oxy28d	Oxy2mo
1	WR	27	740	F	1	35.0	23.5	4	20	800	1	1	0	0
2	SN	25	635	F	2	31.0	21.5	7	41	880	1	1	1	0
3	FN	26	690	M	2	33.0	25.3	8	45	1040	1	2	1	1
4	TN	26	765	M	2	34.0	23.0	9	30	890	0	2	1	0
5	FEN	29	1150	F	2	37.0	24.5	8	45	1390	1	2	1	0
6	GL	25	640	M	2	31.0	28.0	8	45	1200	1	3	1	1
7	FY	26	765	F	2	33.5	25.0	6	61	1475	0	3	1	1
8	AI	28	940	M	2	34.0	25.0	10	41	1140	1	1	1	0
9	RS1	28	1150	F	2	38.0	27.0	23	24	1180	0	3	0	0
10	RS2	28	1110	F	2	37.0	26.5	15	60	1780	0	3	1	1
11	RR1	26	715	F	2	33.5	23.0	6	34	940	0	2	1	0
12	RR2	26	840	F	2	35.0	25.0	8	62	1220	1	2	1	1
13	TS	27	610	F	1	31.0	22.0	26	53	760	1	3	1	1
14	FMN	24	720	M	2	30.0	22.5	8	41	870	1	0	0	0
15	NN	24	560	F	1	30.5	20.5	11	27	850	1	2	0	0

KEY

GA = Gestational age (wks)
BWt = Birth weight (g)
SEX = Male or Female
1S2AGA = SGA (1) or AGA (2)
BHt = Birth height (cm)
Bofc = Birth occipital-frontal circumference (cm)
LWt d = Day at which patient reached lowest wt
EXTB d = Age at extubation (days)
EXTB wt = Wt (g) at extubation
FAILgr = Growth failure at time of extubation; 1=yes, 0=no
BPD1-3 = BPD Grade 1 to 3, or 0=no BPD
Oxy28d = Supplemental oxygen provided at 28 days of age; 1=yes, 0=no
Oxy2mo = Supplemental oxygen provided at 2 months of age; 1=yes, 0=no

	RDS1-4	ASPHYX	SEIZUR	SEPSIS	PDA1-4	IVH1-5	NEC	OTHER	INccV	URccV	INccPV	URccPV	g/kgV	g/kgPV
1	0	0	0	0	3	0	0	0	129	83	136	92	13.8	16.0
2	3	0	0	1	4	0	0	0	123	81	140	76	12.4	14.7
3	1	0	0	0	2	0	0	0	141	93	137	72	17.1	17.2
4	1	0	0	0	0	0	0	0	139	86	137	69	10.5	18.7
5	0	0	1	0	0	0	1	0	153	77	137	61	12.7	8.0
6	4	1	0	1	2	4	0	0	133	95	140	87	11.7	8.4
7	0	0	0	1	0	4	0	0	139	80	122	50	12.5	8.7
8	1	0	1	1	0	4	0	BrnAt	133	81	136	78	8.0	16.3
9	1	0	0	0	2	0	0	0	139	93	130	68	11.9	12.3
10	1	0	0	1	0	0	0	0	134	71	119	60	13.3	11.7
11	0	0	0	1	0	1	0	0	146	62	138	54	12.8	21.0
12	4	0	0	1	2	1	0	0	129	74	140	70	10.1	15.8
13	1	0	0	0	2	1	0	FTT	150	113	130	79	11.2	12.1
14	1	0	0	1	0	0	0	0	151	88	144	76	13.6	15.9
15	2	0	0	1	2	1	0	Pcyst	146	96	136	90	12.9	17.2

KEY

Diagnoses

RDS1-4 = Grade of RDS (1-4)
ASPHYX = Asphyxia; 1=yes,0=no
SEIZUR = Seizures; 1=yes,0=no
SEPSIS = Sepsis; 1=yes,0=no
PDA1-4 = Patent Ductus Arteriosus; Grade 1-4, 0=no
IVH1-5 = Intraventricular hemorrhage; Grade 1-5, 0=no
NEC = Necrotizing enterocolitis; 1=yes,0=no
OTHER = Other major diagnoses:
BrnAt=Brain atrophy
FTT=Failure to thrive
Pcyst=Porencephalic cyst

V = During ventilator support
PV = Post-ventilator support
INccV=Fluids in (cc/kg/day)
URccV=Urine out (cc/kg/day)
INccPV=Fluids in (cc/kg/day)
URccPV=Urine out (cc/kg/day)
g/kgV = Wt gain (g/kg/day)
g/kgPV = Wt gain (g/kg/day)

	CalkgV	CalkgPV	AdjclV	AdcalPV	%PO V	%PO PV	Stl V	Stl PV	NaIN V	NaIN PV
1	61	95	57	89	26.2	42.1	5.9	5.2	3.43	4.26
2	95	106	84	90	80.0	93.4	10.1	7.9	2.09	4.91
3	100	112	98	103	11.0	52.7	1.9	5.1	4.32	3.16
4	98	100	84	87	93.9	86.0	11.6	10.7	2.00	2.15
5	113	104	105	89	46.0	97.1	10.2	17.6	3.33	4.42
6	89	100	76	86	97.8	94.0	9.4	7.1	1.70	3.37
7	101	92	92	82	60.4	76.1	7.1	9.0	2.84	2.00
8	88	95	76	82	87.5	89.5	8.6	6.0	5.61	4.32
9	75	92	75	84	0.0	60.9	1.4	2.8	4.37	3.32
10	83	93	82	92	8.4	3.2	1.8	1.0	3.68	4.74
11	108	106	92	90	96.3	99.0	11.8	5.9	1.94	3.00
12	96	100	85	88	77.1	78.0	9.0	8.0	6.00	2.52
13	73	89	71	83	19.2	41.6	4.4	3.4	4.42	5.24
14	103	117	94	99	60.2	100	7.0	9.0	5.27	5.50
15	107	106	94	91	83.2	95.3	6.7	6.3	2.63	1.76

KEY

V = During ventilator support
PV = Post-ventilator support
Adjcal = 100% IV Cal + 85% enteral Cal
Calkg**V** = Energy intake (Cal/kg/day)
Calkg**PV** = Energy intake (Cal/kg/day)
Adjcl**V** = Adjusted energy intake (Cal/kg/day)
Adcal**PV** = Adjusted energy intake (Cal/kg/day)
%PO **V** = % of total calories fed orally
%PO **PV** =% of total calories fed orally
Stl **V** = Stool output (g/kg/day)
Stl **PV** = Stool output (g/kg/day)
NaIN **V** = Sodium intake (mEq/kg/day)
NaIN**PV** = Sodium intake (mEq/kg/day)

	CalgV	CalgPV	AdclgV	AdclgPV	Chcalg	ChAdclg
1	4.42	5.94	4.13	5.56	+1.52	+1.43
2	7.66	7.21	6.77	6.12	-0.43	-0.65
3	5.85	6.51	5.73	5.99	+0.66	+0.26
4	9.33	5.35	8.00	4.65	-3.98	-3.35
5	8.90	13.0	8.27	11.1	+4.10	+2.83
6	7.60	11.9	6.50	10.2	+4.30	+3.70
7	8.08	10.6	7.36	9.42	+2.52	+2.06
8	11.0	5.83	9.50	5.03	-5.17	-4.47
9	6.30	7.50	6.30	6.83	+1.20	+0.53
10	6.24	7.95	6.16	7.86	+1.71	+1.70
11	8.44	5.05	7.19	4.28	-3.39	-2.91
12	9.50	6.33	8.41	5.57	-3.17	-2.84
13	6.52	7.36	6.34	6.86	+0.84	+0.52
14	7.57	7.36	6.91	6.23	-0.21	-0.68
15	8.29	6.16	7.29	5.29	-2.13	-2.00

KEY

V = During ventilator support
PV = Post-ventilator support
CalgV = Caloric intake per gram of wt gain
CalgPV = Caloric intake per gram of wt gain
AdclgV = Adjusted caloric intake per gram of wt gain
AdclgPV = Adjusted caloric intake per gram of wt gain
Chcalg = Change in caloric intake per gram of wt gain from V to PV
ChAdclg = Change in adjusted caloric intake per gram of wt gain from V to PV

Matched Pairs for Patients
On O_2 at 2 mo and not on O_2 at 2 mo

Patients #3 and #1
Patients #6 and #2
Patients #7 and #4
Patients #10 and #9
Patients #12 and #11
Patients #13 and #15