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Medical Nutrition Therapy in the Management of Preterm and Low Birthweight Infants

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Foreword

Hospitals and clinics around the world offer advanced-level care for high-risk infants, with America as the undisputed leader in forging new pathways within the field of neonatology (the study and care of newborns). Learning experiences at Baylor College of Medicine and Texas Children's Hospital, in the heart of Houston's vast Medical Center, provided the foundation for the preparation of my honors thesis. It was there that I studied infant nutrition by participating in Baylor's neonatal fellowship program. During my time in Houston, I earned a greater appreciation for the delicate yet sophisticated science of infant care. Baylor College of Medicine offers a unique Neonatal Nutrition Rotation, designed to provide advanced-level training in high-risk neonatal nutrition support to practicing physicians and dietitians pursuing specialization in neonatal nutrition. The rotation is clinically-oriented, providing a strong base in management strategies for premature, low birthweight, and other high-risk infants. As an intern, I participated in team rounds and developed infant care plans in the intensive care nurseries of Texas Children's Hospital, all part of the program's objective of training individuals in neonatal nutrition in order to promote provision of the highest-possible quality of care to patients.

As a dietetics major, I entered the setting of Texas Children's Hospital expecting to find dietitians providing premiere nutritional care for infants. What I found was much more. Neonatal dietitians in the units at Texas Children's Hospital are on the cuttingedge of their field. They are involved in on-going research efforts at the national level in cooperation with the United States Department of Agriculture Children's Nutrition Research Center also located within Houston's Medical Center. The dietitians are assertive in providing state-of-the-art care for a population of infants at serious risk both physiologically and nutritionally. They work in close contact with physicians, nurses, pharmacists, and other healthcare professionals, providing team care for infants from the Southwest region of the United States as well as the world at-large.

Although Texas Children's Hospital exemplifies the quality of acute care currently available for high-risk infants, the understanding of neonatal care is still lacking in many respects. Many aspects of neonatalogy remain to be explored by individuals and teams willing to invest the time and effort in such an undertaking. I intend to pursue a career as a registered dietitian, and this thesis project has provided the foundation upon which I will build as I specialize in the field of neonatal nutrition in the years to come.

Preface

In the past, infants born prematurely or of low birthweight simply did not survive. Improved medical care has increased infant survival, as well as subsequent growth and development. The many technological advances in neonatology bring to the forefront countless new challenges in developing nutritional care plans able to adequately meet the needs of extremely fragile and vulnerable infants. Increased knowledge of the nutrient requirements for high-risk infants is needed, along with a clear understanding of how to administer the nutrients in a safe and effective manner.

What exactly must registered dietitians know in order to practice effectively as nutrition experts in the neonatal intensive care setting? The purpose of this paper is to explore the critical role which nutrition plays in the management of premature, low birthweight, and other high-risk infants.

No field in medicine is so compelling and so confusing, so wondrous and so disturbing, as neonatalogy, the care, study, and treatment of the newborn. In no other discipline is the reward for success so great, or the price of failure so horrifying.

–Rasa Gustaitis, A Time to Be Born, A Time to Die

Introduction

Seeing a newborn infant function and grow is literally amazing. An entire discipline has been built around just such a wonder. Neonatology is that field of practice which encompasses the care, treatment, and study of newborns. Recently, nutrition has been recognized for its critical role in the management of high-risk newborns. Neonatal nutrition is a rapidly growing discipline which has the potential to greatly influence the growth and developmental status of premature and low birthweight infants, enhancing infant outcomes and leading to better quality of life.

Many significant advances have been made in recent years in the technology related to neonatology as well as its basic understanding, resulting in a dramatically increased survival rate among infants born prematurely or in an otherwise compromised condition. The trend is clearly reflected in both state and national health statistics. Over the past six years, the neonatal mortality rate, defined as the number of infant deaths before 28 days of life per 1000 live births, steadily declined in both Arkansas and the nation at-large. This figure has been dropping at a considerably greater rate than the total infant mortality rate (number of infant deaths under one year of age per 1000 live births) since the 1960's.[1] The national neonatal mortality rate for 1990 was 5.85 deaths per 1000 live births (24,309 total deaths). The national infant mortality rate for 1991 was 8.9 deaths per 1000 live births (36,766 total deaths), down three percent from 1990.[2] Although America still ranks twenty-second internationally in the total number of infants who die before their first birthday[3], increasing infant survival rates give evidence of the remarkable strides made in the medical care of high-risk infants in recent years.

Many of the advances in infant care, which have led to improving infant mortality rates, may be linked to the increasingly common provision of comprehensive nutritional care at the earliest stages of life. "Medical nutrition therapy" is the terminology used to describe the process of "assessment of the nutritional status of patients with a condition, illness, or injury that puts them at risk. . . by analysis of medical and diet history, laboratory values, and anthropometric measurements [height and weight]."[4] After a thorough assessment has been carried out, appropriate nutritional care measures are taken. Examples of such "specialized nutrition therapies" include the provision of nutrient supplements (neutraceuticals) and delivery of food components through a tube (enteral nutrition) or through the veins (parenteral nutrition). Medical nutrition therapy is an appropriate form of preventative and aggressive care for patients of all ages. For infants in the neonatal intensive care setting, medical nutrition therapy can reduce both hospital costs and length-of-stay. It is clear that the incorporation of nutrition into the management of high-risk newborns is of paramount importance.

ONE

Classification of Newborns

Thousands of healthy, well-functioning infants are born in America every year. For the majority of individuals, giving birth to a child means only an eighteen hour stay in the hospital for routine procedures, after which the new baby may be taken home. In some cases, however, there are complications which require that the infant spend additional time in the hospital nursery. Lengthened stays may be necessary in the case of full-term infants (those born between 37 and 41 weeks of gestation) or preterm infants (those born before the 37th week of gestation).[5] In order to understand the nature of the nutritional care provided in the neonatal setting, it is important to first be familiar with the common classifications for newborn infants.

Low Birthweight Infants

> . . .there are tiny, puny infants with great vitality. Their movements are untiring and their crying lusty, for their organs are quite capable of performing their allotted functions. These infants will live, for although their weight is inferior. . .their sojourn in the womb was longer.
>
> —Pierre Budin, *The Nursling*, 1907

Low birthweight infants, those newborns weighing less than 2500 grams (5 pounds, 8 ounces) at birth, have many associated complications. They are likely to have a longer stay in the hospital and a greater number of return visits than those born at or above 2500 grams, the standard for a healthy infant. Twenty-two million low birthweight infants are born every year on a worldwide basis.[6] In the United States, low birthweight infants account for seven percent of all live births annually,[7] placing the nation behind only 30 other countries for the occurrence of low birthweight.[8] The figure is slightly higher in Arkansas, with 8.2 percent of all newborns weighing less than 2500 grams. Alaska holds the best U.S. record, with only 4.9 percent of infants born at a low birthweight, while the District of Columbia fares the worst at 14.3 percent.[9] Low birthweight is the factor most highly correlated with infant mortality[10], with those infants comprising almost 67 percent of all neonatal deaths on an annual basis.[11] While overall infant mortality rates have steadily declined over the past several decades, the incidence of low birthweight deliveries has remained relatively constant, with an increase from 6.8% of births to 7.1% between 1980 and 1991.[12] This is a troubling trend when considering the prognosis for infants born below ideal weight. Low birthweight babies are 40 times more likely to die in the first month of life than those with higher birthweights[13] and five times more likely to die between 28 days and one year of age (the post-neonatal period).[14] An estimated $3.5 to 7.5 billion is spent each year on the extended medical care of low birthweight infants in America.[15] This figure includes nutritional services, which play a key role in bringing the infants to a stable status and ensuring their future growth and development.

Low birthweight (LBW) infants may be either full-term or preterm. Preterm infants account for two-thirds of all low birthweight deliveries.[16] LBW full-term infants generally experience inadequate growth prior to birth. Poor fetal growth may have various causes, most being maternal in nature. Predisposing factors include the following:

- lack of proper prenatal care
- poor nutrition during pregnancy
- abnormal weight gain patterns
- inadequate accretion of key nutrients
- low socioeconomic status
- age below 17 or above 35 years
- cigarette smoking
- substance abuse
- anemia (low blood iron)[17]

Although maternal factors associated with the occurrence of low birthweight are issues which merit consideration, they will receive limited attention in this paper as I focus on neonatal care.

Preterm Infants

Preterm infants, those born before 37 weeks gestation, commonly have longer than average hospital stays as a result of their compromised development. Premature infants generally comprise the majority of patients in neonatal intensive care nurseries. An infant born at a relatively early stage of pregnancy is almost always born at a low weight, and is commonly compromised in some aspect (this may be physical and/or mental). Accepted classifications of preterm infants are low birthweight (LBW), or less than 2500 grams; very low birthweight (VLBW), or less than 1500 grams; and extremely low birthweight (ELBW), or less than 1000 grams. As recently as 1960, 1000 grams was considered to be the "lower limit of viability" for a newborn. Today, life can be sustained for an infant weighing even less than 500 grams — the weight of an average box of paper clips.

Studies have shown a survival rate of 50 percent for infants born at a weight between 700 and 800 grams, and greater than 75 percent for those at or above 1000 grams.[18]

Gestational Age

Both full-term and preterm infants may also be classified according to the relationship of birthweight to gestational age, perhaps a better measure of physiologic development in newborns than birthweight alone. Small-for-gestational age (SGA) refers to those infants whose birthweight is less than or equal to the tenth percentile for their age in weeks (according to standard growth charts). SGA infants account for one-third of all those born at a low birthweight.[19] Large-for-gestational age (LGA) infants have a birthweight greater than or equal to the 90th percentile, with average-for-gestational age (AGA) infants falling anywhere between the two extremes.[20] These classifications remain vague because there has been no official standard defined by the World Health Organization or the American Medical Association.

In order to determine weight-appropriateness relative to an infant's stage of development, exact gestational age must first be known. This is often difficult to assess, even given the approximate date of the mother's last menstrual period and the infant's original due date. Noting external physical characteristics and functional development of the central nervous system can provide help in determining gestational age at birth. It is critical that a newborn infant be evaluated in regard to physical and neurological characteristics by a physician within a short time after birth. External physical features to be noted at birth include the following: development of creases on the soles of the feet (plantar creases); external ear firmness; degree of blood vessel infiltration of the retina; descension of the genitals (in males); texture and color of the skin; and presence of nipples on the breasts. The stage of neurological development is determined in part by evaluating the following within 24 hours after birth: posture; degree of ankle flexion; amount of arm and leg recoil; and the ability or inability to reach the heel to the ear.[21] Dubowitz, et al., have developed an extensive scoring system which combines both physical and neurologic characteristics to provide a detailed means of evaluating development. The Ballard Method for determining gestational age is the most widely used at neonatal centers around the world. It is a shortened version of the Dubowitz scale which gives the same results, and is therefore suited to the fast pace of most intensive care nurseries. Simple physical measures such as weight, length, and head circumference may also be taken and reviewed relative to standard growth charts; however, the charts which are currently available are at best questionable as to their appropriateness for this population of infants.

Intrauterine Growth Retardation

Knowing both birthweight and relative gestational age can aid dramatically in the provision of nutritional care, playing a large role in the selection of a method of feeding as well as determination of exact nutrient needs.[22] In the case of infants found to be small-for-gestational age, it is important to note that intrauterine growth retardation (IUGR) has occurred. Assessing after-birth growth patterns can aid in identifying at what point during the pregnancy the growth abnormalities took place. An evaluation of the progressing weight-to-length ratio is called the "ponderal index." If weight, length, and head circumference all remain proportionally low the infant exhibits symmetrical growth. This growth pattern indicates that the retardation or some other insult occurred during the first trimester of the pregnancy. Asymmetrical growth patterns, with parameters progressing at a disproportionate rate, is an indicator of placental insufficiency throughout the pregnancy.

Placental insufficiency is only one of the possible causes linked to intrauterine growth retardation. Maternal malnutrition is often pointed to as the culprit in abnormal fetal growth patterns. It is true that malnutrition is a large contributor when an infant is born at a low birthweight, but unlikely that it is the cause of a significant number of cases of intrauterine growth retardation. While deficiencies of specific nutrients from the mother's diet at critical times during the pregnancy may be linked to certain malformations in infants, severe and long-term nutrient deficiencies would have to occur in order to cause serious overall problems of fetal growth.[23] Other possible contributors to IUGR include infections during the gestational period, maternal hypertension, cigarette smoking, and excessive alcohol intake. Small-for-gestational-age infants do not generally die strictly due to their inappropriate relative size. The most prevalent causes of death in SGA infants are asphyxia (lack of oxygen and inadequate blood flow), congenital malformations, and aspiration pneumonia (causing blockage of major airways).[24]

TWO

Management of Newborns

Aspects of Care

There are many aspects to the care of high-risk neonates. Issues of concern for care providers include, but are not limited to, the following:

- the infant's environment — temperature, sound, stimulation
- care of the skin — moisture level and general hygiene
- pharmaceutical therapy — drug/drug and drug/nutrient interactions
- respiratory assistance
- methods of feeding
- care before and after surgical procedures
- parent-infant and infant-sibling bonding
- assessment of other problems — present or potential

All of these are legitimate concerns which must be considered in providing appropriate treatment and preventative care for newborns.

The primary components of an infant's physical environment which should be considered are thermal and sensory in nature. The thermal environment refers to the temperature within the immediate vicinity (within the isolette or crib). Keeping the area at a warm, rather than cool, temperature is associated with increased survival rates, presumably due to a decrease in the amount of oxygen (O_2) consumed as well as the amount of carbon dioxide produced. Establishing a "neutral thermal environment" is important. This refers to the "set of thermal conditions at which heat production (O_2 consumption) is minimal, yet core temperature is within the normal range."[25] A neutral thermal environment, which involves humidity level and air flow as well as temperature, is most often achieved by the use of devices such as incubators and radiant warmers. The room temperature which should be maintained in order to promote a neutral thermal environment falls between 30° and 36° Celsius (depending on gestational age and weight).

The sensory environment refers to any factor which may stimulate the infant. Light, sound, touch, and nearby movement have all been shown to have some effect on the physical and neurological development of premature infants.[26] Further studies need to be conducted to examine the benefit and/or harm of specific environmental conditions.

Nutritional Goals

> Sufficient evidence is available to recommend that greater clinical priority be given to nutrition as a vigorous part of total support in preterm infants.
>
> —National Institute of Health

Of extreme importance within the nursery is the nutritional management of the high-risk infant. This encompasses determination of nutrient requirements relative to size and functional abilities, and the method of administration of those nutrients, among other things. A great emphasis should be placed on proper nutritional management because rapid growth is taking place during the neonatal period, and low nutrient reserves are present in premature infants.[27]

Short-term Goals

The major consideration in nutritional management of preterm, low birthweight, and other high-risk infants is the nature of the short-term goals to be achieved. It is generally accepted that the primary goal of nutritional therapy for infants born prematurely should be to attain a growth rate which mimics what the probable fetal growth would have been at the same gestational age.[28] This in itself is a complicated task given the fact that conditions outside the placenta are quite different from those within the secure boundaries of a mother's womb. It has been argued that the extrauterine environment places new and different demands on all of an infant's body systems, inevitably altering nutrient requirements and patterns of growth.[29] For this reason, exact standards for short-term growth remain somewhat controversial.

Growth Assessment

In an attempt to develop a standard by which growth could be measured in premature infants, Dr. Samuel Fomon, world renowned pediatric specialist from Iowa, proposed the "reference infant" in 1967, now commonly known as the "reference fetus."[30] Dr. Fomon's research on infants born at various stages of gestation has provided invaluable information on average nutrient levels to be maintained throughout fetal life, as well as normal patterns of growth. This data is beneficial based on the previously stated belief that postnatal growth should mimic that of the fetus within the womb. However, in the past quarter of a century many technological advances have occurred. Regrettably, the increasing knowledge base relevant to the medical and nutritional care of high-risk infants has not been paralleled by new information regarding fetal growth patterns. The growth charts which remain in use at hospitals and clinics throughout the United States and abroad are, in fact, the same charts developed in 1948 by Dancis, et al., based on a retrospective study of 100 premature infants in a New York hospital. It is obvious that these growth curves, though widely used, cannot be completely accurate because the data used in establishing them was compiled from a relatively small sample, as well as a quite homogenous and limited population. Consider that in the year 1948, few, if any, infants less than 1000 grams at birth had even been kept alive. The researchers themselves refer to their work as "arbitrary" and without "statistical accuracy."[31] This is not to say that the growth curves may not be a useful tool, only that probable patterns of growth for smaller and younger premature infants must be extrapolated based on the available information; this is, at best, less than ideal in caring for infants as we enter the twenty-first century.

Health care providers at Texas Children's Hospital recognize the value of using growth curves to monitor long-term success in the nutritional management of infants. Emphasis is placed on adjusting the charts to reflect post-conceptual age and birthweight of preterm infants rather than beginning from the normal baseline values for age and weight. It is widely accepted that most infants will experience an initial weight loss of seven to fifteen percent of their original birthweight after birth. However, as neonatologist Stanley Shaffer points out, "prolonged weight loss in the low birthweight infant is not usual and should not be considered a normal event."[32] Weight gain should be resumed by day four to six of postnatal life, and any fluctuations in weight should be closely monitored throughout the course of care. Standards currently followed at Texas Children's Hospital recommend that infants in the neonatal intensive care units gain 10-15 grams per kilogram of body weight each day and increase 0.75-1.2 cm per week in length. Deviations from this pattern are considered cause for further investigation of factors which might be preventing or limiting normal growth.

Long-term Goals

In all neonates, provision of nutrients adequate to promote growth and proper functioning of organ systems is critical. Lucas, et al., have proposed that the quality of nutrition during the early stages of life has a profound and notable effect on development throughout the growing years. His beliefs have been repeatedly substantiated by longitudinal studies carried out over a ten year period.[33]

Long-term goals of nutritional care include concerns such as prevention of mortality, elimination or improvement of conditions which might lead to morbidity, and promotion of optimal functioning at all levels.[34] In the attempt to meet both short and long-term goals related to the nutritional care of neonates, many factors must be taken into consideration. These include appropriate nutrient levels, feeding of high-risk infants, and the medical nutrition therapy for specific disease states and complications of prematurity.

THREE

Nutrient Needs

In order for infants to be healthy, they need to receive a balance of all essential nutrients. Just as adults, they require adequate amounts of fluids, carbohydrates, protein, fat, vitamins, and minerals for survival. Infants, however, require nutrients in smaller quantities than older children or adults, making it important that they eat nutrient-dense foods, containing few "empty calories" (calories providing a relatively small proportion of nutrients usable for growth and functioning). The provision of milk or formula of high nutrient-density becomes extremely important when dealing with infants born prematurely or at a low birthweight. In such small infants, it is critical that every ounce of nourishment count toward growth and development.

The primary objective of neonatal care is measurable growth in each infant. Neonatologist Dr. Ilene Sosenko states that ". . . postnatal growth should approximate in utero growth of a normal fetus of the same post-conceptual age."[35] The fetal growth rate is believed to be 14.4 to 16.1 grams per day during the final trimester of pregnancy.[36] In order to achieve this rate of growth, nutrients must be administered in adequate quantities, in correct proportions, and over the appropriate time period. Each neonatal care unit may practice by a slightly different set of standards, but there are some widely accepted guidelines for appropriate levels of the major nutrients. The most common modes for delivery of nutrients to infants include the following:

- Oral — breastfeeding or bottle feeding
- Enteral — directly into the stomach or small intestine
- Parenteral — an elemental diet delivered directly into circulating blood

Fluid Management

Fluid management is critical and of initial importance in infants of low birthweight, whether preterm or full-term. Sixty percent of total body mass is water in full-term infants; in preterm infants, the figure is even higher, at eighty percent. The physiologically compromised newborn has little capacity to keep moisture within the skin. The skin tissues remain underdeveloped and are therefore not an effective barrier against water loss.[37] Insensible water loss, or water which evaporates without notice, may occur through the skin or the respiratory tract.[38] Factors causing high levels of insensible water loss include the extremely permeable nature of the epidermis of premature infants and the high ratio of surface area to body weight. A primary goal in treating immature newborns is to attempt to minimize the amount of fluid lost. Fluid retention may be accomplished to some extent by the use of incubators in a "thermal neutral" state and by humidity control.

Common recommendations for fluid management in high-risk neonates consist of three main phases: transition, stabilization, and establishment of growth.[39] The transition period occurs during the first 3 to 5 days after birth, and is characterized by high levels of water loss by way of the skin, resulting in above normal levels of sodium. (Because sodium is not excreted proportionally to water, hypernatremia is common.) Weight of the infant may drop by as much as ten to fifteen percent during this period of transition.[40] Suggested therapy includes providing sterile water intravenously in the amount of 80-120 ml/kg/day, depending on birthweight. In extremely low birthweight babies, even more insensible water loss will occur because of the greater ratio of body surface to mass, requiring slightly higher levels of fluid replacement. Preterm infants born before 28 weeks gestation tend to lose a greater amount of water in comparison to the level of sodium losses.[41] No sodium or other electrolytes should be administered during this time. Serum levels of electrolytes should be monitored closely with the goal of maintaining normal values for sodium (135-145mmol/L), potassium (4.0-5.5 mmol/L), and chloride (100 mmol/L).[42]

The second recognizable phase of fluid management is the period of stabilization (about 10-14 days of life). In this stage, water losses are not as serious because the maturation of epidermal tissues allows water to be retained. Sodium should now be given in moderate amounts (2.0-3.0 mmol/kg/day) to promote kidney functioning and prevent hyponatremia. Levels of supplemental potassium should be kept minimal (1.0-2.0 mmol/kg/day), considering that excretion of potassium is lower in preterm infants than in those born full-term.[43]

The period of established growth generally follows the stabilization phase, and is considered to begin at two weeks of life. The objective during this time is to provide adequate fluid and electrolytes to promote formation and growth of all body tissues. The volume of water required increases considerably (generally up to 140-160 ml/kg/day) in order to assure that proper amounts of nutrients for "catch-up" growth can be carried in the body. Kidneys are usually well-adjusted at this stage, and can therefore tolerate increased levels of sodium, chloride, and potassium along with the fluids that are given.[44] Throughout an infant's time in the intensive care unit, it is important to be attentive to any fluctuations in electrolyte concentrations which might lead to hyponatremia or hypernatremia and thus cause further complications. Fluid management is an important component of the nutritional therapy of newborns.

Carbohydrates

Low birthweight infants pose a unique problem in terms of energy needs. Their basal metabolic rates are extremely high due to the tremendous amount of growth taking place. Tissue formation requires energy, as do body temperature regulation, physical activity, and metabolic processes such as the building of body proteins. Premature newborns have high energy needs, but meeting those needs is difficult in such small infants. Many digestive organs remain immature, and enzymes such as lactase (which aids in the breakdown of the carbohydrate lactose into the simple sugars galactose and glucose) are not completely active until late in the pregnancy or after birth even in healthy, full-term infants. This implies that digestion and absorption of carbohydrates would be an even greater complication for the very immature, preterm infant. High basal energy expenditure rates and intolerance to some forms of carbohydrates combine to create quite a challenge for the nutritional management of energy intake.

It is essential that carbohydrates be given because they are the most readily utilized fuel for body functions and are important in brain metabolism.[45] If not administered, the absence of carbohydrates as an energy source causes the breakdown of proteins in body muscle, causing greater stress to the infant already striving to grow and mature.[46] This process is complicated by the fact that premature infants generally possess a limited caloric reserve, providing energy stores which last as little as eight to twelve days in most cases.[47]

Assessing energy needs of the infants requires an estimation of the basal metabolic rate for each infant on an individual basis because the figure is highly variable. Common practice is to begin with a resting metabolism allowance of 36-51 kcal/kg/day. Provision of this amount of energy should succeed in preventing the breakdown of body proteins.[48] Additional kilocalories should then be added for other factors which might be present, for example, physical activity (relatively inactive infants need an extra 1-8 kcal/kg/day), growth (3-6 kcal/kg/day), and the stress of cold (10 kcal/kg/day). The most significant cause of excessively high energy needs stems from problems in of fat absorption. Infants should be closely monitored for fat malabsorption because such a state may consume up to 50 percent of all energy intake.[49] It is important to monitor infants for carbohydrate intolerance, which is indicated by distention of the gastrointestinal organs, colic, diarrhea, excess gas production, and/or drastic changes in activity level.[50] If glucose levels are too high, excess carbon dioxide may be produced, leading to an acidotic condition.

Approximate total energy needs for the preterm infant in a healthy state average 110-130 kcal/kg/day (disease states and malabsorptive disorders may raise this figure to 200 kcal/kg/day).[51] When supplied through a parenteral nutrition solution, glucose should be infused at a rate of 6-8 mg/kg/day. It is generally recommended that carbohydrates provide 40-45 percent of total kilocalories each day.[52] Carbohydrates should be administered in the monosaccharide or disaccharide form (dextrose, glucose, lactose, and glucose polymers), omitting starch and other complex carbohydrates which require greater digestive functioning and the action of certain enzymes which remain non-functional in most preterm infants.[53]

Protein

Protein is a nutrient of great concern in premature and low birthweight babies. Ideally, rapid growth should be occurring in all infants, and this is best supported by the presence of adequate amounts of protein. Exact needs remain controversial, but breastmilk (especially from the mothers of preterm infants) is regarded almost unanimously as the "gold standard" for protein quality because of its amino acid composition.[54] In developing guidelines for the administration of proteins, human milk has been studied in an attempt to reveal its precise pattern of amino acids.[55] The nine known essential amino acids are leucine, isoleucine, valine, lysine, methionine, phenylalanine, threonine, tryptophan, and histidine. It is believed that arginine, cystine, taurine, and tyrosine may also be "conditionally essential" amino acids for preterm infants, and research on the subject continues to be conducted.[56] Though digestive and absorptive capacities are somewhat limited because of the immaturity of the infant's gastrointestinal system, the greatest problem related to maintenance of a proper protein status is the conversion of essential amino acids to non-essential amino acids within the body. Therefore, all amino acids should be supplied in a growing infant's diet.

A daily intake of 3.5-3.6 grams of protein per kilogram of an infant's body weight is generally sufficient to support growth and metabolism, though this value should be attained gradually.[57] Another way to express the value for protein needs is in relation to energy intake, because keeping protein and energy in an appropriate balance is critical in maintaining a positive nitrogen balance (and thus supporting tissue formation) in the infant. Viewed in this way, daily protein intakes should be kept close to 3 grams per 100 kilocalories of energy.

If protein is not given soon after birth, a considerable portion of body protein stores will begin to break down.[58] The little fat present in small infants is generally structural fat which cushions and supports vital organs. During times of metabolic stress, therefore, structural fat is salvaged and body protein is sacrificed to provide for basic energy needs.[59] Catabolic processes may begin within a matter of hours if essential amino acids are not supplied to promote protein synthesis.[60] Plasma levels of protein, albumin, and prealbumin should be monitored to ensure that adequate protein levels are being administered. Because of the immaturity of the premature infant's liver functioning, the possibility of too much protein intake must also be considered. Excessive levels of the nutrient can cause fever, metabolic acidosis, and poor feeding patterns, among other things. At least 150 non-protein kilocalories should be supplied along with each gram of nitrogen given (a 150:1 non-protein to nitrogen ratio).[61] This ratio should promote the most efficient utilization of amino acids provided in the diet. As always in providing nutritional therapy, it is important to individualize care.

Fats and Lipids

The inadequate accumulation of fat deposits found directly beneath the skin may cause of insensible water loss in premature infants. Little fat is present in these infants because the majority of fat is deposited in the final ten weeks of gestation. Sixteen percent of the total body weight of full-term infants is comprised of fat stores; in contrast, preterm infants only possess one percent of weight as fat.

Fat is important in providing protection to all body organs, regulating temperature, carrying certain vitamins, preventing escape of excessive amounts of water, and in the development of the brain and cellular functions. "Brown fat" is that adipose tissue which is able to oxidize its fatty acids to produce heat, thus aiding in thermoregulation. This oxidative process does not consume the glycerol portion of the fatty acids, thereby conserving it for the production of carbohydrates.[62] The oxidation of fats is responsible for the production of energy, and the fact that this capability may be limited in preterm infants is a cause of some concern. However, the factors involved in fat oxidation have been shown to reach maturity quickly after birth.[63] If fat malabsorption is occurring, digestion, absorption, and transport of the nutrient are all hindered. Increasing fat losses through the feces can result in depressed levels of fat-soluble vitamins, nitrogen, water, and minerals, all important to proper nutrition.[64] A relatively large portion of daily kilocalories (40-55 percent) should be provided by fat, which is a concentrated source of energy for infants.

The basis for current recommendations regarding fat intake is human milk. Studies of the composition of fatty acids and the total amount of fat in breastmilk have led to the suggestion that 40-55 percent of total caloric intake be provided by fat (4.4-6.0 grams per 100 kcal), with a minimum of four percent linoleic and one percent linolenic acids. These figures represent the amount believed to be necessary for providing adequate protein-sparing energy and are suited to the metabolic capabilities of premature infants. The percentage of total kilocalories provided as fat is seemingly high because preterm infants have a great need for increased stores of adipose tissue.[65] Provision of adequate amounts of lipids can also aid in maintaining proper glucose levels in the blood, slowing transit time of other nutrients through the gastrointestinal tract, and preventing the increased respiratory rates which accompany carbohydrate overload.

Attention should be given not only to amounts of fat administered, but also to the composition of those lipids. Essential fatty acids are those which must be supplied in the diet; they cannot be produced by the body. Reserves of these essential fatty acids are known to be extremely low in low birthweight babies. Essential fatty acid deficiency is common in neonatal nurseries, interfering with physiologic processes such as normal blood clotting. The deficiency state can develop within a rather short time period (two to seven days) in infants who do not receive either an enteral source of fat or a lipid emulsion along with parenteral solutions. Two fatty acids of interest are linoleic and linolenic acids, which are important in cell membrane integrity and central nervous system development.[66]

The provision of medium-chain triglycerides (MCTs) as an additional energy source should also be considered.[67] Medium-chain triglycerides supply 8.3 kilocalories per gram, a more calorically-dense energy source than either carbohydrates or protein.

MCT oils are liquid at room temperature, making them well suited for inclusion with oral, enteral, or parenteral regimens of feeding. Medium-chain triglycerides are digested, absorbed, and transported more rapidly and completely than are long-chain triglycerides (LCTs).[68] They are, therefore, the lipid of choice, especially when infants exhibit evidence of fat malabsorption. Long-chain triglycerides must still be administered in some small quantity, however, because complete exclusion of LCTs from the diet may result in deficiencies of certain fatty acids not present in MCTs.

Intralipid (IL) solutions are often the mode of administering fats to infants receiving parenteral nutrition therapy. Intralipids were introduced to the market in the early 1960s, but were soon withdrawn upon skepticism regarding their safety and stability in parenteral regimens.[69] Since that time, stable formulations of IL have been marketed, and the solutions are now at use in the medical and nutritional care of patients of all ages. Their use in the first week of neonatal life has been questioned, but recent research has shown that administration of lipids may begin as early as the first day of life at extremely small doses (0.15 gram/kg/day).[70] The American Academy of Pediatrics recommends intralipid solutions be given by continuous infusion at less than or equal to 3 grams/kg birthweight each day.[71] Other research supports this recommendation, claiming the tolerable level of intralipid to be between 0.5 grams and 3 grams/kg/day, with the lower levels appropriate for extremely small or metabolically stressed infants.[72] Regardless of dosage, serum triglyceride levels should be closely monitored to assure that adequate fat clearance is taking place. The mechanisms for fat clearance are often underdeveloped in small-for-gestational-age infants, but are generally adequate in preterm infants provided weight is appropriate-for-gestational-age. Infusing IL over a period of 18-24 hours should allow for adequate fat clearance from the blood in most infants.[73] It is believed that the polyunsaturated fatty acids (PUFAs) supplied by intralipid solutions may be a factor in protecting the lungs from high oxygen levels encountered during respiratory therapy, and thus IL administration is highly beneficial in infants suffering from bronchopulmonary dysplasia or other disorders requiring supplemental oxygen.[74] Intralipids do contribute to an increase in serum levels of triglycerides, phospholipids, and cholesterol. Twenty percent intralipid (with a higher proportion of triglycerides than phospholipids) is recommended for use in most cases rather than ten percent IL (with a higher proportion of phospholipids than triglycerides) because it is not as likely to result in elevated low-density lipoprotein values.[75] The use of long-term intralipid therapy (for greater than a three-week period) remains questionable at the present.[76]

Vitamins

Vitamins are organic substances which provide no energy in the form of calories, but do play an important role in metabolic reactions and other body processes. Varied and extensive problems can arise if an infant becomes deficient in any particular vitamin, as is also the case with all other age groups. Close attention should be paid to vitamins in the nutritional management of newborns for several reasons: organ systems involved in their absorption and utilization are often immature; body stores of the vitamins are generally low in premature infants; and disease states may greatly alter usual requirements of certain vitamins. The two primary categories of vitamins are fat-soluble and water-soluble.

Fat-soluble vitamins are found to be deficient less frequently than water-soluble vitamins in the general population because fat-soluble vitamins can be stored in adipose tissues and are therefore not as readily excreted from the body. However, levels of all vitamins should be monitored in extremely premature infants because such tiny infants have very little body fat present in which to store fat-soluble vitamins. There is also the possibility that placental transfer of nutrients could have been insufficient in an infant born before the completion of the gestational period.

Vitamin A, accumulated almost entirely in the final two months of a normal pregnancy, is a fat-soluble vitamin of primary concern in neonates. Vitamin A deficiency is widespread in premature infants, which is significant considering the function of the vitamin in growth and basic cell differentiation. Vitamin A is involved in the protection of the lungs from tissue damage, as well as the recovery of lung functioning after serious injury or chronic disease.[77, 78] Infants suffering from bronchopulmonary dysplasia (BPD) have vitamin A stores well below the accepted normal values.[79] Infants who must be ventilated within the first forty-eight hours after birth should receive supplements of vitamin A in order to reduce the possibility of the development of chronic lung disease (BPD).[80] The primary form of vitamin A, retinol, also has an important role in vision. Stores of retinol within the liver of infants between 25 and 32 weeks gestation have been found to be less than half the level in infants at 38 to 40 weeks post-conception.[81] The recommended level of vitamin A intake for preterm babies is a minimum of 1500

International Units (IU)/kg/day, also expressed as 450 retinol equivalents (RE).[82] When infants are fed intravenously, fifty to seventy-five percent of retinol may be lost through adherence to the central line.[83] The palmitate form of vitamin A is thus recommended for use in parenteral feedings. Vitamin A administration of 1500 IU/kg/day is considered adequate to meet developmental needs and takes into account expected losses by excretion or malabsorption.

Vitamin D, another fat-soluble vitamin, is an important factor in bone integrity. One of its primary metabolites, calcitriol, effectively enhances the intestinal absorption of both calcium and phosphorus.[84] If vitamin D is deficient, the homeostasis of calcium and phosphorus is upset, and hypomineralization of the bones results, leading to possible fractures and bone deformities.[85] A special consideration regarding vitamin D is its formation by the body in the presence of sunlight; neonates may not be exposed to the sun for weeks at a time if they must be kept in the intensive care unit. Deficiencies are definitely a concern but can be easily prevented since normal vitamin D stores can be maintained in premature infants with a daily intake of about 400 IU, the same as the recommendation for term infants.[86]

Vitamin E acts as an antioxidant in the body, preventing the destruction of cell membranes and other molecules by undergoing oxidation itself. In premature infants, vitamin E can help to prevent certain forms of anemia by promoting synthesis of heme iron, and may also protect against lung disorders and eye problems to some extent. Although tissue levels of vitamin E in the fetus are low, normal infant values (0.5-0.8 mg/dl) are reached within forty-eight hours of birth for full-term infants who are begun on breastmilk or formula feedings. Plasma levels in preterm infants reach normal levels in a short amount of time as well.[87] Suggested supplemental levels range from 5-25 IU of vitamin E each day.[88] Administration of 1 mg alpha(α)-tocopherol (the primary form of vitamin E) for each gram of polyunsaturated fat in the diet will prevent the potential for a deficiency.[89] Vitamin E can be easily incorporated into MCT oil solutions for administration to the infant not fed orally or enterally. Supplemental needs would be lower for the premature infant receiving his mother's own breastmilk, because human milk provides satisfactory quantities of vitamin E. Toxicity of vitamin E is a concern in immature infants, and it is not advisable to administer the nutrient in excessive doses. Some studies have promoted the use of vitamin E in pharmacologic doses for the treatment and/or prevention of visual and respiratory disorders. However, recent research has indicated that administration of the vitamin at high levels is not beneficial in prevention of the problems, and may even lead to further complications such as hemorrhaging.[90] The risks of excessive dosages of vitamin E largely outweigh potential benefits, especially for extremely low birthweight infants.[91]

Vitamin K is a fat-soluble vitamin of which infants are likely to be deficient. Transfer of vitamin K across the placenta from mother to fetus is not generally substantial, and breastmilk is a poor source. It is, thus, common practice to administer 0.5-2.0 mg of the vitamin by intramuscular injection to all newborns at birth.[92] No recommended levels have been established for vitamin K to date.

Water-soluble vitamins should be monitored in providing nutritional care for compromised infants, especially when there is reason to believe a specific deficiency may exist. The water-soluble vitamins act as cofactors in many physiologic reactions, and are therefore an integral part of normal body functioning. Vitamins of special concern for these neonates include vitamin C, thiamin, riboflavin, vitamins B_6 and B_{12}, biotin, folate, and niacin. Administering these nutrients in adequate amounts, and periodically monitoring serum levels is important because the water-soluble vitamins cannot be stored in the body for extended periods. Water-soluble vitamins must be included in the diet on a daily basis to prevent the occurrence of deficiency states.

Vitamin C (ascorbic acid) is involved in the production of collagen (a proteinous connective tissue) and also aids in the absorption of the mineral iron by the small intestine. This vitamin readily crosses the placenta, and though it cannot actually be stored long-term, neonates do have considerable levels of accumulation at birth (which diminish quickly thereafter).[93] Prevention of the vitamin C deficiency disease known as scurvy, as well as enhancement of iron absorption, can be accomplished with the routine administration of 25-31 mg/kg each day.[94]

Thiamin, or vitamin B_1, acts as a cofactor in several body reactions including the metabolism of amino acids and carbohydrates. Therefore, thiamin needs increase with increasing amounts of protein and carbohydrates in the diet.[95] Deficiencies of this vitamin are rare, but have been observed in infants breastfed by undernourished mothers.[96] The recommended dietary allowance (RDA) for thiamin in infants is 300 micrograms(μ)/day. Riboflavin (vitamin B_2) is a water-soluble vitamin which is also important in body reactions. It forms the coenzymes flavin adenine mononucleotide (FAMN) and flavin adenine dinucleotide ($FADH_2$), which are involved in the electron transport of aerobic respiration, critical to the metabolism of all energy sources.[97] Riboflavin is easily destroyed by light, which is a cause of some concern. In order to assure adequate levels of riboflavin in neonates, the RDA has been established as 400 μ/day. In practice, infants should be given about 60 μ/100 kcal.[98]

Vitamin B_6, or pyrodoxine, is intricately involved in all aspects of amino acid metabolism and production. High protein intakes therefore warrant a greater intake of the vitamin. Deficiencies of pyrodoxine, which are relatively uncommon, result in a form of anemia in infants. The amount considered to be adequate to prevent such a state is 150 μ/100 kcal.[99] Vitamin B_{12} is somewhat unique in that it can be synthesized by microorganisms of the human gastrointestinal tract in the presence of an intrinsic factor of the stomach. Deficiencies are rare but serious when they do occur. A lack of vitamin B_{12} has the potential to cause extreme neurological damage.[100] The RDA for premature infants is 0.3 μ/day.

Because biotin has not been studied as extensively as other water-soluble vitamins, no RDA has been established. However, 10 μ/day of biotin is widely accepted as an adequate intake.[101] The vitamin is involved in the metabolism of fats and carbohydrates, and is supplied to some extent by intestinal bacteria (similar to vitamin B_{12}). For this reason, deficiencies are not commonly observed.

Folate is a vitamin which plays a role in protein synthesis. Preterm infants are at risk for developing a deficiency of folate due to their rapid rate of growth and low levels of transfer from the mother during gestation.[102] As a general rule, infants need up to ten times as much folic acid (another name for folate) as do adults relative to body weight.[103]

The anemia caused by a folate deficiency can be avoided by supplementing infants with 0.1 mg/day. Manufactured formulas and fortifiers routinely added to human milk generally supply adequate levels to meet this supplemental need.

Niacin plays an important part in the body's energy-producing glycolysis pathway and electron transport system in its coenzyme forms nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). Niacin can be made by the body from the amino acid tryptophan, indicating that requirements of the vitamin should be based on relative levels of tryptophan present. A deficiency of niacin presents itself as pellagra, with the classic symptoms of dermatitis (skin rash), diarrhea, and dementia. This condition is rare in developed countries. Requirements for niacin are expressed in milligrams of the vitamin in the preformed state or as niacin equivalents (NE), with each NE representing 60 mg tryptophan or 1 mg niacin; 5 mg/day is regarded as an appropriate intake for premature infants.[104]

Minerals

Minerals comprise the final category of nutrients important in providing nutritional therapy to high-risk infants. They are the electrolytes which promote overall homeostasis within the blood by their action across cell membranes. Premature infants can, in a sense, be thought of as "large sacks of gatorade" — a lot of water with only a few electrolytes. As much as 67 percent of the total mineral content in a full-term infant is acquired during the final three months of gestation. Calcium stores increase from 5-28 grams in the final trimester of a normal pregnancy; phosphorus, from 2-16 grams; zinc, from 15-60 milligrams; and copper, from 3-20 milligrams.[105] This indicates that premature infants are at definite risk for possessing low stores of these and other important minerals. Minerals of special significance in the nutritional management of high-risk infants include iron, calcium, phosphorus, and magnesium.

Iron is transferred to the fetus through the placenta during the final trimester of pregnancy, and is therefore commonly inadequate in infants born prematurely. Iron deficiency is a great concern in these infants; even more problematic is the finding that levels of hemoglobin in preterm infants continue to decrease for several weeks after birth. Infants of a birthweight below 1500 grams have been shown to have hemoglobin concentrations of only 70 g/L by two months of age (the normal level in term infants being 110 g/L), indicating that few new red blood cells are being produced.[106] The primary cause of this anemia seems to be the dilution of iron which occurs with rapid growth[107] and increasing blood volume. The suggested supplemental level of iron is 2 mg/kg/day, with a maximum of 15 mg administered within one day.

Calcium, phosphorus, and magnesium are all minerals which are normally abundant in the body. Each is an integral part of bone structure, and each aids in the functioning of other body tissues as well.[108] Calcium and phosphorus are especially important for their role in bone mineralization. Eighty percent of fetal bone density is gained in the last trimester of a normal pregnancy.[109] More than thirty percent of all premature and very low birthweight babies have been shown to display inadequate bone mineralization, which frequently can lead to fractures and other injuries or deformities.[110] Rickets of prematurity has become a serious problem as infants have begun to be kept alive at more immature stages. The diagnosis of rickets is usually subclinical, meaning that it is not recognizable until after physical signs such as fractures have appeared.[111] Serum levels of calcium and phosphorus do not generally reflect bone status accurately because they are maintained at the expense of stores in the bones. Recommended intakes for growing preterm infants are 185-200 mg/kg/day of calcium, 100-140 mg/kg/day of phosphorus, and 5-10 mg/kg/day of magnesium.[112]

Administering adequate amounts of calcium and phosphorus is often difficult because of the limited solubility of the minerals. Their presence in formulas and unfortified human milk has been found to be inadequate to meet the demands of increasing bone density. [113] Special preterm formulas and fortified human milk are believed to possess acceptable levels of calcium and phosphorus for maintaining bone structure. Parenteral nutrition solutions pose a great problem in terms of the delivery of calcium and phosphorus. The minerals tend to settle out of solution and adhere to the delivery line. Measures which may improve the solubility of calcium and phosphorus include the addition of cysteine or other amino acids, inclusion of lipid buffers, and the control of the solution's temperature.[114] Decreasing the pH (increasing acidity) of a solution causes an increase in the solubility of the minerals, while excessive temperatures have the opposite effect. The absorption of minerals from formulas is also thought to be enhanced by the inclusion of medium-chain triglycerides in the feeding regimen.[115, 116] Normal absorption rates should be attempted, with an acceptable range of 36-60 percent mineral retention. Factors which affect absorption and retention include the mineral source, amount of excretion through the feces, and the interaction with other vitamins and minerals.[117] Infants being treated with diuretics should be given additional calcium because diuretic therapy has been shown to increase excretion of the mineral.

Trace Elements

Trace elements are the nutrients which serve as components of metalloenzymes, taking part in many different metabolic reactions.[118] Premature infants have increased requirements for several trace elements compared to infants born full-term. Trace elements required in human metabolism include zinc, copper, iodine, selenium, chromium, manganese, molybdenum, and fluoride. All of the minerals of the body have key functions in maintaining and promoting proper functioning of organs and systems. If not administered in adequate amounts beginning soon after birth, mineral deficiencies will continue, leading to further complications such as weight loss, poor skeletal growth, and impaired metabolism of other nutrients.

Zinc merits further consideration for its involvement in the action of many of the body's enzyme systems. Zinc has roles in reactions of deoxyribonucleic acid (DNA) metabolism, as well as in protein synthesis. Addition of zinc to human milk through the use of chemically engineered fortifiers has been linked to enhanced growth velocity patterns.[119] Suggested levels of administration range from 250-400 μ/kg/day.[120, 121] Deficiencies of the element may stem from inadequate intake or poor absorption rates. Increasing serum alkaline phosphatase levels signal the onset of a zinc deficiency, indicating the need for increased levels of the mineral in an infant's diet.[122]

FOUR

Feeding Regimens

> It is likely that no area in the care of the newborn infant is less critically or more controversially approached than his feeding. What, When, How, and How Often to Feed are questions surrounded by emotions, beliefs, fads, and even commercialism, all of which tend to obscure the basic goals of infant feeding.
>
> —Barness[123]

How should all of the nutrients mentioned here be administered to the premature infant? As Dr. Frank Oski states: "Infant feeding practices are the longest uncontrolled experiment lacking informed consent in the history of medicine."[124] There are various feeding methods which might possibly be utilized for the physiologically compromised newborn. Breastfeeding, bottle feeding, enteral nutrition, and parenteral nutrition are all available options.

In the words of neonatologist Reginald Tsang, "It is neither possible nor desirable to adhere to rigid feeding policies for low birthweight infants."[125] All infants are different, and, therefore, no one regimen can be followed for every situation. In choosing the appropriate method of feeding, there are certain factors which must be taken into consideration. One critical factor is the level of development of feeding skills in the infant. Premature infants will likely be deficient in some basic reflexes such as sucking and rooting, which allow for intake through a bottle or nipple. The rooting and gag reflexes do not fully develop until as late as ten days post-delivery even in full-term infants.[126] Nipple feeding (at the breast or through a bottle) may not be possible in many premature infants of less than thirty-two weeks gestation due to the lack of coordination of sucking, swallowing, and breathing.[127] Determination of feeding readiness should include physical observation of the infant's ability to suck a pacifier or nipple, and to swallow his own saliva. Readiness to feed orally is often determined by the infant's ability to take formula through a bottle. The ability to breastfeed actually precedes the ability to control sucking and swallowing by bottle; therefore, bottle feeding does not seem a reasonable indicator of an infant's readiness to feed. Breastfeeding actually promotes faster coordination of the sucking and swallowing reflex than does bottle feeding. (82) Other factors to be considered in determining readiness to nipple feed are the level of gastrointestinal functioning and respiratory integrity in compromised neonates.

Breastfeeding

> There is no finer investment for any community
> than putting milk into babies.
>
> —Winston Churchill, 1943

What is the "best" food for an infant? Individuals have probed this question repeatedly over the centuries, and yet much debate remains as physicians, dietitians, researchers, and parents alike search for the elusive answer. Breastmilk has long been promoted as the "gold standard" for infant nutrition, but because of a perceived bad social connotation, inconvenience, and numerous other reasons, implementing widespread breastfeeding practices has been resisted on many fronts. An encouraging 1994 survey of Central Arkansas hospitals shows that acceptance of breastfeeding may actually be on the rise as the Twentieth Century comes to a close. The recent report noted that hospitals in

Arkansas' metropolitan area are beginning new programs intended to educate women about the methods and benefits of breastfeeding in order to promote the practice. Their efforts have met with apparent success, as a review of the statistics clearly shows:

Hospital	Incidence of Breastfeeding	
University Hospital, LR	1990 8%	1994 40-50%
Baptist Med Center, LR	1989 65%	1994 75-80%
Doctors Hospital, LR	1992 40%	1994 60%

Table 1.1 Incidence of Breastfeeding at Central Arkansas Hospitals[128]

In 1990, the World Health Organization and the United Nation's Children Fund formed an alliance to promote breastfeeding in a large scale effort to decrease the incidence of disease in underdeveloped countries.[129] Malnutrition has reached epic proportions in Third World countries, contributing largely to high rates of infant death and disease. Breastfeeding is considered by the World Health Organization to be the "single most important immediate remedy for high infant mortality."[130] Early weaning from the breast in such countries is "an established cause of infant morbidity and mortality from infectious disease."[131] The American Academy of Pediatrics (AAP) has also acknowledged the importance of breastfeeding, noting it to be the "foundation of good feeding practices."[132] The AAP supports exclusive breastfeeding (without supplemental formulas or other additional nutrient sources) for at least the first six months of life in all infants.[133] As more information is made available regarding the positive physical, mental, and emotional outcomes of breastfeeding, perhaps the practice will once again be accepted as the standard for infant feeding.

The benefits of breastfeeding are well documented. They are based to a large degree on the characteristic components of human milk. Breastmilk contains important bioactive components such as immunoglobulins, anti-infective agents, hormones, growth factors, and enzymes, all provided in addition to the easily digested nutrients present.[134] The components of human milk together serve to reduce the likelihood of infections in infants, as well as to promote general maturation of all body systems. During fetal life, the developing infant receives nourishment from the placenta. After birth, which brings the initiation of respiration, the infant no longer has need for the oxygen-carbon dioxide exchange provided by the placenta. Nutrients, however, are still vital to growth and development. Breastmilk can be considered a transition from the nourishment previously supplied by the placenta, with the continuing transfer of other bioactive components also vital to extrauterine life. Breastmilk feedings should be initiated at full strength, with a goal intake of 150 cc/kg/day. The volume of the first feeding may need to be as low as 5-25 cc/kg/day, with subsequent feedings gradually advanced until optimum volume is reached.

Breastmilk in women who have given birth prematurely is higher in protein and certain hormones and enzymes than is the milk in women who have carried their infants to term. The main form of carbohydrate present is lactose, and fifty percent of the total kilocalories are supplied by fat. The digestibility of preterm human milk is greater than that of full-term milk, making it well suited for the infant whose digestive functioning remains underdeveloped. Preterm infants fed their own mothers' milk have exhibited greater levels of host protection, faster rates of gastrointestinal maturation, and increased nutrient availability.[135] Studies by Lucas, et al., have also shown marked differences in the cognitive skills during childhood of preterm infants fed breastmilk versus those fed formula, with the breastfed children scoring higher on the Weschler Intelligence Scale for Children.[136]

Colostrum is the yellowish-secretion produced by all lactating women during the first four to seven days post-delivery. Evaluation of colostrum has shown it to be higher in anti-infective properties and many other components than the milk which is produced later during lactation.[137] Women who deliver prematurely may continue the production of colostrum for as many as four to six weeks, providing additional benefits to their underdeveloped infants.[138] Breastfeeding also has a positive emotional effect on both infant and mother, and has been shown to increase oxygen levels and lower heart rate in the infant as a result of the decreased stress and activity level.[139, 140] Along with these positive contributions is the current research which has linked the intake of breastmilk to a decreased incidence of certain intestinal disorders commonly associated with prematurity.[141]

Although it is high in fat, protein, sodium, chloride, magnesium, and iron in comparison to mature human milk,[142] some research has indicated that preterm milk contains inadequate levels of calcium and phosphorus for the prevention of bone loss.[143] For this reason, many clinicians now promote the supplementation of human milk with fortifiers to promote bone density in very low birthweight infants.[144] Commonly used fortifiers supply both additional protein and minerals to the breastmilk. Manufacturers are currently working to improve the quality of fortifiers, struggling with problems such as solubility in the milk and stability at various temperatures.[145] It is unlikely that chemically engineered fortifiers will ever truly match the level of bioavailabitity (absorptive capacity) of nutrients supplied by human milk.

Legitimate concerns related to the practice of breastfeeding center around the fact that many undesirable substances may also be delivered to an infant through the milk. Prescription medications, illegal drugs, and many other substances have the potential to be transmitted through breastmilk. Lists of those substances which should be considered as contraindicators to breastfeeding are available and should be consulted when questions arise. Concerns have surfaced recently regarding the possibility that viruses leading to acquired immunodeficiency syndrome (AIDS) might be transmissable through breastmilk. Research has confirmed these fears, showing that the virus may be received through human milk. The benefits imparted by breastmilk are great enough, however, to outweigh the possible risk of AIDS transmission in many developing countries where malnutrition and infectious diseases abound.

With the increasing emphasis on the many notable benefits of breastmilk, especially for preterm and low birthweight infants, more mothers of infants who are unable to breastfeed (due to their infants' immature sucking and swallowing reflexes or other medical complications) are seeking alternative ways to provide breastmilk for their babies. Texas Children's Hospital (TCH) has long been a leader in this arena. TCH operates a well-established and ever growing human milk bank staffed by registered dietitians specializing in "lactation consultation." The milk bank is open twenty-four hours a day, seven days a week, providing new mothers a place to express their breastmilk periodically using pumps provided on site. The breastmilk is frozen, to be thawed and drawn up later by laboratory technicians for enteral administration to the infants in the intensive care nursery.

The concept of human milk banking is not new. Hospitals in countries such as Britain and Scandinavia have practiced collecting and storing milk since the 1930s.[146] Prior to World War II, milk banks could also frequently be found throughout the United States; however, the practice was abandoned as bottle-feeding came to be viewed as a symbol of wealth in the 1940s and beyond. The decade of the 1950s brought a great decline in the practice of breastfeeding as formulas replaced mothers' milk as "science's answer to the inconvenience of breastfeeding."[147] In the 1960s, women returned to breastfeeding for a time in an attempt to get back to "the basics." With the number of working mothers sharply rising in the decade that followed, breastfeeding once again came to be seen as an inconvenience, and its incidence declined. However, recent years have seen a resurgence in the acceptance of breastfeeding, setting the scene for the return of milk banks here in this country.

Lactation consultants function as mediators between physicians and patients in dealing with many issues related to breastfeeding. The lactation consultant (LC) is often found in a teaching role, educating parents about the benefits of breastfeeding for their infant, as well as instructing new moms on how to make use of the single or double suction pump in order to express breastmilk for storage and subsequent infant consumption. There are both physical and emotional aspects of the job. Much time is spent reviewing principles of anatomy and physiology with patients to promote understanding of the whole process of lactation. Yet perhaps an even more important component is the emotional support the LC provides to her patients, and the confidence she is able to instill in a new mother's ability to provide adequate nutrition for her at-risk infant.

A relatively new technique seen in neonatal nurseries is what is referred to as "kangaroo care." Kangaroo care (KC) is a method of skin-to-skin intervention in which the newborn is placed upon his mother or father's chest in the absence of any coverings. It is so named in reference to the kangaroo, which always gives birth to its young prematurely and then places them in the marsupial pouch where they are held close to the mother until reaching maturity.[148] The technique was begun at a hospital in Bogota, Columbia, in 1979,[149] and has since been studied and implemented in institutions around the world. Research is continuing in places such as the Netherlands, Western Europe, Scandinavia and Kenya. The University of Florida has established a United States Fund for Natural Care Postbirth, which promotes such measures as kangaroo care for high-risk infants.[150] Placing the infant upon his mother's breast has a notable calming effect on both parties. Other results which have been noted in various studies include deep states of sleep in which all extraneous activities cease, as well as slight increases in body temperature.[151] The infant seems to come into "thermal synchrony" with his mother during kangaroo care, leading to self-regulating patterns of temperature between the two.[152]

Kangaroo care is only one of the innovative measures being experimented with in the nation's hospitals. It is obvious that premature and low birthweight infants are rarely able to take large volumes of fluid in a feeding, making it extremely difficult to administer adequate nutrients to the infants at a time when they need them the very most. It is therefore critical that the milk or formula which these infants receive is of premium quality. In the effort to provide such quality, the USDA Children's Nutrition Research Center, Baylor College of Medicine and Texas Children's Hospital have undertaken a joint effort to extensively study the composition of human milk at various stages in maternal production. Recent studies have shown that the milk expressed form mothers in the first few minutes after the let-down reflex of lactation (called "foremilk") is considerable lower in fat than is "hindmilk," that which is released later. By collecting foremilk separately from hindmilk, dietitians are able to administer the higher fat milk to the infants, assuring them a greater amount of fat within the volume they are able to consume. This "lacto-engineering" strategy has met with great success, promoting weight gain in all of the infants currently involved in the study, presumably due to the increase in caloric intake.[153] Innovative measures such as those described here are extremely promising, and indicate the incredible opportunities for continued research in the area of lactation support.

Infant Formulas

There is considerable debate over which is more suited to preterm infants, human milk or man-made formula. Because breastmilk contains previously mentioned bioactive components which cannot presently be duplicated in any man-made formula, it is important that breastfeeding be attempted if at all possible. For the mother who simply chooses not to breastfeed her premature newborn, or who has a declining supply of milk, full bottle-feeding or supplementation with formula may be the best alternative. Preterm formulas are now available which have been developed specifically for infants born prematurely. The nutrient content of these formulas is based on the estimated needs of an infant before full-term. Nutrients are found in greater concentrations than in similar full-term formulas in order to provide the same amount of energy in a smaller volume, often a critical need in infants unable to tolerate large amounts of milk.[154] Most preterm formulations include increased levels of carbohydrates, fat, protein, calcium, phosphorus, and vitamins A and D.[155] Preterm formula has been shown to result in better leg length growth patterns than in infants receiving standard full-term formula.[156]

Formula should not be administered at full-strength to the premature or low birthweight infant upon the first feeding. It should be given at half-strength for the initial feeding; concentrations may then be gradually increased up to full-strength within the seventy-two hours following the first feeding. It is extremely important to note that concentration and volume of either formula or breastmilk should never be advanced simultaneously.

Full-term formulas are appropriate for some infants in the neonatal intensive care setting. Many varieties of formulas are currently on the market — examples include soy-based, iron-enriched, lactose-free, sucrose-free, and hypoallergenic formulations.[157] Choice of the best formula for a particular infant, whether standard or preterm formula is desired, should be based in part on consideration of the following factors:

- Nutrient content — quantity and quality
- Bioavailability of nutrients
- Volume required to meet needs
- Cost — to patient and hospital
- Availability
- Ease of transition to home-feeding[158]

The availability of chemically engineered formulas has been of great benefit in the care of many high-risk infants. However, the importance of providing human milk to all infants capable of breasfeeding cannot be stressed enough. Even after the numerous positive aspects of breastfeeding have been thoroughly documented, some hospitals and healthcare professionals continue to support the use of formula over breastmilk. The United States Government remains the world's largest purchaser of baby formula.[159] Until 1990, the U.S. Department of Health's Supplemental Food Program for Women, Infants, and Children (WIC) did not actively promote breastfeeding, but rather made formula readily available to its participants. Considering that, as a rule, the individuals receiving WIC assistance are of low socioeconomic status, a disturbing paradox seems to exist. Mothers of infants who most need the immunological and developmental benefits which breastmilk can provide are encouraged to abandon the practice of breastfeeding as they are handed free formula. The taxpayer may end up making double payments for this population when the infants return to hospitals and clinics for treatment of infections and disease which might well have been prevented if their parents had simply been educated regarding the benefits of breastfeeding. Not only would hospital costs be reduced, but less formula would have to be purchased — a savings of $800-2,000 per infant annually. Breastmilk is totally free to both the manufacturer and the consumer. WIC is beginning to make such a transition, with reports surfacing that the incidence of breastfeeding increased from 3 percent to 9.25 percent of participants during the 1990-1994 period.[160] An added incentive for those who choose to breastfeed is the provision of additional food vouchers to replace the formula which would be received. The Arkansas survey previously cited also noted that Central Arkansas hospitals are following suit, decreasing the amount of formula which is readily given to new mothers. The formula is now given only upon request.[161]

Enteral Nutrition

Enteral nutrition refers to the process of providing nutrients to an individual by delivering them directly to the stomach or intestinal tract in a digestible form. Direct delivery eliminates the need for chewing and swallowing because the mouth and esophagus are bypassed altogether. Enteral nutrition promotes the development of gastrointestinal hormones and stimulates overall digestive functioning as it nourishes the villi lining the walls of the intestine, which are important reasons to initiate feedings in low birthweight and premature infants. For a period of many years, enteral feedings were delayed in sick and preterm infants to lessen the risk of developing complications.[162] It is now believed that the benefits of early feedings on gastrointestinal development far outweigh the minute risks involved. Thus, enteral feedings may be provided as early as the first day of life if the infant is in stable condition.

For those infants who cannot tolerate full feedings, and must be fed by alternate means, it remains important that some nutrients be introduced to the gastrointestinal tract. The practice of minimal enteral nutrition, or "gastrointestinal (GI) priming," entails administering low-calorie, low-volume feedings to infants receiving intravenous elemental diets in order to stimulate digestive functioning. GI priming has met with much success. It has been shown to improve feeding tolerance, raise serum levels of gastrin (a digestive enzyme), increase the maturation rate of the gastrointestinal tract and its lining, and enhance digestive motor activity, all of which may lead directly or indirectly to the earlier establishment of favorable weight gain patterns.[163, 164] Gastrointestinal priming shows promise as an effective method of maintaining and improving the digestive function capacity in infants who cannot be fed by solely enteral means.

Techniques associated with enteral nutrition include nipple feeding, gastric feeding, transpyloric feeding, and gastrostomy.[165] Gastric feeding is the method in which nutrients are delivered directly to the stomach via a tube inserted through the nose or mouth. Tubes inserted through the nose (the "nasogastric" route) are the most commonly used in neonates. Nasogastric tubes are more easily kept in place than those placed in the mouth, but may in some instances cause greater obstruction of air passageways.[166] Most infants do the majority of their breathing through the nasal cavity; for this reason, tubes inserted through the mouth (the "orogastric" route) often allow for greater ease in respiration.[167] A possible disadvantage to the use of orogastric tubes is the finding that certain infants fed through the tubes for extended periods of time (two to three months) have developed evidence of a grooved upper palate, leading to further feeding complications. Use of an acrylic device molded to the upper palate has been shown to decrease the incidence and severity of groove formation by reducing the pressure of the tube against the oral structure.[168]

In transpyloric feedings, a tube empties directly into a certain section of the intestine. The preferred route is nasojejunal, though the tube may also be inserted into an earlier section of the intestine (the duodenem) by way of the mouth or nose. The primary advantage of transpyloric methods of feeding is that the stomach may be bypassed altogether. This can be of large benefit in infants who have compromised gastric functioning leading to loss of nutrients or gastroesophageal reflux (regurgitation of feedings). However, transpyloric tubes may increase the probability of gastrointestinal bleeding because of the large amounts of hydrochloric acid left in the empty stomach.[169]

A gastrostomy is performed by insertion of a feeding tube directly into the stomach through the abdominal wall. The tube is generally guided by an endoscope, and the method is therefore referred to as PEG (percutaneous endoscopic gastrostomy). The efficacy of gastrostomy methods, as well as the similar technique of jejunostomy (insertion directly into the small intestine), has been questioned.[170] The procedures are generally only done in extreme cases.

There are two primary methods of delivering formula or breastmilk through a tube. The difference between the two methods is in the rate of infusion of the solution. The enteral feedings may be either continuous or intermittent. In continuous infusions, the formula is allowed to drip through the tubing, which is generally kept short to prevent any significant amount of adherence of the solution to the tube. A syringe pump is connected to the tube to control the rate of delivery of formula or milk to the infant. The importance of placing the pump below the infant has recently been documented, showing that in instances of placing it above, up to 33 percent of kilocalories may be lost as the fat surfaces to the top of the tube.[171] Continuous infusion is believed to be an energy efficient method of delivering nutrients to infants, and its use is widespread in neonatal nurseries.[172]

Intermittent infusions are also referred to as bolus feedings. Bolus feedings serve to deliver larger quantities of formula to an infant on a periodic basis (usually every three hours) rather than a continuous delivery of small amounts. For this reason, intermittent feedings are often not suitable for infants who display slow gastric emptying times. Tolerance may be monitored by routinely checking gastric residual volumes and fecal output after feedings. Intermittent feedings are generally less energy efficient than are continuous drips, evidently due to the fact that they stimulate thermogenesis (the energy required to catabolize, absorb, and store nutrients) on a more frequent basis.[173] Perceivable benefits of bolus delivery of tube feedings include the fact that less time is allowed for nutrients within the milk or formula to be lost through interactions with the tubing itself or other components (such as medications) delivered through the tube.[174] Careful monitoring of tube-fed infants is advisable whether continuous drip or intermittent bolus methods are employed. Adequate tolerance of enteral feedings is characterized by gastric residual volumes of less than half the previous feeding, a normal stool pH value (6.0 or higher), and a daily weight gain of 15-20 grams/kg current weight.

Parenteral Nutrition

Parenteral nutrition is an option for feeding high-risk infants which may be used if enteral nutrition is not well-tolerated. Also known as intravenous hyperalimentation, parenteral nutrition involves the infusion of energy and required nutrients directly into the circulatory system through a catheter or butterfly needle implanted into a major blood vessel, thereby eliminating the need for the immature or non-functioning digestive system's participation.[175] The basic concept of parenteral nutrition is the "continuous infusion of a hypertonic nutrient solution into a vessel with rapid flow."[176]

The first report of successful use of the parenteral nutrition technique in infant care came from Helfrik et al. in 1944.[177] It was several decades, however, before the practice was considered safe enough to be used on a routine basis.[178] For many years, parenteral nutrition has been utilized as a last resort, when enteral feedings are not possible or wholly adequate.[179] However, there has been a dramatic increase in the use of TPN in recent years, with full or partial feedings now provided parenterally in the vast majority of premature infants cared for in neonatal intensive care units.[180] Parenteral nutrition has been called a "mainstay in the nutritional support of preterm infants" by Baylor College of Medicine neonatologist Robert Shulman.[181] Low birthweight infants now account for the largest percentage of pediatric patients receiving TPN.[182] A startling eighty-one percent of the 1,765 low birthweight infants involved in a recent study of the National Institute of Child Health and Human Development Neonatal Intensive Care Network were fed by partial or total parenteral nutrition for an average of nineteen days during their hospital stay.[183]

Total parenteral nutrition (TPN) may be administered centrally or peripherally. A central line is one which is inserted through an incision into a primary vein such as the superior or inferior vena cava. Peripheral catheters are those which have their insertion in smaller veins located farther away from the heart. Peripheral parenteral nutrition results in fewer complications such as infection at entry-site, and should therefore be used if at all possible. Because central lines allow for the administration of a more calorically-dense solution, shown to increase rates of weight gain and nitrogen retention, their use is at times warranted in extremely small or sick infants who cannot tolerate an adequate volume to meet nutritional needs.[184, 185] Both intravenous routes allow for slightly lower kilocalorie needs because of the energy conserved as a result of absent digestive functioning. As in all medical and nutritional therapies, the choice of the most appropriate procedure must be based on the condition and needs of each individual patient. In either central or peripheral parenteral nutrition, it is critical that correct placement of the catheter be confirmed before feedings begin.[186]

Specific nutrients of concern when parenteral feeding methods are employed include fat, carbohydrate, protein, vitamins, minerals, and trace elements. It is important to ensure that adequate amounts of fat are administered by TPN. Essential fatty acid deficiency may develop in an infant receiving TPN without a lipid component in as little as three to four days. Lipids are relatively easy to incorporate into a TPN solution because they are iso-osmolar (blood homeostasis is unaffected).[187] Addition of a fat solution to the TPN regimen has the benefits of aiding in maintenance of the line itself, providing a concentrated source of kilocalories, and preventing essential fatty acid deficiency (with 0.5-1.0 grams/kg/day).[188] Some infants have a low tolerance for the carbohydrate glucose, and hyperglycemia is often a problem when it is administered.[189] Therefore, dextrose is often included as the carbohydrate source in TPN. Dextrose should be well tolerated as long as it is kept at a level equal that of normal liver production of glucose (6-8 mg/kg/min).[190] Dextrose, however, provides only 3.4 kilocalories per gram (compared to 4.0 kilocalories per gram of glucose), making it a less concentrated energy source than glucose, fat, or protein. The infusion rate of TPN should be monitored; if the solution is administered too quickly, much of the carbohydrate may be converted to fat in the body.

Crystalline amino acids are incorporated into most TPN solutions to provide the protein component. The factor which is most critical in protein administration is the pattern of amino acids present. Cysteine and taurine are both conditionally essential amino acids for premature infants.[191] The addition of cysteine to TPN solutions has been shown to greatly enhance the solubility of both calcium and phosphorus.[192] These minerals generally form precipitates and settle out of solution, causing the infant to receive less than adequate levels of calcium and phosphorus, needed for bone mineralization. The action of cysteine believed to result in the increased solubility of calcium and phosphorus is a lowering of the pH of TPN solutions.[193] The reason TPN solutions have not previously contained cysteine relates to the fact that the amino acid shortens the shelf life of the solution.[194] Some researchers have proposed that glycerophosphate be added instead of cysteine.[195] It is believed to have relatively the same effect on calcium and phosphorus solubility and poses less of a risk of metabolic acidosis from the excessive lowering of pH levels. Glycerophosphate may be a legitimate alternative to the use of cysteine; however, it is not currently available in the United States. Cysteine and taurine should be included along with the other essential amino acids in any protein solution. Failure to provide adequate levels of protein through TPN may result in fatty infiltration of the liver. Hepatic disease is one of the most widespread problems associated with the use of total parenteral nutrition, and thus protein is of great concern.

Vitamins and minerals in parenteral nutrition solutions should also be considered. In 1972, the United States Food and Drug Administration (FDA) concluded that vitamin and mineral solutions for TPN were "ineffective as currently formulated."[196] The American Medical Association (AMA) devised a new set of standards for the vitamin and mineral content of the solutions, and these received FDA approval in 1981. Even so, seemingly minor modifications of parenteral solution formulations require extensive scrutiny and federal testing for safety before they can be put into use on a large scale.[197] Changes have, therefore, been slow to come in this regard.

The use of TPN is merited in many situations, such as gastrointestinal disorders, severe diarrhea, respiratory distress, malabsorptive states, renal or hepatic failure, and other problems accompanying low birthweight and prematurity.[198] However, much consideration should be given to the fact that total parenteral nutrition is substantially more expensive than any of the enteral feeding methods. The high cost of TPN therapy is one of the reasons that it is advisable to make the transition from parenteral to enteral feeding as soon as an infant is able to tolerate such a change. Reasons regarding the benefits of introducing nutrients into the digestive system to promote functional development should also be considered. Some researchers fear that prolonged periods of TPN therapy may delay the development of feeding skills, causing "feeding aversion" in some infants. The possibility of feeding aversion is of special concern if the infant receives TPN during the critical period for learning feeding skills (believed to be around six to nine months of age).[199] The transition from parenteral to enteral feedings should be made gradually, with other modes of feeding being initiated before the intravenous infusion is stopped completely.

Oral Stimulation

When enteral or parenteral feeding methods are in use, it is important that a program of oral stimulation also be implemented. If the infant is taking nothing by mouth, no further motor skills are developed after birth. Without oral stimulation, the infant may develop physiologic dependence on the enteral or parenteral feedings. The digestive system may also fail to ever take on its work with the extensive use of TPN. One widely accepted means of providing oral stimulation is through the use of non-nutritive sucking behavior (NNS). This is the form of sucking which occurs in all infants both while awake and asleep.[200] NNS is facilitated by allowing the premature infant to suck on a pacifier while receiving enteral or parenteral feedings. The sucking intervention may occur between as well as during routine feedings. It is believed that positive psychological feelings will be associated with the act of feeding when non-nutritive sucking is implemented. Oral stimulation has also been shown by select researchers to increase gastrointestinal transit time, improve weight gain, and shorten the time infants must spend in the hospital.[201] While other researchers who have studied the benefits of non-nutritive sucking have not been as quick to praise the method on these bases, the method is no doubt of significant benefit to many infants. Non-nutritive sucking can serve as a valuable tool in aiding the overall maturation of the suckling reflex.[202] The premature infant learns effective patterns of sucking, even if he is initially only able to "mouth" the nipple.[203] NNS is also believed to stimulate the production of lingual lipase, which is effective in the breakdown of fats and the absorption of their component fatty acids. At least one study has shown that non-nutritive sucking practices cause a notable decrease in infant heart rate[204], which is a promising finding considering that heart rate is widely accepted as a good indicator of overall energy expenditure (EE) in infants. Assuming that the finding of decreased heart rates means that energy expenditures are also lowered during NNS, infants would be conserving much needed energy for use in processes directly related to growth rather than extraneous motor functions. Non-nutritive sucking may also be done on the emptied breast of a mother who is pumping her milk for enteral administration. This method brings the added benefit of increased milk flow secondary to an increase in the production of the maternal hormones prolactin and oxytocin, as well as intangible maternal emotions.[205] As with any medical procedure, the needs of each individual should be considered. If an infant is so premature as to have extreme difficulties coordinating the sucking reflex, more energy may be expended in the process of non-nutritive sucking than its calming effects merit. The physical stress on the infant is an aspect of concern in light of the overall objective of decreasing unnecessary energy expenditure.

Common Problems

There are numerous problems associated with feeding the premature or low birthweight infant. Though they have high caloric needs, digestive functioning and stomach capacity are generally not adequate to meet those needs. Choking is a potential problem due to the lack of proper gag reflexes at such an immature stage of development. Nutrient absorption may also be inadequate due to a low level of intestinal enzymes (which would have been acquired in the final weeks of gestation).[206] Immature motor skills cause poor coordination of breathing with the suck and swallow reflex, which can cause extensive respiratory problems.

Attempts are being made in the neonatal nurseries of many hospitals to accommodate for the widespread problem of poor coordination of sucking, swallowing, and breathing. Before progress can be made, however, there must be an increased understanding of the problem itself. Palmer, et al., have devised a Neonatal Oral-Motor Assessment Scale for the purpose of quantifying an infant's level of oral-motor skills.[207] At Texas Children's Hospital, an Oral-Motor Kinetics (OMK) study is currently underway as well. Research in the OMK study involves identifying normal patterns of sucking, swallowing, and breathing in premature infants by observation. Technologically advanced equipment is also used to assess the exact pressure levels applied to nipples by infants at various stages in sucking and swallowing. Many different devices are being evaluated to determine the size, shape, and other characteristics of rubber nipples which will give the best results and allow for the greatest volume of intake.

Feeding intolerance is another common complication in premature newborns. Feeding intolerance is indicated by abdominal distention due to excess residuals which remain in the stomach after an enteral feeding, by vomiting or diarrhea, or by the presence of blood in the urine and stools.[208] Gastric residual volumes should thus be monitored to assure that the level within the stomach is lower than the level of the previous feeding.

Other feeding problems may be brought on by the use of parenteral nutrition techniques. Such conditions may include the following: problems in metabolism of nutrients (delivered directly into the bloodstream), sepsis, infections at catheter insertion-site, and stunted oral or gastrointestinal development.[209] Despite the potential problems which may occur with the feeding of high-risk newborns, it remains important to attempt the provision of nutrients even in the earliest hours of life.

FIVE

Monitoring Infant Status

During the course of nutritional care for premature and low birthweight infants, it is critical that overall health status be reviewed frequently. Determining the concentration of specific nutrients in an infant's blood and body stores can be a challenge, because levels of one component may (and often do) affect the absorption, retention, and utilization of another important nutrient. As is always the case in nutritional assessment, no one indicator or test should be considered completely diagnostic. It is often advisable to run a series of tests to arrive at a mean value, rather than considering the first known value to be entirely valid. When symptoms are present which indicate a lack or excess of one nutrient, it is crucial to remember that the problem may be caused by a combination of factors. Even growth, one of the primary goals of care, cannot always be relied upon as an absolute indicator of health — underlying problems may still exist without being physically recognizable as such.

Laboratory Values

In the case of several key indicators of nutritional status, blood values which appear to be normal may actually be deceptive. For instance, calcium levels may appear normal for extended periods of time even after bone degradation has begun taking place because the bones sacrifice their stores of calcium in order to maintain homeostasis within the blood and thus protect and conserve vital organ functions. Even moderate deficits of

nutrients can increase the risk for developing certain disease states. Such conditions often go unnoticed because they occur prior to states considered to be true deficiencies and are thus hard to recognize and diagnose.[210] The increased susceptibility to disease is thought to be linked to the increased incidence of infection and poor wound healing which accompany less-than-optimal blood levels of key
nutrients. Proper attention to all aspects of nutritional management should produce positive results and allow for the early detection of any potential problems.

Important blood values which should be monitored by a battery of laboratory tests include levels of sodium (Na), potassium (K), chloride (Cl), calcium (Ca), phosphorus (P), blood urea nitrogen (BUN), hemoglobin (Hgb), albumin and prealbumin. Certain blood gases should also be taken into consideration, primarily carbon dioxide and oxygen. Knowing the levels of the key blood gases is important in determining oxygenation and acid-base status. These should be taken from arterial rather than venous blood since blood from the arteries is more likely to be representative of overall status, coming from various body regions including the lungs.[211] In most neonatal intensive care nurseries, monitoring devices are located at each infant's bedside. The cardiorespirogram (CRG), or oxygen cardiac respiratory graphic recorder (OCRG), allows continual assessment of temperature, heart rate, blood pressure and respiratory status, indicating any sudden shifts in oxygen or carbon dioxide levels by a beeping signal. Premature infants will frequently experience episodes of apnea (cessation of breathing) accompanied by bradycardia (a heart rate of less than 100 beats per minute).[212] Better known as "A's and B's," these conditions place infants at considerable risk if they go unrecognized; therefore, the CRG monitor is an important device in the intensive care setting.

Protein Status

The key indicator of protein status has long been the level of albumin present in the blood. Albumin is the most prevalent plasma protein, and is involved in the control of the osmotic potential of the blood. Below normal serum albumin levels are indicative of malnutrition, generally pointing to deficiencies of both protein and calories. Albumin levels drop very slowly in response to the breakdown and loss of protein, due in part to albumin's long half-life (turnover rate).[213] Monitoring albumin levels is, therefore, a poor diagnostic tool in infants because they are prone to more acute cases of malnutrition. Albumin levels are also subject to change in response to fluid retention, which causes substantial dilution of blood proteins. This is of special significance considering the large proportion of fluid in the preterm infant's body (80 percent). For these reasons, many laboratory technicians and neonatal practitioners have made the transition to an evaluation of transthyretin levels instead. Transthyretin is commonly known as "prealbumin." Prealbumin is not the biochemical name, but rather a reference to its position on most scanner read-outs. Prealbumin has a turnover rate of only 1.8 days. Serum levels not only fall relatively quickly in response to suboptimal protein and calorie intake, but are also restored to appropriate levels once intake is returned to adequate levels. On this basis, prealbumin is a useful indicator of recent dietary intake as well as short-term protein status[214], especially beneficial in the post-surgical management of infants.[215]

Changes in prealbumin levels have been shown to directly correlate to changing weight and other anthropometric measures (length, head circumference, midarm circumference). The physical changes are usually noted within one week of the change in serum transthyretin levels.[216]

In monitoring growth, it is important that clinicians understand the physiological processes of anabolism and catabolism. Anabolism is that metabolic process which involves the synthesis, or build up, of a large molecule or structure from smaller components. Catabolism is basically the opposite process, involving the degradation, or break down, of a large molecule or structure into smaller component parts. During periods of rapid or sustained growth, anabolic processes are taking place. A common approach to determining if an individual is currently in an anabolic or catabolic state is the evaluation of "nitrogen balance." Nitrogen balance is basically the amount of protein intake minus the amount of protein lost through the urine (urea is the primary end product of protein dissociation). The most widely used formula for calculating nitrogen balance is as follows:

$$\text{N-balance} = \frac{\text{Protein intake (grams/24 hrs)}}{6.25} - \text{UUN (grams/24 hrs)}$$

Urine urea nitrogen (UUN) is the product excreted by the kidneys. Total protein intake is divided by the value of 6.25 because every gram of protein represents 6.25 grams of nitrogen intake. A positive nitrogen balance refers to the state of taking in more protein than one excretes, while in negative nitrogen balance more protein is being lost. Positive nitrogen balance is always the goal when growth and/or recovery are the desired outcomes, such as in the nutritional care of immature infants. Urea production will generally be minimal if proper nitrogen uptake is occurring.[217] If the nitrogen balance is found to be negative, inadequate protein intake, excessive protein losses, and general catabolism should be suspected.[218]

Metabolic Studies

One of the metabolic studies currently underway in the nurseries of Texas Children's Hospital takes a unique and innovative approach to evaluating nitrogen balance. As noted previously, nitrogen balance is determined by subtracting nitrogen output through urine from total nitrogen intake in the form of protein. The process itself poses a problem because meticulous care must be taken in calculating all volumes of feedings and precisely measuring urine output. It is difficult, if not impossible, to assess the exact volume of milk an infant receives when breastfeeding. Therefore, for purposes of the nitrogen balance study at Texas Children's Hospital, infants are given their mothers' breastmilk in bottles or through tube-feedings in order to monitor the exact volume of intake at each feeding over a twenty-four hour period. Urine output has traditionally been measured by weighing the infant's saturated diapers over the course of twenty four hours, taking into account the dry weight of each diaper before placement on the infant. This procedure gave imprecise and questionable results, and thus another approach was required. Researchers at the Children's Nutrition Research Center in Houston developed a unique alternative to the traditional method of determining nitrogen losses. In the nurseries of TCH, infants involved in this particular study are placed at a forty-five degree angle on a mesh pad within their isolette. No diaper or other coverings are placed on the infant, and, therefore, urine is allowed to drain freely from the infant through the mesh to be collected in a tray beneath the pad. Losses into the mesh are negligible, and a more accurate measurement of urine output is assured. Information from studies such as this one will also provide beneficial information on the nitrogen-retention of infants at different stages of gestation, as well as the absorption rate of nitrogen from various formulas. This relatively simple procedure gives evidence of the many strides currently being made in the medical and nutritional care of high-risk infants. However, many of the tools currently used to monitor and evaluate physiological status were designed for older populations of children and adults, and are inappropriate for diagnosing premature and low birthweight infants. The critical need for new and definitive testing methods remains.

Anthropometrics

At least one testing method designed specifically for use in the neonatal population has arisen in recent years. The knemometer is a device developed originally for use in children and adults by a physician in Denmark in 1983. A joint effort by researchers at several hospitals and universities in Copenhagen culminated in the development of a neonatal version of the knemometer five years later. The knemometer is an electronic device used to measure knee to heel length; a reading is recorded when a precise preset value for pressure is applied to the device by the infant's foot.[219] Measurement of knee to heel length is believed to be a better indicator of growth than overall height because the stability of the leg bone allows for greater accuracy.

It is generally agreed that growth is a positive occurrence indicating well-being in infants. Growth may be monitored in several different manners. Head circumference (FOC) is often measured periodically and compared to established growth curves. Head circumference is viewed as a good indicator of brain growth and development due to the fact that the number of brain cells continues to increase throughout the fetal period and up to approximately twelve months after birth.[220] Many clinicians also rely greatly on weight values to reveal whether or not adequate growth is taking place. Height (specifically linear growth velocity), however, are arguably better measures of growth considering the great variability of weight secondary to fluid retention and fat deposition in sick neonates.

Because knemometry requires minimal handling of the infant, allowing for undisturbed sleep and uninterrupted ventilation sessions, it seems to be a promising technique for assessing linear growth velocity. Detailed studies[221] have shown that leg length in utero increases at an average rate of 0.43 mm/day. The figure, which is based on a relatively large sampling size, can certainly be beneficial in the intensive care nursery, allowing for the accurate determination of growth (or lack of growth) in infants born prematurely.

A procedure related to that of knemometry is the measurement of bone density in neonates. Bone density measurements show the actual thickness of bones and gives a clear indication of the amount of calcium and phosphorus which are being retained for bone growth. Periodic measurements can be useful in identifying whether or not adequate accretion of nutrients is taking place. Knowledge gained through routine procedures such as bone density measurement will lay the foundation for providing more advanced levels of care to premature and low birthweight infants in the years to come.

SIX

Medical Complications

Certain physiologic complications and disease states are commonly found in neonates, all of which place an infant at risk and lead to longer hospital stays and higher medical costs. Some can be corrected by providing nutritional care; others can only be managed; still others remain to be explored, with little understanding of their relationship to nutritional status at the present time. Common problems seen in both full-term and preterm neonates include: respiratory ailments such as bronchopulmonary dysplasia (BPD); jaundice; rickets; interventricular hemorrhage (IVH); gastrointestinal disorders such as necrotizing enterocolitis (NEC); malabsorptive states; viral and bacterial infections; and visual disorders such as retinopathy. Physiologic complications resulting directly from the infant's immature developmental status are generally associated with one or more of the following:

- respiratory function
- gastrointestinal tract efficiency
- the cardiovascular system
- visual acuity

Respiratory Disorders

Respiratory diseases are the most prevalent disorders resulting from prematurity, with 65,000 cases reported in the United States on an annual basis.[222] Immature lungs do not produce lubricating surfactant and are not fully capable of conducting adequate oxygen-carbon dioxide exchange. The immature lung functioning results in mild to severe limitations in breathing referred to as respiratory distress syndrome.[223] The National Institute of Health and other organizations support the belief that nutrition plays a large role in the structural and functional development of skeletal muscles and overall lung architecture, with poor nutrition contributing to the onset of respiratory diseases.[224] It is critical that lung function be considered in providing nutritional therapy to premature and low birthweight infants whose lungs are still in the developmental stages.

Respiratory distress syndrome (RDS) is the condition evidenced by poor patterns of breathing resulting in inadequate lung oxygenation. In premature infants, RDS is believed to be linked to inadequate levels of pulmonary surfactant (produced after 33 weeks gestation) present in the underdeveloped lungs . The phospholipid surfactant, when present, acts to inflate the alveoli of the lungs to allow for the actual process of respiration.[225] Without the stabilizing action of surfactant, the alveoli atrophy and are rendered unable to do their job. A terrible cycle is set into motion in which the low surfactant volume leads to reduced lung compliance, leading to low alveolar ventilation and decreased pulmonary blood flow, and finally resulting in decreased lung metabolism of the surfactant.[226] Infants suffering from respiratory distress syndrome are maintained on continuous positive airway pressure (CPAP) through the nose, forcing lung expansion to take place and improving oxygen-carbon dioxide exchange. If the stimulation of nasal-CPAP is not sufficient to produce oxygenation, mechanical ventilation is begun, supplying intermittent positive pressure to the lungs through either an oral or endotracheal tube. Mechanical ventilators generally operate by either a time or volume controlled mechanism, which triggers the release of air into the lungs.[227] Use of synchronized intermittent ventilators allows the infant to control his rate of breathing, preventing potential problems which often arise when incoming pressure interferes with an infant's own minimal attempts at respiration.[228] Administration of appropriate levels of vitamin A (cell integrity) and vitamin E (antioxidant properties), as well as the trace elements copper and zinc (antioxidant synthesis) should alleviate some of the symptoms of RDS and prevent its progression toward chronic lung disease.[229]

Bronchopulmonary dysplasia (BPD) is a more severe respiratory disease, characterized by restricted air passageways, fibrosis (hardening) of the lung tissues, and collapse of the alveoli. The clinical definition for bronchopulmonary dysplasia is debatable, but BPD infants have generally been oxygen dependent for a period of at least 28 consecutive days after attempts to ventilate mechanically.[230] The original reason for mechanical ventilation in the development of BPD is usually respiratory distress syndrome, but other etiologies may include pneumonia, meconium aspiration (mucilaginous secretions from the intestines and the amniotic fluid of the placenta which cause blockage of airways), or severe apnea.[231] The severity of BPD is highly correlated to the length of exposure to oxygen, based on the fact that supplemental levels of oxygen produce excess levels of free radicals in the lungs. The immature lungs are deficient in antioxidants, important in protection from such free radicals. Bronchopulmonary dysplasia has nutritional implications because of the large amount of energy used as the infant strives to breathe. BPD can cause an increase of up to 25 percent of resting oxygen consumption;[232] caloric needs are greatly increased to accommodate for the increased energy expenditure. Growth failure, defined as weight and length below the tenth percentile on standard growth curves, is often associated with BPD as a result of the protein-calorie malnutrition state of many of the infants.[233] Weight gain should be promoted by the provision of all nutrient categories, though fluids must be restricted to prevent edema. Inclusion of a lipid component in any nutrient regimen is important because polyunsaturated fatty acids serve to protect the lungs from oxygen toxicity, along with their role in preventing essential fatty acid deficiency.[234]

Gastrointestinal Disorders

Gastrointestinal disorders in premature infants are caused to a large degree by the immaturity of the digestive organs. Infants born prematurely do not receive the benefit of swallowing amniotic fluid during the last weeks of gestation, which plays a large role in the functional development of the gastrointestinal system.[235] Common problems seen in neonatal intensive care units include meconium ileus, necrotizing enterocolitis, gastrointestinal perforations, and short bowel syndrome.

Meconium ileus occurs when a portion of the bowel becomes obstructed by the impaction of a mixture of intestinal secretions, cellular byproducts, and swallowed amniotic fluid.[236] A meconium "plug" forms which prevents proper digestion of nutrients and excretion of wastes. If no further complications follow, meconium ileus has a 92 percent survival rate. However, complications of meconium ileus lead to a 7 percent decrease in the survival rate.[237]

Necrotizing enterocolitis (NEC) is the "most common serious gastrointestinal disorder seen in neonatal intensive care units."[238] The incidence of necrotizing enterocolitis is approximately 2,200 cases per year in the United States alone, with 900 resulting in mortality. The disease is noted most often in infants of 1400-1500 grams and between thirty and thirty-two weeks of gestation.[239] The incidence of necrotizing enterocolitis is inversely related to gestational age; therefore, NEC is often thought of primarily as a disease of prematurity, though cases have occurred in full-term infants as well. The signs which alert to NEC include recurrent episodes of apnea and bradycardia ("A's and B's"), fluctuations of body temperature, abdominal distention, bloody stools, and large gastric residual volumes.[240] A portion of the intestine is almost always rendered nonfunctional, creating serious concerns for the provision of adequate nutrients since malabsorption is likely.[241] NEC also poses a risk for serious gastrointestinal perforation, which may lead to many further complications (40-70 percent mortality).[242]

Necrotizing enterocolitis is known to occur as a result of some form of injury or stress to the mucosal lining of the digestive tract. The classic theory of NEC's etiology, proposed by Santulli, et al., in 1967, still has many supporters. Santulli's theory states that the origin of NEC in any infant requires the presence of three primary conditions: mucosal injury, flourishing bacteria, and an available substrate.[243] Much research related to necrotizing enterocolitis has been conducted over the past twenty years, yet no absolute agreement has been reached regarding its etiology. One broad-based study of 2,681 very low birthweight NEC infants at eight neonatal care centers throughout the United States ended with the finding that no conclusive evidence existed which would point to one specific origin of the disease.[244] Considerable debate exists about whether or not the initiation of feedings in premature infants may lead to the development of necrotizing enterocolitis based on the fact that 95 percent of infants who develop NEC have already been fed.[245] The majority of current research, however, indicates that feedings should not be withheld. Depriving an infant of nutrients is thought not to prevent necrotizing enterocolitis, but only to delay its onset. One possible predisposing (or complicating) factor is the rapid advancement of feeding volume and concentration.[246] For this reason, it is recommended that formula or milk volume never be advanced more than 20 ml/kg/day in low birthweight infants. Interestingly, necrotizing enterocolitis has been noted more frequently in formula-fed infants than in those fed human milk,[247] which suggests that breastmilk may provide protection against the disease's onset. At Glanzing Children's Hospital in Vienna, Austria, researchers are using an innovative approach to prevention. Oral administration of the immunoglobulins IgA and IgB has resulted in a decreased incidence of NEC at their center.[248]

Gastrointestinal disorders such as necrotizing enterocolitis, volvulus (intestinal obstruction), inflammatory bowel disease (IBD), and congenital abdominal wall defects can all lead to short bowel syndrome (SBS). Commonly referred to as "short-gut," SBS is the condition in which a sizable portion of intestine is either entirely missing or rendered non-functional by injury.[249] The reason for an absence of a portion of the intestine may be linked to a birth defect or to surgery required to correct another disorder. Length of the digestive tract is commonly deficient in premature infants because the small and large intestines nearly double in length during late gestation.[250] Full-term infants generally have between 250 and 300 cm of intestine, whereas preterm infants rarely possess more than 230 cm.[251] When less than 200 cm of intestine is present, problems may arise in the digestion and absorption of nutrients. The chance of survival for infants with short bowel syndrome is largely related to the amount of functional intestine remaining to compensate in digestive activities. The pediatric surgeon Willis Potts, in 1955, cited that death was immanent for any infant losing 15 percent of his intestinal length. In 1972, survival was possible with as little as 25-30 cm of intestine remaining (up to a 90 percent loss).[252] By 1994, prognosis was even greater, with infants surviving with only 11 cm of intestine remaining, providing that the ileocecal valve (preventing backflow from the large to small intestine) was unharmed.[253]

A unique physiological mechanism allows for this incredible survival rate after gastrointestinal injury. Known as adaptation, the mechanism involves the increasing circumference, wall thickness, length, and overall cell number of a previously injured intestinal segment. The intestinal villi, which aid in the absorption of nutrients, flourish during the adaptation period, which begins as soon as twelve hours after the initial insult and continues for approximately one year.[254] Adaptation does not occur without enteral stimulation, providing further impetus for early feeding of high-risk infants.[255]

Nutritional management of short bowel syndrome includes provision of a predigested protein source and a minimal amount of fat; replacement of the fat-soluble vitamins A, D, E, and K; and use of simple sugars such as glucose, rather than complex carbohydrates which are more difficult to digest and give added fermentative byproducts.[256] All possible measures should be taken for slowing the gastrointestinal transit time to allow for the greatest level of nutrient-retention.

Cardiovascular Disorders

The most common cardiovascular disorder in high-risk infants is known as intraventricular hemorrhage (IVH). It is the condition in which oxidative injury occurs in the endothelium (tissue) lining the brain, causing excessive internal bleeding. IVH is believed to result from a high level of free radicals (hydroxy ions) which enter the brain after an episode of ischemia (deficiency of oxygen). Once normal circulation is restored, tissue damage occurs in the injured area.[257] The incidence of major morbidity from intraventricular hemorrhage is fifty to 100 percent.[258]

Visual Disorders

Another medical complication commonly seen in neonatal units is retinopathy of prematurity (ROP). ROP is believed to be caused by the toxic effect of oxygen on underdeveloped tissues of the eyes, and is common in infants being treated for lung disorders by the use of supplemental oxygen.[259] Problems stem from the fact that premature infants do not have the cellular ability to protect themselves against the damaging effects of the oxygen. The retina does not reach full development until two to three weeks after birth in term infants. A premature infant's prolonged exposure to high levels of pure oxygen during the final developmental stages alters normal patterns of vascularization of the retina, causing a spectrum of problems from mild visual impairments to total blindness.[260] The final stage of retinopathy, resulting in blindness, is referred to as retrolental fibroplasia (RFP) because it is characterized by the presence of thick tissues behind the lens. An estimated 400-600 infants are blinded by retinopathy of prematurity each year, the majority of those being infants of below 1500 grams birthweight.[261] Other vision problems may stem from a lack of adequate levels of certain fatty acids such as docosahexaenoic acid (DHA). DHA has been shown to increase visual acuity, and some researchers believe that the fatty acid should be promoted as "a conditionally essential nutrient for the preterm baby."[262]

Physical Abnormalities

Major malformations are "anomalies which are prenatal in origin and have cosmetic, medical, or surgical significance."[263] Defects commonly seen in the neonatal setting include the following:

- heart malformations (interventricular-septal defect)
- genital anomalies (of the sexual organs)
- limb deformities
- hydrocephalus (excessive fluid on the brain)
- renal agenesis (absence of the kidneys)
- genetic trisomies such as Down's Syndrome (Trisomy 21)
- abdominal wall defects (omphalocele and gastroschisis)
- cleft lip and/or palate

Congenital malformations occur in approximately 4 out of every 100 live births. The most commonly occurring deformities are genetic trisomies. Other non-genetic anomalies, such as abdominal wall defects, may occur in only 1 out of every 6-10,000 live births.[264] In general, defects are 10-20 percent more prevalent in low birthweight infants than in the overall population of births.[265] A promising 1993 study of nearly 8,000 infants in Budapest, Hungary showed that the incidence of non-genetic abnormalities may be significantly reduced by the practice of taking vitamin and trace element supplements during the pre-conceptual period.[266]

SEVEN

Medical Management

Procedures

With good nutrition, a clean wound will probably heal.
—Hippocrates

Many medical procedures are performed in the neonatal intensive care setting. These range from simple techniques intended to increase an infant's comfort level, to major surgeries requiring much planning and follow-up. All procedures should be evaluated before their administration, with consideration given to the level of invasiveness to the infant, parental concerns, and pre- and post-operative medical and nutritional management. In the case of surgical procedures, metabolic demand is often greatly increased. The compromised nutritional status of infants before the time of surgery also has an effect on the degree of immune functioning which can occur. Therefore, surgery and other procedures must be given much consideration in the nutritional care of newborns.

Extracorporeal life support (ECLS) is currently available at close to eighty medical centers internationally. Also known as extracorporeal membrane oxygenation (ECMO), the procedure is used in cases of severe respiratory failure. The basic concept of ECMO therapy is to remove non-oxygenated blood from the infant's circulation and oxygenate it mechanically through an artificial lung before returning it to the body. ECMO is, in effect, dialysis for the lungs (similar to the kidney dialysis employed in renal failure). ECMO gives the infant's lungs and heart a chance to "rest" while it maintains the exchange of oxygen and carbon dioxide through artificial respiration. Infants who are candidates for receiving extracorporeal membrane oxygenation are those with severe pulmonary hypertension, diaphragmatic abnormalities which prevent proper breathing, or those in the end stages of respiratory distress syndrome. Infants on the waiting list to undergo heart surgery may also receive ECMO support. Congenital heart defect patients are generally not treated with ECMO, because it is not a means of improving the physiologic condition. The first case of infant survival after extracorporeal membrane oxygenation was in 1975. The 1994 survival rate is close to 83 percent after ECMO therapy. The average length of treatment is three to eight days, with artificial oxygenation gradually tapered off before its removal. The time an infant spends connected to the ECMO machine can provide an opportunity to administer parenteral nutrition solutions and lipids through the ECMO line. Resting energy expenditure is decreased since the infant is not struggling to breathe. Provision of adequate nutrients at this time may reverse the catabolism taking place in the physiologically stressed infant.[267]

Pharmaceutical Therapy

Pharmaceutical therapy for neonates is an issue which must be closely monitored. Minimal doses of commonly used medications can have a profound effect on small infants. Many of the medications used regularly in adult patients are not suitable for use in the neonatal population. Medications which are considered safe are usually given at 50 percent or less of the normal adult dosage. The following is a list of medications frequently prescribed for patients in the neonatal intensive care unit, along with their intended use or result:

MEDICATION	USAGE/RESULT
Dexamethasone	Anti-Inflammatory Agent
Zantac	Anti-Gastroesophageal Reflux
Digoxin	Antiarrhythmia (heart murmurs)
Furosemide	Diuretic effect
Lasix	Diuretic effect
Indomethacin	Closure of ductus arteriosus
Insulin	Glucose regulation
Amikacin	Antimicrobial agent
Phenobarbital	Anti-convulsant
Ursodiol	Stimulant of bile acid production
Dopamine	Blood pressure maintenance
Theophylline	Reduction of apnea
Sodium citrate	Reduction of acidosis
Cisapride	Reduction of feeding intolerance

Table 2 Common Neonatal Medications

Most medications are delivered to the infant through a peripheral venous line.[268] Any healthcare professional responsible for administering medications to infants must be aware of the possible side effects of each, as well as the potential for adverse drug-nutrient interactions. The pharmacist should take the responsibility of making others in the neonatal setting aware of the benefits and hazards of commonly prescribed medications.

He or she is also responsible for monitoring each individual infant to assure that no incompatible medications have been combined in a regimen, and that those infants on total parenteral nutrition are not receiving drugs which might settle out of formula or cause deterioration of the intravenous line.

Dexamethasone is an anabolic corticosteroid commonly administered to neonates. Dexamethasone is of great benefit in the treatment of respiratory distress syndrome and bronchopulmonary dysplasia, or for other infants receiving long-term supplemental oxygen. However, the use of steroid therapy on a regular basis has met with much skepticism and opposition in recent years. The potential side effects of dexamethasone are many in number, and questions have been raised regarding the efficacy of using it in such a vulnerable population. Steroids act against the protective mechanisms of the gastrointestinal lining, causing even normal pH levels to bring about erosion and lead to perforations. The negative effect on digestive functioning may be reduced by increasing the pH of the stomach (lowering the acidity level) through the use of another medication, ranitidine.[269] However, the use of ranitidine poses yet another potential problem considering that a reduction in the acidity of the stomach may allow the proliferation of pathogens in the intestinal lining, upsetting the normal gut flora which work in digestion and immunity. Dexamethasone is believed to be responsible for increasing the rate of protein breakdown (catabolism), causing an overall decrease in lean body mass.[270] Studies have also shown that dexamethasone therapy significantly decreases leg length velocity, and is thus "disruptive to normal growth."[271] Steroid therapy remains valuable in the treatment of chronic lung disease, but risks and benefits must be weighed for each individual patient before a prescription is made.

In 1959, a substance known as surfactant was identified for its role in the inflation of lungs during respiration.[272] Since the early 1960's, extensive research and clinical trials have been conducted to produce a suitable surfactant from phospholipid substances which would serve to lubricate an infant's lungs and thereby promote compliance and ease breathing.[273] In 1990, a new class of drugs was formed when the United States Food and Drug Administration (FDA) approved a synthetic surfactant for use in the treatment of respiratory disorders. The following year, a surfactant taken from the lungs of animals was also approved by the FDA.[274] Administration of 100 mg surfactant in 3-5 ml of saline per kilogram of body weight directly into the lungs of an infant experiencing respiratory distress can result in improved oxygenation within minutes.[275] The United States infant mortality curve displayed a significant decline along with the introduction of surfactant treatments to the clinical setting, even when it was only being used on a trial basis (down 8.5 percent in 1989 and 6.3 percent in 1990).[276] Because of its role in decreasing mortality and morbidity rates associated with respiratory distress and bronchopulmonary dysplasia, surfactant replacement therapy has been cited as "one of the most successful therapy interventions in neonatal care in the last two decades."[277]

Administration of inositol, a phospholipid component of cell membranes, is also a potential therapy for infants suffering from respiratory distress syndrome. The substance occurs naturally in colostrum, the form of human milk produced in the earliest stages of lactation.[278] Inositol can endow the developing lungs with enhanced protective capacity, promoting recovery from injury and preventing further tissue damage. Any therapy related to the prevention and management of respiratory disorders should be weighed according to its potential risk and benefit before administration to the patient.

EIGHT

Neonatal Care

Levels of Care

Certain identifiable levels of care exist in neonatal intensive care. Level two nurseries are those which provide intermediate care to high-risk infants receiving total parenteral nutrition and various other therapies including supplemental oxygen. Level three care is more advanced, providing mechanical ventilation through the use of continuous airway pressure support. Level three nurseries generally provide care for infants at more extreme physiological risk. Measures taken in the care of high-risk infants include maximal support, limited care, comfort care, and withdrawal of support. Maximal support entails the provision of mechanical ventilation, total parenteral nutrition, surgical procedures, and medications in an effort to restore the infant to full health. Limited care seeks to maintain the current status of the infant, not increasing treatment measures if health continues to deteriorate. Comfort care is the term used to describe the provision of only basic thermal and nutritive support, without performing procedures to correct problems evident at birth. Withdrawal of support is the removal of the infant from any ventilation or other means of life support. This measure is only taken in extreme cases, when death is imminent and no treatment measures appear feasible.[279]

For most infants, intensive care is only temporary. Current technology and medical knowledge allows for the survival of many infants born in a compromised physiologic state. After the course of treatment in the neonatal intensive care unit, infants are discharged either to normal hospital care or to their own homes. Texas Children's Hospital and other modern care facilities often provide parents with a "rooming-in room," where the infant can be kept for 24-48 hours before final discharge to the home. The amenity of rooming-in rooms is intended to ease the transition from hospital to home for both the infant and parents.

Cost of Care

Improving medical technology has greatly increased the chance of survival for premature and low birthweight infants. However, the technological advances have not come without a price. Costs for neonatal intensive care services are high, and there is continuing debate over who is responsible for payment. In 1990, annual hospital costs for low birthweight infants born in America reached two billion dollars, translating into a cost of $21,000 per baby.[280] An average of $22,500 is reimbursed by Medicaid for the delivery of an infant weighing less than 1500 grams at birth, and $6,500 for each infant under 2000 grams, compared to the average payment of $2,200 for infants above 2500 grams at birth.[281] The care of extremely sick or premature infants may cost up to $1,000 per day. With the average length of stay in the neonatal intensive care unit being three months, costs quickly mount. One 1992 estimate showed average total hospital costs for an infant born at twenty-eight weeks gestation to be $10,600; the figure rose to $35,000 for those born at twenty-four weeks.[282] These figures encompass only the care given during the neonatal period, not taking into account subsequent follow-up visits or future complications related to the initial problems which kept the infants in the intensive care unit. For comparison, consider that the normal delivery of a full-term infant generally costs about $2,800. Only seven percent of all births are low birthweight infants, yet those seven percent account for more than fifty-seven percent of the medical costs for all newborns combined.[283]

Specific medical therapies which are contributors to the high cost of care for high-risk infants include total parenteral nutrition regimens and the use of surfactant as a treatment for chronic lung disorders. Standardized parenteral nutrition solutions average approximately $125/liter, with additional costs for components such as albumin ($100 per bottle) and intralipid ($100 per 500 ml bottle). Thus, the average cost of supplying total parenteral nutrition to an infant at $400-700 each day.

Surfactant therapy for the treatment and prevention of chronic lung disease has greatly increased the rate of survival for infants experiencing respiratory problems. Yet infants of extremely compromised conditions are now being kept alive, requiring more extensive treatment measures to be taken for each infant. Surfactant therapy decreases the cost of medical care for those infants who would have survived even without it, but for each survivor who is kept alive because of the surfactant, an estimated $100,000 in medical costs is incurred.[284] The trends in rising health care costs have caused some to question the efficacy of prolonging the costs to hospitals, insurance companies, and individuals by keeping extremely sick infants alive.

Team Care in the NICU

Improving outcomes for infants in the neonatal intensive care unit are often related to the recent advances in medical technology. However, another aspect which has enhanced the quality of care provided to high-risk infants is the new emphasis on the importance of team care. The inclusion of a team concept in providing medical and nutritional management in any setting can improve outcomes of care. Rather than one individual being assigned to a certain patient, a multidisciplinary team comes together to discuss options for care. The team is ideally composed of individuals from a wide variety of disciplines, bringing both diversity and expertise to enhance the quality of care which can be provided. In many neonatal intensive care nurseries, this concept is being carried out with the addition of nutrition support teams (NSTs) to the care design.

Members of the nutrition support team include a physician, a dietitian, a pharmacist, and a registered nurse, among others. The physician is generally the director of the team, leading rounds and discussions of cases. The dietitian's primary functions are to screen and assess all of the infants who enter the NICU, and to make recommendations for their nutritional management. The pharmacist adds to the team effort by making other members aware of available medications and their possible side effects and interactions with other drugs or nutrients. The registered nurse has an integral role on the team, responsible for daily monitoring of each infant's overall status and for alerting other team members of any potential problems.[285] The main short and long-term goals of a nutrition support team are as follows:

- to decrease the incidence of malnutrition and nutrition-related disorders in the neonatal setting
- to provide consultation to the parents of each infant undergoing care
- to evaluate methods of treatment currently in use and develop protocols for future actions
- to remain abreast of current research on issues related to the care of high-risk infants
- to take part in on-going research projects
- to provide continuing education to other healthcare providers to ease the transition from hospital to home care

NSTs may go on rounds through the unit on a weekly, biweekly, or even daily basis. During their interaction with each other, team members are encouraged to identify problems, improve feeding regimens, assess growth, and determine future care needs for each infant. Proven outcomes of such nutrition support teams include decreases in infant mortality and morbidity, length of stay, hospital costs, and the overall number of days on total parenteral nutrition.[286] A potential disadvantage to team care is the occurrence of "multiple care-giver syndrome."[287] This is the situation in which an infant has his care plan revised so often that little continuity is established, and thus little progress is actually made. While the potential for such an occurrence should be recognized, nutrition support teams have the potential to be a definite asset to the provision of quality care for high-risk infants.

Infant Outcomes

Evaluation of the outcomes of infants born in a physiologically compromised condition has met with mixed results. Studies have shown both positive and negative correlations with the increasing survival rate of premature and low birthweight infants. It is widely accepted that prematurity should not, in itself, be considered a cause of death. The deaths and morbidities which result are generally related to the disorders associated with the immature status of infants and their organ systems, not prematurity alone.

The greatest number of deaths in the neonatal intensive care unit are the result of immature lungs, which are unable to tolerate environmental conditions outside the womb. Respiratory distress syndrome and bronchopulmonary dysplasia lead to approximately 20,000 infant deaths in the United States each year,[288] though this number is gradually decreasing with the widespread implementation of surfactant therapy. Necrotizing enterocolitis (NEC) and other gastrointestinal disorders also add to the mortality rate in infants. However, for infants who survive NEC, the prognosis is quite favorable. Fifty percent of NEC survivors display normal development after leaving the hospital; 35 percent have mild to moderate physiologic impairments; and only 15 percent exhibit severe complications.[289] The outcome of infants who suffer from retinopathy of prematurity (ROP) is generally good. Retinopathy often reverses itself if treatment is begun in its early stages.[290] Ophthalmologic evaluations are recommended for all premature infants by four to six weeks of life in an effort to minimize the long-term effects of the advanced stages of ROP.

The University of Washington School of Medicine in Seattle studied 16 infants born at a weight of less than 800 grams and found that no major neurological problems existed upon follow-up evaluations at six months to three years of age.[291] However, other studies have shown evidence of neurological or other developmental disorders by the time school age is reached in infants born at a low birthweight . For infants born between 1,500 and 2,000 grams, the incidence of problems was ten percent; for those between 1,000 and 1,500 grams, 20 percent; and for infants born below 1,000 grams, the incidence was 30 percent.[292] The relationship of breastfeeding to neurological development of preterm infants has been extensively studied since as early as 1929, and a positive correlation is believed to exist between the two.[293]

For the majority of infants born at a low birthweight, developmental processes are normal by two years of age. Appropriate sizes are reached as the infants experience "catch-up growth" during the period after their initial weight loss. Most infants are discharged from the neonatal intensive care unit by the time they have reached full-term status (37 to 40 weeks gestation).[294] If subsequent hospitalizations occur, they are usually required within the first year of life. The transition from hospital to home care may be difficult for parents unaccustomed to caring for an infant with special needs. Sleep patterns may be disturbed initially because of the changes in the surrounding environment. The overall prognosis for high-risk infants continues to improve as medical technology advances even further than was once believed imaginable.

Ethical Issues

Controversy abounds on the issue of how prematurely infants can and should be kept alive. The fact that infants are being born at earlier stages of development than ever before does not necessarily mean that life can be sustained in any "live-born" infant. As past president of the American Academy of Pediatrics James Strain states, "Not all babies can be born healthy and whole."[295] Recent studies have cited survival rates of up to 50 percent for infants born at 750 grams, with the survival rate for 1000 gram infants nearing 100 percent.[296] The research of Allen, et al., published in November of 1993, showed an 80 percent survival rate for infants born after at least 25 weeks of gestation. Those born at 24 weeks had a 56 percent chance of survival. For infants born at 23 weeks of gestation, the survival rate was only 15 percent, with no infants born at 22 weeks of gestation surviving longer than six months in Allen's study.[297] Statistics such as these reveal the need for hospitals to establish policies regarding such issues as delivery room care of extremely premature or low birthweight infants and methods of decision making related to their medical and nutritional management. Which infants should be actively resuscitated immediately after delivery? Should mechanical ventilation be begun for all infants born with severe breathing disorders? Is supplying parenteral nutrition appropriate for those infants whose digestive organs may never be functional? Is prolonging death of extremely sick infants justified in the light of rising medical costs? The questions are endless, and many remain unanswered.

Ethical issues in the medical care of patients at all ages have received increasing attention in recent years. The practice of neonatology, however, seems to have a greater prevalence of such "bioethical" and "medico-legal" concerns than perhaps any other medical discipline.[298] Many of the issues encountered are not new. The increasing survival rate of extremely premature and low birthweight infants has simply increased the frequency with which they are encountered.[299] Along with increasing concerns have come more extensive federal regulations in an attempt to govern and standardize the decisions made in neonatal intensive care units.

One of the most pressing concerns in the treatment of sick newborns is the issue of who should be responsible for making critical life and death decisions. Some say the federal government, some say the physician, and many believe the decision between treatment and non-treatment is one which only the parents can rightfully make. In most neonatal settings, decisions are currently made based on a consultation between the doctor and the parents. Many hospitals have incorporated the concept of team care into the resolution of ethical issues by developing multidisciplinary teams for the exploration of all possible alternatives when an intervention is being decided upon. In 1983, the American Academy of Pediatrics suggested the involvement of a hospital-wide ethics committee on issues which cannot be easily resolved upon first investigation.[300] Two years later, the United States Supreme Court established the "Baby Doe" regulations. The 1985 federal guidelines call for the institution of infant care review committees (ICRCs) in all neonatal settings. ICRCs are composed of a diverse array of health care professionals including doctors, administrators, and nurses, with additional representatives from the clergy and the legal field.[301] Also known as infant bioethics committees, these groups are intended to be the decision makers on issues such as the limit of viability, treatment of congenital anomalies, withdrawal of life support, and general quality of life concerns. The primary functions of an ICRC are to review individual cases, consult with parents, and then recommend actions to be taken.

Many neonatologists have questioned the worth of infant care review committees, arguing that institutionalizing decisions regarding infant care fails to allow them to practice as experts in their own field.[302] Physicians have also expressed concerns that the regulations alter their practice and disregard much of the consideration they generally give to the needs and desires of the parents. It is clear that the intensive care of high-risk infants is a practice plagued by numerous moral and legal concerns, and that these complex issues may not be easily resolved in the near future.

Conclusion

This paper has explored the critical role of medical nutrition therapy in the management of preterm and low birthweight infants. It is obvious that incredible strides have been made in recent years in the field of neonatology. Medical nutrition therapy for neonates is beginning to be implemented, and continuing efforts to improve the quality of life for these infants are meeting with much success. The trend of increasing infant survival rates indicates the improvements afforded by technology. Apparently, however, not enough changes have been implemented before birth to make a notable difference in the rate of low birthweight deliveries. Initiative must be taken to eliminate maternal risk factors if the occurrence of low birthweight is to subside. Although medicine can now do much to allow and enhance life for infants born in compromised conditions, the well-known maxim holds true that "an ounce of prevention is worth a pound of cure."

Many volumes could be written on the issues addressed here before they would be covered in full. It is easy to recognize the critical role nutrition plays in maintaining health in preterm and low birthweight infants, and in preventing further complications related to their immaturity. The registered dietitian has an important responsibility in working in a field such as neonatology.

In April 1994, neonatal dietitian Melody Thompson conducted a survey of United States perinatal and neonatal centers in an attempt to discover the number of hospitals which currently include a neonatal nutritionist in their intensive care units. The National

Research Council recommends that registered dietitian positions be included at institutions providing care to high-risk newborns. Specific recommendations call for a "registered dietitian with either advanced pediatric training that includes clinical neonatal nutrition or clinical experience in the nutrition care of critically ill newborn infants" in any level III (specialized care) neonatal intensive care unit. However, results of Thompson's survey indicate that only 38 percent of responding neonatal centers have a registered dietitian in the neonatal intensive care unit. Many unit directors (42 percent) have indicated a desire to incorporate a dietitian into their departments. Lack of financial resources is viewed as providing the greatest resistance to developing neonatal dietetics positions. Directors also indicate the lack of an individual qualified to fill such a role as a legitimate problem.[303]

Based on the findings of Thompson's national survey, it is apparent that a need exists for dietitians to specialize in the advanced-level care of high-risk infants. Furthermore, in instances where no registered dietitian is present in the neonatal center, other less qualified individuals take on the role of nutrition manager, providing care of questionable quality to a population of infants at serious nutritional risk. Therefore, the time has come for dietitians to show that they are the individuals most qualified to fill the role of nutritional care provider in the neonatal setting, and that their services are, in fact, integral to the provision of quality infant care.

Many challenges will be faced in managing individual patient care, and the clinical setting will give rise to important questions to be addressed in future research efforts. As technologies advance and more research is completed, it is crucial that dietitians remain abreast of the new knowledge. Continuing education is important in order to provide the highest quality of care to the patients.

Emphasis must be placed on making training opportunities available for individuals willing to specialize in the field of neonatal nutrition. Baylor College of Medicine's Neonatal Nutrition Rotation, along with similar fellowship programs in South Carolina and Indiana, provides a much needed service to students and practicing dietitians seeking advanced-level training in preparation for a career in the specialized care of infants. Experience in the clinical setting, as well as interaction with other qualified individuals already working in the field, will lead to a higher level of care for high-risk infants throughout America.

The provision of high quality infant care by registered dietitians can be viewed as an incredible opportunity to better lives and provide a solid foundation of optimal nutrition which can have a long-reaching effect on the overall health and well-being of infants. Many strides have been made in recent years in relation to the care of neonates in compromised states, and the outlook for the future is increasingly promising.

1. Arkansas Department of Health, Center for Health Statistics, County Trends in Maternal and Child Health - Arkansas, 1987-1991 (Little Rock, 1993) 20.

2. United States Department of Health and Human Services (DHHS), Maternal and Child Health Bureau, Child Health USA '93 (Washington: US Department of Health and Human Services, 1994) 16.

3. J.R. Arena, "Incidence of Low Birthweight in a Hospital-Based Prenatal Clinic: A Quality Assessment/Quality Improvement Project," Department of Nutrition Services, Shore Memorial Hospital, Somers Point, New Jersey, 1994, 1.

4. American Dietetic Association Report, "Position of the American Dietetic Association: Cost-effectiveness of Medical Nutrition Therapy," Journal of the American Dietetic Association 95.1 (1995): 89.

5. Gail Ensner and David Clark, Newborns at Risk (Rockville: Aspen Publishers, 1986) 35.

6. A.F. Williams, "Human Milk and the Preterm Baby," British Medical Journal 306.19 (1993): 1629.

7. American Dietetic Association, Executive Summary of the Legislative Platform, "Economic Benefits of Nutrition Services in Maternal and Child Health," Economic Benefits of Nutrition Services (Chicago, 1992) 11.

8. National Commission to Prevent Infant Mortality, Troubling Trends Persist: Shortchanging America's Next Generation (Washington, March 1992) 8.

9. "US Teen Birth Rate Drops 2%, but Many Babies Born Too Small, Arkansas Democrat-Gazette 26 Oct 1994.

10. "Help for Infants and Pregnant Women," USA Today April 1993: 6.

11. Rasa Gustaitis and Ernie Young, A Time to be Born, a Time to Die (Reading: Addison Wesley, 1986) 210.

12. DHHS 19.

13. Patricia Rowe, "Preventing Infant Mortality: An Investment in the Nation's Future," Children Today Jan/Feb 1989: 18.

14. National Commission to Prevent Infant Mortality, Infant Mortality: Care for Our Children, Care for Our Future (Washington, 1988) 3.

15. ADA 11.

16. Avron Y. Sweet, "Classification of the Low Birthweight Infant," Care of the High-Risk Neonate, ed. Marshall Klaus and Avroy Fanaroff (Philadelphia: WB Saunders, 1993) 86.

17. Elsa Moreno, "Healthy Families Make Healthy Babies," World Health May/June 1993: 23.

18. Elizabeth Ahmann, Home Care for the High Risk Infant (Rockville: Aspen Publishers, Inc., 1986) 2.

19. Sweet 66.

20. Ohio Neonatal Nutritionists, Nutritional Care for High Risk Newborns (Philadelphia: George F. Stickley Company, 1985) 102.

21. Sweet 73-77.

22. Ohio 102.

23. Sweet 69.

24. Sweet 85.

25. Marshall Klaus et al., "The Physical Environment," Care of the High-Risk Neonate, ed. Marshall Klaus and Avroy Fanaroff (Philadelphia: WB Saunders, 1993) 86.

26. Klaus 106.

27. American Academy of Pediatrics, Committee on Nutrition, "Commentary on Parenteral Nutrition," Pediatrics 71.4 (1983): 547.

28. Gordon B. Avery, Mary Ann Fletcher, and Mhairi MacDonald, Neonatology: Pathophysiology and Management of the Newborn (Philadelphia: JB Lippincott Company, 1994) 333.

29. Steven J. Gross and Terri A. Slagle, "Feeding the Low Birth Weight Infant," Clinics in Perinatology 20 (1993): 194.

30. Ekhard Ziegler, et al., "Body Composition of the Reference Fetus," Growth 40 (1976): 329.

31. Joseph Dancis, John O'Connell, and L. Holt, "A Grid for Recording the Weight of Premature Infants," Journal of Pediatrics 33 (1948): 570.

32. Stanley Shaffer, et al., "Postnatal Weight Changes in Low Birth Weight Infants," Pediatrics 79 (1987): 705.

33. Alan Lucas, et al., "Early Diet in Preterm Babies and Developmental Status at 18 Months," Lancet 335 (1990): 1477.

34. Gross 193.

35. Ilene Sosenko and Frank Lee, "Nutritional Influences on Lung Development and Protection against Chronic Lung Disease," Seminars in Perinatology 15.6 (1991): 462.

36. Gillian Lockitch, "Perinatal and Pediatric Nutrition," Clinics in Laboratory Medicine 13 (1993): 388.

37. Reginald C. Tsang et al., eds., Nutritional Needs of the Preterm Infant (Pawling: Williams and Wilkins, 1993) 177.

38. Avroy Fanaroff and Richard Martin, eds., Neonatal-Perinatal Medicine (St. Louis: Mosby-Year Book, 1992) 529.

39. Tsang 9-11.

40. W.C. Heird, "Nutritional Requirements during Infancy and Childhood," Modern Nutrition in Health and Disease, ed. Maurice Shils (Philadelphia: Lea & Febiger, 1994) 751.

41. Fanaroff 510.

42. Tsang 158.

43. Avery 405.

44. Tsang 9-11.

45. Ensner 116.

46. Payne 87.

47. Steven Mayfield, et al., "The Role of the Nutritional Support Team in Neonatal Intensive Care," Seminars in Perinatology 13.2 (1989): 89.

48. Alex Robertson and Bhatia Jatinder, "Feeding Premature Infants," Clinical Pediatrics 32 (1993): 36.

49. Buford Nichols and Reginald Tsang, Nutrition During Infancy (Philadelphia: Hanley and Belfus, Inc., 1988) 12-13.

50. Lockitch 392.

51. Avery 1356.

52. Shirley Walberg Ekvall, ed., Pediatric Nutrition in Chronic Diseases and Developmental Disorders: Prevention, Assessment, and Treatment (New York: Oxford University Press, 1993) 33.

53. J. Neu, Christina J. Valentine, and W. Meetze, "Scientifically-based Strategies for Nutrition of the High-Risk Low Birthweight Infant," European Journal of Pediatrics 150 (1990): 6.

54. Tsang 39.

55. Nichols 11.

56. Ohio 77.

57. Nichols 93.

58. Avery 335.

59. Mayfield 89.

60. Payne 89.

61. Neu 3.

62. Payne 89.

63. Nichols 46.

64. Andre Bach and Vigen Babayan, "Medium-Chain Triglycerides: An Update," American Journal of Clinical Nutrition 36 (1982): 954.

65. Tsang 79.

66. Lockitch 390.

67. Peggy B. Borum, "Medium-chain Triglycerides in Formula for Preterm Neonates: Implications for Hepatic and Extrahepatic Metabolism," Journal of Pediatrics 120 (1992): S139.

68. Bach 950.

69. American Academy of Pediatrics, Committee on Nutrition, "Use of Intravenous Fat Emulsions in Pediatric Patients," Pediatrics (1981): 738.

70. Nicola Gilbertson, et al., "Introduction of Intravenous Lipid Administration on the First Day of Life in the Very Low Birthweight Neonate," Journal of Pediatrics 119 (1991): 615.

71. H. Paust, H. Schroder, and W. Park, "Intravascular Fat Accumulation in the Very Low Birthweight Infant," Journal of Pediatrics 103.4 (1983): 669.

72. W. Park, et al., "Impaired Fat Utilization in Parenterally Fed Low Birthweight Infants Suffering from Sepsis," Journal of Parenteral and Enteral Nutrition 10.6 (1986): 627.

73. Yves Brans, et al., "Fat Emulsion Tolerance in Very Low Birthweight Neonates: Effect on Diffusion of Oxygen in the Lungs and on Blood pH," Pediatrics 78 (1986): 79.

74. Ilene Sosenko, Sheila Innis, and Frank Lee, "Intralipid Increases Lung Polyunsaturated Fatty Acids and Protects Newborn Rats from Oxygen Toxicity," Pediatric Research 30.5 (1991): 413.

75. Dominique Haumont, et al., "Plasma Lipid and Plasma Lipoprotein Concentrations in Low Birthweight Infants Given Parenteral Nutrition with Twenty or Ten Percent Lipid Emulsion," Journal of Pediatrics 115 (1989): 787.

76. Lily Kao, Mary Cheng, and David Warburton, "Triglycerides, Free Fatty Acids, Free Fatty Acids/Albumin Molar Ratio, and Cholesterol Levels in the Serum of Neonates Receiving Long-Term Lipid Infusions: Controlled Trial of Continuous and Intermittent Regimens," Journal of Pediatrics 104 (1984): 434.

77. Sosenko 463.

78. Jayant Senai, et al., "Clinical Trial of Vitamin A Supplementation in Infants Susceptible to Bronchopulmonary Dysplasia," Journal of Pediatrics 111 (1987): 269.

79. Jayant Shenai, Frank Chytil, and Mildred Stahlman, "Vitamin A Status of Neonates with Bronchopulmonary Dysplasia," Pediatric Research 19.2 (1985): 185.

80. V. Chan, et al., "Vitamin A Levels at Birth of High Risk Preterm Infants," Journal of Perinatal Medicine 21 (1993): 147.

81. Nichols 258.

82. Tsang 95.

83. Neu 8.

84. B.L. Salle, et al., "Vitamin D Metabolism in Preterm Infants," Biology of the Neonate 52.1 (1987): 119.

85. W.W. Koo, et al., "Serum Vitamin D Metabolites in Very Low Birth Weight Infants with and without Rickets and Fractures," Journal of Pediatrics 114 (1989): 1017.

86. Nichols 269.

87. Dale Phelps, "The Role of Vitamin E Therapy in High-Risk Neonates," Clinics in Perinatology 15.4 (1988): 955.

88. Tsang 103.

89. Phelps 955.

90. D.L. Phelps, et al., "Tocopherol Efficacy and Safety for Preventing Retinopathy of Prematurity: A Randomized, Controlled, Double-Masked Trial," Pediatrics 79 (1987): 489.

91. L. Johnson, et al., "Effect of Sustained Pharmacologic Vitamin E Levels on Incidence and Severity of Retinopathy of Prematurity: A Controlled Clinical Trial," Journal of Pediatrics 114 (1989): 827.

92. Marcello Orzalesi, "Vitamins and the Premature," Biology of the Neonate 52.1 (1987): 100.

93. Nichols 237.

94. Tsang 126.

95. J.N. Udall and H.L. Greene, "Vitamin Update," Pediatrics in Review 13.5 (1992): 190.

96. Lockitch 400.

97. Nichols 243.

98. Tsang 128.

99. Tsang 129.

100. Nichols 232.

101. Tsang 131.

102. Tsang 187.

103. Nichols 230.

104. Tsang 130.

105. R.A. Ehrenkranz, "Mineral Needs of the Very Low Birthweight Infant," Seminars in Perinatology 13.2 (1989): 142.

106. Lockitch 394.

107. Nichols 219.

108. Tsang 135.

109. G.J. Hoehn, et al., "Alternate Day Infusion of Calcium and Phosphorus in Very Low Birthweight Infants: Wasting of the Infused Materials," Journal of Pediatric Gastroenterology and Nutrition 6.5 (1987): 752.

110. Lockitch 393.

111. Frank Greer, Jean Steichen, and Reginald Tsang, "Effects of Increased Calcium, Phosphorus, and Vitamin D Intake on Bone Mineralization in Very Low Birthweight Infants Fed Formulas with Polycose and Medium-chain Triglycerides," Journal of Pediatrics 100.6 (1982): 951.

112. Gerald B. Merenstein and Sandra L. Gardner, Handbook of Neonatal Intensive Care - Second Edition (St. Louis: The CV Mosby Company, 1989): 187.

113. Richard Schanler, Steven Abrams, and Cutberto Garza, "Bioavailability of Calcium and Phosphorus in Human Milk Fortifiers and Formula for Very Low Birthweight Infants," Journal of Pediatrics 113 (1988): 95.

114. K.A. Fitzgerald and M.W. MacKay, "Calcium and Phosphate Solubility in Neonatal Parenteral Nutrition Solutions Containing TrophAmine," American Journal of Hospital Pharmaceuticals 43 (1986): 93.

115. Greed 954.

116. Bach 952.

117. Ehrenkranz 144.

118. John Cloherty and Ann Stark, eds., Manual of Neonatal Care (Boston: Little, Brown and Company, 1991) 535.

119. P.A. Walravens, et al., "Zinc Supplements in Breastfed Infants," The Lancet 340.8821 (1992): 683.

120. Harry Greene, et al., "Guidelines for the use of Vitamins, Trace Elements, Calcium, Magnesium, and Phosphorus in Infants and Children Receiving Total Parenteral Nutrition: Report of the Subcommittee on Pediatric Parenteral Nutrition Requirements from the Committee on Clinical Practice Issues of the American Society of Clinical Nutrition," American Journal of Clinical Nutrition 48 (1988): 1335.

121. Cloherty 535.

122. American Academy of Pediatrics, Committee on Nutrition, "Zinc," Pediatrics 62.3 (1978): 410.

123. Avory Fanaroff and Marshall Klaus, "The Gastrointestinal Tract - Feeding and Selected Disorders," Care of the High-Risk Neonate, ed. Marshall Klaus and Avroy Fanaroff (Philadelphia: WB Saunders, 1993).

124. Avery 330.

125. Tsang 218.

126. Mary Ann H. Smith, "Nutritional Assessment for Persons with Developmental Disabilities," Topics in Clinical Nutrition 8 (1993): 30.

127. Raanan Arens and Brian Reichman, "Grooved Palate associated with Prolonged Use of Orogastric Feeding Tubes in Premature Infants," Journal of Oral and Maxillofacial Surgery 50 (1992): 64.

128. Karen McAllister, "New Moms Weaned from the Bottle," Arkansas Democrat-Gazette 22 Jan 1995: 1B.

129. McAllister 7B.

130. American Academy of Pediatrics, "The Promotion of Breastfeeding," Pediatrics 69.5 (1982): 654.

131. C.G. Victoria, et al., "Use of Pacifiers and Breastfeeding Duration," The Lancet 341 (1993): 405.

132. AAP, Promotion 654.

133. Gary Freed, et al., "A Practical Guide to Successful Breastfeeding Management," American Journal of Diseases of Children 145 (1991): 917.

134. M. Hamosh and P. Hamosh, "Mother to Infant Biochemical and Immunological Transfer through Breastmilk," A Publication of Georgetown University, 1988.

135. Richard J. Schanler, "Human Milk for Preterm Infants: Nutritional and Immune Factors," Seminars in Perinatology 13.2 (1989): 75.

136. Alan Lucas, et al., "Breastmilk and Subsequent Intelligence Quotient in Children Born Preterm," The Lancet 339 (1992): 261.

137. N.B. Mathur, et al., "Anti-infective Factors in Preterm Human Colostrum," Acta Paediatrica Scandinavia 79 (1990): 1039.

138. Hamosh 158.

139. Nancy Butte, et al., "Heart Rates of Breast-Fed and Formula-Fed Infants," Journal of Pediatric Gastroenterology and Nutrition 13.4 (1991): 391.

140. J.B. Bier, et al., "Breastfeeding of Very Low Birthweight Infants," Journal of Pediatrics 123 (1993): 777.

141. Alan Lucas and T.J. Cole, "Breastmilk and Neonatal Necrotizing Enterocolitis," The Lancet 336 (1990): 1521.

142. Avery 330.

143. Jatinder Bhatia and David Rassin, "Human Milk Supplementation," American Journal of Diseases of Children 142 (1988): 447.

144. Williams 1628.

145. Bhatia 445.

146. American Academy of Pediatrics, Committee on Nutrition, "Human Milk Banking," Pediatrics 65.4 (1980): 854.

147. McAllister 1B.

148. S.M. Ludington-Hoe, et al., "Kangaroo Care: Research Results and Practice Implications and Guidelines," Neonatal Network 13.1 (1994): 19.

149. Richard Leeuw, et al., "Physiological Effects of Kangaroo Care in Very Small Preterm Infants," Biology of the Neonate 59 (1991): 149.

150. Gene Anderson, "Current Knowledge about Skin-to-Skin (Kangaroo) Care for Preterm Infants," Journal of Perinatology 11.3 (1991): 217.

151. Luddington-Hoe 22.

152. Anderson 217.

153. Christina J. Valentine, Nancy Hurst, and Richard Schanler, "A Lacto-Engineering Strategy that Promotes Weight Gain in Human Milk-Fed Low Birth Weight (LBW) Infants," Abstract in FASEB Journal 6.5 (1992): A1958.

154. Ross Laboratories, Using Concentrated Formulas and Caloric Supplements to Meet Special Infant Feeding Needs (Columbus: Ross Laboratories, 1987) 4.

155. Christina J. Valentine, "Neonatal Nutrition in the 1990's:Milking It for Everything You Can," Feeding Guidelines of Baylor College of Medicine, Houston, TX.

156. Gibson 502.

157. Mead-Johnson Pediatrics, Pediatric Products Handbook (Evansville: Mead Johnson & Company, 1993) 6.

158. Valentine, Neonatal 4.

159. McAllister 7B.

160. McAllister 1B.

161. McAllister 7B.

162. Gross 197.

163. William Meetze, et al., "Gastrointestinal Priming Prior to Full Enteral Nutrition in Very Low Birthweight Infants," Journal of Pediatric Gastroenterology and Nutrition 15.2 (1992): 169.

164. C.L. Berseth, "Effect of Early Feeding on Maturation of the Preterm Infant's Small Intestine," Journal of Pediatrics 120 (1992): 951.

165. Gilberto Pereira and Moritz Ziegler, "Nutritional Care of the Surgical Neonate," Clinics in Perinatology 16.1 (1989): 238.

166. Avery 340.

167. Pereira 239.

168. Arens 65.

169. P.D. Macdonald, et al., "Randomised Trial of Continuous Nasogastric, Bolus Nasogastric, and Transpyloric Feeding in Infants of Birthweight Under 1400 grams," Archives of Disease in Childhood 67 (1992): 431.

170. Tsang 217.

171. Frank Greed, "Changes in Fat Concentration of Human Milk during Delivery by Intermittent Bolus and Continuous Mechanical Pump Infusion," Journal of Pediatrics 105.5 (1984): 747.

172. Judith Grant and Scott Denne, "Effect of Intermittent versus Continuous Enteral Feeding on Energy Expenditure in Premature Infants," Journal of Pediatrics 118 (1991): 928.

173. Grant 928.

174. Valentine, Neonatal 5.

175. Gustaitis 36.

176. William Heird, Sudha Kashyap, and Michael Gomez, "Parenteral Alimentation of the Neonate," Seminars in Perinatology 15.6 (1991): 493.

177. K.W. Helfrick and N.M. Abelson, "Intravenous Feeding of a Complete Diet in a Child," Journal of Pediatrics 25 (1944): 400.

178. Beth Leonberg McCoy, "TPN in the Pediatric Patient," Support Line 13.5 (1991): 1.

179. Robertson 41.

180. Ekvall 32.

181. Richard J. Shulman, "Protein Deficiency in Premature Infants Receiving TPN," American Journal of Clinical Nutrition 44 (1986): 610.

182. Heird, Parenteral 493.

183. M. Hack, et al., "Very Low Birth Weight Outcomes of the National Institute of Child Health and Human Development Neonatal Network," Pediatrics 87 (1991): 587.

184. Cloherty 548.

185. William Heird, et al., "Pediatric Parenteral Amino Acid Mixture in Low Birthweight Infants," Pediatrics 81 (1988): 49.

186. AAP, Commentary 547.

187. Heird, Parenteral 493.

188. Texas Children's Hospital(TCH), "Parenteral Nutrient Requirements," an In-Service Publication, 5.

189. Pereira 247.

190. TCH 3.

191. AAP, Commentary 548.

192. Kristie Fitzgerald and Mark MacKay, "Calcium and Phosphorus Solubility in Neonatal Parenteral Nutrient Solutions Containing Aminosyn PF," American Journal of Hospital Pharmaceuticals 44 (1987): 1399.

193. Fitzgerald 1399.

194. Laura Laine, et al., "Cysteine Usage Increases the Need for Acetate in Neonates Who Receive Total Parenteral Nutrition," American Journal of Clinical Nutrition 54 (1991): 565.

195. Friedrich Manz, "L-Cysteine in Metabolic Acidosis of Low Birthweight Infants," American Journal of Clinical Nutrition (1993): 455.

196. Greene 1324.

197. Greene 1324.

198. McCoy 1.

199. McCoy 4.

200. Fanaroff 767.

201. Gross 204.

202. Mario Decurtis, et al., "Effect of Non-Nutritive Sucking on Nutrient Retention in Preterm Infants," Journal of Pediatrics 109.5 (1986): 890.

203. Indira Narayanan, et al., "Sucking on the 'Emptied' Breast: Non-Nutritive Sucking with a Difference," Archives of Disease in Childhood (1990): 241.

204. R. Woodson and C. Hamilton, "The Effect of Nonnutritive Sucking on Heart Rate in Preterm Infants," Developmental Psychobiology 21.3 (1988): 210.

205. Narayanan 244.

206. Avery 333.

207. J.B. Bier, et al., "Breastfeeding of Very Low Birthweight Infants," Journal of Pediatrics 123 (1993): 774.

208. Avery 64.

209. Ekvall 37.

210. Denis R. Benjamin, "Laboratory Tests and Nutritional Assessment - Protein-Energy Status," Pediatric Clinics of North America 36.1 (1990): 140.

211. Joseph Broughton, "Understanding Blood Gases," A Publication of the University of Colorado Medical Center.

212. Cloherty 222.

213. Benjamin 140.

214. Benjamin 146.

215. W.J. Chwals, et al., "Serum Visceral Protein Levels Reflect Protein-Calorie Repletion in Neonates Recovering from Major Surgery," Journal of Pediatric Surgery 27.3 (1992): 319.

216. M.K. Georgieff, S.R. Sasanow, and G.R. Pereira, "Serum Transthyretin Levels and Protein Intake as Predictors of Weight Gain Velocity in Premature Infants," Journal of Pediatric Gastroenterology and Nutrition 6 (1987): 775.

217. Payne 89.

218. Benjamin 152.

219. Kim Michaelsen, et al., "Short-Term Measurement of Linear Growth in Preterm Infants: Validation of a Hand-held Knemometer," Pediatric Research 30.5 (1991): 464.

220. Sweet 68.

221. Alan Gibson, Richard Pearse, and Jeremy Wales, "Knemometry and the Assessment of Growth in Premature Babies," Archives of Diseases in Childhood 69 (1993): 501.

222. John Travis, "Helping Premature Lungs Breathe Easier," Science 261 (1993): 426.

223. Ahmann 2.

224. N. Edelman, R. Rucker, and H. Peavy, "Nutrition and the Respiratory System," National Institute of Health, Workshop Summary, June 2-4, 1985.

225. June Brady and George Gregory, "Assisted Ventilation," Care of the High-Risk Neonate, ed. Marshall Klaus and Avroy Fanaroff (Philadelphia: WB Saunders, 1993) 260.

226. Klaus 185.

227. Brady 211.

228. T.P. Strandjord and Alan Hodson, "Neonatology," Journal of the American Medical Association 268.3 (1992): 377.

229. Sosenko 465.

230. Bier 775.

231. Eduardo Bancalari and Tilo Gerhardt, "Bronchopulmonary Dysplasia," Pediatric Clinics of North America 33.1 (1986): 2.

232. Sosenko 463.

233. Sharon Kurzner, et al., "Growth Failure in Infants with Bronchopulmonary Dysplasia: Nutrition and Elevated Resting Metabolic Expenditure," Pediatrics 81.3 (1988): 379.

234. Sosenko 466.

235. Josef Neu, "Functional Development of the Fetal Gastrointestinal Tract," Seminars in Perinatology 13.3 (1989): 224.

236. Neu, Functional 230.

237. F. Rescoria, et al., "Changing Patterns of Treatment and Survival in Neonates with Meconium Ileus," Archives of Surgery 124 (1989): 840.

238. Avery 333.

239. Michelle Walsh, et al., "Necrotizing Enterocolitis: A Practitioner's Perspective," Pediatrics in Review 9.7 (1988): 219.

240. Walsh 222.

241. Ahmann 7.

242. Dickens St. Vil, et al., "Neonatal Gastrointestinal Perforations," Journal of Pediatric Surgery 27.10 (1992): 1341.

243. Ann Kosloske, "A Unifying Hypothesis for Pathogenesis and Prevention of Necrotizing Enterocolitis," Journal of Pediatrics 117.1 (1990): 568.

244. Ricardo Uauy, et al., "Necrotizing Enterocolitis in Very Low Birthweight Infants: Biodemographic and Clinical Correlates," Journal of Pediatrics 119 (1991): 637.

245. Walsh 220.

246. Diane Anderson and Robert Kliegman, "The Relationship of Neonatal Alimentation Practices to the Occurrence of Endemic Necrotizing Enterocolitis," American Journal of Perinatology 8.1 (1991): 62.

247. Lucas, Breastmilk 1519.

248. M. Eibl, et al., "Prevention of Necrotizing Enterocolitis in Low Birthweight Infants by IgA-IgG Feeding," New England Journal of Medicine 319.1 (1988): 1.

249. Marshall Schwartz and Kosaku Maeda, "Short Bowel Syndrome in Infants and Children," Pediatric Clinics of North America 32.5 (1985): 1265.

250. R.J. Touloukian and G.J.W. Smith, "Normal Intestinal Length in Preterm Infants," Journal of Pediatric Surgery 18.6 (1983): 721.

251. Douglas Wilmore, "Factors Correlating with a Successful Outcome Following Extensive Intestinal Resection in Newborn Infants," Journal of Pediatrics 80.1 (1972): 89.

252. Wilmore 89.

253. Christina J. Valentine, "Feeding Strategies for the Infant Post-Necrotizing Enterocolitis and with Short Bowel Syndrome," A Baylor College of Medicine Publication, 1.

254. Moritz M. Ziegler, "Short Bowel Syndrome in Infancy: Etiology and Management," Clinics in Perinatology 13.1 (1986): 167.

255. Jon Vanderhoof, et al., "Short Bowel Syndrome," Journal of Pediatric Gastroenterology and Nutrition 14 (1992): 349.

256. Ziegler, Short 170.

257. Phelps 960.

258. Marilee Allen, P.K. Donohue, and A.E. Dusman, "The Limit of Viability - Neonatal Outcome of Infants Born at 22 to 25 Weeks' Gestation," New England Journal of Medicine 329.22 (1993): 1597.

259. Ahmann 8.

260. Cloherty 595.

261. Phelps 959.

262. J. Raloff, "Fish Oil Sharpens Young Preemies' Focus," Science News 144 (1993) 38.

263. Cloherty 109.

264. Christina J. Valentine, "Congenital Anomalies of the Alimentary Tract," Nutritional Care for High-Risk Newborns (Chicago: Precept Press, Inc., 1994) 297-8.

265. Sweet 84.

266. Andrew Czeizel, "Prevention of Congenital Abnormalities by Periconceptual Multivitamin Supplementation," British Medical Journal 306 (1993): 1645.

267. Rebeccah Brown, Jacqueline Wessel, and Brad Warner, "Nutrition Considerations in the Neonatal Extracorporeal Life Support Patient," Nutrition in Clinical Practice 9 (1994): 25.

268. Stephanie Phelps and Richard Helms, "Risk Factors Affecting Infiltration of Peripheral Venous Lines in Infants," Journal of Pediatrics 111 (1987): 389.

269. E.J. Kelly, S. Chatfield, and K. Brownlee, "The Effect of Intravenous Ranitidine on the Intragastric pH of Preterm Infants Receiving Dexamethasone," Archives of Diseases in Childhood 69 (1993): 39.

270. K. Brownlee, et al., "Catabolic Effect of Dexamethasone in the Preterm Baby," Archives of Disease in Childhood (1992): 4.

271. Alan Gibson, Richard Pearse, and Jeremy Wales, "Growth Retardation after Dexamethasone Administration: Assessment by Knemometry," Archives of Disease in Childhood 69 (1993): 507.

272. Alan Jobe, "Pulmonary Surfactant Therapy," New England Journal of Medicine 328.12 (1993): 861.

273. Travis 426.

274. Jobe 861.

275. Jobe 862.

276. Jobe 862.

277. Arthur Eidelman, "Economic Consequences of Surfactant Therapy," Journal of Perinatal Medicine 13.2 (1993): 138.

278. Mikko Hallman, et al., "Inositol Supplementation in Premature Infants with Respiratory Distress Syndrome," New England Journal of Medicine 326.19 (1992): 1233.

279. Brian Carter, "Neonatologists and Bioethics after 'Baby Doe'," Journal of Perinatology 13.2 (1993): 144.

280. Arena 1.

281. ADA Reports 88.

282. "What Price Life?" The Economist 326.7796 (1993): 52.

283. Arena 1.

284. Eidelman 137.

285. Mayfield 90-91.

286. Mayfield 88.

287. Mayfield 89.

288. Robert Berkow, ed., The Merck Manual of Diagnosis and Therapy, 14th ed. (Rahway: Merck & Company, Inc., 1982) 1759.

289. Kosloske 573.

290. Cloherty 595.

291. F.C. Bennett, N.M. Robinson, and C.J. Sells, "Growth and Development of Infants Weighing Less than 800 Grams at Birth," Pediatrics 71 (1983): 319.

292. M.L. Hulseman and L.A. Norman, "The Neonatal ICU Graduate: Part I. Common Problems," American Family Physician 45.3 (1992): 1301.

293. Walter Rogan and Beth Gladen, "Breastfeeding and Cognitive Development," Early Human Development 31 (1993): 181.

294. M.L. Hulseman and L.A. Norman, "The Neonatal ICU Graduate: Part II. Fundamentals of Outpatient Care," American Family Physician 45.4 (1992): 1696.

295. American Academy of Pediatrics, Committee on Bioethics, "Treatment of Critically Ill Newborns," Pediatrics 72.4 (1983): 565.

296. Hulseman, Part I 1301.

297. Allen 1597.

298. Carter 149.

299. William Weil, "Issues Associated with Treatment and Nontreatment Decisions," American Journal of Diseases in Children 138 (1984): 519.

300. Carter 144.

301. Weil 522.

302. L.M. Kopelman, T.G. Irons, and A.E. Kopelman, "Neonatologists Judge the 'Baby Doe' Regulations," New England Journal of Medicine 318 (1988): 680.

303. Melody Thompson, Pamela Price, and Douglas Stahle, "Nutrition Services in Neonatal Intensive Care: A National Survey," Journal of the American Dietetic Association 94.4 (1994): 440-441.