Born in the USA – The History of Neonatology in the United States: A Century of Caring

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Introduction

It is hard to believe that during my lifetime the first neonatal unit was established and neonatology became a subspecialty of pediatric medicine; it is hard to believe that I was a minted nursing school graduate working in a neonatal intensive care unit that took part in the surfactant trials. It is hard to believe that we relied solely on a bear-cub ventilator and extremely high inspiratory pressures to support infants with respiratory distress syndrome. My mind's, eye allows me to look back and see the fragile skin of the preterm infant with a perfectly circular-shaped transcutaneous oxygen monitor burn. I can almost feel the corrugated vent tubing throbbing with humidity.

Considering that the average age of a nurse today is 49 years, I am not alone with my memories. Many of us, including nurses, physicians, and respiratory therapists who work in the NICU, share the same experiences. With quiet pride and grounded responsibility, we look back on the infants and families we have cared for and we feel satisfied. We look back on the dramatic advances that have taken place in neonatology and the responsibilities we have carried as neonatal nurses and we wonder how time has passed so quickly, especially the last two decades. In the U.S., it is widely agreed that modern neonatology began in the 1960s. However, for more than a century, countless nurses and physicians have dedicated their professional lives to improving the standards of care provided for high-risk and preterm infants. Since I was a small child, my father would remind me: "To know your future, you should study your past." The purpose of this article is to provide a brief but illuminating look back on the history of neonatology, and to encourage all of you to recognize that you are a part of this journey.

In the Beginning, Turn-of-the-Century America

As the 19th century bid its farewell, Americans looked over their shoulder with awe at remarkable strides that characterized the industrial revolution. Yet, despite urban explosion and technological advance, nearly 20% of all infants in American cities never lived to see their first birthday. Industrialization in the 19th century, characterized by employment of women in factories, decrease in breast feeding, child abandonment, and increasing need for foundling homes, resulted in the highest recorded infant mortality: more than 230/1,000 births in 1870.[1] Many infants died immediately from respiratory distress syndrome, and others died in the first few weeks of life from hypothermia, infection, or weight loss. By the early 1900s, pediatricians began to take increasing interest in improving the health of newborns and preventing death by emphasizing adequate feeding and prevention of infection. Moreover, with a newly constructed U.S. birth registry in 1915, showing an infant mortality rate of 99.6/1,000 live births,[2] there was increasing awareness (public and political) that infant mortality reflected the overall health and welfare of our nation. Since 1900, especially in the past 50 years, dramatic improvements in the care of preterm and term infants have taken place in all areas of neonatal care.

Thermoregulation

The Incubator

America's first hospitals for premature infants were established at the turn of the 20th century at fairs, amusement parks, and expositions. In 1896, Martin Couney, a former student of Parisian physicians, Stéphane Tarnier and Pièrre-Constant Budin, inventors of the incubator, is credited with bringing the incubator to the United States. Doctor Couney, known as the "Incubator Doctor," was the first person to offer specialized care for premature infants in the US. In 1901, Couney set up his first incubator show at the Trans-Mississippi Exposition in Omaha, Nebraska. From there, Couney went on to exhibit his premature babies at the Pan-American Exposition in Buffalo, New York.[3] In the 40 years following, the *"Incubator Baby Side-Shows"* were at nearly all of the large expositions or World's Fairs in America, beginning in 1898 and continuing until 1943. Couney's longest running incubator exhibit was at Coney Island, New York. This exhibit, called the Luna Park Incubator Exhibition, was the longest running show at Coney Island. The incubator baby shows featured entire rows of incubators, staffed by rotating shifts of physicians and nurses. By the 1930s, Julius Hess, Chief of Pediatrics at the Michael

Reese Hospital in Chicago, became the leading expert on prematurity. He developed the Hess incubator, which was capable of delivering oxygen to the baby inside. The Hess incubator was used in the U.S. in the first dedicated transport vehicle in Chicago. The incubator was heated by coils and plugged into the ambulance.

By the 1940s, a modern-like incubator with clear plastic walls was introduced. The visibility afforded by the modern clear plastic incubator was recognized immediately, "Nurses and doctors stared at the naked babies as if they were seeing them for the first time." Naked infants were examined more completely, observed more closely, and treated more actively than ever before.[4]

Thermal Regulation

Although various incubators were designed and used in Europe and the U.S., it was not until the 1950s, with the work of William Silverman, Richard Day, and colleagues at Columbia Presbyterian, (known then as Babies Hospital), in New York, that the benefits of modifying body temperature were demonstrated. In one of the first randomized, controlled trials in neonatology, they were able to demonstrate improved survival in preterm infants who were kept in incubators that were 4° warmer than in the control infants.[5] Soon thereafter, the factors that affect the equation of heat loss *versus* heat production were elucidated.[6] The importance of radiant heat loss led to the introduction of radiant warmers, both in the delivery room and in premature nurseries. It was also noted that an important component of heat production was the presence of brown fat.[7] It was demonstrated that not all infants of low birth weight (LBW) were born preterm but might be small for gestational age or experience IUGR.[8] Some were found to have difficulty maintaining their body temperature, largely because they lacked brown fat. Because other substrates were used to produce heat, they also developed low blood glucose levels. For different-sized infants, at different postnatal ages, a range of temperatures, called the neutral thermal environment,[9] was found to minimize energy expenditure. In 1958, Dr. William Silverman's seminal report showed that maintaining body temperature by controlling the thermal environment significantly decreased low-birth-weight mortality.[10] With this discovery, thermal management became a cornerstone of neonatology.

Growth and Nutrition

Growth Categories

Beginning in the late 1950s, Farquhar in Scotland[10] and Gellis and Hsia[11] and Cornblath[12] in the U.S. reported that infants of poorly controlled diabetic mothers were "overgrown" and at increased risk for hypoglycemia, respiratory distress syndrome (RDS), hyperbilirubinemia, hypocalcemia, and hypertrophic cardiomyopathy. On the other end of the growth curve, Gruenwald[13] recognized that fetal undergrowth might be the result of placental insufficiency. Warkany et al.[14] are credited with introducing the term "intrauterine growth retardation," commonly known today as intrauterine growth restriction. In 1967, Lulu Lubchenco, from Mile High City in Denver, Colorado, published the seminal paper reporting a growth classification based on birth weight, categorizing newborns into three groups: small, appropriate, or large for gestational age.[15] Lubchenco's work led to improved assessment and management of problems that were unique to specific growth categories and provided a standard for postnatal growth for preterm infants.

Nutrition

As early as the 1850s, preterm infants were reported to be gavage fed with soft rubber catheters;[16] polyethylene tubes were introduced in the 1950s.[17] Secondary to concerns about oxygenation, respiratory status, and infection, it was common practice to withhold feeding the preterm infant for the first few days of life, or longer. Clinical disorders such as hypoglycemia and hyperbilirubinemia coupled with difficult IV access, reinforced the need to re-think traditional feeding practices and ultimately led to present-day feeding management. After the discovery of the chemical composition of milk in the 1890s, various percentages of protein, fat, and carbohydrate were used for infant feeding, with formula feeds introduced in the 1920s. To improve the health of poor women and children, the U.S. Congress enacted the National Supplemental Feeding Program for Women and Children (WIC) in 1972. Whey-predominant formulas for preterm infants were introduced in the 1980s.[18]

Parenteral Nutrition

The infusion of intravenous fluids was a major turning point for the care of preterm infants. Initially, peripheral venous nutrition was primarily in the form of glucose. Development of micro-infusion pumps facilitated the accurate administration of IV fluids to extremely preterm infants. Numerous investigators attempted to infuse protein hydrolysates to the preterm or postsurgical infant, but it was Dudrick and Wilmore who worked initially with laboratory animals in Rhoads' department and developed the basis by which high caloric IV preparations, with appropriate nitrogen concentrations, could be infused into large-caliber vessels.[19] These techniques were rapidly applied to the care of the low-birth-weight infant.

Delivery Room Resuscitation

The Apgar Score

In 1957, Doctor Virginia Apgar suggested that a newborn should be assessed in the delivery room with a scoring system based on 5 parameters—heart rate, respiration, reflex activity, tone, and color— within the first minute, and if necessary at 5 minutes.[20] The following year (1958), Dr. Apgar proposed that someone other than the delivering obstetrician or midwife should be caring for the infant and giving the Apgar Score.[20] Since then, the Apgar Score is used in delivery rooms throughout the world. Improved delivery room assessment and management led to respiratory management immediately at birth that included bag-and-mask ventilation or endotracheal intubation and assisted ventilation for infants failing to establish spontaneous respiration. Suctioning of the oropharynx with the head on the perineum, followed by prophylactic endotracheal intubation and suctioning to prevent meconium aspiration became delivery room protocol.[21] The establishment of a national resuscitation program in the United

States codified neonatal resuscitation in a way that could be taught to thousands of physicians and nurses.[22]

Respiratory Disorders

In the early 1900s, the treatment for apnea or cyanosis was spirit of ammonia and a small dose of whiskey.[23] By the 1930s, premature and cyanotic infants were given oxygen. The notion of "if a little is good, a lot should be better" was espoused and liberal use of oxygen was the standard of treatment for cyanotic infants.[24] Without the ability to measure the infant's interior oxygen level, the only way to determine whether or not an infant was getting enough oxygen was to observe color. Unfortunately, liberal oxygen use, coupled with inability to measure arterial oxygen tension, proved to have devastating consequences, and many preterm infants developed retrolental fibroplasia, now called retinopathy of prematurity (ROP). RLF was responsible for more childhood blindness—an estimated 8,000 cases—than all other causes combined. The association between oxygen therapy and RLF was eventually determined by Kate Cambell of Australia in 1951[25] and liberal use of oxygen was directly linked to ROP and blindness. Consequently, respiratory management strategies shifted to the other extreme, characterized by oxygen restriction. Oxygen concentrations greater than 40 percent were considered dangerous and incubators were designed so that no more than 40% oxygen could be delivered, unless a baffle on the back of the incubator was closed. Undoubtedly, many infants died because they were deprived of adequate amounts of oxygen. By the end of the 1960s, measuring arterial oxygen tension for all neonates receiving supplemental oxygen became standard of practice. Our ability to measure PO_2 with micro samples of blood, decreasing from 2 ml to 0.5 mL, and subsequently to 0.2–0.3 mL, enabled us to improve respiratory function of preterm infants, prevent ROP, and care for infants of lower birth weights and younger gestational ages.

Surfactant

In 1959, Dr. Mary Ellen Avery and her colleague, Dr. Jere Mead, described the mechanism underlying the failure of premature infant's lungs to expand, and to retain air. For the first time, Avery and Jere reported that hyaline membrane disease was not caused by the *presence* of something in the lungs but rather by the *absence* of something.[26] They recognized that infants who died of hyaline membrane disease lacked a substance in the lung called *surfactant.* When it became clear that the problem involved retaining air, mechanical respirators were modified to provide positive pressure in the alveoli at the end of expiration, as well. In addition, understanding the cause of the so-called hyaline membrane disease pointed the way to two new treatments: steroid injections for pregnant women to encourage a fetus at risk for premature birth to speed up the production of natural surfactant, and development of surfactant products that could be placed in the lungs of babies born before they were able to produce this substance on their own. Mary Ellen Avery's and Jere Mead's description of surfactant deficiency as the etiology of HMD, a disease that caused an estimated 25,000 deaths per year, soon followed. This led to what many consider the greatest success in modern neonatology, the development and administration of surfactant to premature infants. The use of surfactant to treat what we now know as respiratory distress syndrome has revolutionized the field of neonatal medicine, reducing neonatal mortality from RDS by 40%.

Advances in Respiratory Management

Respiratory monitoring improved with transcutaneous oxygen assessment, followed by transcutaneous carbon dioxide, pulse oximetry, routine blood gas monitoring, and noninvasive apnea, heart rate, and blood pressure monitoring. The use of CPAP resulted in a dramatic improvement in the successful respiratory support of premature infants. The first generation of ventilators designed specifically for neonatal use, the Baby Bird I and Bournes BP 200, were introduced. The first successful use of extracorporeal membrane oxygenation (ECMO) took place in 1975.[27] ECMO eventually reduced infant mortality from 80% to 25% for critically ill infants with acute reversible respiratory and cardiac failure unresponsive to conventional therapy in conditions such as persistent pulmonary hypertension, meconium aspiration, and sepsis. By the mid 1970s, umbilical lines were routinely used and by the 1980s, pulse oximetry was introduced,[28] rapidly gaining popularity because it was a non-invasive way to measure oxygen saturation. Furthermore, because there was no heating device, the position did not need to be changed frequently. Remarkable advances in the respiratory management of preterm infants soon followed.

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Evolution of the Neonatal Intensive Care Unit

With hospital births increasing from fewer than 5% in 1900 to more than 50% in 1921, hospital nurseries began appearing, and pediatricians assumed a larger role in neonatal care.[29] The care of the newborn entered the academic setting through the work of Julius Hess, Chief of Pediatrics at Michael Reese Hospital in Chicago. In 1922, the Sarah Morris Premature Center, the first unit solely for premature infants, opened. Julius Hess' textbook "Premature and Congenitally Diseased Infants," was the first book devoted to newborns.[30] Hess established concepts of research in the newborn, developed the Hess Incubator, and became the leading American expert on prematurity. The Sarah Morris Hospital at Michael Reese Hospital promoted advances in aseptic techniques, neonatal transport service, and nasal feeding. By 1948, both the American Academy of Pediatrics and World Health Organization

uniformly defined prematurity as infants with a birth weight less than 2,500 grams.

On August 7, 1963, Patrick Bouvier Kennedy, the third child of President John F. Kennedy and First Lady Jacqueline Bouvier Kennedy was born. He was born at 34 1/2 weeks' gestation with a birth weight of 2,112 grams (4lbs, 10oz), by repeat cesarean section at the Otis Air Force Base Hospital, in Cape Cod (Massachusetts). Because of progressive respiratory distress, the baby was transferred to Boston Children's Hospital, where he was placed in a hyperbaric oxygen chamber, and died at 39 hours of life from hyaline membrane disease. The morning after his death, Patrick's obituary in *The New York Times* pointed out that, at that time, all that could be done "for a victim of hyaline membrane disease is to monitor the infant's blood chemistry and to try to keep it near normal levels. Thus, the battle for the Kennedy baby was lost only because medical science has not yet advanced far enough to accomplish as quickly as necessary what the body can do by itself in its own time." More than any other single event, the death of this infant served to ignite public and medical awareness to the need for neonatal intensive care and soon led to the establishment of NICUs around the country.

Just two years later, in 1965, the first American newborn intensive care unit (NICU), designed by Dr Louis Gluck, was opened at Yale Hospital in New Haven, Connecticut.[31] In 1975, the American Board of Pediatrics established the Subspecialty Board of Neonatology. After the 1976 report *Toward Improving the Outcome of Pregnancy* by the AAP, American College of Obstetrics & Gynecology, and the National Foundation, premature care became increasingly centralized in regional NICUs, with dramatic improvements in survival. The concept of concentrating the sickest patients in regional centers persists. For those infants who are less acute, the expanding numbers of neonatologists, neonatal nurses, and respiratory therapists have enabled the establishment of nurseries that are capable of providing a high level of care in community hospitals. As a result, some degree of de-regionalization has occurred, with many infants being cared for in state-of-the-art neonatal units, by board-certified neonatologists, closer to home.

Hyperbilirubinemia

In 1942, the link between Rh factor and erythroblastosis fetalis was identified. In 1946, Doctor Louis Diamond described double-volume exchange transfusion through the umbilical vein for treatment of erythroblastosis fetalis.[32] Phototherapy, introduced in United States by Jerold Lucey in the 1960s, became the mainstay of treatment for both preterm and term infants.[33] There was contentious debate about its safety in the early days, but it now is an established and accepted treatment modality. Between 1990-2000, there was a rise in kernicterus cases, attributed to many factors, including early discharge, late preterm birth, and exclusive breast feeding.[34] Newer phototherapy strategies include bili-blankets that can be wrapped around the infant to obviate the need for eye protection.[35] Within the past few years, a new phototherapy light source, using high-intensity light-emitting diodes, has been shown to be at least as effective as conventional phototherapy.[36]

The Micropreemie

The '90s are widely considered the decade of the micropreemie. Successful treatment of these newborns, with gestational ages of 23 to 25 weeks and birth weights of 500 to 750 grams, was made possible by surfactant replacement therapy, improved perinatal management (including prenatal steroids), new technologies for maintaining temperature, precision micro-management of fluid delivery, sophisticated nutritional management, and continued improvement in ventilatory management (e.g., patient-triggered ventilation, high-frequency ventilators, pressure and volume support ventilators, and computerized pulmonary function graphs and trends).

Developmentally Supportive Care

Beginning in the 1970s, there was increasing awareness that the parents and families were important participants in the care provided for preterm infants. Maternal-infant bonding was fully described, and fathers obtained "nonvisitor" status. Heidelise Als introduced the Newborn Individualized Developmental Care and Assessment Program, which supported family-centered, individualized developmental care for premature infants while shortening ventilator days and improving developmental outcomes of NICU graduates. In the late '80s, family-centered care expanded, with sibling visitation policies, support groups, antepartum consultations, parental rooming-in, kangaroo care (skin-to-skin contact between parents and infants), and multidisciplinary developmental committees.

Genetics and the Human Genome

In 1952, James Watson and Francis Crick identified and described the double helical structure of DNA, for which they received the 1962 Nobel Prize in Medicine. In 1959, Dr. Jerome Lejeune, in Paris, described trisomy of chromosome 21 in Down Syndrome. This was followed by extensive investigations of chromosomal syndromes in man, further advanced by techniques for banding and identifying deletions and translocations. In 1963, Dr. Robert Guthrie described a test for detecting phenylketonuria in the newborn period. This was followed by methods for detecting other metabolic, genetic, and endocrinologic diseases by mass neonatal screening, now carried on throughout the United States. In 2000, Drs. Francis S. Collins and J. Craig Venter completed the mapping of the human genome.

2010 and Beyond

Over the past 100 years, there have been remarkable advances in the care of the neonate and dramatic progress in reducing the infant mortality rate. Each year in the U.S., over 500,000 infants are born premature. Infants at the borderline of viability in both weight and gestation are surviving. Over the past century, the outlook for infants with birth weights of 1 kg has changed from 95% mortality to 95% survival. With the enormous progress made in neonatology during the past decade, and with every indication that it will continue, neonatal nurses and physicians should be proud of their accomplishments and look forward to the future. ●

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