

# The Last Fifty Years of Neonatal Surgical Management

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**Neonatal surgical mortality has steadily fallen over the last five decades. Improved survival does not appear to be related to the introduction of new operative procedures. Most of the basic procedures were developed by 1960. Eight developments appear to be responsible: (1) The growth of pediatric surgery resulted in widespread availability of neonatal surgeons and dissemination of knowledge about newborn surgical emergencies. (2) The parallel growth of pediatric anesthesia, beginning in 1946, provided specialized intraoperative management of the neonate. (3) Understanding neonatal physiology is the key to successful management; major advances occurred between 1950 and 1970. (4) New inventions revolutionized patient care; the transistor (1947) made it possible for medical devices to sense, amplify and control physiologic responses and opened the communication and computer age. (5) Neonatal mechanical ventilation had a prohibitive mortality and was seldom utilized; the development of CPAP and a continuous flow ventilator in the 1970s allowed safe ventilatory support. (6) Total parenteral nutrition (1968) prevented starvation that frequently affected infants with major anomalies. (7) The effective treatment of infection began with the clinical use of penicillin (1941); antibiotics have reduced mortality but infants suffering from the septic syndrome have a prohibitive mortality; cytokine, proinflammatory agent research, and the development of anti-inflammatory and blocking agents in the 1980s have not affected mortality. (8) The establishment of newborn intensive care units (1960) provided an environment, equipment, and staff for effective physiologic management. *Am J Surg.* 2000;180:345-352. © 2000 by Excerpta Medica, Inc.**

In 1949 the overall mortality of neonatal surgery was 72%, leading Peter Rickham<sup>1</sup> to state that “except in the hands of a very few, very expert surgeons, operating on a small number of highly selected cases, the mortality

for major operative procedures was forbiddingly high.” Over the last 6 decades there has been a striking reduction in mortality. A series of reports<sup>2</sup> from the University of Michigan describes the experience with esophageal atresia and tracheoesophageal fistula from 1935 to 1985. Cameron Haight<sup>3</sup> performed the first successful primary repair in 1941. From 1935 to 1950 operative mortality was 52% and long-term survival, 35%. By 1966 mortality had fallen significantly to 24% and long-term survival had improved to 65%.<sup>4</sup> Over the next 10 years there was a drop in operative mortality to 6% and a high late survival rate of 77%.<sup>5</sup> Currently, overall survival rates vary between 85% and 95%.<sup>6</sup> Manning et al,<sup>7</sup> discussing the Michigan experience, observed that in the last half century esophageal atresia has been transformed from an anomaly with 100% mortality to one with an expected survival rate exceeding 80%. The authors stated that the improvement was only in part the result of improved operative technique but “more important due to the perioperative management of the high risk neonate” (Figure 1).

There has been a similar decrease in mortality for gastrochisis. When Moore and Stokes<sup>8</sup> established the present-day classification criteria in 1953, the mortality was 100%. From 1960 to 1970, mortality remained high at 64%. By 1975 mortality had fallen to 31%. Cooney<sup>9</sup> reported a 91% survival rate from 1982 to 1992. Ninety-seven percent of the infants were managed by primary closure, suggesting that the introduction of staged closure by the silo technique in 1967 (a modification of Schuster's technique) was not the primary factor in the low mortality rate.<sup>9</sup>

A 50-year review of treatment of thoracic and abdominal abnormalities suggests that the almost universal improvement in survival is not due to new or improved surgical techniques. Most of the basic surgical procedures were in use by the 1950s. Eight medical and industrial developments appear to be primarily responsible: (1) growth of pediatric surgery, (2) growth of pediatric anesthesia, (3) advances in neonatal physiology, (4) establishment of the neonatal intensive care unit (NICU), (5) invention of the transistor, (6) advances in airway management and mechanical ventilation, (7) introduction of total parenteral nutrition (TPN), and (8) discovery of antibiotics (Table I).

## GROWTH OF PEDIATRIC SURGERY

Seventy-one years ago, when William Ladd was appointed surgeon-in-chief of Boston Children's Hospital, there were only two other full-time pediatric surgeons and no training programs. Unless an infant with a major surgical condition was fortunate enough to be born at or near one of the medical centers that had a pediatric surgeon he or she had little chance of receiving effective treatment. The increased number and distribution of trained pediatric

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Manuscript submitted June 19, 2000, and accepted in revised form August 7, 2000.

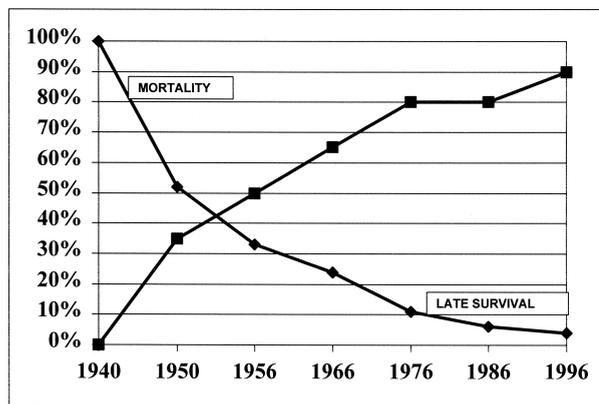


Figure 1. Trends in mortality from surgery for esophageal atresia.

surgeons has now made skilled surgical treatment available to almost every infant. Boston Children's Hospital was the principal pediatric surgical training institution during the 1940s and 1950s. Ladd and his successor Robert Gross trained or directly influenced the majority of pediatric surgeons who went on to develop pediatric surgical training programs. Formal approval of training programs began in 1952. A committee of the Surgical Section of the American Academy of Pediatrics (AAP) approved 11 programs. Certification by the American Board of Surgery occurred in 1973 and program review was taken over by the Residency Review Committee. From 1977 to 1978, 15 pediatric surgical training programs were approved. Today there are 32 programs and approximately 30 new graduates enter pediatric surgical practice each year.<sup>10</sup> The average resident performs 870 operations during his or her 2 years of training. Ninety of the operations are performed on neonates, including 9 repairs of esophageal atresia and tracheoesophageal fistula and 14 closures of abdominal wall defects (personal communication, Residency Review Committee, October 1996). Currently, there are 631 practicing pediatric surgeons. Only three states—Idaho, North Dakota, and Wyoming—do not have pediatric surgeons but their population is small and widely distributed.<sup>11</sup> The current status of pediatric surgery is summarized in Table II.

Fifty years ago major congenital anomalies were frequently diagnosed late and stabilization and initial management of babies were inadequate. Infants were transferred to a surgical facility in extremely poor condition contributing to the high mortality. As pediatric surgeons began practicing in children's hospitals, university medical centers, and urban and community hospitals, they took on the role of missionaries spreading the word on early diagnosis and effective treatment of newborn surgical conditions. Locally, lectures were given at pediatric conferences, grand rounds, medical student classes, and medical society meetings. Nationally, information was disseminated through articles, textbook chapters, postgraduate courses, and presentations at national meetings.

## PEDIATRIC ANESTHESIA

No matter how skillful and experienced the pediatric surgeon, safe conduct of the newborn patients through the perioperative period requires an equally competent pediatric anesthesiologist. Multiple studies have shown that an-

TABLE I

### Factors Improving Survival in Neonatal Surgery

- Growth of pediatric surgery
- Growth of pediatric anesthesia
- Improved understanding of newborn physiology
- Technological advances allowing improved monitoring
- Advances in airway management
- The development of total parenteral nutrition
- The advent of effective antibiotics
- The establishment of neonatal intensive care units

TABLE II

### The Current Status of Pediatric Surgery

Residency	Practicing Surgeons
Programs: 32	In community: 661
Graduates: 30 per year	Operations: 456 per year
Operations: 870 per 2 years	States: 47
Newborn operations: 90 per 2 years	

esthesia-related mortality has been disproportionately high in the infants group. Rackow et al<sup>12</sup> reported significantly higher operative mortality during the first year of life. The incidence of cardiac arrest was 1 in 525 cases. The Baltimore Anesthesia Study Commission found that 20% of pediatric anesthesia deaths occurred in the first week of life.<sup>13</sup> A prospective survey of 40,240 pediatric anesthetics conducted in France found that anesthetic deaths and the risk of serious complications were significantly higher in infants and children compared with adults, 0.5 per 100 versus 43 per 1,000.<sup>14</sup> Keenan et al<sup>15</sup> found a higher frequency of cardiac arrests when nonpediatric anesthesiologists delivered anesthesia to infants. The National Confidential Inquiry into Perioperative Deaths for Pediatric Anesthesia<sup>16</sup> conducted in England found a higher incidence of anesthetic mortality and morbidity when anesthesiologists who do not spend "a substantial part of their professional time with children" administered anesthesia. The Commission of Professional Liability of the American Society of Anesthesiology compared pediatric and adult closed malpractice claims.<sup>17</sup> Respiratory complications and mortality were greater in the pediatric claims. The Commission found that adequate monitoring of the patient could have prevented 89% of the pediatric claims.

Pediatric anesthesia as a subspecialty had its origin in the 1930s. Robson, as the first full-time chief of anesthesia at Toronto Hospital for Sick Children, first described techniques specifically devised for children. Ayre introduced the "T" piece for pediatric endotracheal anesthesia. Leigh and Belton wrote *Pediatric Anesthesia*, the first book in the new subspecialty.

Pediatric anesthesia as a recognized subspecialty was established during the period from 1946 to 1966. Robert M. Smith became the director of anesthesia at the Boston Children's Hospital in 1946. He made many contributions to the physiology of neonatal anesthesia and utilized endotracheal anesthesia and muscle relaxants. Dr. Smith trained future leaders in pediatric anesthesia and wrote the first truly comprehensive textbook of pediatric anesthesia.

In 1966 the Pediatric Anesthesia Section of the AAP was established. The Society of Pediatric Anesthesia was founded in 1986.<sup>18</sup>

Today pediatric anesthesia residency programs are certified by the Accreditation Council for Graduate Medical Education and the American Board of Anesthesia. Forty-nine fellowship programs graduate approximately 100 fellows annually. The Society for Pediatric Anesthesia has approximately 1,600 members, the Anesthesia Section of AAP, approximately 200 members (personal communication, Francis X. McGowan, February 10, 2000). At present no certification process exists for pediatric anesthesia.

## NEONATAL PHYSIOLOGY

There are no standard newborn surgical patients, and the most constant feature of neonatal physiology is change. The surgeon must have a management system that permits individualization and flexibility. This requires basic knowledge of the physiologic and pathophysiologic factors that affect the newborn patient. During the perinatal period, rapid and profound physiologic changes enable the infant to make the successful passage from intrauterine to extrauterine life. All babies must complete these transitional tasks. However, if the infant is born before term, fetal tasks normally accomplished in the final weeks of gestation are unfinished. To ensure survival, the preterm infant has the added burden of quickly completing the fetal tasks as well. Added to these obligatory burdens, the newborn surgical patient must respond to the pathophysiology of a life-threatening surgical condition.

Over the last 5 decades great strides were made in understanding the physiology and pathophysiology of the perinatal period. This new knowledge was disseminated through Clement Smith's text, *The Physiology of the Newborn Infant*,<sup>19</sup> first published in 1954 and Dawes' book *Fetal and Neonatal Physiology*<sup>20</sup> published in 1968. Several major advances will be briefly reviewed.

In 1900 Budin<sup>21</sup> reported an increased mortality rate in premature infants with low body temperature. In 1958, Silverman et al<sup>22</sup> demonstrated that survival of premature infants was directly related to the ambient temperature the infant was exposed to rather than to body temperature. Bruck<sup>23</sup> 3 years later reported that term and premature infants are thermogenically active. To maintain a constant core temperature, infants exposed to a cold environment increase metabolic activity and heat production without shivering. Heat is produced at a high energy and oxygen costs to the newborn. Hammarlund and associates<sup>24</sup> in a series of studies of evaporative water loss beginning in 1977 clarified the relationship between heat and water loss and gestational age, relative humidity, and environmental conditions.

The pioneering studies by Friis-Hansen et al<sup>25</sup> of body water compartments in the fetus and infant beginning in 1954 form the basis of much of our present knowledge of prenatal and postnatal changes in body fluid distribution and water requirements of premature and term infants. Clinical studies by Lorenz et al<sup>26</sup> demonstrated that postnatal reduction in extracellular fluid volume is of high physiologic priority and is achieved by changes in water and sodium excretion. Stevenson<sup>27</sup> in 1977 and Bell and associates<sup>28</sup> in 1990 demonstrated the deleterious effect of

TABLE III

### Remaining Obstacles in Neonatal Care

Unable to prevent prematurity
Uncorrectable congenital anatomic abnormalities (heart, lung, kidney, central nervous system)
Inborn errors of metabolism
Persistent high mortality from sepsis

fluid overload. Aperia et al,<sup>29</sup> Engle and Arant,<sup>30</sup> and Sulyok et al<sup>31</sup> clarified perinatal renal water excretion, sodium and potassium excretion, and the affect of hormones such as aldosterone on the newborn kidney.

The therapeutic use of surfactant is an excellent example of how basic physiologic and pathophysiologic studies can lead to a significant decrease in neonatal mortality. Prattle<sup>32</sup> in 1956 observed that stable foam was found in the airway of rabbits with lung edema. Clements<sup>33</sup> 1 year later described the changing surface tension of lung extracts at varying surface areas. Stimulated by the work of Clements, Avery<sup>34</sup> wondered why infants who died with hyaline membrane disease (HMD) never had foam in their airways, and reasoned they lacked foam because "they did not have surfactant with the capacity to reduce surface tension when surface area was reduced." In 1959 Avery and Mead<sup>34</sup> demonstrated surfactant deficiency in the lung extracts of infants with HMD. According to LaPlace's Law, surface tension is greatest in small alveoli because of their small radius. In the absence of surfactant, the small alveoli collapse and the larger alveoli distend, leading to the characteristic lesion of HMD. Buckingham and Avery<sup>35</sup> later identified type II cells as the site of surfactant synthesis. Over the next 22 years research defined the composition of surfactant and its relationship to pulmonary function. In 1980 Fujiwara and coworkers<sup>36</sup> performed the first successful clinical trial with surfactant replacement. Surfactant treatment for HMD results in improvement in respiratory function, reduced oxygen and airway pressure requirements, decreased air leaks, and increased survival. Since the advent of surfactant therapy in 1980 congenital malformations have replaced HMD as the leading cause of death in preterm infants.

## THE TRANSISTOR

Knowledge of neonatal physiology and pathophysiology alone will not allow the surgeon and anesthesiologist to effectively manage the critically ill newborn patient. Monitoring devices must be available to "read the baby" and detect early, subtle changes so that new therapy can be initiated or existing therapy modified. Small, reliable, relatively inexpensive, and sensitive monitoring devices were not available prior to the invention of the transistor. For a monitoring device to be effective it must contain components that will amplify and switch electronic signals. The vacuum tube, invented in 1906, could perform both of these functions. However, vacuum tubes were expensive, large, gave off too much heat, burned out rapidly, and were inefficient. In 1945 Bell Laboratories assembled a team consisting of Shockley, Brattain, and Bardeen to develop a solid-state semiconductor switch to replace the vacuum tube. They invented the transistor in 1947. The three team

members won the Nobel Prize in 1956. The transistor is arguably the most significant invention of the century. It amplifies electronic signals, acts as a switch, has no moving parts, gives off little heat, and is extremely reliable and inexpensive. A single memory chip in a computer has as many as 6 million transistors measuring 0.35 microns across and costing 0.00005 cents per transistor. Solid-state neonatal monitoring devices include pulse, pressure, respiratory, oxygen, and temperature monitors. The transistor's switching characteristic allows medical devices such as intravenous pumps, radiant warmers, incubators, mechanical ventilators, and extracorporeal membrane oxygenation (ECMO) and dialysis machines to be precisely controlled.

The microchip made by creating and interconnecting transistors to form complex electronic systems on a sliver of silicon has made the computer possible. The transistor can switch an electronic current on and off at lightning-fast speed, an essential function in a digital computer. The transistor's small size and its ability to amplify and switch signals have launched the communication revolution. Pagers, cellular telephones, facsimile machines, and the Internet have made communication mobile and instantaneous.

### AIRWAY MANAGEMENT AND MECHANICAL VENTILATION

Respiratory failure leads to retention of carbon dioxide, progressive hypoxia, and in some patients shunting from left to right across the ductus arteriosus and foramen ovale. Inadequately treated, it invariably progresses to death. There are multiple causes for respiratory insufficiency in the neonatal surgical patient. These include intrinsic lung disease such as pneumonia and HMD, inadequate ventilation due to fatigue, restricted ventilation in patients with distended abdomens or tight abdominal closure, and in the case of congenital diaphragmatic hernia, decreased pulmonary parenchyma. These patients are now successfully managed by prolonged endotracheal intubation and mechanical ventilation. Ventilator management seems almost routine in today's newborn intensive care units. It is shocking to realize that only 30 years ago the use of the endotracheal tube and mechanical ventilation were considered experimental, largely unsuccessful and to be reserved only for moribund infants. In the 1960s medical personnel often considered the ventilator a "death machine."

Although Chaussier<sup>37</sup> described endotracheal intubation in 1806, tracheostomy was the standard method for airway control until the late 1960s. Tracheostomy in the infant, however, had a high complication and mortality rate. Endotracheal tubes were made of rubber and often had "shoulders" (Cole tube). Because of the risk of pressure injury to the glottis and trachea there was considerable reluctance to utilize these tubes. In 1949, Dwyer and coworkers<sup>38</sup> in order to reduce mucosal injury modified plastic tubes to conform to the anatomic shape of the airway. Briggs,<sup>39</sup> in 1950, reported the first prolonged endotracheal intubation with a plastic tube. The patient, an adult, was maintained on mechanical ventilation for 42 days. The physical properties of polyvinyl chloride (PVC), its malleability and plasticity at body temperature and its biologic inertness, appeared to make this material ideal for infant endotracheal tubes. Brandstater<sup>40</sup> was the first to intubate infants and children with PVC endotracheal tubes. Allen and

Stevens,<sup>41</sup> 10 years later, reported their experience with prolonged endotracheal intubation utilizing PVC tubes in 61 infants and children. Following these successful reports prolonged endotracheal and nasotracheal intubation with plastic tubes became the accepted method for airway control in the newborn.

Donald and Lord<sup>42</sup> in 1953 were probably the first to successfully use positive pressure ventilation in the newborn. The significance of their pioneering work seemed to go unrecognized. Over the next 11 years there were only three reports in the world literature of neonatal mechanical ventilation. Of the 18 babies ventilated, only 1 survived.<sup>43</sup> In 1965 Thomas and coworkers<sup>44</sup> reported successful ventilation of a group of infants with severe pulmonary insufficiency. In spite of the encouraging results of Donald and Thomas there was little enthusiasm for utilizing mechanical ventilation except as a last resort. Five years later, Gregory and colleagues<sup>45</sup> reported the use of continuous positive airway pressure (CPAP) for the treatment of HMD; 16 of the 20 patients survived. Kirby<sup>46</sup> and Delomos reasoned that the benefits of CPAP should be incorporated into mechanical ventilation. They designed a pneumatically driven, time-cycled, pressure-limited ventilator that delivered a continuous flow of gas and intermittent mandatory ventilation (IMV) to the patient. The infant was able to take spontaneous breaths between mechanical breaths. Their first ventilator, the Baby Bird I, was introduced in 1971 and proved successful.<sup>46</sup> Other models incorporating Kirby's theoretical breakthrough, a continuous flow of fresh gas to the patient, were quickly introduced. With the invention of the transistor and integrated circuits precise control of inspiratory and expiratory time, rate, positive end expiratory pressure (PEEP) and peak inspiratory pressure (PIP) became possible. Advances in microcircuitry soon made it possible to directly measure tidal volume, compliance and resistance.

### TOTAL PARENTERAL NUTRITION

Dudrick and colleagues<sup>47</sup> began their classic paper, "Long-term total parenteral nutrition with growth, development and positive nitrogen balance," with the following sentence: "The best route for satisfying nutritional requirements is the gastrointestinal tract." Unfortunately, newborn surgical patients often have inadequate gastrointestinal function for prolonged periods. Premature infants, particularly the extremely low birth weight baby and infants maintained on mechanical ventilation, are usually unable to tolerate enteral feedings. Patients with necrotizing enterocolitis, jejunal atresia, and gastroschisis often cannot be fed for periods ranging for 14 to 60 days. Heird and associates<sup>48</sup> estimated that a 1 kg baby has only a 4-day nutritional reserve, and full-term infants may live for no more than 1 month without nutrition. These estimates did not take into consideration the added nutritional demands of the newborn surgical patient. There is little doubt that prior to the development of TPN in 1968, starvation was a major factor in the morbidity and mortality of newborn surgical patients who were unable to be fed.

The development of TPN began in the early 1940s when Rhoads<sup>49</sup> and Starr attempted to achieve nitrogen balance in adult surgical patients. They found three limiting factors: (1) the caloric value of carbohydrate and hydrolyzed

protein was four kilocalories per gram, (2) total fluid intake was limited by the danger of pulmonary edema, and (3) strongly hypertonic solutions caused peripheral vein thrombosis. Several years later they successfully infused concentrated solutions in dogs through catheters placed in large veins. In 1949 they placed vena cava catheters in terminal cancer patients and found extensive clot formation on the catheters. Rhoads stated that the clots were "sufficiently alarming to frighten us away from this approach." It was not until 1966 that Dudrick began his experiments on beagle puppies infusing concentrated glucose and protein hydrolysate solutions into the central venous system. He found that puppies receiving TPN matched their littermates in growth and development. Dudrick and his coworkers then utilized the infraclavicular approach to subclavian vein cannulation to administer concentrated solutions into adult patients with gastrointestinal fistulae.<sup>49</sup> In the classic paper by Dudrick et al<sup>47</sup> published in 1968, they described these patients and an infant with jejunal ileal atresia who was maintained on TPN for more than 22 months. The infant doubled her body weight in 75 days and had an increased head circumference.

By 1970 TPN had been used successfully on a large number of pediatric surgical patients. It became apparent that the newborn infant, particularly the premature baby, had special nutritional requirements that were not provided for in adult formulas. As a result TPN formulas were modified. In addition to the classic essential amino acids there are three or four additional essential amino acids unique to the newborn. They are cysteine, taurine, tyrosine, and perhaps proline. TPN solutions including crystalline amino acids essential for infants are now available. The development of osteopenia and pathologic fractures in infants receiving TPN led to the development of formulas high in calcium and phosphorus.

## THE DISCOVERY OF ANTIBIOTICS

Neonates, particularly extremely low birth weight infants, have increased susceptibility to bacterial infection. Their neutrophil storage pool is diminished. Neutrophil and monocyte chemotaxis is abnormal, and cytokine and complement production is decreased. Natural killer cell and B cell function are immature. There are reduced levels of type-specific immunoglobulin G (IgG), secretory IgG, IgA, and IgM.<sup>50</sup> Because of their compromised host defense, all newborn infants are at risk of developing infection. However, the surgical neonate has the added burdens of invasive procedures and exposure to pathogenic bacteria in the hospital environment. Although antibiotics have decreased deaths due to infection, sepsis is still a significant cause of death in the newborn surgical patient. Often, sepsis is the final common pathway to death in a critically ill neonatal patient who suffers from a postoperative complication or requires long-term mechanical ventilation and TPN. Current attempts at immunotherapy and blocking the inflammatory cascade have been unsuccessful.<sup>51</sup> Antibiotics and supportive care remain the mainstay of treatment.

The antibiotics era had its origin in 1929 with the discovery of penicillin by Alexander Fleming.<sup>53</sup> He found that bacterial lysis of *Staphylococcus* was produced by the

mold *Penicillium*. Crude extracts of the mold had antibacterial properties. Fleming's discovery raised little interest. In 1935, Domagk<sup>53</sup> developed the first clinically effective antibacterial drug, protosil, that is hydrolyzed in vivo to an active compound, sulfanilamide. The first patient treated was a child, his daughter, who was near death from a streptococcal infection. She made a dramatic recovery. Domagk was awarded the Nobel Prize in 1939. In 1940, Chain and colleagues<sup>54</sup> isolated penicillin from Fleming's mold and made production on an industrial scale possible. Fleming, Florey, and Chain won the Nobel Prize in 1945. Charles Fletcher was the first physician to use penicillin clinically in 1941.<sup>55</sup>

The clinical use of penicillin began the antibiotics era. Its phenomenal success led to the search for other antibiotic-producing microorganisms. Schatz, Bugie, and Waksman<sup>56</sup> discovered streptomycin from the soil organism actinomycete. Actinomycetes, especially *Streptomyces* species, have yielded a large number of the antibiotics used in clinical medicine including amphotericin B, erythromycin, neomycin, tetracycline, and vancomycin.

Antibiotic-directed therapy is very effective in combating established infection when the organism and its antibiotic sensitivity are known. Empiric antibiotic therapy may be life-saving when a serious infection is suspected but not proven. The presumed organism and site of infection, the clinical status, and consideration of the risks and benefits to the patient determine the therapy.

An attempt was made to use antibiotics prophylactically soon after their discovery. Clinical trials in the 1950s reported either no benefit or higher infection rates with the antibiotic prophylaxis.<sup>57</sup> Burke<sup>58</sup> in a series of animal experiments demonstrated the critical dependence of prophylactic efficacy on timing of administration of antibiotics. Polk and Lopez-Majoy<sup>59</sup> conducted a double-blind prospective randomized trial utilizing cephaloridine given preoperatively and intraoperatively. The infection rate was 30% in the control group and 7% in the treatment group. Subsequent research demonstrated that prophylaxis was dependent on the presence of peak tissue antibiotic levels at the time the tissue concentration of bacterial are high. Unfortunately there are no parallel studies of antibiotic prophylaxis in the newborn surgical patient. However, most pediatric surgeons administer preoperative antibiotics on the basis of the adult studies.

Within 4 years of the introduction of penicillin, the dark side of antibiotics, bacteria resistance, was first detected. The first penicillin-resistant organism was *Staphylococcus aureus* rapidly followed by penicillin-resistant *Streptococcus pneumoniae*, *Gonococcus* organisms, and *Enterococcus* organisms. As bacteria resistance increased, antibiotics such as vancomycin became drugs of last resort. However, even these drugs proved vulnerable. Vancomycin-resistant enterococci (VRE) were first reported in England and France in 1987. They appeared in one American hospital in 1989. By 1991, 38 American hospitals had isolated VRE.<sup>60</sup> Microbiologists fear that a transfer of vancomycin-resistant genes from *Enterococcus* to other organisms such as *Staphylococcus* will eventually occur. Most microbiologists believe antibiotic resistance is inevitable but can be slowed by the judicious use of antibiotics, improvement in public

health measures, and development of new agents by the drug industry.

### THE NEWBORN INTENSIVE CARE UNIT

A growing knowledge of neonatal physiology and rapidly advancing technology made it apparent that special units staffed and equipped to meet the unique needs of neonatal medical and surgical patient were needed. The origin of neonatal intensive care units can be traced to the establishment of premature nurseries. In 1934, the Chicago Department of Health developed a city plan to expedite early transport of preterm infants to premature infant stations at two hospitals.<sup>61</sup> The Colorado Premature Program began in 1947.<sup>62</sup> Premature centers became common throughout the United States but admission was strictly limited to low birth weight infants. Term infants with medical and surgical illnesses and babies with infection were managed in separate areas for fear of cross-infection.

In 1949 the Liverpool Regional Hospital Board investigated the fate of infants born with major congenital malformations. They found that surgical mortality was 72%. Three factors were believed to be responsible for the high mortality: failure or delay in diagnosis, failure to concentrate critically ill infants in one hospital, and failure to concentrate them in one ward. The Board recommended that all infants born with life-threatening abnormalities should be admitted to one unit and cared for by a team of pediatric surgeons, anesthesiologist, pediatricians, and specially trained nurses. As a result, the first neonatal surgical unit was established by Peter Rickham at the Alder Hey Children's Hospital in 1953.<sup>1</sup>

The first neonatal intensive care unit (NICU) in the United States was established at Grace New Haven Hospital in 1960. Louis Gluck reasoned that segregation of full-term, premature, and infected infants in different parts of the hospital resulted in dispersion of trained personnel and equipment. Critically ill infants could be managed more effectively in a single unit that enabled experienced personnel and special equipment to be concentrated in one area. The risk of cross-contamination could be reduced by hand washing, and bathing infants with antibacterial soaps and isolating them in incubators.<sup>63</sup>

The successful development of mechanical ventilators stimulated the growth of NICUs in the 1970s. Because NICUs required specialized personnel and facilities beyond those available at most hospitals, national efforts were made to regionalize their locations. Regionalization was considered the interhospital transfer of newborn patients from community hospitals to a medical center. There were more than 125 NICUs in North America primarily at major university medical centers by 1975. In 1994, 500 hospitals reported having NICUs, for a total of 12,000 NICU beds or 3 per 1,000 live births.<sup>64</sup>

With the success of regional NICUs, the concept of regional perinatal centers was introduced. The goal was to further improve neonatal outcome by earlier identification of high-risk pregnancies and referral to tertiary perinatal centers before delivery. By 1978 perinatal centers were operating in 28 states. A Robert Wood Foundation demonstration program in 1985 concluded that the rapid growth of regional perinatal centers closely correlated with the decline in neonatal mortality.<sup>65</sup>

The increase in the number of neonatologists and pediatric surgeons, the large number of NICUs, new technology, the high cost of neonatal care, competition, and the advent of managed care have recently resulted in a reversal in the general trend toward regionalization. This shift has been called deregionalization. More infants are receiving intensive care in smaller nonuniversity hospitals with level II and III nurseries. Increased competition by hospitals for well-insured obstetrical patients has spurred a rapid proliferation of NICUs in suburban areas. Managed care programs influence access to NICU services by their ability to channel obstetrical and newborn patients to specific providers and facilities. It is feared that managed care organizations will direct obstetrical and neonatal care to lower level hospitals because of their significantly lower operating costs. Deregionalization appears to have had an effect on pediatric surgical practice. Gieger and coworkers found in a recent survey that 50% of recently graduated pediatric surgeons cover an average of 2.8 hospitals and 27% cover 4 to 10 hospitals (personal communication, J.D. Gieger, May 1999). One half of all board-certified pediatric surgeons who have been in practice 10 to 20 years operate in more than one hospital.

The long-term effect of deregionalization is not clear. The concept of "getting the right patient to the right hospital at the right time" has been shown to be effective not only for newborn patients but also for trauma victims. The proliferation of small NICUs raises the question whether small units will have a sufficient number of patients to maintain the skill of the providers. The justification for a hospital to have a NICU should be based solely on quality of care, not on economic or social factors. To preserve quality, it must be measured and constantly monitored. Unfortunately, no such system is presently in place in the United States.

### COMMENT

The principal causes of neonatal surgical mortality are now complications of premature, uncorrectable abnormalities of the heart, lungs, kidney, and central nervous system, inborn errors of metabolism, and infection. There has been a significant reduction in premature deaths, particularly in infants below 1,000 g. Unfortunately, there has been no progress in preventing prematurity. Prevention of prematurity alone would have a profound effect on all newborn mortality. At present it is not possible to predict what the effect of improved prenatal diagnosis of congenital abnormalities will have. Three approaches are available or being developed when the diagnosis of malformation is made before birth. Abortion is an option fraught with ethical, philosophic, and religious controversy. Fetal surgery is still in its pioneering stage as a practical method of treating anomalies. A few centers have had success with intrauterine correction of carefully selected abnormalities. Gene therapy holds great promise but is still at the experimental stages. New antibiotics are rapidly being developed but resistance is a biologic phenomenon that will not be prevented by new drugs. Immunotherapy and blocking the inflammatory cascade has not proven effective in treating the septic syndrome. However, considerable progress has been made in understanding the inflammatory process and

may bring us closer to an effective treatment for overwhelming sepsis and multiple organ failure in the future.

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