Chapter 15

Assisted Ventilation in Newborn Infants

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The first recorded reference to assisted ventilation is in the second Book of Kings 4:32-35, "And when Elisha was come into the house, behold the child was dead . . . and he went up and lay upon the child and put his mouth upon his mouth, and his eyes upon his eyes, and his hands upon his hands: and he stretched himself upon the child; and the flesh of the child waxed warm."[1] I am indebted to Dr. Virginia Apgar for this reference, who said, "They didn't record that he blew, but he did!" Although this instance of mouth-to-mouth resuscitation was used in a small child and not a newborn infant, undoubtedly this form of short term assisted ventilation has been used to resuscitate newborn infants since ancient times.

In the mid 16th Century, the Flemish anatomist and physician, Andreas Vesalius, first applied artificial respiration to animals.[2] It had become evident to the ingenious anatomist that it was only necessary now and then to blow a little air into the lung of an animal with opened thorax, to keep it alive for some time. However, his experiment, using a rush tube placed in the windpipe, through which air must be blown, was only intended to demonstrate the movements of the heart with the chest opened. It was for the physiologist, Robert Hooke, in 1667,[3] to describe first the prolonged preservation of life in an open-chested dog by artificial ventilation, the dog being allowed to "die" and be revived repeatedly by continually inflating the lungs with bellows attached to the trachea. Hooke recognized that "bare motion of the lungs without fresh air contributes nothing to the life of the animal, he being found to survive as
well, when they were not mov'd, as when they were; so it was not the subsiding or movelessness of the lungs that was the immediate cause of death, or the stopping of the circulation of the blood through the lungs, but the want of a sufficient supply of fresh air."

Moving to the 18th Century, we see a crude endotracheal tube and hand-operated bellows, for use in infants, described before the Royal Humane Society in 1780. It is doubtful, however, if this apparatus was very widely used.

In 1889, Alexander Graham Bell designed and built a body-type respirator for use in newborn infants. I am indebted to Dr. Leo Stern for unearthing this valuable historical information.[4] Bell expressed his views with respect to its use as follows: "Many children, especially those prematurely born, die from inability to expand their lungs sufficiently when they take their first breath. I have no doubt that in many of those cases, lives could be saved by starting the respiration artificially by means of apparatus operating in the manner described above." Following what appear to be encouraging results in small animals, he presented his views to a meeting of the American Association for the Advancement of Science held in Montreal but this was met with little enthusiasm, and the apparatus probably was never used on human infants.

The tank-type respirator designed by Drinker in 1929 was used successfully in 21 of 35 newborn infants for resuscitation of asphyxia at birth, by Murphy and his colleagues in 1931.[5] Most of the unsuccessful attempts were in premature babies.

In 1950 Dr. Alan Bloxsom invented the Bloxsom air-lock for newborn resuscitation, a box in which the infant was enclosed; it was filled with oxygen and the pressure inside was slowly cycled.[6] Three premature were successfully treated in the air-lock for as long as 12 days but its primary use was in resuscitation of asphyxiated newborns. No controlled trials or measurements were possible, and its questionable success may have been due to the prevention of physician or nurse mis-handling of the asphyxiated infant who was locked away from their interference.

Although many unpublished trials of home-made apparatus designed to assist ventilation of newborn infants with apnea or severe respiratory distress undoubtedly had occurred during the 60 years following Bell's respirator, the next scientific explorations of such equipment appear to be those of Ian Donald and his collaborators. In a series of articles published in 1952, 1953 and 1954, they described early models of the servo-controlled respirator, designed to augment ventilation of newborn infants both acutely, and over a period of time.[7,8,9] An early version of this respirator appears in a 1953 publication which describes 3 and possibly 4 survivors attributed to its use. In 1954 the "emergency positive pressure patient cycled respirator" was described, designed to "cover delays in preparing the servo respirator or to meet respiratory emergencies, and it could be used at once via a mask, with the child still in its cot or incubator." This apparatus became known as "the puffer." Success with both respirators was encouraging, and by 1954, 11 infants of 28 treated with the servo respirator had survived; and of 21 infants treated with the "puffer" alone, 9 had survived.
During this medical era poliomyelitis was epidemic, and respiratory muscle weakness and bulbar respiratory failure was often successfully treated with tank-type negative pressure ventilators of the Drinker design or by manually delivered continuous positive pressure through an endotracheal tube or tracheostomy. Many polio patients were weaned to a negative pressure chest cuirass or to a foot-tilt rocking bed as they improved. In the mid 1950's, we, and undoubtedly many others, used home-designed rocking beds in a largely futile attempt to artificially ventilate small apneic infants. Ours was triggered by a truck windshield wiper, and occasionally it served to tide over an infant with recurrent apnea and minimal lung disease.

In 1956 the Monaghen Company, a manufacturer of polio respirator equipment, held a meeting in Ann Arbor, Michigan asking about the need and desirability for development of an infant-sized negative pressure tanktype respirator. I was privileged to attend this meeting where Jim Wilson, among others, described his largely unsuccessful attempts at using homebuilt respirators. The answer to the Monaghen Company's question was a qualified "yes," and, subsequently, 4 prototype miniature "iron lungs" were built. One of these was placed in our hospital, but because of our lack of confidence or experience, it was placed in the basement, and remained unused for some time.

By 1957, Professor Donald reported treatment of 151 newborn infants with his successive respirator models, and 50 survived, "a large number of which were under 3 lbs, and even under 2 lbs."[10] Much, but not all, of the application was for brief resuscitation and not for continuous use, and hyaline membrane disease and intraventricular hemorrhage continued to take their toll.

The magnitude of the catastrophic 1952 poliomyelitis epidemic in Copenhagen made a deep impression on medical opinion. Though the mortality in spino-bulbar poliomyelitis had been reduced from 80% at the commencement to 25% with the revolutionary new treatment of tracheostomy and manually-controlled respiration, the manpower required for this success was so large that it occupied 1400 students, almost the whole student body of the medical school. All teaching activities had to be suspended until it was over. A rash of activity occurred throughout Europe and a number of positive pressure, usually volume controlled, ventilators were designed and put into use in Europe, the tank being largely considered obsolete. By 1959, 2 such apparati had been used on newborns, a volume controlled ventilator (the Engstrom respirator) in Sweden, and the East Radcliff pump, also a volume controlled ventilator, in South Africa. Benson, Celander and Haglund reported the successful use of the Engstrom, coupled with neuromuscular block and a tracheostomy in 3 of their first 9 infants with "pulmonary insufficiency of the newborn."[11]

Pat Smythe, also using neuromuscular block and a tracheostomy, reported the successful treatment of 2 of 9 infants with tetanus neonatorum with the modified Radcliff pump; an additional 2 patients, surviving seven weeks, succumbed from problems other than tetanus.[12]

In the summer of 1961, Dr. Jim Sutherland asked us if we would be interested in testing the relative merits of a new negative-pressure infant ventilator, supplied to him by Jack Emerson, with our Monaghan model still residing in the hospital basement. The trial of relative effectiveness would be
done on term, healthy, newborn infants using the non-invasive techniques I had developed for measuring total ventilation, alveolar ventilation and end-tidal PCO$_2$ in newborn infants. Jim and a summer student research fellow spent 2 weeks in Nashville with us measuring the changes in alveolar ventilation and PCO$_2$ which were produced by each ventilator.

The Emerson consisted of a turkey-sized plastic bag over a plastic hood, with clamps to seal around the neck connected at the other end to an intermittently cycled vacuum cleaner pump.

We learned from these trials that we could, in fact, increase alveolar ventilation in normal newborns with both ventilators, but in Jim's it was extremely difficult to maintain body temperature, because of leaks and the lack of a warming device, except for externally applied heat lamps.

Important to any future success, the metabolic problems associated with prematurity, cold stress, starvation and circulatory problems, so frequently associated with ventilatory failure in the newborn, were being recognized and rational treatments designed. Oxygen, long withheld because of the fear of blindness in preemies was recognized to be necessary for survival of critically ill infants with respiratory problems. However, the techniques for measuring blood oxygen, pH and PCO$_2$ levels were still those used in adults, requiring large amounts of blood from small infants for repeated monitoring, and lengthy analysis using the Van Slyke Manometric Machine.

However, continuous temperature probes had been developed, and heart rate monitors and pressure transducers were used in cardiac catheterization laboratories.

Meanwhile, the National Heart Institute had decided to fund a laboratory concerned with the study of the transitional circulation and its relation to neonatal cardiorespiratory disease. Our small research grant was selected to receive a sizable supplement to renovate and equip laboratory space immediately adjacent to our premature nursery. In the Fall of 1961, this laboratory was opened and we began to study infants with respiratory distress with our new tools, using brief introduction of umbilical arterial and venous catheters, as we had learned from Stan James. For the first time, we began transferring infants into our nursery who were born elsewhere, utilizing NIH funds for their study and care. Within a few weeks of opening our laboratory, an infant was born in our hospital with severe hyaline membrane disease. It happened to be the baby of a senior medical student. We thought the infant would surely die, despite oxygen by mask and scalp-vein buffer, which were the extent of our therapeutic armamentarium at that time. We offered to put the baby in our negative-pressure tank-respirator, if the parents were willing. They agreed, and after placing an umbilical venous catheter in the left atrium (we were unable to enter an artery), the baby was sealed in the tank where she remained for five very tiring, but enormously instructive days. She was successfully weaned from her ventilatory assistance and, much to our relief, her umbilical catheter could be removed, and she is now a beautiful 20 year old girl with an I. Q. of 140.

Initial success was important. We had learned how to use an indwelling catheter for monitoring blood
gases and pH, not only during the course of a disease, but also for regulating the use of a ventilator. We used pin electrodes in the intercostal muscles to monitor the EKG on our oscilloscope, a rectal thermistor to regulate the temperature of the tank, and an intraesophageal catheter to reflect intrapleural pressure. "Intensive Care" had arrived!

About the same time, Paul Swyer and Maria Delivoria, in Toronto and H. de V. Heese in Cape Town were modifying the Bird positive pressure respirator used in adults for neonates with hyaline membrane disease, each with some success.

We continued to use the negative tank-type respirator, combined with manually operated positive pressure when necessary and, in 1965, the Air Shields Company developed a more easily managed model. Other types of infant respirators, notably the Bourns volume controlled model, were developed and widely used.

Intensive Care nurseries, almost always in conjunction with active research laboratories, sprang up in almost every major medical center in the 1960's, and much understanding of the underlying processes that lead to the abnormal outcome of pregnancy, labor and delivery, especially in premature infants, was developed, both in America and abroad. Refinements were made on equipment, such as blood gas machines requiring small volumes of blood, ventilators, infant heart rate monitors and heat regulatory mechanisms in incubators.

What may have been of even more importance was the gradual development of the role of the neonatal nurse, who added the "caring intensively" to Nick Nelson's definition of "intensive care." A better monitor has yet to be devised than an alert, intelligent, informed and caring bedside nurse in a Newborn ICU.

Physicians were also educating themselves to think, not small, but appropriately for the premature infant's needs, and they began to call themselves Neonatologists -- one who has not only knowledge, but understanding of the newly born.

It was, however, almost ten years before a real conceptual breakthrough occurred. Gregory, an anesthesiologist, developed a method of delivering constant distending airway pressure to the newborn lung through an endotracheal tube. This system had the possibility of maintaining open terminal airways at end expiration, thereby avoiding atelectasis when surfactant was deficient, and maximizing ventilation-to-perfusion ratios. The risks of prolonged use of high inspired oxygen concentrations and high peak airway pressures were thereby often averted. This concept was added to both positive and negative ventilator use, and was further modified by Bancalari who designed a constant distending negative pressure chest cuirass and by Kattwinkle who developed nasal prongs to avoid the use of an endotracheal tube when a ventilator was not needed. The use of constant distending airway pressure, although often misused, as are many tools, including ventilators, has been an important contribution toward successful management of a wide variety of newborn lung problems.
Ventilators have been successively modified and designed specifically for use on very small infants, and the omission of demand valves and addition of continuous flow gases has allowed their effective use, even on the smallest subjects.

Recently, the experimental development of high frequency oscillation ventilators for newborns shows hope of successful ventilation while avoiding the risks of barotrauma to the airways and air dissection. Extracorporeal Membrane Oxygenators (ECMO) have also occasionally been successfully used in certain types of serious life-threatening disorders of the newborn, such as massive meconium aspiration syndrome.

The ultimate method for safe and effective artificial ventilation of the newborn lung, especially when it is diseased or anatomically extremely immature, has yet to be devised. However, I am sure, as long as serious sequelaes result from our imperfect attempts, we shall continue to seek better ways, not only to salvage lives but also to do so without harm. "Primum non nocare."

REFERENCES


3. Philosophical Transactions, giving some account of the present undertakings, studies, and labours of the ingenious in many considerable parts of the world. Vol. I for Anno 1665 and 1666, p. 539.


