Chapter 2
Negative Pressure Noninvasive Ventilation (NPNIV): History, Rationale, and Application

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Dedication

This chapter is dedicated to Jack Haven Emerson (1906–1997), who designed the most effective, widely used noninvasive negative pressure ventilator, the iron lung, in the first half of the twentieth century, and to Dr. Dudley F. Rochester, my mentor, who did so much of the research to begin our understanding of the basis of their physiologic effectiveness, and to my patients who have taught me more than they can know.

Introduction

Man has recognized the vital role of breathing since antiquity, beginning with archeological findings depicting inhalation therapy using herbs, oils, and other substances since 6000 BC [1]. Man has taken the automaticity of breathing for granted, expecting its adequacy for all activities whether awake or asleep. Dickinson W. Richards, MD, Nobel Laureate, said in 1962: "Breathing is that essential physiologic function that is straddled between the conscious & the unconscious and subject to both" [2]. The understanding of the components of this critical physiologic function that starts at birth, and must be continuous and widely adaptable to support all levels of physical, metabolic, and functional needs, has evolved slowly over the millennia by many brilliant scientists from a combination of keen observation, imagination,

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daring experimentation, trial and error, and necessity, while overcoming dogma, religious inhibitions and politics. It is this gradual chronologic process, still evolving, which guides what we do for patients today.

Breathing is an automatic, unconscious act until it is not sufficient—when symptoms of breathlessness and distress develop, or when life itself is threatened. All normal breathing is by negative pressure, accomplished by the development of negative intrathoracic, or below atmospheric pressure, when the inspiratory muscles contract, predominantly through diaphragmatic descent, distending the rib cage, thus allowing the pressure gradient from the higher atmospheric pressure to cause air to flow through open airways into the elastic lungs and chest wall. Simply relaxing these muscles allows for recoil of the lungs and chest wall to effect exhalation until higher workloads require the recruitment of additional muscles. It took hundreds of years to learn to recognize and understand this.

The slow and gradually accelerating evolution of knowledge regarding the vital connection of breathing to life and how its loss needed to be addressed was recognized as early as 3150 BC. To appreciate this process, it will be necessary to address its evolution from managing primarily respiratory emergencies with both "invasive" and "noninvasive" positive pressure ventilation (NIPPV) to the development and successful use of negative pressure noninvasive ventilation (NPNIV), enhanced by the polio epidemics, by ingenious designs, by better communications, by the availability of reliable power, by the necessary financial support, and from improved systems of care whose highlights will be chronologically described below.

The History of Ventilatory Failure and the Beginnings of Assisted Ventilation

An unknown philosopher stated "The lungs are the center of the universe and the seat of the soul [3]". The earliest reference for attempts to restore breathing was about 3150 BC when Egyptian physicians tried to save drowned victims by placing a reed in the throat and blowing into the lungs [4]. The Chinese in 2000 BC described *lien ch'i*, as a transfer of inspired air into the "soul" (life): mouth positive pressure. In the Old Testament book of Genesis 2:7, written between 1450 and 1410 B.C. by Moses, God is described "as breathing life into his dust created man by breathing into his nostrils" & thus "man became a living thing" and "when his breath was taken, he died & returned to dust." Further, it was written in 2 Kings 4: 34–35 that the Prophet Elisha "…went up…placed his mouth upon his mouth…and again…the child sneezed seven times…opened his eyes [5]."

There were long hiatuses in recorded history with sporadic descriptions on the essence of breathing and/or its restoration. In 570 BC a Greek physician, Anaximenes, emphasized that the essence of all life was *"pneuma"* or breath [6]. Hippocrates (460−375 BC) wrote the first directions for intubation in "Treatise on Air" by placing a "cannula into the trachea along the jaw bone so that air can be drawn into the lungs [7]." However, it was Claudius Galen, a physician, in 128 AD, who followed on this by experimentation by breathing into a hollow reed placed in the throats of many different animals, and noted that their chests expanded. Human experimentation was strictly, legally forbidden. In 160 AD, as the physician to the gladiators in the arena, Galen was the first to conclude that the head controlled breathing when he observed that those gladiators who had their heads cut off at the neck ceased breathing immediately and those injured below the neck continued to breathe [8]. His scientific studies through careful dissection in animals became the basis, the "Bible," for the practice of medicine. He assumed that the anatomy of pigs, apes, dogs, and oxen were the same as in humans. His doctrines were considered so sacrosanct and inviolate by the clergy that their contradiction was punishable by death. This greatly inhibited studies in humans and severely limited the growth of knowledge about breathing in man.

It took more than another thousand years, in 1543, for Andreas Vesalius, a Dutch physician, to dare to do studies in humans. He was a meticulous physician who secretly performed detailed human dissections, despite the church's prohibitions. This massive work led to his appointment as Professor of Anatomy in Padua at age 23. He was the first to successfully resuscitate a drowning victim by "placing a tube in his throat & bringing him back to life with a return of a pulse." Previous experimenters found in opening the chest that this caused the lungs to collapse, and was always associated with cessation of heart beats and death. He observed when he opened the chest of animals that "when the lung …collapsed, the beat of the heart and arteries appear wavy, creepy, twisting; but when the lung is inflated at intervals, the motion of the heart and arteries …" resumed, the first description of ventricular fibrillation restored to a regular rhythm with the use of intermittent positive pressure breathing (IPPB). He did this by placing a tube through an "opening" in the trachea of a pig through which he could blow which caused the lung to "rise" and "restore the animal." This concept of positive pressure breathing lasts to the 21st century, intermittently abandoned, then resurrected. Vesalius stole the body of a criminal, boiled it, and thus acquired the first complete human skeleton. When he was not yet 29-years old, his seven volume book, *de Humani Corporis Fabrica*, printed in 1555, beautifully illustrated by a pupil of Titan, detailed correct human anatomy for the first time, contradicting Galen's work. This was considered heretical, creating professional and theological storms. The story is told that Vesalius performed an autopsy on a Spanish nobleman and observed that his "heart started to beat again" after he inflated his lungs through a tube placed into the trachea. This, along with his contradicting work, earned him the designation of heretic. Since the Pope had decreed that a heretic was guilty of a form of "spiritual treason" when a system of fines and exile was replaced by execution since 1200, a declared heretic was in mortal danger.It was only because of the wealth of his father and his connections to Charles V, Emperor of Spain and the Netherlands, that he was condemned to a "pilgrimage to the Holy Land" rather than execution. It was on this pilgrimage that his brilliant and audacious career ended in his premature death in a ship wreck off Greece on the Ionian island of Zante. Since the clergy were often the only educated, literate people throughout the middle-ages, their dictums were law. Anyone could be accused of being a traitor who was then summoned before a tribunal, "per inquisitionem," where there was little recourse for self-defense, and sentencing decided. This period, The Inquisition, lasted 800 years, from 1000 to 1800, when countless people were executed, including Joan of Arc, who was executed after torture for heresy in 1431 [9]. This prolonged period dominated by fanatical ignorance with the mortal threat it imposed benefited the clergy and the monarchy both politically and financially and dramatically impeded medical progress [9].

The first recorded attempt of "mechanical" ventilation was in 1550, attributed to Paracelsus, when he used a fire bellows as a device connected to a tube inserted in the patient's mouth to blow air into the lungs to assist breathing, an "IPPB [10]."

Although first mentioned in the bible in Genesis 35:17, midwives have been practicing neonatal resuscitation of apneic infants by mouth-to-mouth breathing since the 15th century although no systematic data were reported as to consequences or the rate of success [11, 12].

Without an efficient means for information dissemination or a common language, it took more than another 100 years for Robert Hooke, an English "Leonardo" in 1667, to apply Paracelsus's IPPB idea experimentally by attaching a pump he made for his mentor, Robert Boyle, to a cut in the trachea of dogs with open thoraces to "blow air in regularly and intermittently to keep them alive," noting the difference in color between venous and arterial blood [10]. Excepting for Vesalius's work, prior to this, opening the chest always resulted in collapse of the lungs, cardiac standstill, and death.

It was John Mayow, an English physician-scientist in 1673, who first conceived and built an external negative pressure ventilator, which consisted of a unit with a bellows and a bladder to pull and expel air, suggesting that this mimicked the action of the inspiratory muscles [13]. While he was also the first to show the necessity of oxygen for life, preceding Priestley, he did not name it. His work remained obscure until 1832.

In Scotland in 1732, W.A. Tossach, a surgeon, reported the miraculous rescue of a suffocated coal-pit miner from the pit when he performed mouth-to-mouth breathing: "I… blowed my breath as hard as I could raising his chest fully" when the heart restarted, after noting that he had to pinch the nostrils to prevent the air from escaping. One hour later the miner began to move and yawn and was said to have walked home after 4 h. His duration of death "was between half an hour and three quarters." Details of the miner's age and subsequent health were not given [14].

It took another 12 years for John Fothergill, in 1744, to successfully revive a drowning victim choosing mouth-to-mouth resuscitation, because he feared lung overdistension with use of the bellows. He also believed that warm rather than cold air would be "more beneficial" that led to its promotion as effective noninvasive positive pressure resuscitation. He founded the British Humane Society in 1750 to promote this method to save lives. A common belief at that time was that a drowned person was already dead, that the lungs were already collapsed and thus not capable of responding to resuscitation. John Fothergill showed that this was not true. Another fear that worked against resuscitation efforts was that a victim brought to a home may obligate the owner for the burial expenses [15].

Twenty-three years later, in 1767, due to the continued frequency of drowning victims in the Netherland waterways, the Society for the Rescue of Drowned Persons, or The Humane Society, was formed to rescue such persons. The first protocols were expounded which included keeping the victims warm, using mouth-to-mouth breathing and the addition of hand compression of the chest or chest and abdomen to "assist expiration" for resuscitation. This inadvertently added cardiac compression to the rescue effort although no records were published as to the rate of its success [16].

Lack of such records and the slowness of information dissemination contributed to developing a litany of other local practices. Many useless ideas were espoused for reviving victims of drowning, as it was thought that strong and stimulating practices could revive a subject. These included being rolled over barrels, thrown over a trotting horse face down, being subjected to loud noises, or having bright lights shone in the eyes, or burned with hot irons. The Humane Society recommended blowing tobacco smoke into the "great bowel" as an "accessory means" to aid resuscitation. When insufficient persons or lack of any implement to blow tobacco smoke were available, induction of vomiting with emetics, pouring warmed wine down the throat, or inducing sneezing with "spirits of quick lime" on a rag placed under the nose were also recommended and practiced with no beneficial outcome. Venesection was promoted as "particularly necessary" if any life returned. Since such accidents occurred ubiquitously, similar Humane Societies were formed in England and other European countries using some combinations of effective and useless techniques [17]. The choice of mouth to mouth or bellows varied by their local popularity or by individual practitioners in the absence of controlled trials.

Between 1772 and 1774, the simultaneous but independent rediscovery of oxygen for its capacity for life support in mice placed under airtight glass domes and to keep a flame lit with "pure," "vital," "dephlogisticated air" from which nitrogen (phlogiston) had been removed by Joseph Priestley (English), and Carl Wilhelm Scheele (Swedish), led to the abandonment of mouth-to-mouth efforts in favor of the use of bellows with oxygen for resuscitation. It was thought that more oxygen could be given by the bellows than by mouth-to-mouth attempts. It was the combined work of Joseph Black, isolating carbon dioxide in 1757, Henry Cavendish, isolating hydrogen in 1766 AD, and Daniel Rutherford, isolating nitrogen in 1772 that facilitated the French chemist, Antoine Laurent-Lavoisier, to name the gas Oxygen. Born an aristocrat of independent means, and intensely dedicated to studying respiratory physiology, Lavoisier with Pierre Simon Laplace, in 1780, discovered that the nature of respiration was a process of combustion where oxygen is used and carbon dioxide and water produced. This concept also led Lavoisier to work on public health for the poor because he found the air unclean where they lived. The French Revolution was in full force and for his aristocratic connections and his investment interests his career was cut short by the guillotine. He was labeled "an enemy of the people" in part because his chemistry lab was supported by the King [18]. His work fostered the use of oxygen in resuscitation [19].

During this time in England, John Hunter in 1776 tried to improve on resuscitation efforts by devising a double bellows so that one could be used to blow in "fresh air" or oxygen and the other used to suck out the "bad air;" the first cyclic "ventilator." This consolidated the use of oxygen for resuscitation. To prevent air from entering the stomach, Hunter applied gentle tracheal pressure to compress the esophagus [20]. He forbade venesection as being useless. The addition of oxygen to mechanical bellows resuscitation was expanded by its promotion by an Englishman, Edmund Goodwyn, MD. He was given a Gold Medal for his acclaimed dissertation "The Connexion of Life and Respiration: On an Experimental Injury Into the Effects on Submersion, Strangulation and Several Kinds of Noxious Airs in Living Animals… and the More Effectual Means of Cure" published in 1805 [21]. This was the first "evidenced-based" study published. It fostered Lord Cathcart, representing Scotland in the House of Lords, to encourage ordinary laymen to use such artificial respiratory resuscitation by offering incremental monetary rewards for saving lives this way based on the extent of action each resuscitator had taken; from a half crown for reporting a drowned victim to a surgeon or to minister, to the largest sum of four guineas for a life saved. Even providing a house for the victim and rescuer was rewarded for "covering expenses" plus one guinea for the "trouble [22]."

The first published hand book for "Life-Saving Measures for Drowning Persons" was in 1796, in Danish, by John Daniel Herbholdt, MD and Carl Gottlob Rafn, botanist. They collaborated on detailed specific resuscitation methods, and described the use for victim retrieval by several types of grappling hooks and boats. What they added was evaluation and critical analysis to their findings that led to similar techniques now still used. Lack of translated copies limited its wider application until the work was translated in 1960 by the Scandinavian Society of Anesthesiologists, on their founding [22].

By 1802, E. Coleman, a Scots veterinary professor, refined a catheter by making it in silver and of larger bore, and introduced it into the trachea to which a bellows was attached and oxygen added. He was also the first to describe the use of electrical current through placing electrodes over the base and the apex of the heart as part of the resuscitation effort [23]. The tripartite successful use of manual bellows or IPPB respiration, with or without intubation, chest-abdominal compression and electrical heart stimulation, innovative then, was overlooked for over a hundred years.

While the fireside bellows of Paracelsus and Hooke had been the "mechanical" tool used, no systematic data were collected as to its success or failure rate, or of any complications, until Leroy d'Etoille, of France, in 1827. He was the first to report a complication when he described its causing "emphysema and tension pneumothorax" and warned against its "improper use [24]." Even though Robert Hooke had suggested that this method of forcing air into the chest might cause "emphysema" in 1667, he provided no data. The lack of volume control using a bellows and the lack of ability to regulate the device for the size and weight of the victims led to Leroy's challenge to its use. A report of poor survival by Sir Benjamin C. Brodie of the Royal Humane Society in England in 1867 ended this form of positive pressure resuscitation and the societies formed to promote it [25]. Ignorance that proper use could be associated with a better outcome, and discouragement by the high mortality from infections, especially when the trachea was entered, led to the abandonment of this form of IPPB for more than 100 years.

The need for safe, effective resuscitation, however, continued for medical emergencies such as for still born infants, for victims of drowning and for asphixiations from chloroform, fire or other occupational exposures. Manual devices of individual creation were used without systematic study or analysis.

Negative Pressure "Noninvasive" Ventilation (NPNIV)

With the work of John Mayow from the 1670s "lost," between the 1830s through 1925 many scientists/physicians began to think again about "more normal, physiologic" negative pressure methods to support respiration. They set to designing devices that would develop sub-atmospheric or "negative" pressure around the body that would draw air into the lungs for persons with inability to breathe, not just victims of drowning. Early models generally failed, with often prolongation of dying for those so treated by the devices. The failure rate contributed to additional designs even when limited by the absence of available, reliable continuous power to run them.

Four main types of negative pressure devices were designed: the tank ventilator, the "iron lung," the cuirass with a variety of chest shells, and the differential pressure chamber of Sauerbruch.

The tank, the iron lung, and cuirasses will be considered together due to their overlap in development, design, and similarities of action for breathing support, although they are different in their effectiveness for different patient disorders and ages.

The initial devices were cumbersome, were largely manually operated and, except for a few reports, mostly failed. Their perceived persistent need, however, supported the enthusiasm for new designs by many physicians and scientists who collaborated with engineers.

The first unit was made of a rigid wood box housing the whole patient except for the head, around which was an airtight neck collar or "dam" by which intermittent negative pressure, alone or with positive pressure, generated manually or via a mechanically operated pump, using steam, water or electric power, which developed the pressure changes to induce air flow into the chest.

In 1832, Dr. John Dalziel, a Scottish physician from Drumlanrig wrote an easy "On Sleep, and an Apparatus for Promoting Artificial Respiration," the first account of sleep (nocturnal) and artificial respiration [26]. He created the first automatic respirator by designing a box enclosing the seated body with a seal around the head and neck and manually connected to a pair of bellows inside the box, worked from the outside by a piston rod with a one way valve, to develop sub-atmospheric pressure around the thorax so that positive atmospheric pressure caused air to flow into the lungs. The windows at the box's side allowed observation of chest movements. It was not until 1840 that Dr. Robert Lewins of Leith, England, used this model to "produce breathing" in a drowned seaman [26]. He modified it by replacing the bellows with a large syringe. The fact that breathing was restored was measured by the extinguishing of a lit candle under the victim's nostril during exhalation.

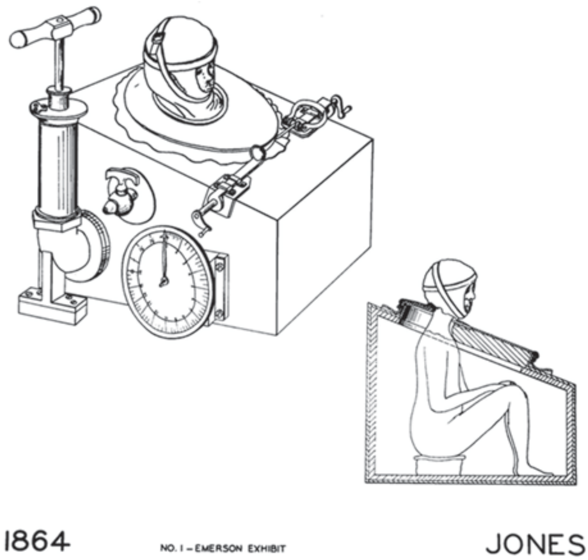

Fig. 2.1 Alfred E. Jones of Lexington, Kentucky patented first American tank respirator. (Used with permission from J. H. Emerson Co.)

Alfred E. Jones from Lexington, Kentucky, USA, following a similar design, patented the first American tank respirator in 1864 also using a large syringe to develop negative pressure for a seated subject. He treated asthma and bronchitis with his device and claimed "cures" for a host of diseases including "paralysis, neuralgia, asthma, bronchitis, rheumatism, dyspepsia, seminal weakness, deafness and … others" when "properly and judiciously" used [27] (Fig. 2.1).

In 1876 Ignez von Hauke from Austria experimented with both continuous positive pressure applied to the mouth via a mask and, initially, continuous negative pressure ventilation for up to 15 min intervals for the treatment of pneumonia, atelectasis, and emphysema. He discovered that intermittent negative pressure ventilation in phase with the patient's inspiration could be used for respiratory failure. He then made an iron cuirass covering the chest with an air-filled rubber edge to "seal." Agitated patients made this device unworkable, which led to the design for the first tank-type respirator, covering the whole body, "*Pneumatische Apparate* [28]." The whole subject was enclosed supine in this tank, including the scalp covered with an elastic cap which was sealed to the tank edge with elastic plaster, leaving the face free. It was hand operated for 2–3 h per "treatment." He used it for many conditions including neonatal asphyxia, atelectasis, pneumonia, tracheitis, croup, and diphtheria. L. Waldenburg, his colleague, reported that it kept a small girl alive for 3 months suffering from "great debilitation and double pneumonia" when she improved, and gained weight. It also "straightened" her rachitic chest wall [29].

In the same year, 1876, Eugene Joseph Woillez from France, designed a workable manually operated negative pressure tank respirator he called a "Spiroscope". Repeating the work of John Mayow, he stated that "the primary reason for the entry of air into the lungs is not the pressure of the air but the expansion of the thoracic

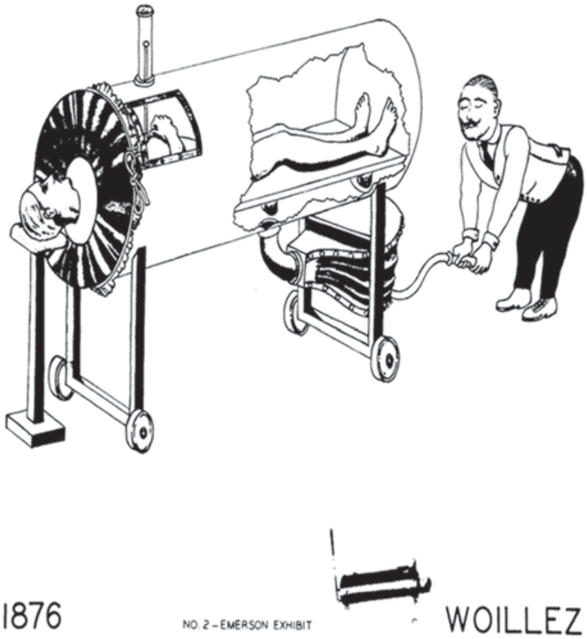

Fig. 2.2 Spirophore of Woillez: a negative pressure tank ventilator which was manually operated with the unique feature of observing chest movements with a rod resting on the patient's chest. (Used with permission from J. H. Emerson Co.)

cavity by the respiratory muscles." He then made an improved model encasing the whole body called the "Spirophore" with an adjustable rubber collar to seal around the neck with the head protruding, resting on a shelf, and a sliding bed, which became the prototype for all the negative pressure tank units that followed. A manually operated bellows generated the pressure changes from the opposite end. It had a unique feature, a rod resting perpendicular to the supine patient's chest which signaled the motion of the chest cage with each breath cycle, thus allowing for its detection [30] (Fig. 2.2). A unit lent to a Dr. Voisin for three drowned victims failed to revive the already dead victims. Woillez refused to patent his unit. His goal was to place these units all along the river Seine for drowning victims but lack of financial support doomed the project, possibly due to the failed attempts.

In 1887 Charles Breuillard, MD of Paris designed an impractical "bath cabinet" for a seated patient which required the patient to operate a valve to shift between vacuum for inhalation and release to atmospheric pressure for exhalation, requiring a conscious subject who could not fall asleep [31]. But it was the first unit to be continuously powered by steam from a boiler heated by a "spirit lamp" rather than manually (Fig. 2.3).

Alexander Graham Bell, the inventor of the telephone, and not a physician, after the death of his 1-day-old son in 1881 designed a metal vacuum jacket in 1882 which developed negative pressures with a separate hand pump to artificially "expand' the lungs to save lives. It was a unit made of two rigid halves with soft linings held to the chest by a strap, with negative pressure provided by large bellows. He successfully experimented with healthy volunteers. Even after he presented the

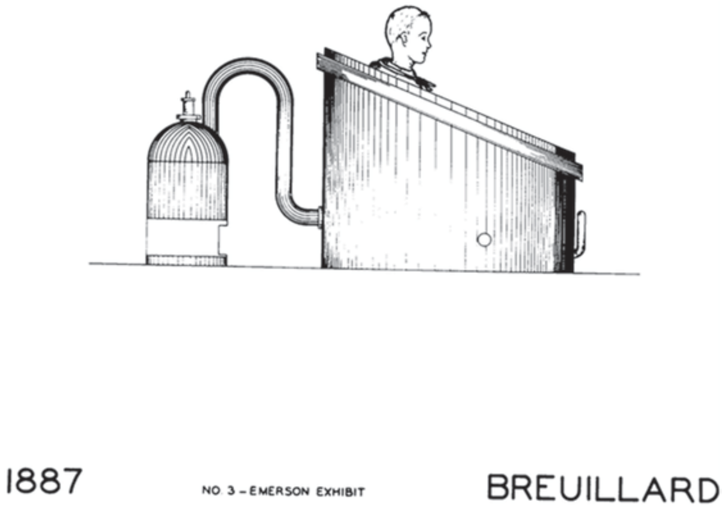

Fig. 2.3 Bath cabinet of Breuillard where the patient had to operate the valve to switch from negative to atmospheric pressure to support breathing. (Used with permission from J. H. Emerson Co.)

results to a meeting of the Advancement of Science and loaned it to someone at the University College in London, however, it generated little interest and went unused, perhaps because Bell was not a physician [32].

In 1889, Dr. Egon Braun of Vienna devised an infant "resuscitator" consisting of a box in which was placed a small supporting plaster mold conforming to an infant's body, with a rubber diaphragm seal around the head, leaving the nose and mouth exposed to air. Through a tube at the base of the box the operator would blow into the pipe to force chest compression, causing the air to exhaust out of the infant, allowing for chest recoil to generate a suction, or negative pressure, to inflate the chest (Fig. 2.4). This was repeated 20–30 times a minute by volunteers and reported to be "completely successful in 50 cases" reported by OW Doe [33].

In 1901, a Hungarian physician, Rudolph Eisenmenger, patented the first portable negative/positive pressure "cuirass" ventilator used for cardiopulmonary arrest from drowning or intoxication, consisting of a two part box enclosing the chest and abdomen, allowing the throat and limbs free. A foot operated bellows was later replaced by motors in 1904 (the "Biomotor") and was reported as "extraordinarily successful" when he reported the resuscitation of a man who had hung himself [34] (Fig. 2.5).

Aside from these issues of negative pressure ventilators to allow for resuscitation, there had been no system that allowed a surgeon to operate on the lung without its collapse until 1904, when Ernst Ferdinand Sauerbruch of Germany designed and built an airtight continuous negative pressure operating room, a giant "pleural space," where the subject's head protruded through a hole, exposed to atmospheric pressure, allowing for inflow of air to the lungs, and where the surgeon, also in the room, could work on a patient with an open chest. It was completely abandoned due

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