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The History of Deep Hypothermic Circulatory Arrest in Thoracic Aortic Surgery

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Abstract

Depending on the extent of aortic disease and surgical repair required, thoracic aortic surgery often involves periods of reduced cerebral perfusion. Historically, this resulted in detrimental neurological dysfunction, and high risk of mortality and morbidity. Over the last half century, rapid improvements have revolutionized aortic surgery. Among these, deep hypothermic circulatory arrest (DHCA) has drastically reduced the risk of mortality and morbidity following surgery on the thoracic aorta. This progress was facilitated by experimental pioneers such as Bigelow, who studied reduced oxygen expenditure consequent on induction of hypothermia in dogs. These encouraging findings led to trials in human cardiac surgery by Lewis in 1952 and further made possible the first successful aortic arch replacement by Denton Cooley and Michael De Bakey. Modern day surgery has come a long way from the use of immersion of the patient in ice baths and other primitive techniques previously described. This paper explores the development of deep hypothermic circulatory arrest from its origins to the present.

Key Words

Deep hypothermic circulatory arrest · Aortic aneurysm · Thoracic aortic surgery · History · Cerebral protection

Introduction

"History Teaches Everything Including the Future"—*Alphonse de Lamartine, 19th Century French Poet*

The earliest use of deep hypothermic circulatory arrest (DHCA) can be traced to Ancient Greece and the Hippocratic School of Medicine in the 4th century BD [1,2]. Denton A. Cooley, in his inaugural article in this journal, *AORTA*, on the history of aortic aneurysm surgery, described aortic disease as a fundamental problem of mankind [3]. Depending on the anatomic involvement of aortic disease, a surgical repair may mandate periods of reduced cerebral and visceral perfusion. Historically, such interventions were coupled with harrowing rates of death, and led to neurological complications and major visceral organ dysfunction. These facts led pioneering surgeons and researchers to dedicate their lives in the search for methods to reduce such outcomes. Among the advances is hypothermia, a technique that is now employed in a wide range of situations, including post cardiac arrest, aortic arch and thoracoabdominal surgery, and specialized cerebrovascular surgery. DHCA requires the use of cardiopulmonary bypass and cools the body to lower degrees than standard hypothermia alone [4]. Its modern day use resides mainly in cardiothoracic surgery (and neurosurgery) as a mechanism of cerebral protection. Its use has dramatically reduced the incidence of neurological damage following aortic surgery [5,6].

This review will elicit key milestones in the development of deep hypothermic circulatory arrest (Table 1).

Deep Hypothermic Circulatory Arrest

The first reported use of hypothermia as a therapeutic intervention dates to the Hippocratic era, from the Hippocratic School of Medicine, where it was described as a treatment for tetanus [1]. Hippocrates himself pro-

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Table 1. Key Innovators and Their Contributions to DHCA

Year	Contributor	Contribution
4th century BD	Hippocrates (Greece)	Use of snow to cause hypothermia to aid healing
1812	Larrey (France)	Use of ice on injured soldiers
1950	Bigelow (Canada)	Canine and Rhesus monkey experiments on hypothermia to reduce body oxygen requirements to allow exclusion of the heart from circulation
1950s	Gollan (Czechoslovakia/US)	Use of an oxygenator with a heat exchanger to cause hypothermia and rewarming in animals
1952	Lewis (US)	Performed the first successful human open-heart surgery to close an atrial septal defect using cooling blankets to induce hypothermia
1953	Swan (US)	Experimented with hypothermia further, and used this knowledge to the success of his first open-heart surgery. Swan went on to use this on hundreds of patients, with low mortality
1955	Cooley (US)	First use of hypothermia for cerebral protection during first aortic arch aneurysm repair with a homograft
1955	Lillehei and Kirklin (US)	Noticed and published that better outcomes occurred when body temperature cooled spontaneously during oxygenation
1959	Sealy (US)	Continued Lillehei and Kirklin's development and added a heat exchanger to a DeWall oxygenator to use hypothermia alongside it
1959	Drew (England)	First employed his own technique to use the patient's lungs instead of an oxygenator alongside hypothermia, and went on to apply this throughout his surgical career
1960s	Meshalkin (Russia)	Used ice and snow to operate without cardiopulmonary bypass
	Delorme (Scotland) and Boerema (Holland)	Developed methods of cooling in patients through experiments on dogs, passing the cannulated blood through an ice bath and returning it through a vein
1959	Ross and Brock (England)	Popularized using hypothermia alongside cardiopulmonary bypass
1963	Barnard and Schrire (South Africa)	First used DHCA and CPB at the same time on an ascending and arch aortic aneurysm
1975	Griepp (US)	Used surface cooling with CPB to resect aortic arch aneurysms in four patients

DHCA, deep hypothermic circulatory arrest; CPB, cardiopulmonary bypass.

moted the use of snow and ice packed around the injured soldier to promote healing [7]. In 1812, Dominique Larrey, surgeon to famous military leader Napoleon, used ice to alleviate injured soldiers' pain during amputations [8]. Despite a history of well over two thousand years, hypothermia did not gain popularity until the 21st century. In modern medicine, mild therapeutic hypothermia is widely used post cardiac arrest with return of spontaneous circulation in an effort to reduce the incidence of neurological damage [9]. DHCA is, however, reserved for aortic surgery and cerebrovascular surgery as a method of cerebral protection [2,5].

The birth of hypothermic cooling techniques for use in cardiac surgery began in earnest with the work of William Bigelow (Fig. 1) [10]. Today, Bigelow is famous for writing two books, including one called "Cold Hearts." He is further recognized for his role in the development of the pacemaker. He was awarded the title of Officer of the Order of Canada, the second highest honor of merit awarded by the Queen to civilians, and he was inducted into the Canadian Medical Hall of Fame in 1997.

In 1950, a research team in Toronto led by Bigelow published their two years' work on oxygen uptake and expenditure in canines at temperatures considered hypothermic [10]. They hypothesized that a reduced body oxygen requirement could be achieved through a reduced metabolic drive secondary to hypothermia. This in turn would enable the heart to be excluded from circulation and allow the possibility of cardiac surgery. Their work was published before the invention of cardiopulmonary bypass by John Gibbons, who began clinical application of his heart-lung machine in 1952 [11]. Bigelow's experiments encompassed 176 dogs, who were cooled with the aid of muscle relaxants to control homeostatic temperature regulation resulting in severe shivering, venesection as a method of reducing pressure within the venous system, and phrenic nerve stimulation to induce artificial respiration. Bigelow was able to successfully exclude the

Figure 1. Wilfred G. Bigelow (1913-2005), initiated cardiac surgery under hypothermia. Reproduced with permission [8].

Figure 2. Open-heart surgery performed in 1955. The patient is currently submerged in an ice bath. Courtesy of the US National Library of Medicine.

heart from circulation without arrest at a core temperature of 20°C in 39 of his dogs. Of these 39, 51% of dogs were successfully revived. Cardiac arrhythmias, particularly ventricular fibrillation, were the major hindrance in the dogs who were successfully revived [10].

In these early experiments, a common theme was to avoid ventricular fibrillation or at least to correct it as soon as it developed. We must remember this, as in the current era of cardiopulmonary bypass, we are immune to the impact of ventricular fibrillation, which is expected as part-and-parcel of deep hypothermia.

Despite these promising advances, the team continued to search for better methods of cooling. They knew that a hibernating mammal, such as the groundhog, could survive a temperature of 3°C. They wished to reduce the current limit of 20°C [10,12]. The team performed further research on Macacus Rhesus monkeys, once again using cooling blankets, this time to below 20°C [12]; 11 of 12 monkeys cooled to temperatures between 16 and 19°C survived between 15 and 24 minutes. Whereas in previous experiments on dogs, at which their respirations ceased around 24°C, monkeys continued to respire at 8 respirations per minute at 20°C. Similarly, Bigelow et al. used groundhogs cooled below 5°C (as in their natural hibernating state), operated, and successfully revived 5 of 6 animals [12].

A physiologist named Frank Gollan worked in the 1950s using hypothermia and an oxygenator of his own invention, and presented his work in 1955 [13–15]. Gollan made an important step in that his bubble oxygenator included a heat exchange device, whereby he could induce hypothermia as well as carry out rewarming [16]. He was able to achieve measured core temperatures of 4°C and published revival of the animals. Despite this, his research was not widely recognized and was largely ignored among the surgeons at the American Association for Thoracic Surgery [17]. In Sweden, Juvenelle and colleagues were also coming to conclusions similar to Gollan's—specifically, that the use of a pump-oxygenator and hypothermia of 12°C would decrease oxygen requirements of the body to allow open cardiac operating times of up to two hours without adverse consequences [17,18]. However, Juvenelle's method produced little in the way of long-term survival [18].

The first successful human operation utilizing a period of hypothermia was performed in 1952 at the University of Minnesota by Dr. John F. Lewis [19]. Armed with knowledge of William Bigelow's experiments on hypothermia, and his own extensive experiments involving several hundred canines, he was successful in closing a secundum atrial septal defect in a 5-year-old girl [20]. For two hours he wrapped the anesthetized patient in refrigerated blankets until her rectal temperature had fallen to below 28°C. Lewis describes the operation in his landmark paper [20]. "The chest is opened with a transverse, sternal splitting incision through the 4 interspaces, the heart is explored digitally through the right auricular appendage. Cardiac inflow and outflow are occluded and the right atrium is opened widely to allow repair. The left and right heart are filled with saline and atrium closed". Following the operation, the patient was placed in hot water at 45°C to increase her rectal temperature to 36°C. This operation is heralded in cardiac history as the first ever successful operation within the open human heart under direct vision.

Subsequently, Lewis used this technique on 29 more patients, with only three deaths. Without cardiopulmonary bypass, hypothermia still carried an inherent risk of ventricular fibrillation, which remained a significant danger of hypothermia, previously noted by Bigelow et al. and Lewis et al., who used cardiac massage, intracardiac adrenalin, and electrical shock successfully in more than 90% of patients for restoration to normal sinus rhythm [12,20]. The success of Lewis's operations gained worldwide medical recognition, and they represent a major milestone in cardiac surgical history. However, with the introduction of the cardiopulmonary bypass machine, the sole use of hypothermia as a technique to allow intracardiac operations was short-lived, in view of the limited operating time this technique provided and the associated complications it carried.

In 1953 came Henry Swan, who had repeated the work of Bigelow to investigate impact on the variables of pH, serum sodium, chloride, potassium, phosphorus, plasma protein, and hematocrit under the influence of hypothermia, with particular interest in prevention of the well documented complication of ventricular fibrillation [21]. On February 19th of the same year, Swan carried out open-heart surgery, a pulmonary valvulectomy, using hypothermia for the first time [8,21]. Swan then applied these findings in a surgical setting, prior to the use of cardiopulmonary bypass, using 26-28°C hypothermia on hundreds of patients, with a low mortality rate [8]. As such, Swan was considered to have the most surgical experience using hypothermia.

The renowned surgeon Dr. Denton Cooley employed hypothermia for cerebral protection during his first attempt at total resection and replacement of the aortic arch in 1955 [22,23]. The 49-year-old gentleman was suffering from a syphilitic aneurysm involving the arch and a further aneurysm affecting the descending aorta. Cooley used surface cooling to achieve 33°C, and temporary shunts were placed to provide blood to the carotids and distal aorta. In this case, the patient went on to suffer a stroke and then death, although this was attributed to an 8 minute occlusion of the right carotid shunt. This case not only represented the first ever aortic arch resection and replacement, but exploited the use of hypothermia as an adjunct in aortic arch surgery, as it is still used today.

Further, important developments in 1955 were introduced by Lillehei and Kirklin, who used the pump-oxygenator for intracardiac surgery [24]. During their operations, it was noticed that body temperature would often cool spontaneously, as early oxygenators lacked heat exchangers. In this way it was noted that allowing spontaneous cooling alongside pump-oxygenators could produce better outcomes. Lillehei and Kirklin published their successful work, and their techniques became fashionable [17].

Sealy et al. fronted this development throughout the late 1950s and, in 1959, were the first to add a heat exchanger alongside a DeWall oxygenator [17,25]. This allowed rapid active cooling and rewarming of patients to a temperature of 32°C [25]. They confirmed the compatibility of using hypothermia alongside an oxygenator. Sealy reported this technique for 95 patients in a variety of open cardiac surgeries including tetralogy of Fallot, complete transposition, valvular disease, septal defects, and reported a mortality rate of 17% [26].

From 1959 onwards, Charles Drew, a surgeon at the London Westminister Hospital, began developing his own methods for intracardiac surgery after disappointing results using other popularized methods [17]. Drew first used his technique, developed through experimentation on dogs, on a 1-year-old child with Down's syndrome in congestive heart failure from an endocardial cushion defect, although the child later died after recovery. He successfully repaired his following two patients, who underwent ventricular septal defect (VSD) closure, and they recovered without complications in 1959 [27]. His technique involved a circulatory support system to cool patients to 15°C. His cynicism toward oxygenators led to using the patient's own lungs for oxygenation. This technique was gradually advanced to children and adults across a career of 22 years, with varying degrees of success. But, eventually this technique lost ground [17]. Drew's work represented a cardinal contribution to today's knowledge of hypothermia, and this was recognized in 1961, when Drew was invited to present the renowned Hunterian lecture at the Royal College of Surgeons.

In Siberia, Professor E. N. Meshalkin, who is credited as the pioneer of Soviet cardiac surgery, used hypothermia during the 1960s on a variety of patients. He was notorious for operating on congenital defects without cardiopulmonary bypass, with only mild hypothermia [28]. It is documented that Prof. Meshalkin's method of cooling was the utilization of the abundance of snow and ice available in Siberia for surface cooling [29].

Meanwhile, methods of cooling were being advanced by Delorme and Boerema via the insertion of a cannula into the femoral artery of canines, passing the blood through an extracorporeal coil immersed within an ice bath, and returning the cooled blood through the femoral vein [30,31]. They were both able to cool canines to 22 to 26°C (except in 1 dog) without causing fibrillation, a dreaded complication of surface cooling. armed with this knowledge, Delorme concluded that operating on a bloodless field would become possible in cardiac surgery. However, arteriovenous cooling was subject to complications, including fistula formation and thrombosis. Furthermore, the technique required initiation before surgery.

Mr. Donald Ross, well known for leading the team that performed the first cardiac transplant in the United Kingdom, is further credited with popularizing venovenous cooling, a method he had devised in canine experimentation by cannulating the external jugular vein for blood drainage and providing return through the superior vena cava [32,33]. He reported improved success using venovenous cooling over surface cooling due to the greater control over the stages of cooling, preventing core temperatures from dropping too low, or too rapidly, reducing the risk of cardiac irregularities. The recognized detrimental effect of ventricular fibrillation from rapid cooling was still a very real risk. Ross did not commence cooling until the chest was open and, thus, was able to observe the heart and deal with any irregularities.

In 1959, Ross and Sir Russel Brock, from Guy's Hospital London, declared "deep hypothermia by means of a heart lung bypass machine or a differential cooling technique holds promise of longer safe periods of intra cardiac surgery in the future" [34]. Following this pronouncement, there was a wave of experiments in the use of cardiopulmonary bypass with hypothermia.

World renowned Dr. Christiaan Neethling Barnard and Velva Schrire in 1963 were the first to use deep hypothermic circulatory arrest and cardiopulmonary bypass simultaneously, on two patients with aortic aneurysm involving the ascending aorta and arch. They cooled the patients to a temperature of approximately 10°C measured in the esophagus [35]. They were successful in one of their patients. Following this, multiple renowned surgeons began reporting success with combinations of hypothermia and cardiopulmonary bypass, including Borst and Lilliehei.

In 1975, Professor Randall Griepp published a series of four patient operations for aortic arch aneurysms using hypothermia via a combination of surface cooling and cardiopulmonary bypass [36]. He published successful resection of aneurysms in all four patients. Griepp et al. would later (1991) report the limitations of using hypothermic circulatory arrest alone for cerebral protection, noting a relationship between duration of hypothermic arrest and mortality [37,38].

These concerns were echoed by Haldenwang et al. [39], who noted that temporary or permanent neurologic dysfunction incidence rose when HCA exceeded 40 minutes and mortality rates increased above 60 minutes of HCA. It was this observation that led to the development of further techniques: antegrade cerebral perfusion (ACP) and retrograde cerebral perfusion (RCP), which are used in combination with DHCA today.

Summary

History surrounds cardiac surgery in the form of many successes and failures of pioneering individuals in the face of difficult challenges. The past fifty years have been monumental for the refinement of aortic surgery and decreasing the risk of patient mortality and neurological deficit. DHCA started from small laboratory experiments, to the use of ice baths, and is still used in aortic surgery today (Fig. 2). The relative infancy of deep hypothermic circulatory arrest means the near future is extremely promising and will surely hold many new exciting developments and innovations within this field.

Conflict of Interest

The authors have no conflict of interest relevant to this publication.

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