Best Practice & Research Clinical Anaesthesiology 29 (2015) 99–111

Contents lists available at ScienceDirect

Best Practice & Research Clinical Anaesthesiology

journal homepage: www.elsevier.com/locate/bean

1

History of cardiopulmonary bypass (CPB)

Eugene A. Hessel II, MD, FACS, Professor Anesthesiology, Surgery (Cardiothoracic), Neurosurgery, and Pediatrics [*, 1]

University of Kentucky College of Medicine, Lexington, KY, USA

Keywords:
extracorporeal circulation
heart–lung machines
cardiopulmonary bypass
cardiac surgery
history

The development of cardiopulmonary bypass (CPB), thereby permitting open-heart surgery, is one of the most important advances in medicine in the 20th century. Many currently practicing cardiac anesthesiologists, cardiac surgeons, and perfusionists are unaware of how recently it came into use (60 years) and how much the practice of CPB has changed during its short existence. In this paper, the development of CPB and the many changes and progress that has taken place over this brief period of time, making it a remarkably safe endeavor, are reviewed. The many as yet unresolved questions are also identified, which sets the stage for the other papers in this issue of this journal.

Introduction

The development of cardiopulmonary bypass (CPB) to permit cardiac surgery is considered one of the greatest advances in medicine in the 20th century. Many do not appreciate how recently this has developed. This has occurred during the lifetime of many who are still practicing. The first successful series of open-heart surgery utilizing heart–lung (H–L) machines occurred exactly 60 years ago in the spring and summer of 1955. In this article, the historical development and technological advancement of extracorporeal circulation and CPB are reviewed. Much of this material is based upon or extracted from other publications by this author [1–3], and based upon other papers and books related to the history of cardiac surgery and CPB [4–15]. *Cardiopulmonary Bypass Bibliography,* covering 1667–1989,

* Tel.: +1 859 533 0756 (cell), +1 859 323 5956x80050 (office); Fax: +1 859 323 1080.
E-mail address: ehessel@uky.edu.

[1] Administrative assistant: Charles York.

http://dx.doi.org/10.1016/j.bpa.2015.04.006
1521-6896/

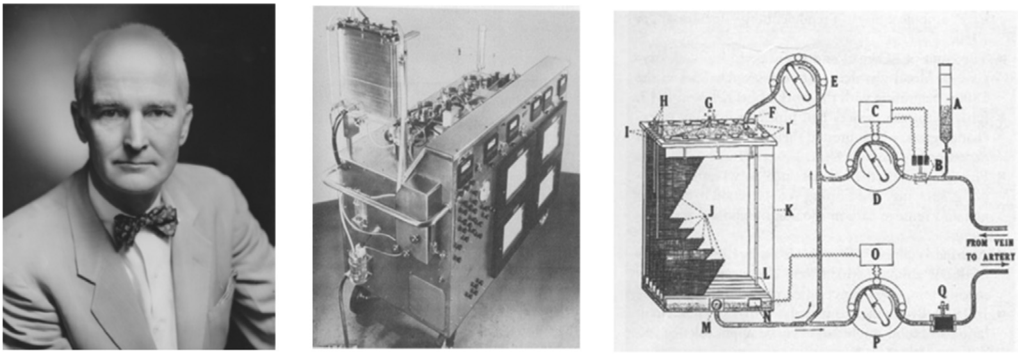
by Utley and colleagues is a particularly valuable resource [16]. Unfortunately, my review has likely overlooked many of the important contributions that have occurred in other countries, if not published in the English language literature.

The birth of use of mechanical H–L machines for CPB in cardiac surgery

The concept of ECC to support organ function was first suggested and explored in animals in the 19th century, but many scientific discoveries and techniques were necessary before clinical CPB could be achieved including blood types and transfusion, heparin and protamine, and the use of silicone antifoam [3,11,17]. A number of surgical teams in the early 1950s attempted to develop H–L machines and used them to perform open-heart surgery without success, but this was finally accomplished by John Gibbon Jr. (Fig. 1A) on 6 May 1953 [18–20]. Dr. Gibbon was inspired to develop an H–L machine while caring for a patient in 1930 as a surgical research fellow. Despite being dissuaded by his mentors, he spent the next 20 years working alongside his wife and finally developed an H–L machine with the assistance of the engineers at IBM (Fig. 1 B and C), with which he achieved 90% survival in dogs. This led to his first clinical application, which failed due to wrong diagnosis, but his second attempt, on an 18-year-old woman with an atrial septal defect (ASD), was successful. Unfortunately, his next two patients, died and he declared a moratorium on further application of his H–L machine. Only one other successful open-heart surgery was performed using an H–L machine during 16 other attempts by six other teams between 1952 and 1954, leading to an attitude of hopelessness. Some hypothesized that human patients, as compared with animal subjects, were too sick to tolerate CPB. However, in March 1954, C. Walton Lillehei (Fig. 2A) and his colleagues at the University of Minnesota initiated a remarkable series of direct-vision intracardiac surgery with total CPB using another adult as the "heart–lung machine" (so-called "controlled cross-circulation"), in which the adult's femoral artery and vein were connected to the child's arterial and venous system, respectively [21] (Fig. 2B). Over the next 16 months, they operated on 45 seriously ill children with congenital heart disease with 28 survivors and thus clearly demonstrated the potential for CPB to permit even complex open-heart surgery in sick patients once a satisfactory artificial H–L machine was available for use by a skillful cardiac surgical team. This was accomplished during the spring and summer of 1955 when two groups, one led by John Kirklin (Fig. 3A) at the Mayo Clinic starting on March 22nd [22] and the other by C. Walton Lillehei (Fig. 2A) starting on May 13th [23], working 90 miles apart, using vastly different H–L machines and approaches to the conduct of CPB, each operated on about 40 cases.

The Mayo Clinic group used the IBM-Gibbon machine, freely provided by Gibbon and IBM, which they modified and called the "Mayo–Gibbon" H–L machine (Fig. 3B). Their H–L machine was capable of oxygenating at flows of 2.4 L/min per square meter, and it included inline arterial and venous saturation and a vaporizer for administering a volatile anesthetic. Lillehei's team employed a helical reservoir bubble oxygenator (BO) (Figs. 2C and D) developed by a young physician, Richard A. DeWall, who was working in the cardiac surgical research laboratory and as a perfusionist for the open-heart cross-circulation procedures.

Lillehei and Kirklin were truly the giants of the development of open-heart surgery, with vastly different styles and personalities. Kirklin was methodical and academic [24], whereas Lillehei was impulsive and action oriented [14], but both made tremendous contributions to the practice of CPB. While searching for a method to conduct open-heart surgery between 1950 and 1955, besides inventing and successfully applying human cross-circulation, Lillehei helped his colleagues at the University of Minnesota develop and apply clinically (but unsuccessfully) an *H–L* machine employing a screen oxygenator and the first successful use of circulatory arrest under moderate surface-induced hypothermia to perform open-heart surgery. He also introduced epicardial pacing to treat surgically induced heart block, and he pioneered the use of median sternotomy and femoral artery cannulation for inflow in the late 1950s. Before it was given a name, Kirklin practiced evidence-based cardiac surgery and perfusion ("show me the data"), stressing the acquisition and the appropriate statistical analysis of objective data. He authored or coauthored many papers, exploring the pathophysiology and optimal conduct of CPB. He was the editor of *The Journal of Thoracic and Cardiovascular Surgery* from 1987 to 1994 [24].



A B C

Fig. 1. John Gibbon and the first successful clinical use of the heart–lung machine for open-heart surgery. **1A**. John H Gibbon, Jr. (1903–1973). Fig. 1 in Theruvath TP and Ikonomidis JS. Historical perspectives of The American Association for Thoracic Surgery: John H. Gibbon, Jr. (1903–1973). Journal of Thoracic and Cardiovascular Surgery 2014; 147: 833-836. Used with permission from Elsevier. **1B**. Photo of Gibbon Model II H–L machine. Used by Gibbon for the first successful clinical open-heart surgery with a mechanical H–L machine, 6 May 1953. Note the stationary vertical screen oxygenator and roller pumps and elevation of HL machine above the floor requiring active venous drainage. Figure from Romaine-Davis A. *John Gibbon and His Heart-Lung Machine*. Philadelphia, University of Pennsylvania Press, 1991. Used with permission. **1C**. Diagram of Gibbon H–L machine. Stationary vertical screen oxygenator (K); roller pumps for active venous drainage (D) and arterial return (P) and a third (E) for recirculation; (A) blood reservoir, (B) venous pressure transducer, (C) automatic venous pump shutdown control, (F) oxygen input, (G) reservoir pressure relief valve, (H) Oxygen exhaust, (J) stainless steel screens, (O) automatic electronic artery pump motor control, and (Q) reverse flow filter. Figure 14 from Romaine-Davis A. *John Gibbon and His Heart-Lung Machine*. Philadelphia, University of Pennsylvania Press, 1991. Used with permission from Wolters Kluwer Health, Inc.

In the last half of the 1950s, many groups initiated open-heart programs employing CPB, mainly to treat congenital heart disease. Much has changed with regard to the equipment and components employed and the conduct of CPB, which I have been fortunate to witness during my career in medicine, starting as a medical student in 1957, then as a cardiac surgeon until 1982, and subsequently as a cardiac anesthesiologist.

Subsequent developments

Oxygenators (Fig. 4)

Early on, crude membrane oxygenators (MOs) and biologic oxygenators (animal lungs) (Fig. 4A) were investigated, but most groups employed BOs of their own design or copied from DeWall's. However, the rotating disc oxygenator developed by Kay and Cross in the late 1950s [25] became widely used and favored by many for longer and more complex cases, but it required large priming volume and reusable parts. Thus, many adopted the unitized plastic-bag disposable BOs (Fig. 4B), which were introduced in the early 1960s and subsequently replaced by hard-shell disposable BO with integrated heat exchangers (Fig. 4C). In the early 1970s, disposable but relatively inefficient MOs were introduced separately by Lande and Kolobow; however, in the mid-1970s, more efficient and commercially available microporous polypropylene MOs became available, and by the end of the decade, these were being *used* in nearly 20% of cases. In the early 1980s, hollow-fiber technology led to the adoption of MOs, which virtually replaced all oxygenators by 1994. In the early 2000s, a new nonporous true diffusion membrane constructed from poly-(4-methyl-1-pentene) (PMP) was introduced, which is thought to be more biocompatible and more suitable for long-term perfusion (e.g., extracorporeal membrane oxygenation (ECMO)). In recent years, some manufactures have integrated screen microfilters into MOs, thereby perhaps eliminating the need for a separate arterial line microfilter.

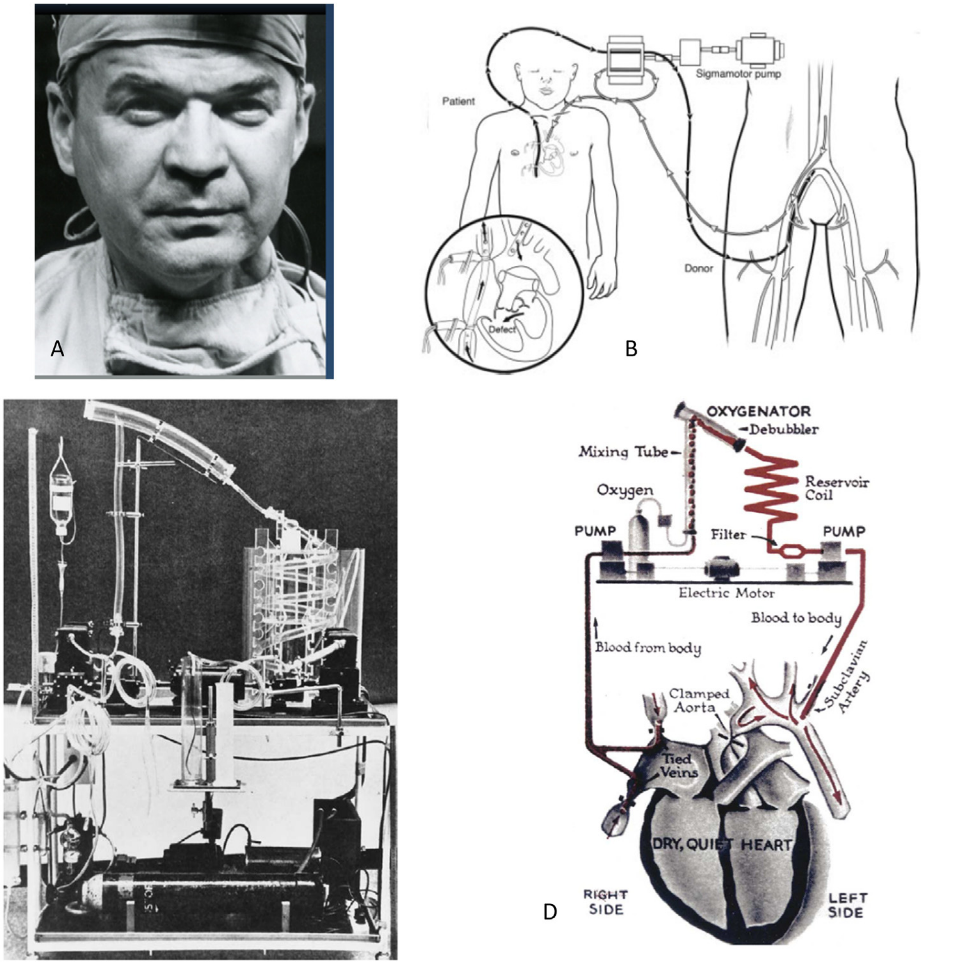


Fig. 2. CW Lillehei and early CPB. **2A**. C. Walton Lillehei. (1918–1999). Used with permission of the Lillehei Heart Institute at the University of Minnesota. **2B**. Lillehei's cross-circulation procedure using an adult as the H–L "machine." The adult's femoral artery was connected to the child's left subclavian artery. A single SVC cannula drained both SVC and IVC into the adult's femoral vein. A single Sigmamotor pump controlled both the flow out of the adult into the child and the flow out of the child into the adult to keep blood volumes in each stable. Figure 7 in Stoney WS. Evolution of Cardiopulmonary Bypass. Circulation 2009; 119; 2844-2853. Used with permission from Wolters Kluwer Health. **2C**. Photograph of H–L machine employing a DeWall helical reservoir bubble oxygenator used by Lillehei for the first series of open-heart surgery performed at the University of Minnesota in the summer of 1955. Note the use of Sigmamotor pumps. Fig. 2 in DeWall RA. The Evolution of the Helical Reservoir Pump- Oxygenator System at the University of Minnesota. Ann Thorac Surg 2003; 76: S2210 –5. Used with permission from Elsevier. **2D**. Diagram of early H–L machine used at the University of Minnesota. Note the bubble oxygenator a with debubbling chamber, a helical coil debubbling reservoir, and separate Sigmamotor venous and arterial pumps. Arterial inflow into subclavian but venous drainage through separate cannulas in IVC and SVC. Fig. 1 in DeWall RA. The Evolution of the Helical Reservoir Pump- Oxygenator System at the University of Minnesota. Ann Thorac Surg 2003; 76: S2210 –5. Used with permission from Elsevier.

Arterial pumps

Initially, Sigmamotor ("finger") pumps were commonly used, but they were quickly replaced with roller pumps. However, in the 1980s, perhaps due to their use in ECMO and as ventricular assist devices, and their purported improved safety and reduced blood trauma, centrifugal pumps began to

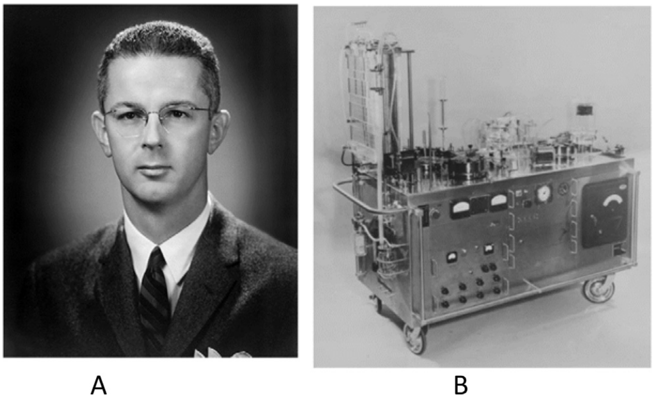


Fig. 3. John Kirklin and early CPB. **3A**. John W Kirklin (1917–2004). Circa 1957, 2 years after accomplishing the first successful series of clinical open-heart surgeries using an H–L machine (Mayo–Gibbon). Fig. 1, from Stephenson L J. Historical perspective of The American Association for Thoracic Surgery: John W. Kirklin, MD (1917–2004). J Thorac Cardiovasc Surg. 2007; 134: 225-8. Used with permission from Elsevier. **3B**. The Mayo–Gibbon H–L machine employed for open-heart surgery at the Mayo Clinic in the spring of 1955. Figure 11 in Stoney WS. Evolution of Cardiopulmonary Bypass. Circulation 2009; 119; 2844-2853. Used with permission from Wolters Kluwer Health, Inc.

compete with roller pumps. Throughout the development of CPB, there has been a continuing debate about the advantages of providing pulsatile flow with numerous preclinical and clinical studies providing conflicting data [26]. Pulsatile modes of CPB seem to be more popular in Europe than in the USA.

Arterial cannulation

In the early days of cardiac surgery, which was most commonly performed through a lateral thoracotomy or an transverse sternal bilateral anterior thoracotomy, arterial inflow was directed into the

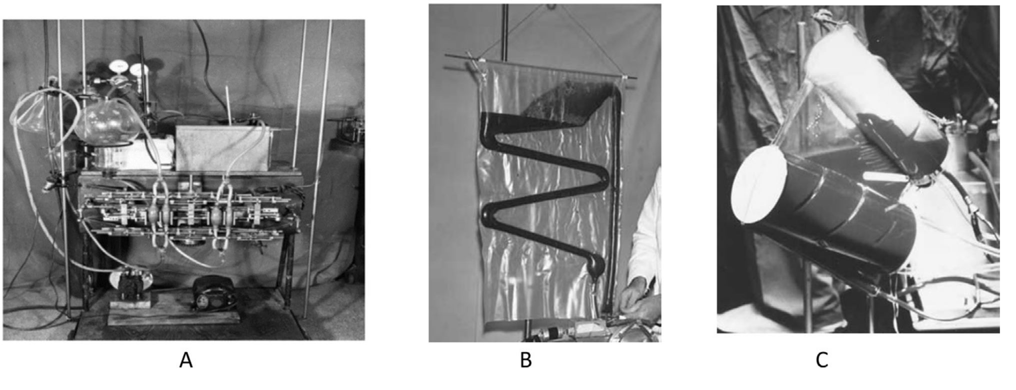


Fig. 4. Early oxygenators. **4A**. Mustard's H–L machine employing a biologic (monkey) lung. (Clinically unsuccessful.) Rhesus monkey lungs were suspended in the glass flask and used as the oxygenator. Fig. 3 in Stoney WS. Evolution of Cardiopulmonary Bypass. Circulation 2009; 119; 2844-2853. Used with permission from Wolters Kluwer Health, Inc. **4B**. Disposable plastic sheet bubble oxygenator with reservoir. Modified from Fig. 3 in DeWall RA. The Evolution of the Helical Reservoir Pump- Oxygenator System at the University of Minnesota. Ann Thorac Surg 2003; 76: S2210 –5. Used with permission from Elsevier. **4C**. Hard-shell disposable bubble oxygenator with integrated heat exchanger (Bentley "Temptrol"). Modified from Figure 6 in DeWall RA. The Evolution of the Helical Reservoir Pump- Oxygenator System at the University of Minnesota. Ann Thorac Surg 2003; 76: S2210 –5. Used with permission from Elsevier.

subclavian artery, but by the end of the 1950s femoral artery cannulation became dominant. By the late 1960s and early 1970s, direct cannulation of the ascending aorta, advocated by DeWall in 1963 [27], became standard, partly related to the more common use of median sternotomy and because of the significant incidence of retrograde dissection associated with femoral cannulation. This complication reappeared with the introduction of "port-access" surgery in the mid-1990s. The reason why cannulating the ascending aorta was not adopted for a long time remains an unanswered question to the author. Because the role of dislodging atheroemboli and the management of ascending aortic dissections were of concern, the use of subclavian cannulation was reintroduced in the mid-1990s [28].

Venous cannulation and drainage

Initially active venous drainage accomplished and controlled by a separate venous pump was used mainly to help balance venous and arterial flow, but soon gravity drainage became standard. This remained true until the reintroduction of augmented venous return, with either pumps ("kinetic") [29] or vacuum [30], in the mid-1990s, initially to facilitate drainage through the long narrow femoral venous cannulas used for "port-access" minimally invasive cardiac surgery, but now often used to facilitate reduced prime volume by utilizing smaller venous lines and raising the level of the H–L machine up from the floor level.

Temperature management

During its early days, CPB was conducted at normothermia, but in the late 1950s Sealy and others introduced efficient heat exchangers utilizing moderate hypothermia (28–32 °C). This rapidly became standard practice both to improve the tolerance to the limited flow and oxygenation capacity of early H–L machines and to hemodilution and for neuroprotection. Until the early 1980s, temperature-corrected (i.e., corrected to the patient's actual temperature) pH and $PaCO_2$ were kept at 7.40 and 40, respectively (so-called pH-stat strategy). However, in 1982, Ream and colleagues advocated the use of alpha-stat management to produce alkalemia and hypocapnea during hypothermia [31], and alpha-stat quickly became standard practice. The use of moderate hypothermia during CPB remained common until normothermic or "tepid" bypass, advocated by the group in Toronto, Canada [32], became popular starting in the 1990s, partly to reduce the risk of cerebral hyperthermia and injury during rewarming; this led to emphasis on monitoring nasopharyngeal instead of rectal or bladder temperature [33] with the recommendation of maintaining the arterial inflow temperature at $\leq$37 °C.

In 1959, Drew in London, UK, introduced the technique of deep hypothermic circulatory arrest (DHCA) [34]. DHCA was not widely adopted at the time, but it was reintroduced in the mid- and late 1960s separately by Dillard [35] and Barratt-Boyes [36] to facilitate infant heart surgery and by Griepp in 1975 for conducting aortic arch surgery [37].

Anticoagulation and bleeding

Until 1975, heparin was administered by protocol without any objective monitoring of its effect. In that year, Bull at Loma Linda University documented the limitations of this approach and advocated the use of objective monitoring with the activated clotting time (ACT) being aimed at a rather arbitrary target of 480 s [38]. The proper level of anticoagulation and the method of monitoring it continue to be debated, but by the end of the 1970s, some type of objective monitoring and control of heparinization was employed by most teams. In 1987, Royston [39] and other groups introduced the use of aprotinin to reduce perioperative bleeding, and soon the use of aprotinin and other synthetic anti-fibrinolytics during CPB became ubiquitous, although aprotinin was withdrawn from the market in 2007 due to safety concerns. Heparin-coated circuits were introduced partly with the potential of reducing heparin requirements, but this has remained controversial. In recent years, the nearly ubiquitous use of drugs affecting platelet function and the recognition and management of heparin-induced thrombocytopenia have led to the development and use of new point-of-care monitoring of coagulation and platelet function during CPB (e.g., thromboelastography (TEG)) and the introduction of alternatives to heparin for conduct of CPB (e.g., bivalirudin). In 2007, cardiac surgeons, anesthesiologists, and perfusionists collaborated on the development and publication of blood management guidelines which were updated in 2011 [40].

Hemodilution, anemia, and hemofiltration

Initially, whole blood (and a large volume of it!) was used to prime H–L machines. However, in the late 1950s and the early 1960s, several groups introduced hemodilution and asanguineous priming to reduce the adverse effects of blood, conserve this valuable resource, and improve tissue perfusion during hypothermia. Thereafter, hemodilution, sometimes to extreme degrees, became standard practice. This became problematic with the adoption of tepid or normothermic bypass, and since 1997 a number of observational studies have detected increased morbidity and mortality associated with low hematocrit during CPB. Conversely, the adverse effects of RBC transfusion (beyond the infectious risks) were becoming more apparent. Thus, interventions to reduce the severity of anemia during CPB were instituted including the use of retrograde arterial priming (RAP) in 1998 [41], reduction of the priming volumes of extracorporeal circuit (ECC), and the development and use of miniaturized circuits. The use of hemofiltration during CPB was first reported by Darup and colleagues in 1979 [42] to remove excess crystalloid, to raise hematocrit and plasma protein concentration, and to remove inflammatory mediators. In 1991, Naik et al. introduced the practice of modified ultrafiltration (MUF) to the practice of pediatric CPB [43], and in 1996 Journis et al. advocated zero-balance ultrafiltration (Z-BUF) during CPB [44].

Modifying the ECC and conduct of CPB to improve organ preservation

Gross air embolism was an early concern during CPB (and the cause for the failure of a number of early attempts at using CPB); thus, most early H–L machines included a macro-bubble trap on the arterial line. However, in the early 1970s, recognition of the presence and significance of microemboli including gaseous microemboli (GME), especially by Roy Swank and Russell Patterson, led to the development and placement of microfilters on both the cardiotomy suction and the arterial line. The in-depth Dacron wool filter developed by Swank was soon supplanted by the screen filter from Patterson. By the mid-1990s, the use of arterial line microfilters was nearly 100%. Because activated leukocytes are thought to be a major contributor to the inflammatory response (systemic inflammatory response syndrome (SIRS)) associated with CPB, the use of leukocyte-depleting filters in various sites in the ECC was introduced in the 1990s; however, the lack of high-level evidence for benefits to clinically important outcomes [52] has curtailed their widespread use. In the 1990s, more attention was redirected at the cardiotomy suction as a major source of microemboli and of activation of other blood components. This led to the emphasis on minimizing or eliminating the use of cardiotomy suction when possible or the preprocessing of cardiotomy suction blood before returning it to the ECC using cell saver/processors. The latter were first introduced by Jack Latham and his company, Haemonetics, in 1971.

Optimal conduct of CPB for brain protection has been of concern since the early days of CPB. In the early 1980s, the groups at University of Alabama and Copenhagen reported on the objective measurement of cerebral blood flow during CPB [53,54], which partly led to the adoption of alpha-stat pH/ $PaCO_2$ management [31,55]. In 1986, Nussmeier and colleagues [56] reported that barbiturate administration decreased the incidence of neurologic injury during cardiac surgery. Although not confirmed by a subsequent study [57], this observation stimulated investigation of other drugs and methods to reduce adverse neurologic sequelae. In 1992, the Washington University group called attention to the probable role of ascending aortic atherosclerosis and manipulation of the aorta, and they introduced the use of epivascular ultrasound scanning to guide cannulation [58]. Recognition of the increased incidence of neurologic dysfunction of the brain during longer periods of circulatory arrest during deep hypothermia led Ueda et al. [59] to resurrect retrograde cerebral perfusion (first described by Mills and Ochsner in 1980 to treat massive cerebral air embolism [60]). Shortly thereafter, antegrade cerebral perfusion was advocated as a superior method of cerebral protection during induced circulatory arrest. Strategies for neurocognitive protection are reviewed in a subsequent article in this issue.

To protect the heart, initially brief periods of ischemic arrest were often induced by administration of high concentrations of potassium into the aortic root [61]. With the advent of aortic valve replacement surgery in the early 1960s, continuous perfusion of oxygenated blood from the H–L machine directly into the coronary ostia was common practice, although Shumway at Stanford University advocated simply topical cooling of the heart with ice and ice-cold fluid. This did not always reliably protect hypertrophied left ventricles, and in 1972 Cooley et al. described the phenomenon of ischemic contracture of the LV, so-called "stone heart." In 1973, Gay and Ebert [62] in the United States and others in England and Europe introduced intermittent infusion of cold low-concentration potassium crystalloid cardioplegia, and this was rapidly adopted to facilitate all types of cardiac surgery. Cardioplegia was initially administered antegrade, but in the early 1980s retrograde administration was introduced and cold blood cardioplegia was introduced in the late 1970s. Although warm blood cardioplegia was discussed in the late 1970s, it was not until the early 1990s that it was strongly advocated, especially by the Toronto group [32]. Myocardial protection is discussed further in a subsequent article in this issue.

In 1981, Kirklin's group at University of Alabama identified the systemic inflammatory reaction (SIR) induced by CPB as a cause for much of the morbidity associated with cardiac surgery [63]. This contributed to the introduction of drugs such as aprotinin, heparin-coated circuits, hemofiltration, leukofiltration, low-surface-area minimized circuits, minimized use of cardiotomy suction, and off-pump coronary artery bypass graft (CABG). The inflammatory response related to CPB is discussed more thoroughly later in this issue.

Monitoring

Initially, left heart filling was estimated by CVP, but this was soon recognized as being unreliable and placement of the left atrial (LA) line for direct monitoring of the left atrial pressure (LAP) was introduced by the group at the Mayo Clinic. Placement of an LA line was widely practiced until supplanted by the use of the pulmonary artery catheter (PAC) developed by cardiologists Swan and Ganz in 1970. The PAC was quickly adopted in cardiac surgery by the groups at MGH and Emory, and it soon became standard practice until the introduction of transesophageal echocardiography (TEE) to cardiac surgery in the 1980s. Perioperative TEE was introduced initially, at least in the USA, by anesthesiologist Michael Cahalan at the University of California Medical School in San Francisco [45], and followed soon thereafter by multiple other groups [46–48]. TEE is used not only to guide cardiac surgery but also to assist with conduct of CPB (e.g., assessing atherosclerosis in the aorta, cannulation strategies, decompression of the left ventricle and residual air, and possible aortic dissection.)

Although the early H–L machines used by the Mayo group included monitors of arterial and venous oxygen saturation, these, along with low-level monitors and bubble detectors, were only slowly adopted until they became standard [49]. In recent years, manufacturers have provided data management and computerized monitoring and alarm systems, including some that control arterial pump flows, to H–L machine consoles. Although the Mayo Clinic group employed electroencephalographic (EEG) monitoring in their early experience, this was not widely practiced and little cerebral monitoring was used until the introduction of processed EEG (e.g., bispectral index) and cerebral oximetry (by Somanetics) in the early 1990s. Murkin's trial demonstrating the benefit of cerebral oximetry [50] has led some to advocate routine cerebral monitoring [51], and although widely practiced its use remains controversial because of the lack of high-level evidence.

Less invasive cardiac surgery

In an effort to reduce some of the adverse effects and cost associated with CPB, and to compete with percutaneous coronary intervention, a revolution started by the Swiss cardiologist Andreas Gruntzig with his letter to the editor of *Lancet* in 1978 [64], cardiac surgeons Benetti of Argentina [65] and Buffolo of Brazil [66] began performing direct coronary revascularization without the use of CPB (off-pump coronary artery bypass (OP-CAB)) in the late 1970s and the early 1980s. Others began adopting this practice in the 1990s, and soon it was widely practiced by groups throughout the world. Although there continues to be debate about the benefits and proper indication for OP-CAB, one notable observation has been that many of the complications, including stroke, neurocognitive decline, renal failure, inflammatory responses, and other morbidity and mortality, were only modestly reduced or not reduced as compared with CABG accomplished with CPB, suggesting that CPB is not the major cause of the complications associated with cardiac surgery.

In 1996, the "port-access system" was introduced for minimally invasive cardiac surgery [67]. Its use was associated with some unanticipated morbidity (including the reappearance of retrograde aortic dissection) and mortality, but it led to the further development of minimal-access surgery. This led to the reintroduction of augmented venous drainage, required by the use of long and narrow venous cannulas, yet it was also associated with some catastrophic complications. These unfortunate experiences emphasized the risk of the premature adoption of new techniques prior to adequate evaluation and the need to carefully prepare before the introduction of any changes in CPB practice. Partly in response to the challenge of OP-CAB, beginning in 2002 [68], minimized extracorporeal circuits began to be offered by several different manufactures and evaluated by many different groups. However, their use posed other limitations on the conduct of CPB and demanded specialized care by the entire team, and thus it has not been widely adopted in the USA.

Safety and accident surveys

Risk and risk containment has been a concern since the beginning of clinical CPB, but interest became more focused with the publication of the first national survey of perfusion accidents by Stoney et al., in 1980 [69] followed by multiple subsequent surveys in various countries over the next 20 years [70–72]. These have led to additional educational efforts and adoption of safe practices and safety equipment on H–L machines, and promulgation of guidelines such as those issued by the American Society of ExtraCorporeal Technology (AmSECT) International Consortium for Evidence-Based Perfusion [49]. The Australian and New Zealand College of Perfusionists (ANZCP) has initiated a model Perfusion Incident Reporting System (PIRS). In 2007, the Society of Cardiovascular Anesthesiologists (SCA) started the FOCUS (Flawless Operative Cardiovascular Unified Systems) initiative through the SCA Foundation [73], and in 2013 the American Heart Association (AHA) published a scientific statement on patient safety in the cardiac operating room emphasizing human factors and teamwork [74].

Perfusionists

In the early days, H–L machines were managed by surgeons (often residents) and laboratory technicians working in the research laboratories. Gradually, at least in the USA, this task was taken over by "technicians" drawn from various fields, who received "on-the-job training." A group of these "perfusionists" (a designation credited to Bennett Mitchell) began meeting in 1964, and they established the American Society of ExtraCorporeal Technology in 1968. In the late 1960s and the early 1970s, the demand for perfusionists increased dramatically with the introduction of coronary artery surgery and more successful valve surgery. In 1974, AmSECT established the American Board of Cardiovascular Perfusion (ABCP).The first baccalaureate program in perfusion was established by James Dearing at the Ohio State University in 1969 and the famed Texas Heart Institute School of Perfusion was established by Charles Reed in 1971. In 1991, the European Board of Cardiovascular Perfusion was established.

A survey of 811 perfusionists practicing in North America (USA and Canada) in 1980 by this author and his colleagues provides a snapshot of the nature of perfusion practice 25 years after it began [75]. Although 68% received their training on the job, 76% were ABCP certified. Disposable BOs were used in >90% of cases, roller pumps in 94%, and arterial filters in 64%. Low-level alarms were used in 45% of cases, oxygen sensors in 26%, and bubble alarms in 10%. Asanguineous priming was used in 72%. Two-thirds monitored heparinization prior to initiation of bypass, mostly with the ACT. Most employed moderate hypothermia (26–30°), and 84% added carbon dioxide to the oxygenator. Cold cardioplegia was employed in 99% of cases, but 50% of the time it was administered by a pressurized bag (usually controlled by the anesthesiologist). Changes in these practices are reflected in more recent surveys of practice in the USA and elsewhere [70–72,76–78].

Evidence-based practice and guidelines

The concept of basing medical practice on a critical review of the best evidence available in the medical literature was developed and promulgated by David Sakett and his colleagues at the McMaster University in Hamilton, Ontario, Canada beginning in 1981. This group included GH Guyatt who is credited with coining the term “evidence-based medicine” (EBM). They posited a hierarchy of levels of evidence, with a meta-analysis of several large well-conducted randomized controlled trials (RCTs) at the top. In recent years, the practice of EBM has been adopted for CPB. Unfortunately, as in many other fields of medicine, the existence of high-level evidence to guide most aspects of CPB is lacking [26,79], and there remains a great need and opportunities to generate such evidence to guide the conduct of CPB, especially in high-risk patients [3,26]. The development of small animal models (e.g., rabbit and rat) of CPB in the 1990s and the early 2000s has permitted the detailed analysis of the impact of various aspects of the conduct of CPB [80,81]. In the late 1980s, Mangano and colleagues initiated large multicenter studies involving thousands of patients, which have generated important observational data related to the conduct of cardiac surgery and CPB, as has the Northern New England Cardiovascular Disease Study Group. To promulgate EBM practice of CPB, the ANZCP inaugurated the annual “Perfusion Down Under” and AmSECT established the International Consortium for Evidence Based Perfusion in 2007, and several EBM guidelines for conduct of CPB have been published in recent years [26,40,49,82,83].

Education and simulation

In the early days, education mainly occurred through meetings of surgical and cardiology societies and publications in their journals. AmSECT inaugurated the first journal devoted to CPB (*Journal of Extracorporeal Perfusion*) in 1966, and a second journal, *Perfusion*, was inaugurated in 1986. In 1962, Galletti and Brecher published the first comprehensive textbook on CPB that served as the definitive treatise on CPB until other texts began to appear about 13 years later. Meetings devoted to CPB were first sponsored by AmSECT. In 1978, the SCA was established, which quickly devoted much attention to education regarding CPB. In 1980, cardiac surgeon Joe Utley initiated the San Diego Cardiothoracic Surgery Symposium mainly devoted to the conduct of CPB.

As in other fields of medicine and high-tech industries, the development of simulators and the use of simulation for training and evaluation have recently expanded into the practice of CPB. However, the use of computer simulation for basic education in perfusion was first described by Riley and O'Kane at the Mayo Clinic in 1977 [84]. The use of simulation was greatly enhanced by the development of the “Orpheus” simulator by Morris and Pybus in 2007 [85], and in the last decade various low- and high-fidelity simulators have been introduced and many groups have demonstrated their value in introductory perfusion education, maintenance of core skills, the practice of emergency situation responses, and the development of team resource management and multidisciplinary team education. This stimulated the AmSECT to establish a Simulation Taskforce in 2011.

Summary

Practical clinical CPB began only 60 years ago, and tremendous changes and advances have been made over that period of time, making it a remarkably safe and effective procedure (as this author can attest to personally, after his CABG utilizing CPB about 5 years ago.) Over this period, some accepted practices have been discarded (e.g., pH-stat strategy for blood gas management, routine use of moderate hypothermia, and prolonged DHCA), whereas previously discarded techniques have been brought back (e.g., subclavian artery inflow, potassium cardioplegia, and augmented venous return). In recent years, enhanced attention has been directed to safety, including devices and monitors for the ECC, establishment of guidelines, and enhanced education and evaluation including introduction of simulation. An important lesson is that the premature use of new equipment or techniques can lead to unexpected adverse consequences. Finally, much of our practice of CPB is not based upon a high level of evidence, and thus there is great opportunity for future research and improvement, therefore adding to this fascinating history of CPB.

Practice points

1. CPB has evolved over a short period of time, and it has become remarkably safe but is far from perfect.
2. The practice of CPB including choice of equipment and conduct is largely based on experience rather than high-level evidence.
3. The entire team (surgeon, perfusionist, and anesthesiologist) should be involved in selecting the equipment and deciding how to monitor and conduct CPB
4. Thorough evaluation of new techniques and equipment should be conducted before introducing them into one's clinical practice.

Research agenda

1. High-level evidence is still needed to guide selection of equipment and conduct of CPB and to identify in which patients these are critical
2. Some of the many unresolved issues include desirability of pulsatile flow, benefits and use of minimized circuits, importance of excluding cardiotomy suction, optimal hematocrit, type of arterial pump, need for and optimal surface coating, importance of GME and optimal filtration, and role of leukocyte-depleting filters.

Funding

The author wrote this entire manuscript and received no outside funding.

Conflict of interest

None.

References

*[1] Hessel 2nd EA. History of cardiac surgery and anesthesia. In: Estafanous FG, Barash PG, Reves JG, editors. Cardiac anesthesia: principles and clinical practice. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001. p. 3–35.
*[2] Hessel 2nd EA. Evolution of cardiac anesthesia and surgery. In: Kaplan JA, Reich DL, Lake CL, et al., editors. Kaplan's cardiac anesthesia. 5th ed. Philadelphia: PA Saunders/Elsevier; 2006. p. 3–32.
*[3] Hessel II EA. A brief history of cardiopulmonary bypass. Semin Cardiothorac Vasc Anesth 2014;18(2):87–100.
[4] American Society of ExtraCorporeal Technology. History and Heritage of cardiovascular surgery, perfusion and the american society of ExtraCorporeal technology. 1885–2011. Richmond, VA: American Society of ExtraCorporeal Technology; 2012.
*[5] Shumacker Jr HB. The evolution of cardiac surgery. Bloomington, IN: Indiana University Press; 1992.
[6] Shumacker HB. The birth of an idea and the development of cardiopulmonary bypass. In: Gravlee GP, Davis RF, Stammers AH, et al., editors. Cardiopulmonary bypass: principles and practice. 3rd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008. p. 21–32.
[7] Lillehei CW. Historical development of cardiopulmonary bypass in Minnesota. In: Gravlee GP, Davis RF, Stammers AH, et al., editors. Cardiopulmonary bypass. principles and practice. 3rd ed. Philadelphia, PA: Wolters Kluwer/Lippincott Williams & Wilkins; 2008. p. 3–20.
[8] Westaby S, Bosher C. Landmarks in cardiac surgery. Oxford, England: Isis Medical Media; 1997.
[9] Edmunds Jr LH. The evolution of cardiopulmonary bypass: lessons to be learned. Perfusion 2002;17:243–51.
[10] Galletti PM. Cardiopulmonary bypass: a historical perspective. Artif Organs 1993;17:675–86.
[11] Galletti PM, Mora CT. Cardiopulmonary bypass: the historical foundation, the future promise. In: Mora CT, editor. Cardiopulmonary bypass. Berlin, Germany: Springer- Verlag; 1995. p. 3–21.
[12] Stoney WS. Evolution of cardiopulmonary bypass. Circulation 2009;119:2844–53.
[13] Cooper DKC. Open heart. The radical surgeons who revolutionized medicine. New York, NY: Kaplan; 2010.

[14] Miller GW. King of hearts. The true story of the Maverick who pioneered open heart surgery. New York, NY: Crown; 2000.
[15] Utley JR. Early development of cardiopulmonary bypass. Perfusion 1986;1:1–14.
*[16] Utley JR, Johnson HD, Morgan MS. Cardiopulmonary bypass bibliography. Spartanburg, South Carolina: Cardiothoracic Research and Education Foundation; 1989.
[17] Comroe Jr JH, Dripps RD. Ben Franklin and open heart surgery. Circ Res 1974;35:661–9.
[18] Romaine-Davis A. John Gibbon and his heart-lung machine. Philadelphia: University of Pennsylvania Press; 1991.
*[19] Shumacker Jr HB. A dream of the heart. The life of john H. Gibbon, jr. Father of the heart-lung machine. Santa Barbara, CA: Fithian Press; 1999.
[20] Gibbon Jr JH. Application of a mechanical heart and lung apparatus to cardiac surgery. Minn Med 1954;37(3):171–85.
[21] Lillehei CW, Cohen M, Warden HE, et al. The direct-vision intracardiac correction of congenital anomalies by controlled cross circulation; results in thirty-two patients with ventricular septal defects, tetralogy of Fallot, and atrioventricularis communis defects. Surgery 1955;38(1):11–29.
[22] Kirklin JW, Dushane JW, Patrick RT, et al. Intracardiac surgery with the aid of a mechanical pump-oxygenator system (Gibbon type): report of eight cases. Proc Staff Meet Mayo Clinic 1955;30:201–6.
[23] Lillihei CW, DeWall RA, Gott VL, et al. The direct vision correction of calcific aortic stenosis by means of a pump-oxygenator and retrograde coronary sinus perfusion. Dis Chest 1956;30(2):123–32.
[24] Stephenson LW. Historical perspective of the american association for thoracic surgery: john W. Kirklin, MD (1917-2004). J Thorac Cardiovasc Surg 2007;134(1):225–8.
[25] Cross FS, Kay EB. Direct vision repair of intracardiac defects utilizing a rotating disc reservoir-oxygenator. Surg Gynecol Obstet 1957 Jun;104(6):711–6.
*[26] Murphy GS, Hessel 2nd EA, Groom RC. Optimal perfusion during cardiopulmonary bypass: an evidence-based approach. Anesth Analg 2009;108:1394–417.
[27] DeWall RA, Levy MJ. Direct cannulation of the ascending aorta for open-heart surgery. J Thorac Cardiovasc Surg 1963;45: 496–9.
[28] Sabik JF, Lytle BW, McCarthy PM, et al. Axillary artery: an alternative site of arterial cannulation for patients with extensive aortic and peripheral vascular disease. J Thorac Cardiovasc Surg 1995;109:885–90.
[29] Toomasian JM, McCarthy JP. Total extrathoracic cardiopulmonary support with kinetic assisted venous drainage: experience in 50 patients. Perfusion 1998;13:137–43.
[30] Taketani S, Sawa Y, Masai T, et al. A novel technique of cardiopulmonary bypass using vacuum system for venous drainage with pressure relief valve: an experimental study. Artif Organs 1998;22:337–41.
[31] Ream AK, Reitz BA, Silverberg G. Temperature correction of PCO_2 and pH in estimating acid-base status: an example of the emperor's new clothes? Anesthesiology 1982;56:41–4.
[32] Lichtenstein SV, Ashe KA, Dalati H, et al. Warm heart surgery. J Thorac Cardiovasc Surg 1991;101:269–74.
[33] Nathan HJ, Lavallée G. The management of temperature during hypothermic cardiopulmonary bypass: Canadian survey. Can J Anaesth 1995;42:669–71.
[34] Drew CE, Anderson IM. Profound hypothermia in cardiac surgery: report of three cases. Lancet 1959;1(7076):748–50.
[35] Dillard DH, Mohri H, Hessel 2nd EA, et al. Correction of total anomalous pulmonary venous drainage in infancy utilizing deep hypothermia with total circulatory arrest. Circulation 1967;35(4 Suppl):I105–10.
[36] Barratt-Boyes BG, Simpson M, Neutze JM. Intracardiac surgery in neonates and infants using deep hypothermia with surface cooling and limited cardiopulmonary bypass. Circulation 1971;43(5 Suppl):I25–30.
[37] Ergin MA, O'Connor J, Guinto R, et al. Experience with profound hypothermia and circulatory arrest in the treatment of aneurysms of the aortic arch. Aortic arch replacement for acute arch dissections. J Thorac Cardiovasc Surg 1982;84(5): 649–55.
[38] Bull BS, Korpman RA, Huse WM, et al. Heparin therapy during extracorporeal circulation. I. Problems inherent in existing heparin protocols. J Thorac Cardiovasc Surg 1975;69(5):674–84.
[39] Royston D, Bidstrup BP, Taylor KM, et al. Effect of aprotinin on need for blood transfusion after repeat open-heart surgery. Lancet 1987;2(8571):1289–91.
[40] Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris VA, Brown JR, et al. 2011 update to the society of thoracic surgeons and the society of cardiovascular anesthesiologists blood conservation clinical practice guidelines. Ann Thorac Surg 2011;91:944–82.
[41] Rosengart TK, DeBois W, O'Hara M, et al. Retrograde autologous priming for cardiopulmonary bypass: a safe and effective means of decreasing hemodilution and transfusion requirements. J Thorac Cardiovasc Surg 1998;115(2):426–38.
[42] Darup J, Bleese N, Kalmar P, et al. Hemofiltration during extracorporeal circulation (ECC). Thorac Cardiovasc Surg 1979; 27(4):227–30.
[43] Naik SK, Knight A, Elliott MJ. A successful modification of ultrafiltration for cardiopulmonary bypass in children. Perfusion 1991;6(1):41–50.
[44] Journois D, Israel-Biet D, Pouard P, et al. High-volume, zero-balanced hemofiltration to reduce delayed inflammatory response to cardiopulmonary bypass in children. Anesthesiology 1996;85(5):965–76.
[45] Cahalan MK, Kremer P, Schiller NB, et al. Intraoperative monitoring with two-dimensional transesophageal echocardiography (Abst.). Anesthesiology 1982;57:A-153.
[46] Kaplan JA. Transesophageal echocardiography. Mt Sinai J Med 1984;51(5):592–4.
[47] Cahalan MK, Litt L, Botvinick EH, et al. Advances in noninvasive cardiovascular imaging: implication for the anesthesiologist. Anesthesiology 1987;66:356–72.
[48] Clements FM, deBruijn NP. Perioperative evaluation of regional wall motion by transesophageal two-dimensional echocardiography. Anesth Analg 1987;66:249–61.
*[49] Baker RA, Bronson SL, Dickinson TA, et al. Report from AmSECT's international consortium for evidence-based perfusion: American society of ExtraCorporeal technology standards and guidelines for perfusion practice. J Extra Corpor Technol 2013;45:156–66.
[50] Murkin JM, Adams SJ, Novick RJ, et al. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. Anesth Analg 2007;104:51–8.

[51] Edmonds Jr HL. 2010 standard of care for central nervous system monitoring during cardiac surgery. J Cardiothorac Vasc Anesth 2010;24:541–3.
[52] Warren O, Alexiou C, Massey R, et al. The effects of various leukocyte filtration strategies in cardiac surgery. Eur J Cardiothorac Surg 2007;31(4):665–76.
[53] Henriksen L, Hjelms E, Lindeburgh T. Brain hyperperfusion during cardiac operations. Cerebral blood flow measured in man by intra-arterial injection of xenon 133: evidence suggestive of intraoperative microembolism. J Thorac Cardiovasc Surg 1983;86:202–8.
[54] Govier AV, Reves JG, McKay RD, et al. Factors and their influence on regional cerebral blood flow during nonpulsatile cardiopulmonary bypass. Ann Thorac Surg 1984;38:592–600.
[55] Murkin JM, Farrar JK, Tweed WA, et al. Cerebral autoregulation and flow/metabolism coupling during cardiopulmonary bypass: the influence of PaCO2. Anesth Analg 1987;66(9):825–32.
[56] Nussmeier NA, Arlund C, Slogoff S. Neuropsychiatric complications after cardiopulmonary bypass: cerebral protection by a barbiturate. Anesthesiology 1986;64:165–70.
[57] Zaidan JR, Klochany A, Martin WM, et al. Effect of thiopental on neurologic outcome following coronary artery bypass grafting. Anesthesiology 1991;74:406–11.
[58] Wareing TH, Davila-Roman VG, Barzilai B, et al. Management of the severely atherosclerotic ascending aorta during cardiac operations. A strategy for detection and treatment. J Thorac Cardiovasc Surg 1992;103:453–62.
[59] Ueda Y, Miki S, Kusuhara K, et al. Surgical treatment of aneurysm or dissection involving the ascending aorta and aortic arch, utilizing circulatory arrest and retrograde cerebral perfusion. J Cardiovasc Surg Torino 1990;31:553–8.
[60] Mills NL, Ochsner JL. Massive air embolism during cardiopulmonary bypass. Causes, prevention, and management. J Thorac Cardiovasc Surg 1980;80:708–17.
[61] Melrose DG, Dreyer B, Bentall HH, et al. Elective cardiac arrest. Lancet 1955;269(6879):21–2.
[62] Gay Jr WA, Ebert PA. Functional, metabolic, and morphologic effects of potassium-induced cardioplegia. Surgery 1973;74(2):284–90.
[63] Chenoweth DE, Cooper SW, Hugli TE, et al. Complement activation during cardiopulmonary bypass: evidence for generation of C3a and C5a anaphylatoxins. N Engl J Med 1981;304:497–503.
[64] Gruntzig A. Transluminal dilatation coronary-artery stenosis. Lancet 1978;1(8058):263.
[65] Benetti FJ, Naselli G, Wood M, et al. Direct myocardial revascularization without extracorporeal circulation: experience in 700 patients. Chest 1991;100:312–6.
[66] Buffolo E, Andrade JC, Succi J, et al. Direct myocardial revascularization without cardiopulmonary bypass. Thorac Cardiovasc Surg 1985 Feb;33(1):26–9.
[67] Stevens JH, Burdon TA, Peters WS, et al. Port-access coronary artery bypass grafting: a proposed surgical method. J Thorac Cardiovasc Surg 1996;111:567–73.
[68] Fromes Y, Gaillard D, Ponzio O, et al. Reduction of the inflammatory response following coronary bypass grafting with total minimal extracorporeal circulation. Eur J Cardiothorac Surg 2002;22(4):527–33.
[69] Stoney WS, Alford Jr WC, Burrus GR, et al. Air embolism and other accidents using pump oxygenators. Ann Thorac Surg 1980;29:336–40.
[70] Jenkins OF, Morris R, Simpson JM. Australasian perfusion incident survey. Perfusion 1997;12(5):279–88.
[71] Mejak BL, Stammers A, Rauch E, et al. A retrospective study on perfusion incidents and safety devices. Perfusion 2000;15(1):51–61.
[72] Charrière JM, Pélissié J, Verd C, et al. Survey: retrospective survey of monitoring/safety devices and incidents of cardiopulmonary bypass for cardiac surgery in France. J Extra Corpor Technol 2007;39(3):142–57.
[73] Martinez EA, Marsteller JA, Thompson DA, et al. The society of cardiovascular anesthesiologists' FOCUS initiative: locating errors through networked surveillance (LENS) project vision. Anesth Analg 2010;110:307–11.
*[74] Wahr JA, Prager RL, Abernathy 3rd JH, et al. Patient safety in the cardiac operating room: human factors and teamwork: a scientific statement from the American heart association. Circulation 2013;128:1139–69.
*[75] Miller Jr DW, Binford JM, Hessel 2nd EA. Results of a survey of the professional activities of 811 cardiopulmonary perfusionists. J Thorac Cardiovasc Surg 1982;83(3):385–9.
[76] Silvay G, Ammar T, Reich DL, et al. Cardiopulmonary bypass for adult patients: a survey of equipment and techniques. J Cardiothorac Vasc Anesth 1995;9(4):420–4.
[77] Tuble SC, Willcox TW, Baker RA. Australian and New Zealand perfusion survey: management and procedure. J Extra Corpor Technol 2009;41(2):64–72.
[78] Warren OJ, Wallace S, de Wit KL, et al. Variations in the application of various perfusion technologies in Great Britain and Ireland–a national survey. Artif Organs 2010;34(3):200–5.
[79] Bartels C, Gerdes A, Babin-Ebell J, et al. Cardiopulmonary bypass: evidence or experience based? J Thorac Cardiovasc Surg 2002;124:20–7.
[80] Ballaux PK, Gourlay T, Ratnatunga CP, et al. A literature review of cardiopulmonary bypass models for rats. Perfusion 1999;14:411–7.
[81] Grocott HP, Mackensen GB, Newman MF, et al. Neurological injury during cardiopulmonary bypass in the rat. Perfusion 2001;16:75–81.
[82] Shann KG, Likosky DS, Murkin JM, et al. An evidence based review of the practice of cardiopulmonary bypass in adults: a focus on neurologic injury, glycemic control, hemodilution, and the inflammatory response. J Thorac Cardiovasc Surg 2006;132:283–90.
[83] Hogue Jr CW, Palin CA, Arrowsmith JE. Cardiopulmonary bypass management and neurologic outcomes: an evidence based appraisal of current practices. Anesth Analg 2006;103:21–37.
[84] Riley JB, O'Kane KC. A computer simulation of maintaining total heart lung bypass for basic education. J Extra Corpor Technol Proc 1977:42–9.
[85] Morris RW, Pybus DA. "Orpheus" cardiopulmonary bypass simulation system. J Extra Corpor Technol 2007;39(4):228–33.