Cardiopulmonary Bypass and Cardioplegia

33

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Abstract

This chapter describes the history and techniques of cardiopulmonary bypass, a process that effectually excludes the heart from the general circulation and leaves it empty so that it can accommodate open cardiac surgical intervention. Since its first implementation, cardiopulmonary bypass has improved significantly to become a very highly sophisticated, but reliably performed procedure. The near future promises even more improvements because research and innovations continue to make cardiac operations safer and more efficient.

With the advent of coronary bypass in the late 1960s and early 1970s, surgeons became increasingly interested in finding ways to protect the heart during the period of global ischemia via infusion of cold perfusates into the coronary circulation (i.e., cardioplegia). Therefore, this chapter further details the advantages and disadvantages of various cardioplegia solutions which have been developed at several separate institutions, including extracellular- and intracellular-type solutions.

Keywords

Cardiopulmonary bypass • Cross-circulation • Anticoagulation • Heart–lung machine • Cardioplegia

33.1 Cardiopulmonary Bypass

Extracorporeal circulation and *cardiopulmonary bypass* are synonymous terms denoting a method by which the blood that usually returns directly to the heart is temporarily drained from superior and inferior vena cavae. The blood is diverted into a reservoir where it is oxygenated and subsequently returned to the patient's arterial circulation. This process effectually excludes the heart from the general circulation and leaves it empty so that it can accommodate surgical intervention (Fig. 33.1).

The breakthrough technologies that first allowed this type of *open-heart* operation were developed by two separate centers in the USA in the early 1950s. Importantly, Lillehei and Varco [1] at the University of Minnesota developed a cross-circulation technique. This technique utilized a human donor (usually the parents of a child undergoing cardiac surgery) who, in essence, functioned as an extracorporeal pump for the patient's circulatory system. This type of extracorporeal circulation also allowed the blood to be drained from the child's vena cava so that the surgical procedure could be performed within the empty heart. The subsequent development of the heart–lung machine by Gibbon [2] was considered revolutionary in that it eliminated the need for a support donor (a second patient). Gibbon's system has been improved since the mid-1950s and has gradually evolved into the standardized, but very complex and sophisticated machine it is today. The bubble oxygenator developed by DeWald and Lillehei in 1955 was additive technology that also aided in the advancement of this field (see also Chap. 25).

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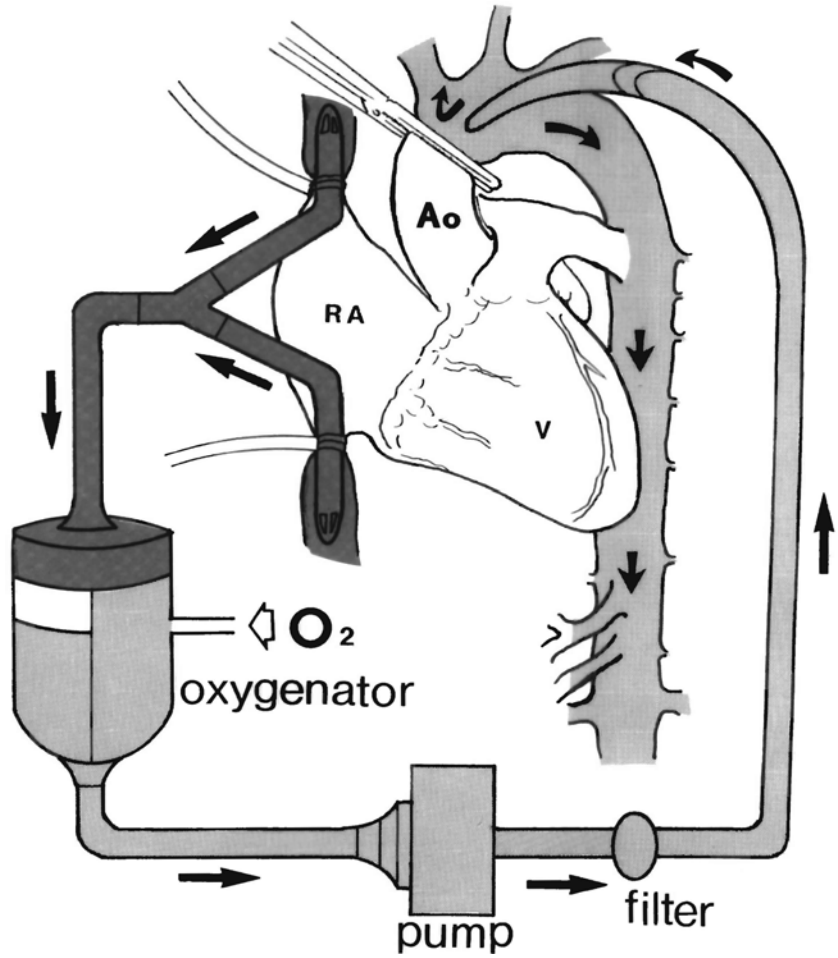

Fig. 33.1 Total cardiopulmonary bypass showing the venous cannulas in the superior and inferior vena cavae with constrictions placed around the respective veins. The venous blood is draining to the oxygenator and is propelled by the pump into the distal ascending aorta to maintain perfusion of the entire body. A cross-clamp is applied to the ascending aorta, and all chambers of the heart therefore are excluded from the perfusion system. Note that modern day systems often place the pump ahead of the oxygenator such that blood from the reservoir is actively pumped through the oxygenator. *Ao* aorta, *RA* right atrium, *V* ventricle

The basic components of an extracorporeal circuit include: (1) a reservoir into which the patient's blood is diverted; (2) an oxygenator that replaces the function of the lungs; and (3) a pump that propels the oxygenated blood back into the patient's arterial circulation. In this manner, the machine bypasses both the heart and the lungs while maintaining the function of other organs during surgical interventions within the heart.

A solid understanding of cardiopulmonary bypass and ways to control the patient's physiology is just as important as efficient and meticulous techniques to achieve the best outcomes in cardiac surgery. Today, dedicated perfusionists work closely with the surgical team to ensure that bypass runs properly; they rely on detailed communication from the operative field. This chapter details the components of cardiopulmonary bypass.

33.1.1 Venous Drainage

The venous blood that is normally delivered to the right atrium is commonly diverted to the heart–lung machine, either by cannulating the veins themselves or by cannulating the right atrial chamber. Surgery performed in or through the right atrial chamber requires that both the right atrium and right ventricle be empty. To do so, cannulas are typically placed directly into the superior and inferior vena cavae. Constricting tourniquets are then placed around the vein over the cannulas, and thus blood is diverted into the heart–lung machine (Fig. 33.1). This constitutes *total cardiopulmonary bypass*.

Cannulation of the superior vena cava (SVC) is normally performed by placing a purse string suture either directly in the SVC or in the right atrium. The cannula is advanced either directly into the SVC or indirectly through the right atrium. It should be noted that direct cannulation of the SVC generally provides more room for any work that may need to be done inside the right atrium. Conversely, for large ascending aortic aneurysms it may be necessary to advance the cannula indirectly through the atrium.

Cannulation of the inferior vena proceeds through purse strings placed on the inferior portion of the right atrium. By placing tourniquets around both cannulas and snaring down on them, the surgeon establishes total cardiopulmonary

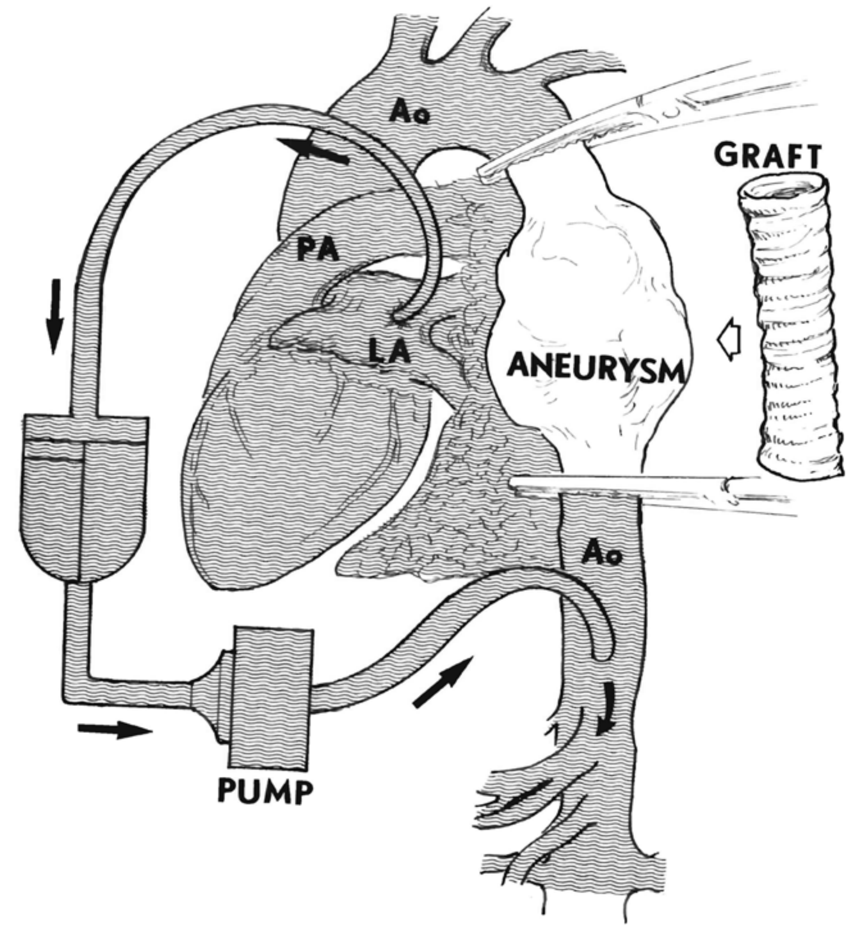

Fig. 33.2 Left heart bypass showing a cannula inserted in the left atrium draining approximately half of the cardiac output into the oxygenator through the pump, and reinfusing it in the distal aorta for perfusion of the abdominal organs. The excluded portion is only the descending thoracic aorta (between clamps). The left heart continues to beat and pumps half of the cardiac output to the head and upper organs. The graft is shown in the position in which it will be implanted after the aneurysm is resected. *Ao* aorta, *LA* left atrium, *PA* pulmonary artery

bypass. The only flow that enters the right atrium is that from the coronary sinus, i.e., until the aorta is clamped. With the aorta cross-clamped and no flow entering the aortic root and coronary arteries, the surgeon can work inside the atrium in a completely bloodless field. Typically, access to the left atrium is obtained by opening the fossa ovalis. A bloodless field here allows insertion of the retrograde coronary artery catheter directly into the coronary sinus for direct cardioplegia, as discussed later.

A modification of this type of bypass can be used when the cardiac chambers are not surgically entered, such as in coronary bypass operations involving procedures on the surface of the heart. In such cases, a double-staged cannula is placed with the tip of the cannula in the inferior vena cava and the side drainage holes positioned at the level of the right atrium. Coronary bypass surgery does not involve direct vision of the inside of the cardiac chambers so there is no need to constrict the superior or inferior vena cava. This configuration is often referred to as *full cardiopulmonary bypass* rather than total cardiopulmonary bypass. When coronary bypass operations are undertaken simultaneously with cardiac valve repairs or replacements, total cardiopulmonary bypass is typically implemented.

If venous drainage is not optimal, then two critical issues may result: (1) the heart may become distended with warm systemic blood, resulting in persistent myocardial activity or undue strain on the myocardium leading to injury; and (2) venous congestion may result in hepatic impairment. Thus, adequate venous drainage must be ensured prior to proceeding with these types of operations.

33.1.2 Arterial Return

Once the blood has been oxygenated in the heart–lung machine, it is returned to the patient's general circulation via cannulas placed directly in the arterial system (Fig. 33.1). The most common method involves the placement of a cannula in the highest portion of the ascending aorta below or at the origin of the innominate artery. This is typically the first cannula that is inserted. The aorta must be free of calcific disease in order to cannulate it without increased risk of stroke. The axillary artery is the next best alternative in the setting of calcific aortic disease and/or for cases requiring circulatory arrest for replacement of all or parts of the aortic arch [3].

Depending on the type of surgery, other sites are also used, including cannulation of the femoral artery in the groin and infusion of the arterial system in a retrograde manner. This is useful for minimally invasive heart surgery in younger patients without calcific disease in whom the thoracic incision does not allow exposure to the ascending aorta. Yet, if calcific disease is present the retrograde flow can shower plaque up toward the carotids with increased risk of stroke.

Once the arterial cannula is secured and both the forward flow and venous drainage are adequate, the ascending aorta is cross-clamped. At this point no systemic blood enters the coronary artery circulation. The heart is, therefore, totally excluded from the circulation. Thus the heart needs to be protected by using one of a number of methods to infuse cardioplegic solutions (see Sect. 33.2). Any blood remaining in the operative field is removed via cardiotomy suction lines which are used to aspirate it back to the heart–lung machine, where it reenters the bypass circulation with the rest of the removed blood.

In some operations involving the descending thoracic aorta, total cardiopulmonary bypass is not necessary. For example, if the portion of the aorta that needs to be isolated lies between the left carotid artery and the diaphragm, only part of the total blood volume needs to be removed, and partial bypass can be implemented (Fig. 33.2). The blood is removed by the heart–lung machine via a cannula inserted into either the left atrium or left superior pulmonary vein. Then, the blood is infused back into the descending thoracic aorta beyond the level of distal aortic cross-clamp. Doing so allows the heart to continue to beat normally and helps maintain the viability of the proximal organs (head, neck, and arms), while the rest of the lower body is perfused and thus maintained by the pump. This technique is called *left heart bypass* because it involves only removal of blood and decompression of the left-side cardiac chambers. As shown in Fig. 33.2, after a descending thoracic aorta aneurysm operation is completed, the bypass is discontinued. The clamps which were placed to occlude the aorta in the arch and the descending portion are removed. The normal physiological perfusion of the body (which was interrupted during surgery without ever stopping the heartbeat) is thus reestablished.

After an operation applying full or total cardiopulmonary bypass and cardiac arrest, the aortic clamp is released, allowing the general circulation to reperfuse the coronary arteries and to rewarm the heart. After the air is expelled from the cardiac chambers, the heart often elicits ventricular fibrillation. Such fibrillation normally requires cardioversion with an electric shock administered directly to the heart by employing paddles that deliver currents that vary from 20 to 30 W/s. The patient is then ventilated using the endotracheal tube connected to the anesthesia machine, which reinflates the lungs. After the normal sinus rhythm of the heart is reestablished, the patient is gradually weaned off the extracorporeal circulation until the heart takes over full function. At this point the heart–lung machine is stopped, and all cannulas are removed and access areas closed

In some complex surgical cases involving the aortic arch, separate independent perfusion of the arch vessels may require implementation, that is, in addition to the perfusion of the lower part of the body through the cannula inserted in the femoral artery. This is most commonly seen in situations where the arch and descending aorta are bypassed simultaneously. The perfusionist must monitor two separate infusions to regulate pressures and make certain that a balance and sufficient perfusion is achieved in both the upper and the lower areas of the patient's body. With the advent of staged aortic procedures such as the "elephant trunk procedure" and hybrid stent grafting, it is less common to deal with such an extensive amount of aortic replacement in a single setting [4].

Another specialized bypass method that needs description is the *deep hypothermia and total circulatory arrest* technique. This type of total cardiopulmonary bypass requires decreasing body temperature to very low levels (15°–25 °C); this is typically accomplished using heat exchangers installed in the heart–lung machine circuits. Circulation is stopped altogether when the proper temperature is reached, and the heart is emptied for several minutes with the entire volume of the patient's blood remaining in the reservoir of the heart–lung machine. The pump is then stopped and the arterial perfusion ceases. The venous return line, however, is left open to continue emptying the patient's blood volume completely into the reservoir of the heart–lung machine.

This technique is used in special cases to allow repair of very complicated conditions. The period of total circulatory arrest induced during deep hypothermia is usually less than 45 min [5, 6]. This time restriction is to insure that the patient does not suffer neurological deterioration or central nervous system damage during such global ischemia. In general, cooling alone is sufficient for circulatory arrest times less than 20 min. However, since the time required to perform the aortic arch repair can be unpredictable, most surgeons will utilize some sort of brain perfusion strategy. Retrograde brain perfusion is commonly used for periods of 30–45 min. It requires the arterial outflow from the pump to be connected to the SVC cannula either directly or through a separate circuit. By snaring the SVC, oxygenated blood is delivered up the vena cava to perfuse the brain in a retrograde fashion. The flow rates are typically 300–500 mL/min and the central venous pressure is kept no higher than 35 mmHg.

Antegrade brain perfusion is more typically used for planned circulatory arrest periods ranging 45–90 min. In this mode of perfusion, the axillary artery graft is used to deliver oxygenated blood up the carotids once the innominate artery is snared; typical flow rates vary between 500 and 1000 mL/min. The patient should have some evaluation of the brain vessels beforehand to ensure a complete *Circle of Willis*, an anastomotic system of arteries that sits at the base of the brain.

As soon as the repair is completed, normal cardiopulmonary bypass is reestablished. The patient is gradually rewarmed to a normal core temperature of 37 °C prior to removal from extracorporeal circulation. The use of deep hypothermia always requires careful evaluation by the surgical team. In such clinical cases, the danger of inducing neurological damage must be weighed against the benefits of correcting a major cardiac anomaly. Conversely, the long-term quality of the arch repair should not be compromised by concerns over circulatory arrest, especially with proper usage of selective brain perfusion techniques.

It is important to note that aortic cannulation can have important consequences (pitfalls) associated with it. The patient must be completely anticoagulated before instituting flow through the cannula. If there is calcific disease, cannulating or clamping the aorta has been associated with increased incidences of stroke or distal embolic events. Finally, during aortic cannulation, there is commonly a 1–2 % incidence of aortic dissection related to a tear caused by the cannula. If such a condition is suspected due to high line pressures or enlargement of the ascending aorta, the flow through the cannula should be immediately stopped; a transesophageal echo can be used to confirm the diagnosis, and then an alternative cannulation strategy should be identified. This situation often requires circulatory arrest to repair the tear.

33.1.3 Anticoagulation

To prevent the formation of clots during cardiopulmonary procedures, both within the body and within the extracorporeal heart–lung machine, it is necessary to anticoagulate the patient's blood. The most common agent used for such anticoagulation is heparin. It is commonly administered intravenously before cannulation at a dose of 300 units/kg. There are two types of heparin: (1) the lung beef type which is extracted from a bovine source; and (2) the porcine mucosal type which is from a swine source. Since the mid-1980s, the porcine mucosal heparin has been preferred because it is less likely to lead to thrombocytopenia and/or the production of heparin antibodies in the patient, a condition known as HIT syndrome [7].

A small percentage of patients have experienced heparin-induced thrombocytopenia (HIT) from prior heparin exposure. They have antibodies to heparin molecules which attack heparin-platelet aggregates and this, in turn, depletes their platelet pool to dangerously low levels.

The effectiveness of anticoagulation therapy requires testing, usually by measuring the activated clotting time (ACT) of the patient's blood. These test results are expressed in seconds, with normal values ranging between 100 and 120 s. Heparinization is deemed adequate for cardiopulmonary bypass when the ACT runs above 400 s. Typically, the anticoagulant effects induced during such surgeries must be reversed postoperatively. Still today, porotamine sulfate is the drug of choice to neutralize the effects of the heparin and allow the patient to elicit normal clotting values. Yet, this drug is a macromolecule compound that may produce pulmonary vasoconstriction and severe hypotension [8, 9], particularly in diabetic patients. Nevertheless, such side effects are rare and, in most patients, this drug can be used safely, as it neutralizes the effects of heparin. Naturally, the amount of protamine necessary to achieve neutralization depends on the amount and timing of therapeutic heparin administered. Initially, a test dose is given; if no reaction occurs, protamine is then administered in the appropriate amounts. Its effects are monitored by measuring ACTs until they return to a normal range. It should be noted that if any reaction or side-effects occur, additional treatments are commonly employed, such as the administration of epinephrine, calcium, steroids, or fluids [9].

Occasionally patients cannot be given heparin because they have developed heparin antibodies from previous exposure. Other anticoagulant agents are studied and occasionally used in such cases, including hirudin (Lepirudin) [10], a potent anticoagulant that is extracted from leaches and lampreys. Other drugs include the heparinoids [11] like Orgaran (Org10172, Organon Company, West Orange, NJ, USA), for which a different monitoring protocol is implemented. Unfortunately, to date, no drug has been identified that can reverse the effects of Orgaran, thus it must be metabolized by the human body. For such patients bleeding is a constant, and often very difficult, postoperative complication. Bivalrudin (Angiomax) is currently the most commonly used agent for cardiac surgery in patients with HIT [12].

If the cardiopulmonary bypass takes an extended time, coagulopathies often pose complications. In such cases, the body, primarily the liver, is unable to produce the appropriate clotting factors to reverse the anticoagulation status. Other factors that can contribute to coagulopathies include ischemia of the abdominal organs, particularly if necrosis occurs in the liver cells and/or in the intestine. Bleeding, therefore, can be a very serious and difficult complication to treat; in such patients, the administration of multiple coagulation factors, platelets, and cryoprecipitates may be required.

33.1.4 Temperatures of Perfusion

Since their inception, cardiopulmonary bypass and extracorporeal circulation have been implemented using some degree of hypothermia. Lowering core body temperature decreases the overall oxygen demands of body tissues, and a more desirable protective state during pulseless circulation is provided by the heart–lung machine.

Several degrees of clinical hypothermia are commonly identifiable relative to extracorporeal circulation interventions. *Normothermia* indicates that core body temperature is between 35.5° and 37 °C [13], *mild hypothermia* is between 32° and 35 °C, and *moderate hypothermia* is between 24° and 32 °C. An important distinction must be made between mild and moderate hypothermia. If the heart is perfused at mild levels (above 31 °C), the heart will continue to beat although at slower rates. Therefore, this mild level of hypothermia allows surgical correction of some congenital anomalies without arresting the heart. An additional level of hypothermia used occasionally is *deep or profound hypothermia*, which usually brings the body temperature below 20 °C.

Currently, most open-cardiac operative procedures are conducted under conditions somewhere between moderate and mild hypothermia. Some centers routinely use moderate hypothermia, while others employ normothermia [14, 15]. One reason to maintain normothermic perfusion is to avoid coagulopathies that may develop when body temperature is lowered to the moderate levels, and thus allow for normal function of the body's enzyme systems. Normothermic temperatures also enable the kidneys to respond better to diuretics.

Several reports have indicated the relative safety of normothermic perfusion [13–19], but an equal number have suggested complications with this modality [20, 21]. As a result, the spontaneous drifting to mild hypothermic levels is generally preferred. Deep or profound hypothermia is associated with the implementation of total circulatory arrest as mentioned before. With this level of hypothermia, body temperature is lowered to between 15° and 18 °C. Such operations are usually prolonged given the time it takes to cool the body to those levels before surgery and also by the required time to rewarm it afterwards. The goal of systemic cooling is not so much to decrease metabolic demands in the peripheral organs, but rather to drop the temperature of collateral arterial flow that reaches the heart such as the bronchial arteries. If one stays normothermic and has difficulty maintaining cardiac arrest, it is likely that the warm bronchial artery flow is making its way through the pulmonary arteries or veins and warming the inside of the heart.

33.1.5 Perfusion Pressures

Under normal physiological conditions, the heart provides a pulsatile pressure and flow. The systolic pressure depends on the ventricular function. The diastolic pressure in normal states is primarily regulated by the blood volume and the vascular tonus (the degree of constriction experienced by venous vessels relative to their maximally dilated states). During cardiopulmonary bypass, the heart–lung machine facilitates pulseless perfusion; there is no systolic or diastolic pressure, but rather one steady mean pressure throughout the arterial circulatory system. Therefore, this pressure should be high enough to provide adequate blood oxygen to all organs of the body, particularly the brain and kidneys. Since the patient is typically hypothermic, the oxygen requirements are lower; the perfusion pressure is usually maintained around 70 mm of mercury Hg. Occasionally, specifically in patients with severe obstructive carotid disease, a higher perfusion pressure is recommended to ensure proper perfusion of the brain. Nevertheless, this recommendation is somewhat debated because the brain is known to have its own regulatory system to maintain low resistance near obstructed areas [15, 17]. A useful rule of thumb is to keep the mean arterial pressure close to the patient's decade of life (i.e., 74 years old = 70 mmHg, 86 years old = 80 mmHg).

During cardiopulmonary bypass, if the patient shows decreased vascular tonus (despite adequate volume of fluid), vasoconstrictors are routinely used; a typical therapy is a bolus or drips of neosynephrine [13]. A decreased vascular tonus is common in septic patients with bacterial endocarditis, for whom an emergency operation sometimes is necessary to replace the affected valve and reverse the profound heart failure. Remember that the perfusion pressure is a product of the cardiopulmonary flow and resistance. If the flow has been optimized (ideal flow = 2.4 × body surface area) then the resistance needs to be increased to meet the desired perfusion pressure. Markers of end organ perfusion during bypass include: urine output, mixed venous saturation, lactic acid, and base deficit.

33.1.6 Hemodilution

Up to a certain level, hemodilution can be a desirable side effect of cardiopulmonary bypass. Lowering the hematocrit prevents *clumping* of the red cells or *sludging*, thereby providing better circulation at the capillary level; viscosity of the circulating blood is decreased, on the other hand, to also ensure that oxygen is adequately delivered to the body's tissues during cardiopulmonary bypass. Hematocrit levels are monitored and maintained at a minimum between 22 and 26 %. Toward the end of the bypass operation, typically the perfusionist deliberately removes some of the fluid from the patient's circulation to hemoconcentrate the blood toward more normal hematocrit levels [22, 23]; this rises to above 30 % by the time the patient is removed from cardiopulmonary bypass. Subsequent diuresis and/or removal of red blood cells (RBC) will further aid in reestablishing the hematocrit to normal levels.

Transfusion of RBC is sometimes necessary if the hematocrit cannot be maintained above 22 %. Risk factors for a low hematocrit on bypass include: (1) the female gender; (2) older age; (3) lower body mass index; (4) a high New York Heart Association class and combined valve and coronary bypass procedures; and/or (5) anemia, the strongest risk factor [24].

It is important to note that there are multiple problems associated with RBC transfusion including: (1) increased renal dysfunction; (2) arrhythmias and infections; and, (3) increased long-term mortality [24]. Interestingly, anemia and RBC transfusions for the bypass patient have additive adverse effects [25]. Therefore, every effort should be made to prevent severe anemia without transfusion, including: (1) use of smaller bypass circuits and less priming volumes; (2) proper preoperative hemoglobin optimization; (3) increasing RBC transfusion thresholds; (4) retrograde autologous priming; and (5) meticulous hemostasis [26].

Pulseless perfusion, as provided by the heart–lung machine, and hemodilution will both invariably lead to a transfer of fluid across the capillary walls into the third space (interstitial). Therefore, all patients develop, to some degree, peripheral third spacing or edema, which often develops within the first 24–72 h after bypass. This usually manifests as pulmonary edema, pleural effusions, atrial fibrillation, and lower extremity edema. This is why patients often require diuresis on day 2–4 following bypass. In an attempt to avoid edema, plasma expanders (such as albumin, hetastarch, dextran, and mannitol) are usually added to the priming solution of the heart–lung machine.

33.1.7 Heart–Lung Machine Basics

The basic components and sequence of modern day heart–lung machines are as follows: venous drainage (vacuum assist) → reservoir → perfusion pump → oxygenator (with heat exchanger) → arterial line filters → aorta. The reservoir of the cardiopulmonary bypass machine is important for proper drainage and emptying of the heart. Without the reservoir, the blood in the human body and the blood in the machine would be in a constant equilibrium of roughly 1:1. With the reservoir, approximately 100 mL to 2 L of volume can be housed outside of the body during perfusion. This negative volume balance drains the human venous capacitance system and leaves the heart flat and empty. An empty heart does little work and consumes minimal oxygen. This is different than the modern day extracorporeal membrane oxygenator circuits which do not have a reservoir and do not allow decompression of the ailing heart.

Although the classic heart–lung machine used gravity to drain the venous blood into the reservoir, modern machines like the Performer CPB (Medtronic, Inc., Minneapolis, MN, USA) (Fig. 33.3) employ an active vacuum in a very small system that reduces the need for large volumes in the reservoir [27, 28]. The Performer CPB is smaller in size and can be placed closer to the operating table, saving tubing length, and it accommodates to any position. In addition, the tubing used for the heart–lung machine where the blood circulates has undergone significant improvement with the use of Carmeda [29, 30], which is a bioactive surface with which the inner side of the tubing is coated. Carmeda is bonded to the wall tubing, mimicking the human endovascular endothelium to reduce coagulation and inflammatory responses of the patient's body, due to the blood-material surface interaction. The Performer CPB machine displayed in Fig. 33.3 incorporates multiple safety features consisting of alarm sensors for air bubbles, debris, pressure changes, and temperatures, making its use practically fool proof for protection of the patient.

In addition, the newer centrifugal pumps (Fig. 33.3), like the Bio-Medicus and the Performance CPB (both from Medtronic, Inc.), offer a distinct advantage over the older roller-type pumps such as the standard DeBakey type. More specifically, the roller pumps use occlusive pressure to propel the blood within the tubing, and can cause damage to the RBC and dislodge debris from the tubing material. In contrast, the newer centrifugal pumps minimize trauma to the RBC because the motion required to move the blood does not constrict the tubing. Although the bubble oxygenator has been used for many years, it has been largely supplanted by the membrane oxygenator. The membrane oxygenator is associated with less trauma to RBC and is less likely to produce micro-bubbles that might pass into the patient's arterial system and cause air embolism.

As the blood is oxygenated, it passes through heat exchangers that cool or rewarm it as necessary for a given stage of the operation. Typically, one heat exchanger provides temperature control for systemic perfusion to the patient's body, whereas a second exchanger controls the temperature within the cardioplegia line. In most current systems, the temperature within each circuit is separately controlled by a central regulatory unit. The blood is then filtered which helps prevent microembolization when it is returned to the patient's arterial system. In addition, two suction lines are employed to aspirate any blood from the operative field, thus recovering and returning the blood to the reservoir where it is oxygenated before being pumped back into the patient's arterial system.

Importantly, the perfusionist needs to monitor the general circulation flow, electrolyte parameters, anticoagulation parameters, and the ultrafiltration system (which extracts fluids from the patient's arterial system to avoid over hydration). The perfusionist is also responsible for maintaining the proper pressures within each circuit and monitoring the temperature of the cardioplegic solution that will be used to protect

Fig. 33.3 Performer CPB cardiopulmonary bypass machine manufactured by Medtronic, Inc. (Minneapolis, MN, USA) shows a smaller size adjustable to any position. Attached to the machine is the Resting Heart Device which eliminates most of the large size reservoirs. It contains the filters and monitoring devices. All tubing is coated with Carmeda (see description in the text)

the heart during the period of its exclusion from general circulation. Normally, at 15- to 20-min intervals, the perfusionist apprises the surgeon of the elapsed time of perfusion and reinfuses the heart as necessary to maintain a temperature within the appropriate range (below 15 °C). The perfusionist also remains in direct communication with the anesthesiologist to coordinate administration of any drugs or any other action necessary to maintain the balance of the patient's other organ systems. Finally, at the end of cardiopulmonary bypass, the perfusionist administers protamine in an amount sufficient to neutralize the effects of the heparin, thus returning the patient's coagulation system to normal function.

At the conclusion of the surgery, cardiopulmonary bypass is discontinued and the patient's heart resumes systemic blood circulation. A small volume of blood often remains in the pump and needs to be reinfused into the patient. This remaining blood is sometimes reinfused directly from the reservoir or it may be concentrated and reinfused later.

33.1.8 Heart–Lung Machine Priming

Before cardiopulmonary bypass is undertaken, the heart–lung machine needs to be primed. For an adult patient, a typi-

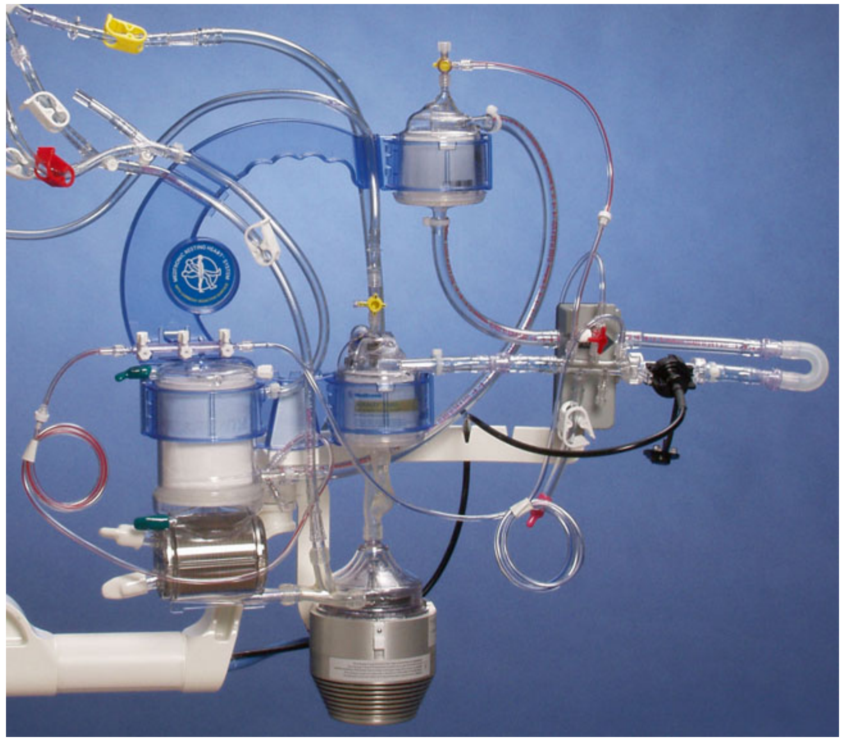

Fig. 33.4 Close-up image of the Resting Heart System showing the small reservoir in the center. The centrifugal pump is shown at the bottom. The rest are filters provided with alarm systems for air venting

cal 1500 mL of priming fluid is primarily a basic crystalloid solution. Plasmalite is the preferred crystalloid solution to which albumin or hetastarch (about 500 mL for a normal sized patient) is typically added. Doing so helps maintain osmolality and volume in the intravascular space, and helps prevent peripheral third spacing and edema. Red cell sludging usually is prevented within the system by the addition of extra heparin, however with the new systems like the Performer CPB, this is no longer required. In the pediatric patient, ideally one should have much less volume than what is required in adults. In such cases, the so-called Resting Heart System provided by Medtronic, Inc. (Fig. 33.4) can be integrated into the regular Performer CPB system to significantly reduce the entire volume needed for priming the pump. This integrated unit also provides for an automatic venous air removal and integrated air removal from the cardioplegic system. As mentioned before, at the end of the perfusion the blood is hemoconcentrated to normal levels by eliminating the extra fluid from the circulation; all the air is eliminated as well.

33.1.9 Hemodynamics

As cardiopulmonary bypass is implemented, the patient's blood pressure usually drops briefly as the blood is diverted from the heart to the heart–lung machine. This drop is precipitated by the cold (ambient) temperature of the fluid, that was used to prime the machine and which the heart–lung machine has now introduced into the patient's aorta. It also results from the emptying of blood from the heart. This drop should last no more than a minute or two, i.e., before the proper pressure and flow is reestablished. The surgeon should not continue with the procedure unless s/he is confident that forward flow and drainage are optimized. In general, it is preferable to maintain a systemic pressure of approximately 70 mmHg and flows between 1500 and 2500 mL-m^2 of body surface area throughout the entire surgical procedure (ideally 2.4 × body surface area). If the systemic pressure tends to sag, which can happen because of the various factors (e.g., loss of vascular tonus), the anesthesiologist and perfusionist must coordinate administration of vasoconstrictor agents (such as neosynepherine). If the pressure is too high, vasodilators are administered and/or the rate of perfusion is decreased to restore safe pressures.

Importantly, venous pressure and oxygen saturations should be monitored very carefully throughout any bypass procedure. An altered venous pressure is one of the most important indicators that a potential obstruction in the venous return has occurred, either at the level of the venous cannula or within the superior or inferior vena cava. Such obstructions will often lead to major procedural complications if they are not monitored and immediately corrected. Typically the perfusionist reports any concern to the surgeon so that s/he can check whether any obstruction may exist. During cardiopulmonary bypass, the venous pressure should usually be near zero and saturation above 70 % because all the blood is completely diverted into the heart–lung machine. Once the pressures are equilibrated, the temperatures must be maintained at the level of hypothermia that the surgeon has chosen.

Elevated central venous pressures and pulmonary artery pressures suggest poor drainage, as does a heart that is distending. Markers of end organ perfusion during bypass include: urine output, mixed venous saturation, lactic acid, and/or base deficit. Acidosis, low urine output, and decreased mixed venous saturation suggest poor oxygen delivery to the tissues.

The written records for the cardiopulmonary bypass are normally called *pump records*. They must contain all pertinent information including: (1) pressures; (2) flows; (3) temperatures; (4) medications; (5) periods of ischemia; and (6) beginning and end times. These records provide important information and trends that add to our understanding of cardiopulmonary bypass. Precise monitoring during cardiopulmonary bypass is extremely important especially in patients with compromised renal function (i.e., those who cannot produce urine to remove extra fluid from their own systems). In such patients, the most important electrolyte to monitor is potassium which, after any major operation, usually rises above the normal level of 4.0–4.5 mEq/L. Potassium must be very strictly monitored to prevent associated severe bradycardia and/or cardiac arrest. A dialysis system can be used during cardiopulmonary bypass, if necessary, to prevent such serious complications. Even in large medical centers, patients who are normally on dialysis rarely receive potassium during cardiopulmonary bypass.

In general, after weaning from cardiopulmonary bypass, most patients will display various degrees of bradycardia, usually due to the persistent effect of large amounts of β-blockers administered preoperatively or because of large amounts of cardioplegia solution. Few patients will elicit heart beats greater than 80 beats/min when taken off cardiopulmonary bypass. Most patients are commonly provided with a temporary pacemaker system postoperatively. This consists of wires placed on the surface of the heart (external leads) and connected to an external pacemaker unit (much like the first wearable pacemaker developed by Earl Bakken in 1958, see Chap. 25). Based on many years of research and experience, the optimal post cardiopulmonary heart rate has been determined as 70–90 beats/min in an adult; atrial pacing is set at that rate, with appropriate ventricular sensing. Such pacing is usually necessary for only 24–48 h which, in general, provides higher cardiac output and significantly improved hemodynamics, and allows the patient to eliminate the extra water that is usually third spaced during such an operation. Ventricular leads are routinely implanted in all patients as a very simple and safe prophylactic lifesaving measure [31]. This practice is highly advisable during the postoperative period because serious problems such as complete heart block are frequently unpredictable regardless of the patient's age or general health. If serious problems occur, there is no substitute for the ability to pace the ventricle immediately. Once the acute recovery period is over and the patient is stable (typically 5 days after surgery), the temporary pacemaker wires can usually be removed. In rare cases when heart block or severe bradycardia occurs, a permanent pacemaker system may be necessary to implant. See Chap. 30 for more details.

33.1.10 Weaning from Cardiopulmonary Bypass

In order to discontinue cardiopulmonary bypass the patient needs to be warm (37 °C) with a perfusing heart rhythm and good ventilation. These are the most important elements for weaning from bypass. However, there are several other important details that can be summed up in a simple pneumonic suggested by Lars Svensson from Cleveland Clinic [32]. The pneumonic is as follows:

A—Anastomosis (check all surgical bleeding sites)
B—Beat of the heart, Breathing (defibrillate if needed, place pacing wires, suction out the pleural spaces to allow proper ventilation, slowly ventilate the heart watching for any tethered bypass grafts)
C—Circulation (forward flow and drainage; fill up the heart with volume and allow it to eject)
D—Degrees (normothermia 37 °C); Deair (have the root vent on and check the echo to ensure that the heart has been adequately deaired)
E—Electrolytes (potassium is the main factor; some add calcium to optimize contraction); Echo (confirm function, valves, air)
F—Flows (start coming down on the bypass flows toward about 2 L/min and reassess blood pressure, heart distention, and contractility)
G—Gasses (ensure that blood gasses are normalizing)
H—Hypertension/Hypotension (treat any swings in blood pressure with the appropriate agents)
I—Ionotropes (select appropriate ionotropes, i.e., epinephrine for longer pump runs or sluggish heart, vasopressors for systemic vasoplegia)—ideal pressure for coming off bypass is 70 mmHg.
J—Juices (ensure adequate urine output and potassium. If urine is sluggish and K^+ is high, then you may need to dialyze the patient to wean from bypass)

33.2 Cardioplegia

In the 1950s, the consensus among cardiac surgeons was that the results of the surgical methods were satisfactory [33]. Yet, numerous reports described low cardiac output syndromes occurring after surgical correction of congenital anomalies [34]. Unfortunately, at that time no definite connection was provided between the lack of proper myocardial protection during surgery and the potential for postoperative cardiac dysfunction and/or high mortality rates. Not until the advent of coronary bypass in the late 1960s and early 1970s were intraoperative myocardial infarctions or deaths clearly attributed to poor protection of the myocardium [35, 36]. At that time, several reports also noted that the levels of cardiac enzymes after surgery were significantly elevated, indicating that additional myocardial damage had occurred even during the operation [36]. As a result, surgeons of that era showed an increasing interest in attempting to protect the heart during the period of global ischemia (aortic cross-clamping) via infusion of cold perfusates into the coronary circulation. Cold infusion of any solution into the heart separate from the total body perfusion is one of the methods known collectively as *cardioplegia*. After continued demonstration of its effectiveness, the use of hypothermic cardioplegia became quite widespread. In order to implement the use of cardioplegia, the general circulation to the coronary arteries must be interrupted. This is achieved by placing a vascular clamp across the aorta just above the coronary arteries; in this manner, as the heart is excluded from the general circulation, the infusion of cardioplegic solution is done in the aortic root entering in the coronary circulation to achieve a rapid and complete stoppage of the cardiac activity. Other modes of inducing cessation of cardiac activity employ chemical additions to perfusates or shocking the heart with electrical stimuli.

Yet, today many issues still need to be investigated concerning optimizing cardioplegic methodologies, such as: (1) what type of solution to use; (2) how much solution to inject; (3) how often to reinfuse these solutions; (4) how long to extend global ischemia safely using cardioplegia approaches; (5) how well a specific solution protects the energy reserves of the myocardium; and/or (6) the optimal route of delivery to ensure proper distribution to the right and left ventricles. As mentioned above, operative settings requiring the injection of cardioplegia involve aortic cross-clamping and coronary infusion (Fig. 33.5) of usually a cold chemical solution [37–41]. Some cardiac surgeons prefer to inject warm [42, 43] or tepid [44] solutions that have been mixed with chemical components (e.g., high potassium concentrations). However, normal warm myocardial cells require uninterrupted coronary perfusion. The principles of applying cardioplegia are aimed at: (1) conserving energy through the rapid induction of diastolic arrest; (2) slowing the metabolic demands and degenerative processes that inevitably follow global myocardial ischemia; (3) preventing unfavorable ischemic changes; and (4) preventing myocardial edema through adequate venting, drainage, and osmolality of the protective solutions. Extensive research over the past 30+ years has provided several formulations of chemical components, with or without cooling, to obtain these goals. Interestingly, the relative use of these solutions still varies widely, likely because they have been independently developed at several separate institutions.

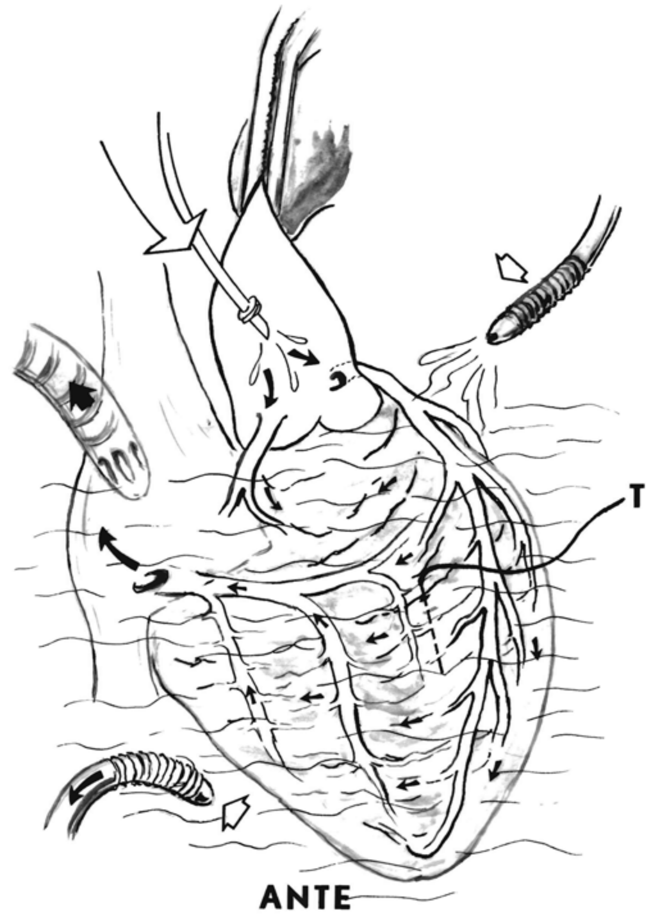

Fig. 33.5 Antegrade cardioplegia (*ANTE*). The ascending aorta is cross-clamped and cardioplegia is infused into the root of the aorta. The solution runs through the coronary arterial system and leaves the heart via the coronary sinus in the right atrium. At the upper right corner is an irrigating catheter that provides continuous topical hypothermia. This solution is removed by the suction line at the lower left (*clear arrows*). *T* temperature probe positioned in interventricular septum for monitoring purposes

33.2.1 Types of Solutions

Crystalloid solutions generally can be divided into two categories based on their approximate formulation—extracellular or intracellular. Extracellular solutions contain calcium and sodium, the primary determinants for transcellular calcium exchange. Cardioplegic cardiac arrest can still be achieved by extracellular solutions containing only moderate amounts of potassium or magnesium. Cold blood cardioplegia solution [39–45], the most commonly used throughout North America, is considered an extracellular ionic formula. The principle advantage to extracellular-type solutions is that they make it simpler to control equilibration characteristics within the ischemic myocardial tissue. Because no calcium or sodium variant exists in the extracellular fluid, subsequent replacement is easily achieved without any major reequilibration with the intracellular fluid. The disadvantage of extracellular solutions is that they are more easily washed out by noncoronary flow, but this effect can be counteracted by adding calcium channel blockers or procaine. Cardioplegic solutions that mimic intracellular ionic concentrations usually contain no sodium or calcium. Their advantage, at least in theory, is that their lack of sodium or calcium generates a large osmolar space which is available for other potentially protective components. In turn, this allows the solution to contain a high concentration of glucose, dextrose, mannitol, or histidine without eliciting excessive hyper-osmolarity. Another advantage of intercellular-type solutions is that their minimal or reduced levels of extracellular calcium will limit contraction or restrict ischemia-induced calcium entry. The primary disadvantage of such solutions is that the lack of sodium and calcium may, under extreme conditions, predispose the heart to elicit the so-called *calcium paradox*. Another disadvantage is the potentially complex pattern of subsequent reequilibration then required. As Hearse et al. [46] pointed out, low-volume infusion of intracellular solutions offers good protection, intermediate volumes offer only marginal protection, and high volumes may actually exacerbate injury to the myocardium.

Each of the described crystalloid cardioplegic solutions is considered to contain several components that have been "proven" by various researchers to provide enhanced protection. For example, in one study published by Hearse et al. [37], the effects of changing the composition of the simple cardioplegic solution when used during a 30-min period of ischemia were compared. It was shown that, at the end of a period of ischemia when no cardioplegia was used, the percentage of ventricular function recovery was practically nil, only about 3 %. However, if potassium was added, the recovery increased to about 30 %. Furthermore, if both potassium and magnesium were added, the recovery was even better (up to 68 %). And if potassium, magnesium, and adenosine triphosphate were used in combination, the recovery reached 86 %. Finally, if a combination of potassium, magnesium, adenosine triphosphate, creatine phosphate, and procaine was used, the recovery peaked at a dramatic 93 %.

After using crystalloid cardioplegia alone for several years, it was considered whether mixing cold blood with the crystalloid solution would offer better protection than the crystalloid alone; it was suggested that the ability of the blood to carry oxygen to the tissues and its buffering capacity particularly if the period of ischemia was more than 90 min and, in such cases, the ventricular function was less than normal. Although the idea of protecting the heart with blood cardioplegia originated in the early 1950s with Ebert et al. [47], it was not until 20 years later when it was reintroduced by Buckberg and associates [39, 43, 45, 48, 49] that it became popular among most surgeons in the USA and throughout the world to use cold blood cardioplegia. Nevertheless, controversy persists regarding the "optimal" formulation to protect and prevent damage to the heart. The following solutions are some of the most commonly used for such procedures today.

33.2.2 St. Thomas II Solution

The formulation for the St. Thomas II solution (Plegisol: Abbott Laboratories, Abbott Park, IL, USA) originated with the published research of Hearse, Braimbridge, Stuart, and Jynge [37, 46, 50, 51] from the St. Thomas Hospital in London. The basic vehicle was Ringers solution to which potassium chloride, procaine, and magnesium were added (Table 33.1).

St. Thomas II solution is an extracellular-type formulation. It is used extensively as an isolated clear cardioplegic solution and also as the base mix for the cold blood cardioplegic solution proposed by Buckberg et al. It is usually injected into the root of the aorta at temperatures between 4° and 6 °C (Fig. 33.5), depending on the surgeon's preference with an initial volume of about 1000 mL for a 70 kg adult, followed by 100 mL infusions intermittently every 15–20 min. This method has long been combined with or without topical hypothermia to maintain the heart's temperature below 15 °C. The size of the catheter used for its infusion and the pressure for injection are discussed in Sect. 33.2.8.

Table 33.1 Composition of St. Thomas II solution

Sodium chloride	120 mmol/L
Potassium	16 mmol/L
Sodium bicarbonate	10 mmol/L
Calcium	1.2 mmol/L
Magnesium	16 mmol/L
Procaine	1 mmol/L
Osmolality	280 mOsm/kg H_2O
Oncotic pressure	0.4
pH	7.8

Table 33.2 Composition of Birmingham solution

Sodium	100 mmol/L
Potassium	30 mmol/L
Calcium	0.7 mmol/L
Glucose	5 g/L
Chloride	84 mmol/L
Albumin	50 g/L
Mannitol	5 g/L
Osmolality	300–335 mOsm/L

Table 33.3 Composition of Bretschneider (Custodiol) solution

Sodium	15 mM
Potassium	9 mM
Magnesium	4 mM
α-Histidine	180 mM
α-Histidine Hcl	18 mM
Calcium chloride	0.015 mM
Mannitol	30 mM
Tryptophane	2 mM
Ketoglutarate	1 mM
pH	7.1–7.2
Osmolality	295–325 mOsm/kg H_20

Fig. 33.6 Antegrade infusion of the Bretschneider (HTK, "Custodiol" solution containing Histidin-Tryptophane-Ketoglutarate). The solution is infused in an antegrade manner into the aortic root while the aorta is cross-clamped. Because this method requires a large volume of solution, the right atrium is open and the solution exiting in the coronary sinus is aspirated and discarded. The superior and inferior vena cavae are individually cannulated to allow the right atrium to remain empty so that the HTK solution can be evacuated. Topical continuous hypothermia is shown with the irrigating cannula at the upper right and the suction catheter at the lower left. *T* temperature probe

33.2.3 Birmingham Solution

Various extracellular solutions were also developed in the USA. Most solutions sought to attain relatively high extracellular concentrations of potassium as an arrest-inducing agent. More specifically, Birmingham solution was developed by Conti et al. [52]; its effectiveness was primarily demonstrated by the publications of Kirklin et al. [53]. The importance of the Birmingham solution is that glucose was included as a substrate for the myocardium (Table 33.2). The development of this solution gave origin to many other formulations that use the basic additions of glucose, potassium, and insulin.

33.2.4 Bretschneider Solution (Custodiol)

During the early 1960s and 1970s, Bretschneider in Goettingen, Germany published his studies introducing HTK (Histidine-Tryptophane-Ketoglutarate) also known as Custodiol crystalloid cardioplegic solution (Dr. F. Köhler Chemie GmbHD-6146 Alsbach-Hähnlein, Germany) [54, 55] (Table 33.3). This intracellular-type solution has also been shown to be very effective in protecting the heart during surgery. It has been used extensively in Germany since its introduction and has also been used widely throughout Asia, North Africa, and Latin America. It is used not only as a protective solution for the heart during periods of surgical ischemia, but also as a preservation solution for hearts [56–58], livers, and kidneys [59] prior to transplantation. According to Preusse et al. [55], this solution must be provided in large amounts, between 3000 and 4000 mL per organ. Therefore, double cannulation of the right atrium with exclusion of this chamber must be implemented during surgery in order to allow opening of the atrium and to eliminate the large volume of solution from the coronary sinus orifice to prevent the fluid from reaching the general circulation (Fig. 33.6). For Custodiol solution to be most effective, the period of equilibration is crucial [54, 55]; that is, it takes about 7 min of infusion to equilibrate the extracellular and intracellular spaces before the patient's operation should proceed. This solution has also been used for both antegrade and retrograde (through the coronary sinus) perfusions. One of the considered significant advantages of this solution is its buffering capacity, which even surpasses the buffering properties of blood. Importantly, Custodiol solution needs to be stored at a specific temperature (12°–16 °C) to prevent denaturation of the components.

Table 33.4 Composition of Crystalloid Potassium Insulin (University of Minnesota) solution

Dextrose	50 g/1000 mL
Sodium	3.5 mEq/L
Potassium	30 mEq/L
Chloride	30 mEq/L
Sodium bicarbonate	3.5 mEq/L
Regular insulin	10 units
Mannitol	12.5 g
Albumin	12.5 g
Osmolality	364 mOsm/L
pH	7.8
Oncotic pressure	3

33.2.5 Glucose–Insulin–Potassium Solutions

Most of the research performed on glucose–insulin–potassium (GIK) solutions was done in the USA. Multiple formulations with these components have been widely used for the past 30 years. Studies by Hewitt et al. [60] and later by Lolley et al. [61] demonstrated that continuous infusion of a solution containing 278 mmol/L of glucose, 20 mmol/L of potassium, and 20 U insulin with 69 mmol/L of mannitol dramatically improved myocardial protection. Those studies illustrated that the combination of glucose, insulin, and potassium improved anaerobic glycolysis and the washout of toxic substances. A slight modification of this basic solution, which included albumin to increase osmolality, was used extensively for many years at the University of Minnesota (Minneapolis, MN, USA) [62–64] (Table 33.4). The only concern with the use of GIK solution is the inevitable degradation of its constituent insulin over time. Therefore GIK solutions must be prepared fresh for each use and cannot be stored for prolonged periods of time.

Many investigators contributed to the formulation of GIK solutions, among them Follete et al. [45] and Todd and Tyers [65]. We consider here that Roe et al.'s classical solution [41] also belongs in this category. The common denominator among these formulations is the use of dextrose as the basic vehicle. Multiple publications have shown protective effects. However when used alone, GIK solutions often provide insufficient protection during long periods of ischemia (i.e., beyond 120 min) or when the left ventricular function is marginal initially.

Several crystalloid solutions have been formulated without dextrose. The main difference among these is the basic vehicle which could be formulated with Ringers or Krebs-Henseleit. Potassium is commonly added at doses between 15 and 125 mmol/L. Some solutions in this group are the University of Wisconsin [57, 66] and Celsior [67] solutions which are also used to preserve organs for transplantation. Several agents are considered available to help increase the osmolality of cardioplegic solutions (Table 33.5); for example, mannitol has been included in such solutions to stabilize osmolality and to act as a potential scavenger for oxygen radicals.

Table 33.5 Components used to raise osmolality

Component	Oncotic pressure (mmHg)	Osmolality (mOsm)
Hespan (hetastarch) (6 % in 0.9 % saline solution)	18.4	311
Mannitol 25 % (12.5 g/50 mL)	0.1	–
Albumin 25 %	>200	239
Dextran (10 % in dextrose)	130.2	319
Plasmanate (5 % albumin)	16.86	239
Tris hydroxymethyl aminomethane (THAM)	–	370

Table 33.6 Composition of Buckberg's Cold Blood cardioplegic solution

5 % dextrose with ¼ normal saline	422 mL
Potassium chloride	2 mEq/mL
Tris hydroxymethyl aminomethane (THAM)	72 mL CPD 6
Diluent volume	500 mL
Blood hematocrit	22 % = 500 mL
Osmolality	360 mOsm/kg
Potassium	22 mEq/L
pH	7.8
Calcium	0.3 mEq/L
Hematocrit	10 %

33.2.6 Additional Components

Other components have been added to crystalloid cardioplegic solutions by various investigators based on their own research. These include aspartate as the substrate to generate adenosine triphosphate [48]; glutamate as a substrate [49]; 1.5 % hetastarch as an additive [68]; procaine as a membrane stabilizer [46, 51]; nifedipine to prevent calcium paradox [69]; phosphates as a base for adenosine triphosphate regeneration [70–72]; and/or steroids (methylprednisolone) as a cellular wall stabilizer [73–75]. Other elements found to help maintain an alkaline pH include Tris hydroxymethyl amimomethane (THAM), as advocated by Buckberg [39], and histidine as in the HTK solution.

Del Nido cardioplegia uses lidocaine to prolong the period of myocardial arrest. It uses a 1:4 blood to crystalloid mixture, and is commonly employed for pediatric surgery. This is particularly useful in minimally invasive surgery where the retrograde access is not always reliable and avoids stopping for antegrade at multiple points throughout the procedure. Use of Del Nido requires a normal coronary circulation without obstructions. Microplegia is another form of cardioplegia that is being investigated; it contains much smaller volumes than standard solutions and presumably causes less myocardial edema.

Fig. 33.7 Roller pumps of cardioplegia infusion system. The upper pump utilizes ¼ inch tubing to move the blood, and the lower pump runs crystalloid cardioplegic solution using 1/16 inch tubing. The blood and cardioplegic solution are automatically mixed in a 4:1 proportion in the outflow line before entering the ascending aorta

33.2.7 Cold Blood Cardioplegia

The mixture of blood with crystalloid cardioplegia has become the most favored formulation for cardioplegia among cardiac surgeons both in the USA and throughout the world. It is considered superior to any other cardioplegic solution alone. The standard proportion of blood to crystalloid solution has remained fairly constant at 4:1 (4 parts of blood to 1 part of crystalloid cardioplegia), although some surgeons prefer a proportion of 8:1 in special circumstances. Nevertheless, as mentioned before, the actual formulation of the crystalloid portion varies across institutions [76].

Administration of cold blood cardioplegia in the proportions proposed by Buckberg (Table 33.6) can be easily accomplished using the appropriate equipment available as a kit. This contains the necessary caliber of tubing which is placed in a roller pump that automatically mixes the blood with the clear solution before injection into the root of the aorta (Fig. 33.7). As an example, the Performer CPB machine can accommodate any mixing proportion desired (4:1, 4:6, 4:8). The kit includes a heat exchanger which maintains the temperature of the solution between 4° and 6 °C and allows the myocardial temperature to decrease even below 15 °C. The significant advantage of cold blood cardioplegia is that it is considered to provide oxygen and nutrients to the ischemic myocardium and offer optimal buffering capacity. This mixture can be injected antegrade (in the root of the aorta) or retrograde (by coronary sinus cannulation using a self-inflating balloon to perfuse the entire heart) [77] (Fig. 33.8). Cold blood cardioplegia has endured many years of testing, both in its initial form of providing cardioplegia at cold temperatures and in its more recent adaptation to warm cardioplegia as promoted by Lichtenstein et al. [78]. The cold blood method is widely used in the pediatric population as well for surgeries to correct all types of congenital anomalies.

33.2.8 Cardioplegia Administration

Our previous clinical work showed that cardioplegic solutions should be administered at a rapid rate and under moderate pressure. Doing so shortens the prearrest period, provides better flow distribution, and accelerates the decreasing myocardial temperature. In addition, rapid injection results in postoperative isoenzyme levels that are lower than those in patients who undergo slower cardioplegic injections [62].

Experimental studies on animals with normal coronary arteries have shown that low infusion pressures (less than 30 mmHg) and peak flow rates less than 125 mL/min result in a higher incidence of cellular ischemia, focal necrosis, and uneven flow distribution [64]. Consequently, patients with obstructive coronary disease who undergo low-pressure or low-volume cardioplegic injections will inevitably experience an increase in flow distribution problems.

Conversely pressures higher than 110 mmHg and peak flow rates greater than 1500 mL/min may result in a higher incidence of mechanical and physical trauma to the vascular endothelium [64]. These higher levels, however, greatly enhance cellular protection. It should be noted that the use of

Fig. 33.8 Cold blood cardioplegia. This may be administered by antegrade infusion into the root of the aorta below the cross-clamp. It may also be accomplished in a retrograde manner through a catheter inserted in the coronary sinus provided with a balloon which is inflated to prevent reflux into the right atrium. Continuous topical hypothermia is used in conjunction with cold blood cardioplegia to potentiate the hypothermic protection of the heart. *P* pressure monitoring line of the coronary sinus, *T* temperature probe

high pressures in the aortic root of patients with coronary obstructions does not necessarily raise a concern. Rapid administration of cardioplegic solutions causes the temperature of the myocardium to fall rapidly within seconds to the protective range below 15 °C and induces immediate cardiac arrest. This is important because one would prefer not to have the heart beating against the clamp for more than a few seconds, as it wastes myocardial energy and can lead to edema and injury.

Cardioplegic solutions are most commonly administered via cannulas placed into the aortic root below the level of the aortic cross-clamp (Fig. 33.5). This site provides a normal antegrade flow to all areas of the heart. Several aortic valve procedures, however, require the aortic root to remain open for long periods of time. Therefore, infusion of cardioplegia can be done by direct injection into the coronary ostia by handheld cannulas or, alternatively, cardioplegic solution may be administered retrograde through the coronary sinus. This gives the added advantage of not having to stop the procedure to administer cardioplegia and allows the surgeon to flush out the coronary system of air and debris. This option may be used to slow and continuously protect the heart (Fig. 33.9). Yet, this approach has some limitations that are dependent on the degree of hypertrophy of the myocardium due to the preexisting condition. The delivery pressures in the coronary sinus must be intentionally kept between 20 and 50 mmHg. Too low suggests a lack of occlusion by the catheter balloon in the coronary sinus with inadequate perfusion and too high may lead to vessel ruptures. Decompression of the left ventricular chamber is helpful to facilitate the perfusion of all areas of the heart [79].

The perfusion to the right heart is one of the most challenging issues that surgeons face. Antegrade and retrograde very reliably provide good flow to the left ventricle, unless there is a significant coronary blockage that needs to be considered. As mentioned, hypertrophy may limit perfusion to the left ventricle and cooling systemically and topically is a useful adjunct. However, perfusion of the right coronary system is not always as predictable. Retrograde catheters often miss the middle cardiac vein which is required to perfuse the right ventricle (see Chap. 8). Direct retrograde insertion prevents this error but relies on opening the right atrium. This is an important technique to be able to perform. A saphenous vein graft to a distal right coronary artery or branch also allows reliable right ventricular perfusion but is only used if a blockage is present in the right system. A temperature probe in the right ventricle can reveal the degree of right ventricular cooling.

General conduct of cardioplegia at our institution using the Buckberg's cold blood cardioplegia protocols is as follows:

1. 500–1000 mL cold antegrade induction dose with high potassium, followed by 500 mL retrograde
2. 300 mL maintenance doses through the retrograde route and down vein grafts with high potassium and higher glucose concentrations every 15–20 min
3. Final "hot shot" dose with a high glucose, substrate replete solution and low potassium
4. Once the hot shot is complete and the root is deaired, the cross-clamp is removed

Over the past 30 years, to increase the safety of such operations, the use of cardioplegic solutions has been noted as one of the most significant advances in cardiac surgery. Continued research will search for optimal systems and methods to provide even better protection of the heart during cardiac surgery.

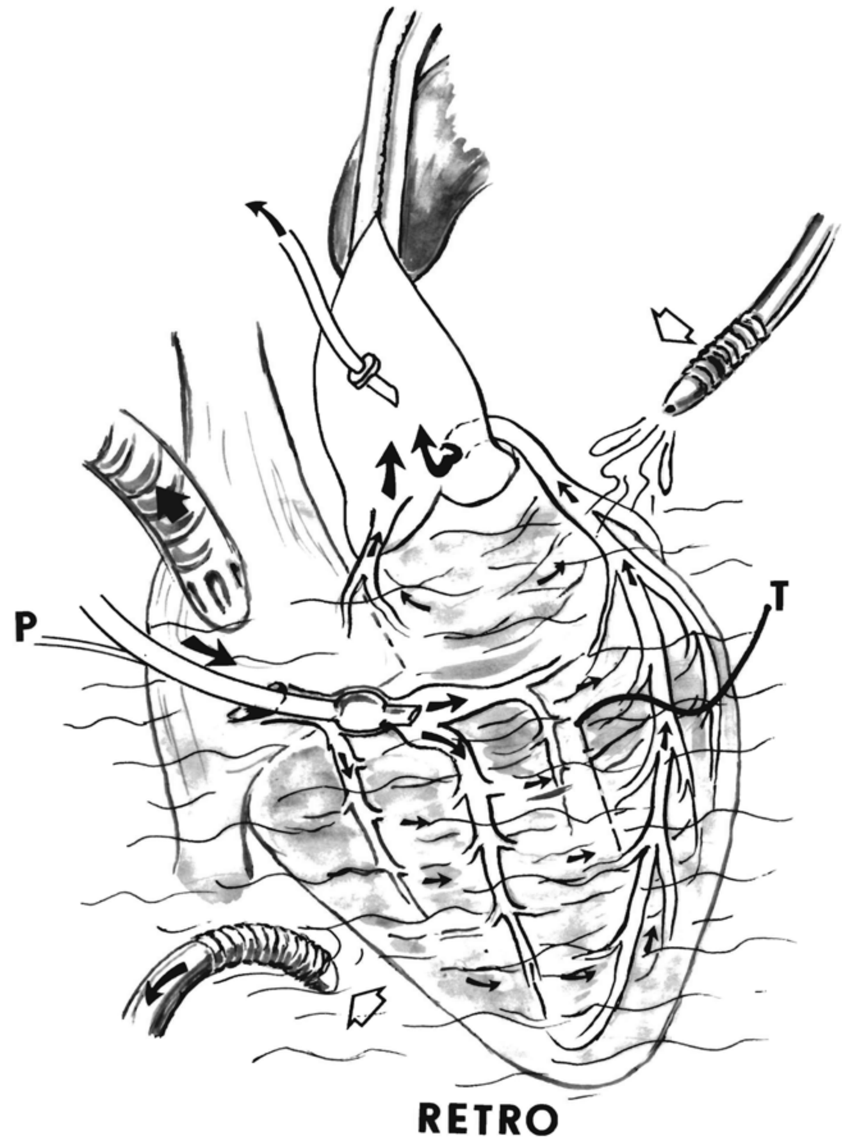

Fig. 33.9 Retrograde (*RETRO*) administration of crystalloid cardioplegia. This is accomplished via the coronary sinus with a catheter provided with a balloon that is inflated to prevent reflux into the atrium. The solution eventually reaches the aortic root from where it is aspirated. It may also be allowed to drain into the left ventricle which is vented to the pump. Continuous topical hypothermia is again shown using cold saline over the heart. *P* pressure line monitoring, *T* temperature probe

33.2.9 Adjunct Topical Hypothermia

The use of cardiac hypothermia has been one of the most important tools for increasing the safety of cardiac operations. The application of topical hypothermia in the form of ice slush was first introduced in the 1960s by Shumway, Lower, and Stofer [80, 81], and was used exclusively through the 1970s until the introduction of crystalloid cardioplegia. Still today, topical hypothermia is considered to potentiate the use of all methods of cardioplegic perfusion, keeping the temperature of the heart in the safe range to tolerate global ischemia. This is particularly important for hypertrophied ventricles where uniform distribution of the cardioplegia to the microvascular subendocardium is unpredictable. The heart can be effectively cooled externally by a continual flow of cold (6 °C) saline or Ringers solution over the heart, eliminating the overflow solution using wall suction (Figs. 33.5 and 33.9). This technique is preferred to the older method of applying slush ice over the heart; the latter method has been blamed for causing frostbite lesions to the muscle and damage to the phrenic nerve which runs along the pericardial sac. To avoid these problems, insulated pads have been designed to be placed around the heart to protect the phrenic nerves. Several types of plastic jackets were proposed and designed in the past, through which cold water was pumped continuously, while the jacket wrapped the heart entailing both ventricles. They are currently rarely used due to cumbersome application and crowding of the operative field. The topical cooling (whichever method is used), as well as the infusion of cold cardioplegia in the coronary circulation, is discontinued when the operation is completed and rewarming of the patient begins. The aortic clamp placed in the ascending portion isolating the heart from systemic circulation is removed, and the heart receives the systemic warm blood from the body into the coronaries, reestablishing the normal perfusion of the organ. Once the

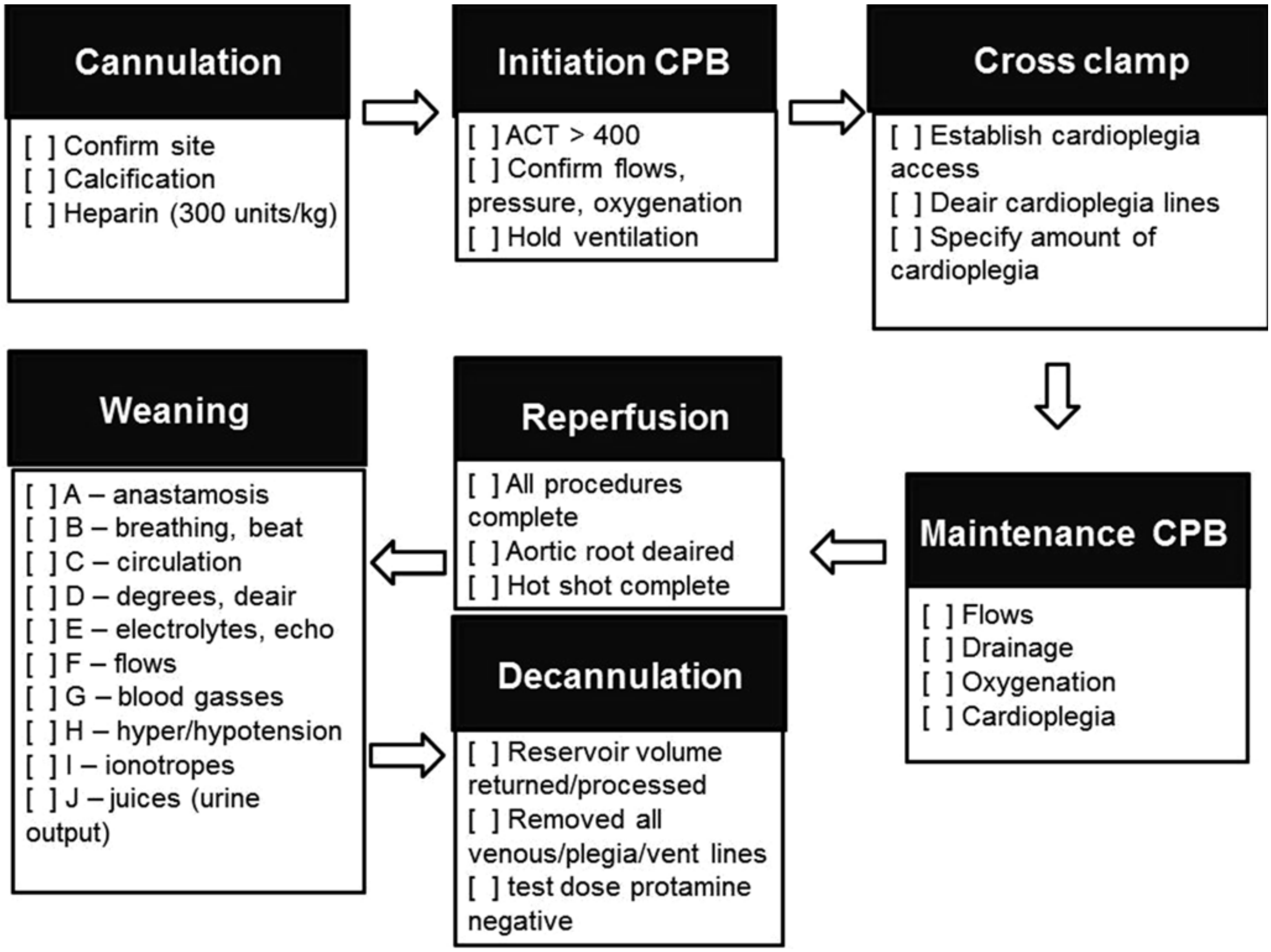

Fig. 33.10 Overview of critical events in cardiopulmonary bypass (*CPB*). Good communication between the operative field and perfusion is required at each step to ensure safety. There is no advancement along the algorithm unless the individual component has been clearly checked off by the team. The process begins with cannulation of the ascending aorta and atrium and continues with initiation of bypass. Cross clamp occurs next, followed by reperfusion and weaning. Aortic decannulation is the very last part of the process

heart temperature reaches 37 °C and its function is reestablished, cardiopulmonary bypass is terminated and all cannulas are removed. Sometimes the normal beating of the heart reappears spontaneously but, if not, electrical cardioversion is implemented using external paddles until a normal heart beat is reestablished.

33.3 Summary

Figure 33.10 summarizes the various parts of cardiopulmonary bypass and emphasizes critical events confirmed at each step. The process typically begins with cannulation of the ascending aorta and atrium and continues with initiation of bypass. Cross-clamp occurs next, followed by reperfusion and weaning. Once complete, aortic decannulation is the very last part of the process. Both cardiopulmonary bypass and the use of cardioplegia represent major medical breakthroughs that have extended the lives of millions of people worldwide. It is impossible to provide the level of surgical precision required for complex cardiac surgical procedures without a firm understanding of the components and steps involved in cardiopulmonary bypass.

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