Technique

Perfusion Techniques for Heparin-Bonded Circuits

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ABSTRACT

Recent advances in cardiopulmonary bypass techniques include the development of durable, covalently bonded heparin coated surfaces using end-point attachment techniques. Advantages of heparin-coated cardiopulmonary bypass include reduced systemic heparin, avoidance of protamine sulfate at the completion of the procedure, enhanced biocompatibility of the circuit, successful application of cardiopulmonary bypass in cases where bleeding may become a problem, and in application of assist devices.

Our experience with this technology has led to the development of guidelines and management strategies. We generally consider application for two categories: 1) pharmacotoxicity, i.e., allergic reaction to heparin or protamine; and 2) progression of problems, such as prolonged bleeding tendencies (aspirin) or hemorrhage from cerebral vascular accident. Applications of this technology require tip to tip heparin-bonding, "streamlining" the circuit, meticulous attention to fluid mechanics, crystalloid cardioplegia, precise heparin management, and reversed Trendelenburg position for post-cardiopulmonary bypass volume.

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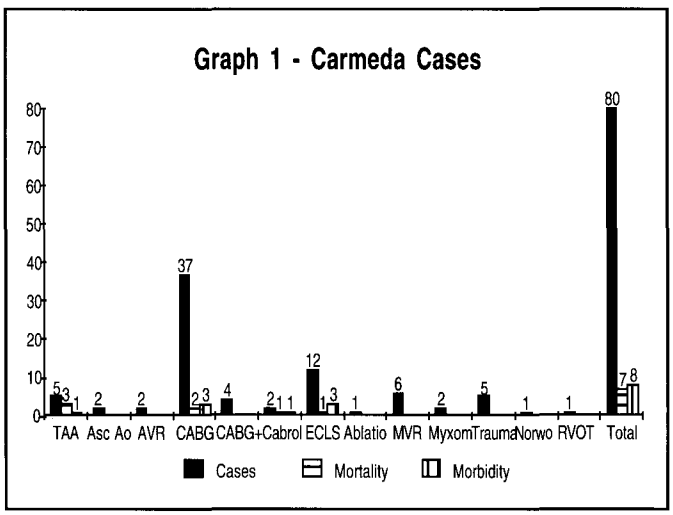
INTRODUCTION

The introduction of heparin-bonded perfusion circuits to the perfusion community has caused debate in the utilization and application of this unique system. As with any new technique, case studies and descriptions of technique are reported to expand the clinical base and evaluate results. As a result of numerous clinical cases performed at our institution(see Graph 1, Carmeda Cases), a technique is under development that offers conformity and reproducibility in results. As with any dynamic technique, ongoing refinements are under development and review.

The descriptions of heparin-bonded perfusion techniques offered in the literature are often incomplete and difficult to follow, yet standard practices in many centers adhere to protocols. The utilization of pump sucker and sump return is one example of the vagueness in these descriptions that has caused considerable consternation to the perfusion team. This example is often ignored (1,2) or the technique is avoided by utilizing the cell saver (2,3). There are other examples of even greater importance that need to be discussed prior to addressing pump sucker and sump return problems.

INDICATIONS FOR HEPARIN-BONDED CIRCUITS

The surgeon and perfusion team should review animal and clinical trials before attempting heparinless or reduced heparin cardiopulmonary bypass. The first question to address is the need for applying such an approach. Many times the answer will determine how the circuit should be utilized. We generally consider application for two categories: 1) pharmacotoxicity, i.e., allergic reaction to heparin or protamine; and 2) progression of problems, such as prolonged bleeding tendencies (aspirin) or hemorrhage from cerebral vascular accident (CVA). One exclusion from utilization is excessive bleeding requiring pump sucker return, although this is being sidestepped by von Segesser (4) with the utilization of a heparin-bonded cardiotomy. Table 1 reviews our indications and exclusions.



Why should the patient be offered a heparinless procedure using a heparin-bonded circuit? If reduction in complement activation together with the basic biocompatibility of such a circuit is desired, then the surgeon and perfusionist can use heparin in standard dosage. Protamine toxicity is a not uncommon clinical entity, so one must be careful (5-7). The risk of leukocyte depletion can also complicate the decision tree. Reduced postoperative ventilator support from decreased complement activation is seen with heparin-bonded circuits (7,8).

PERFUSION CONSIDERATIONS

Once the decision to use a heparin-bonded circuit is made, the perfusionist must address problems of non-heparin-coated surfaces, sites of stagnant flow, and potential air-blood interfaces. These potential hazards must be avoided. Presently, the greatest shortcoming in the circuit design is in the cardiotomy, which is prone to stagnation, a large air-blood interface, and resultant thrombus generation. Tip-to-tip heparin coating is necessary (Table 2). The cardioplegia cannula must also be biocompatible. Contact with a non-heparin-bonded surface can activate both coagulation and complement cascades.

Areas of stagnation in the circuit must be avoided and the circuit constructed for streamlined blood flow (Figures 1 and 2) (6). Critical areas of the cardiopulmonary bypass system such as the cardiotomy line may not be able to be modified. Intensive forethought regarding another potential stagnant area is the arterial filter bypass line. Whether the perfusionist elects to exclude or include this line (with occasional flushing) is a debatable discussion.

Venous return and storage can create difficulties. Conventional closed membrane systems with 1000 ml venous reservoir

Table 1: Indications and exclusions:

Patients ideally suited for inclusion:

- Allergic reactions:
  - Insulin dependent diabetics (possible cross-reaction w/protamine).
  - History of vasectomy.
  - History of shellfish allergic reaction.
  - History of protamine allergic reaction.
  - History of iodine dye reaction.
- Active or suspected bleeding site (e.g. gastric ulcer, intra-renal bleeding, recent CVA)
- Cardiogenic shock requiring assist device(s) (including trauma)

Patients who may be ideal:

- Potential for post-operative bleeding (e.g. aspirin usage, warfarin, heparin, etc. usage prior to surgery)
- Ejection fraction <35%
- Valve or aortic repair procedure
- Under 18 years old
- Biocompatibility (avoidance of complement activation)

Exclusion criteria:

- Excessive need for pump sucker (e.g. cannulation difficulty)

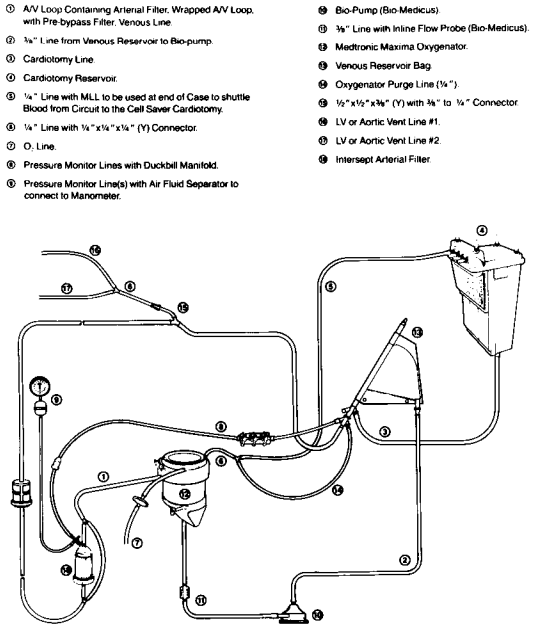
Table 2: Carmeda BioActive Surface coated "software"

Sarns 6.5mm arterial cannula & 51/36Fr venous cannula[a]
Medtronic 1/2 x 3/32" tubing[b]
Medtronic venous resorvoir bag[b]
Medtronic 3/8 x 3/32" tubing[b]
Medtronic BioHead (DP80)[b]
Medtronic BioFlow probe[b]
Medtronic Maxima (adult) oxygenator[b]
Medtronic Intersept arterial filter[b]
Medtronic "Intersept" cardiotomy resorvoir[b]
DLP 14 gauge cardioplegia needle w/vent[c]

Non-CBAS heparin coated "software"

Gish cardioplegia resorvoir[d]

Figure 1: Circuit design of standard cardiopulmonary circuit utilizing heparin-bonded oxygenator, vortex pump (Medtronic-BioMedicus), and tubing



Note: sashed wrapped 1/4" suction/vent lines are handed to table and then placed through the pump heads as sucker and vent line. An extra purge line w/duckbill is used from #13 (venous reservoir bag) to the cell suction cardiotomy to remove unwanted air--controlled with a stopcock #5 1/4" line (w/yellow stripe packaged in clear peel packet) w/MLL - I use this off the oxygenator to purge the cardiotomy (priming) and to empty circuit contents to the cell saver at the end of the case. It can be cut for extra 1/4" tubing (e.g. cardioplegia raceway tubing for GISH cardioplegia system

bags usually drain to the cardiotomy. Letting the blood stagnate in a non-heparin-bonded cardiotomy can generate thrombus, especially with low or no heparin use. The following techniques regarding methods have worked well for our institution.

FLUID ADMINISTRATION & BLOOD CONSERVATION

Administration of fluids can create problems. The basis for the decision to add colloid, crystalloid or blood should not change. If the patient can tolerate lower hemoglobin levels as documented by adequate saturations and minimal vasopressor support, an attempt to avoid homologous blood transfusions should be made. Hematocrits greater than 16% usually increase in the post-cardiopulmonary bypass period when the contents of the perfusion circuit are processed through a cell saver and returned to the patient.

The cell saver is paramount for blood conservation. It should be utilized throughout the operative case and to process the perfusion circuit volume to elevate the patient's post-cardiopulmonary bypass hematocrit. CPD is the best anticoagulant, but remain aware of and monitor the effects of chelation by measuring ionized calcium levels.

Anesthesia must be conservative with fluids. Whole blood pre-donation methods require the anesthesiologist to withdraw one to two units of the patient's blood from a central venous line before cardiopulmonary bypass (CPB). CPB with hemodilution allows the hemoglobin to fall to approximately 7-8 grams/dl. Fluid resuscitation is achieved with pH-balanced solutions and albumin.

One beneficial technology is platelet-rich plasma (PRP) sequestration involving plasmapheresis and hemodilution. In this technique, blood is withdrawn from the patient and separated into packed cells and PRP (approximately 20-25% of the patient's plasma volume is processed). Initial volume replacement is with 5% albumin and the patient's packed red cells to enhance oxygenation, saving the PRP for postoperative use when enhanced coagulation is desirable. Perhaps the easiest and, if properly supervised, economical approach is perioperative autologous blood cell washing using any of the numerous cell savers currently on the market. Care must be observed as these circuits are all non-heparin-coated and biocompatibility may be compromised.

The perfusionist can also reduce the circulating volume (while the patient is on CPB) by draining excess volume into blood bags containing CPD. Using a 1400-1600 ml venous reservoir bag and minimizing the prime volume will preserve the integrity of the bypass circuit and obviate the use of the cardiotomy for storing excess volume. Manufacturers have developed and are producing heparin-bonded cardiotomy sets. Heparin-bonded cardioplegia devices and ultrafiltration units are also under development.

Finally, concerns regarding homologous blood transfusions during the perioperative period must be addressed. If the decision has been reached to avoid homologous blood products, meticulous monitoring of the patient throughout the perioperative course is required. Numerous physiologic abnormalities that occur as a result of cardiopulmonary bypass with reduced heparin

a Sarns/3M Healthcare, Ann Arbor, MI 48103
b Carmeda Inc., Stockholm, Sweden, in conjunction with Medtronic Cardiopulmonary, Anaheim, CA 92807
c Medtronic DLP, Inc., Grand Rapids, MI 49501
d Gish BioMedical Inc., Santa Ana, CA 92705

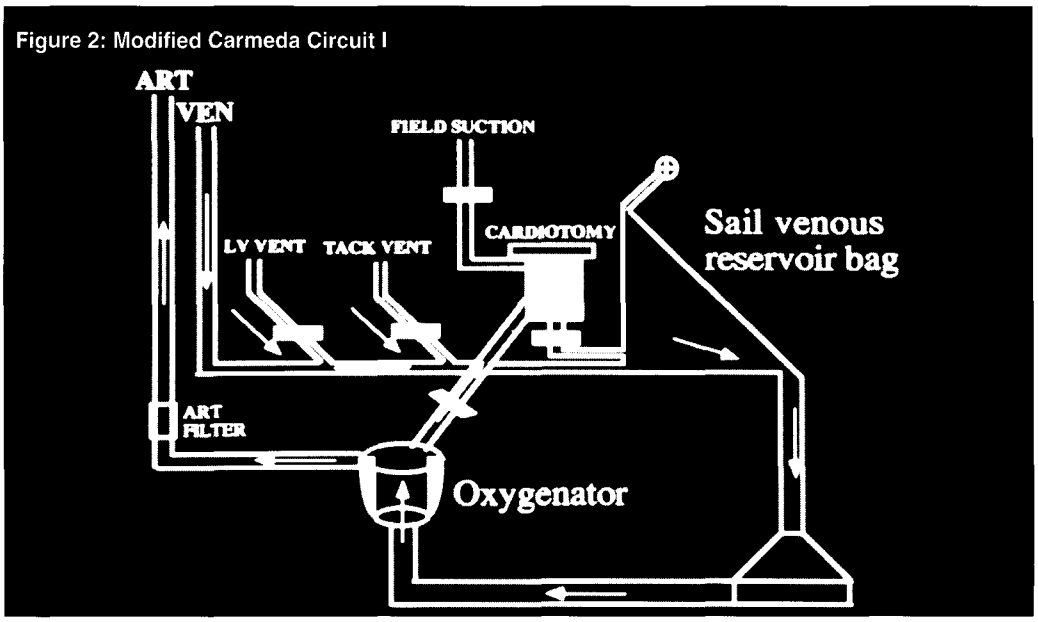


Figure 2: Modified Carmeda Circuit I

can potentially decrease the need for homologous blood. Low hemoglobin levels in the early post cardiopulmonary bypass intraoperative period will elevate to acceptable levels as autologous blood conservation techniques increase the patient's hematocrit. If a low hemoglobin creates hemodynamic problems (suggested by increased vasopressor support) or falling venous saturations, then the associated risk to the patient may exceed the risks related to blood reaction problems; in this situation blood administration is required. Apparent postoperative coagulopathies may temporarily appear, indicated by abnormal laboratory values, but our experience with heparin-bonded circuits suggests that these values do not reflect patient bleeding as measured via mediastinal drainage. Abnormal postoperative laboratory values usually return to normal ranges with time (2).

CARDIOPLEGIA

Cardioplegia administration presents several problems. Fluid overload and osmotic imbalances can occur with crystalloid preparations. Activation of complement and coagulation cascades can develop if blood cardioplegia is desired and non-heparin-bonded surfaces are employed. Presently, crystalloid cardioplegia is infused (modified St. Thomas' Hospital solution - Plegisol[e]) to flush the coronary vessels and to avoid blood contact with non-heparin-bonded surfaces. Careful calculation of the cardioplegia dose is required to avoid fluid overload and maintain myocardial preservation. We presently calculate the initial crystalloid cardioplegia dosage at 10 ml per kg patient body weight. If cardiac arrest occurs after 20-25% of the volume has been infused, the remainder of the calculated dose is delivered. If cardiac arrest does not occur after this initial volume is infused, the total dosage is increased to 15 ml/kg. We routinely monitor myocardial temperature and aim for a temperature under 15 degrees Centigrade. Prolonged fibrillation is addressed as per the protocol of each institution.

CARDIOTOMY & PUMP SUCTION

The greatest difference between cardiopulmonary bypass either with or without heparin lies in the utilization of the pump suction. We recommend that blood be prevented from stagnating in the cardiotomy, although no specific standard has been established. Using a cell-saving device with rapid processing of the blood to return it via infusion into the bypass circuit can be successful. Lack of pump suction continues to be a detracting aspect of heparin-free cardiopulmonary bypass.

In situations where systemic heparinization is minimized or avoided and profound hypothermia is employed (< 20° C.), we have used roller pump suction. Blood collected in the cardiotomy is meticulously visualized for fibrin deposition and clot formation. To avoid over-hemodilution, pump suction must be used in situations where blood loss may be massive. Minimal to moderate blood loss can be processed with autotransfusion. When moderate (>28° C.) to normothermic temperature is used, however, roller pump suction must be avoided, necessitating the use of autotransfusion devices. The decision to either cell wash or return the CPD blood to the perfusion circuit must be made. While minimal amounts of blood can be washed without difficulty, scavenging large amounts of blood with washing may lead to significant plasma protein depletion, loss of biocompatibility and potential reduction in circuit volume, necessitating homologous blood transfusion (2).

CARDIOTOMY & SUMP (AORTIC, LV) DRAINAGE

Sump return (either left ventricular venting, aortic root venting, or other approaches) can be difficult. In several of our cases involving aortic valve replacement, left atrial myxoma removal, or pulmonary embolus removal, we have managed to avoid excessive blood loss by meticulous operative methods (careful dissection, bovie, and good surgical hemostasis). Left ventricular venting can be successfully accomplished by incorporating the vent line into the venous drainage line with a 1/2"x 1/2"x1/4" connector and 1/4" tubing (Figure 2). The vent holes must be under the fluid surface to prevent air entrapment. If air enters the line, the perfusionist or surgeon must quickly clamp the line and preserve the fluid hydroseal that allows drainage. In some instances, decompression of the left ventricle may be

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difficult with passive venting via gravity and siphon suction through the venous line. Minimal roller pump suction and return of blood to the venous line may be employed. It is extremely important to adjust the roller pump suction so that decompression of the ventricle is achieved without air entrapment. Similarly, during aortic valve procedures, the aortic vent should be used when an adequate hydroseal is present and blood can be suctioned through the venous line. The minute amounts of air are usually easily handled. Connecting these sumps to the cell-saver (suction) cardiotomy may precipitate massive volume shifts (2). This can be especially dangerous when employing an aortic or ventricular vent upon release of the aortic clamp. While de-airing of the ventricle is crucial at this juncture, the sudden shift of blood volume to the cell-saver cardiotomy may compromise circuit volume and prompt the need for homologous blood transfusion.

The traditional one-way valves incorporated in many sump lines must be deleted to avoid air embolism into the modified heparin-coated perfusion circuit (Figure 1). This loss of safety must be carefully supervised by the perfusionist to avoid mishaps. It is prudent to test the hydrostatic suction to assure adequate drainage and direction. It has been our experience to watch air in the gravity drained, siphoned tube that incorporates a one-way valve. Air must be avoided in this line to prevent entrance into the venous line. Successful decompression has been obtained in our experiences with direct (no one-way valve) sumping to the venous line as diagrammed in Figure 1.

THORACIC ANEURYSMS

Thoracic aneurysms present a major challenge for the perfusionist. Attempts to maintain a heparinless environment can be successful if the perfusionist maintains a closed circuit. Two circuit designs are presented (Figures 4 and 5). A simple design incorporating a Carmeda-coated[f] vortex pump, heparin-bonded tubing, and cannula is well-described in the literature and easily applied (Figure 4) (9). In other situations where partial or full support is anticipated, an in-line heparin-coated oxygenator[g] can be used (Figure 5) (9). In some cases, systemic heparinization may have to be used if pump suction is required and a cardiotomy is inserted. However, with the arrival of heparin-bonded cardiotomies, reduced systemic heparinization and cardiotomy pump suction can be practically applied (4).

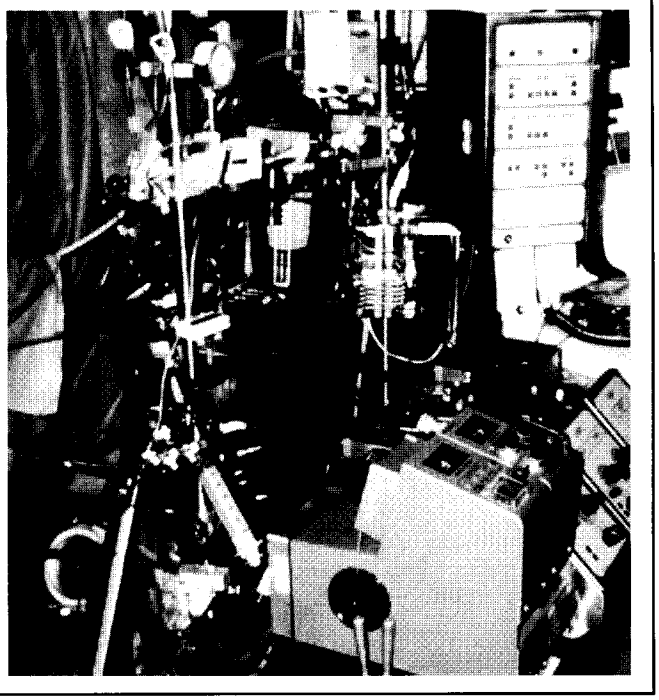
CONDUCT OF PERFUSION

The conduct of perfusion intensifies the need to maintain adequate flow through the circuit. This can be documented by placing a flow probe in line. Usual problems with vortex pumps can be avoided by careful supervision. Some problems that can occur are: 1) decreased flow and increased revolutions per minute (rpm) suggesting occlusion, an immediate signal that requires checking the circuit to find the cause, and 2) an unstable reservoir level that requires checking the lines to determine whether kinking, peri-cannular collapse, or potential thrombus is the cause of impediment. Kinks are straightened and peri-cannular collapse is resolved by retarding flow, but the presence of clot demands immediate exchange. If thrombus is detected, heparinization, (possibly thrombolytic therapy) and rapid exchange of the circuit must be performed immediately.

Thrombolytic therapy will have to be discussed and protocols established according to individual institutions. Thrombolytic agents produce a better resolution of massive thrombus (experiences with pulmonary embolus) and better improvement of cardiopulmonary hemodynamics than heparin alone (10). Lysis can be achieved, but bleeding is compounded three times more frequently. The late beneficial effect of thrombolysis and post-thrombotic syndrome is not well established. There are many thrombolytic agents that either activate plasminogen directly (urokinase, saruplase, alteplase) or indirectly (streptokinase, anistreplase). All must be reviewed regarding their individual dosages and consequences. None have an established optimal dose. In addition, there is poor correlation between the laboratory parameters, thrombolytic efficacy and the incidence of bleeding. We have not had this problem and would hesitate to suggest protocols to other institutions.

Arterial occlusion that is not obvious (mechanical failure, kink or inappropriate calibration of flow probe) suggests thrombus in the: a) centrifugal pump (does light reflect through the cone?) b) Oxygenator (is there adequate oxygenation, especially carbon dioxide exchange?) c) Arterial filter (is there a pressure gradient change of pre- and post-filter measurements?) d)

Figure 3: Operational design in the OR



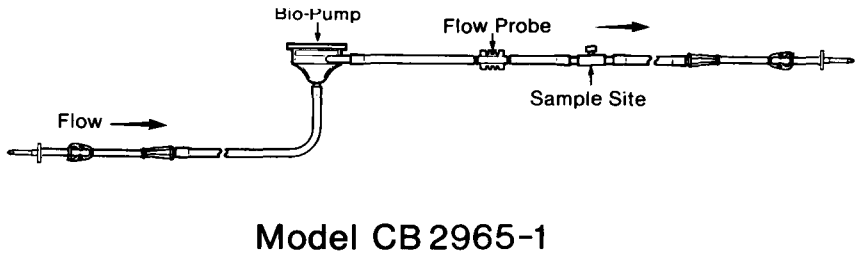
f Carmeda Inc., Stockholm, Sweden, in conjunction with Medtronic Cardiopulmonary, Anaheim, CA 92807 USA

g Medtronic Cardiopulmonary, Anaheim, CA 92807 USA

Cannulas - DO NOT have the surgeon squeeze the line to palpate for a clot! Immediate exchange is recommended with full heparinization as outlined above.

Cardiotomy drainage lines create areas of stagnation that can produce thrombus formation. To avoid this problem, maintain 300 - 400 ml of a crystalloid solution in the cardiotomy and occasionally flush the cardiotomy line to maintain dilution and flow. The rest of the circuit is assembled to promote easy visibility and rapid exchange. Streamline the circuit to avoid stagnant areas, especially at the venous reservoir bag, oxygenator, and bypass line of the arterial filter (Figure 3) (9).

Figure 4: Circuit design of left heart support utilizing heparin-bonded tubing and vortex pump (Medtronic-BioMedicus and tubing)



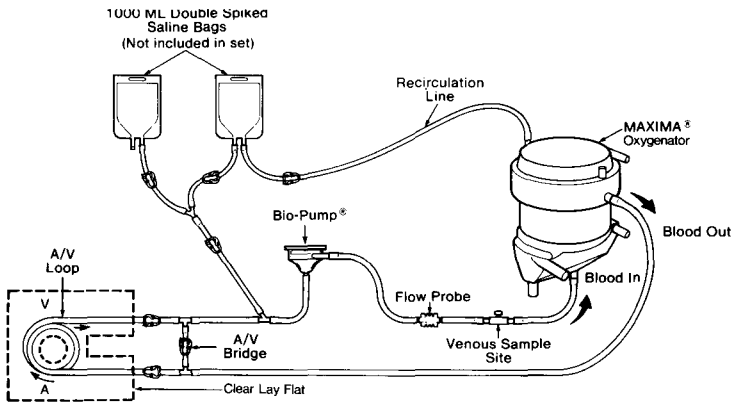
Model CB 2965-1

HEPARIN MANAGEMENT

Clotting times measured by activated clotting time (ACT) machines can be notoriously misleading. Avoid response to a single isolated value and assess the entire situation. Always plan on having a backup or secondary measurement from another source (Hemochron[h] and HemoTec ACT device[i]). Always chart results as you would with any perfusion case whether you use low or no systemic heparin.

Current monitoring techniques stress thrombin generation for end-point generation of clot. One of the easiest measurements that can help monitor heparin activity levels is the Medtronic-HemoTec H.M.S. system. This has helped in the measurement of circulating heparin and appropriate protamine dosage if low-dose heparin therapy is used. A technique to predict thrombin generation or "coagulability" must be developed that can adapt to the demands of these emerging heparin-free techniques.

Figure 5: Circuit design of ECLS circuit utilizing heparin-bonded oxygenator, vortex pump (Medtronic-BioMedicus), and tubing



Model CB 2505

WEANING OFF CARDIOPULMONARY BYPASS

Preparation to wean off cardiopulmonary bypass is different from conventional (with heparin) strategies. The patient is pharmacologically optimized and intravascular volume is expanded (pulmonary diastolic pressures around 10 mmHg). Partial bypass flows , greater than two L/min, are maintained while the anesthesiologist and perfusionist stabilize the patient's hemodynamics. As filling pressures approach optimum levels, the patient is placed in reversed Trendelenburg (feet down position) to increase circulatory volume in the patient's legs. This acts as a reservoir for rapid volume(auto-infusion) postoperatively. As the hemodynamic status stabilizes, saturations are rechecked.

The surgeon surveys the operative field for any potential problems that may require resumption of bypass. As the perfusionist maintains flows greater than 1.5 L/min, venous drainage is abruptly discontinued, the surgeon clamps and cuts the venous cannula from the tubing, clamps the arterial line, cuts the tubing, and re-connects the arterial and venous tubing with a 3/8"x1/2" heparin-bonded connector. The perfusionist immediately recirculates and adds crystalloid solution to the venous reservoir to dilute the prime. At the same time, the perfusionist begins to transfer the circuit volume to the cell saver. The transferred volume is washed and concentrated as rapidly as possible for return to the patient.

If filling pressures fall, the patient's legs can be gently

h International Technidyne Co., Edison, NJ 08820
i Medtronic HemoTec, Inc., Englewood, CO 80112

raised for autotransfusion. As cannulas are removed the surgeon must be meticulous to avoid bleeding or mishap. Our surgeons differ in which cannula to remove first. Debate continues whether to remove the arterial cannula first in case aortic disruption occurs and volume replacement is needed via the venous line or remove the venous cannula first to avoid preload depression and thrombus generation in a low flow area. If bypass is urgently required, the perfusionist should have maintained an intact, though hemodiluted, circuit. Again, arterial cannulation requires minute infusions of crystalloid to maintain a degree of hemodilution in the cannula tip to avoid stagnation and thrombus development.

CONCLUSION

While perfusion techniques vary among perfusionists, standard considerations are always employed throughout perfusion practices. West Virginia University (in conjunction with Ruby Memorial and Monongalia General Hospitals) has been involved in ongoing analysis of heparin-bonded cardiopulmonary bypass systems. As with any investigation, further research must be completed before definite advantages are realized (11). Animal research must be employed to concentrate on long-term, pathophysiological effects. Different techniques and potential complications continue to be investigated and explored.

Biocompatibility has been investigated by our team as well as by others (3,7,8). Coagulation effects have also been recorded and observed. While experiences have been encouraging, application of heparin-bonded circuitry has been restricted to those patients with indicated needs (Table 1). One of the restrictive elements of further utilization has been the lack of a heparin-bonded cardiotomy; we hope to investigate cardiotomies developed by several manufacturers in the future. Concern will also revolve around blood-air interfaces with roller pump suction and the cardiotomy. As with any new device and technique, further refinement in technique as well as analysis of results needs to be fully completed before protocols are established. We hope to enlarge upon our experiences over the next few months.

Post-bypass problems rarely occur. Interestingly, with biocompatibility comes decreased complement activation and minimal pulmonary congestion. This usually results in decreased ventilator time, rapid intensive care recovery, and general pulmonary recovery on the ward. As our series expands, we hope to see patient outcomes improve together with faster recovery and earlier discharge times (10).

Low-dose heparin as well as heparin-free bypass procedures are suitable for indicated problems. Avoiding the pharmacotoxic effects of heparin and protamine and enhancing the biocompatibility of the perfusion circuit with decreasing complement activation will benefit the patient. Minimizing homologous blood products and reducing potential harmful exposure to the patient are obvious goals for the perfusionist. As techniques improve, expanded use of heparin-bonded circuits into the pediatric population as well as routine open-heart procedures may not only reduce patient risk and avoid serious mishaps, it may impact economic sensibility with reduced hospital stays, especially in intensive care environments. Standardization and sharing techniques among the perfusion community will increase the knowledge applied to this unique and exciting technology. As this technique is applied to more and more patients, case reports and discussions will improve and refine our perfusion practice.

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