

## Abstracts

### A METHOD TO IDENTIFY THE SUBPOPULATION OF CARDIOPULMONARY BYPASS PATIENTS WHO RESPOND TO HYPOTHERMIA INDUCED PLATELET AGGREGATION

Hypothermic temperatures (24–32°C) are routinely reached during cardiopulmonary bypass (CPB) to reduce the oxygen requirements and to provide a margin of safety for the patient. Despite precautions and advancements in surgical techniques, undesired outcomes still occur without explanation in a number of CPB patients. It has been found that hypothermic temperatures, in association with extra-corporeal circulation, promote the formation of platelet aggregates in whole human blood. This response, termed hypothermic-induced platelet aggregation (HIPA), is limited to a subpopulation of patients, which has been classified into three separate response groups (Low, Medium, and High) based upon the number of aggregates and the duration of their appearance. In a previous population, it was identified that 14% were High Responders, 18% were Medium Responders, and 68% were Low Responders at 24°C.

It has been postulated that occlusive platelet aggregates may contribute to the undesired outcomes associated with hypothermic CPB surgery. A method is described to pre-operatively identify HIPA responders by video microscopy and the apparatus was tested in-vitro. A video of a Low versus High Responder to HIPA will be presented as evidence. If the High or Medium Responder subpopulations are identified preoperatively, there are modifications that perfusionists can make to their protocols to decrease the risk of having undesired outcomes, such as neurocognitive dysfunction and circuit device flow obstruction, during hypothermic CPB surgery. Pharmacological intervention has been postulated to reduce the risk of such complications.

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### THE EFFECTS OF LEUKOCYTE REDUCTION ON MATRIX METALLOPROTEINASE RELEASE IN CARDIOPULMONARY BYPASS

Matrix metalloproteinases (MMPs) are a family of enzymes responsible for degrading the extracellular matrix, a process likely responsible for the development of altered vascular permeability. Past studies in patients undergoing cardiopulmonary bypass (CPB) have documented increased levels of MMPs with CPB. The MMP species MMP-9, highly expressed in neutrophils, was increased post-CPB. In light of the mechanistic relationship between MMP activity and vascular permeability, interruption of MMP release in CPB would be a novel interventional strategy. This study is aimed at measuring MMP release in patients undergoing elective coronary revascularization and CPB in which a leukocyte reduction filter (LRF) was employed.

Patients are consented for participation and randomly assigned to either the LRF group or the standard CPB circuit with no LRF. MMP levels are serially measured at baseline and up to twelve hours post-CPB. The LRF circuit contains two filters (LeukoGuard-6 and LeukoGuard-BC, Pall Corporation, East Hills, NY). The MMP levels were measured by enzyme-linked immunoassay.

Four patients have been randomized to date (2 non-LRF, 2 LRF). Baseline MMP-9 levels were 62±16 ng/ml. At six hours post-CPB, MMP-9 levels were 45±9 ng/ml in the non-LRF group and were 50% lower in the LRF group (26±15 ng/ml).

While this study is ongoing (target sample size of 20 patients), modifying MMP release through selectively sequestering mediators of the inflammatory response (i.e., leukocytes) may hold clinical relevance in patients undergoing CPB.

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## DIASTOLIC DYSFUNCTION IN THE AGED

The prevalence of cardiovascular disease in the U.S. dramatically increases with age. A hallmark feature of the aged myocardium is increased fibrosis resulting in diastolic dysfunction. Moreover, the survival of patients subsequent to a myocardial infarction is inversely related to age due to a certain extent to maladaptive remodeling mediated by cardiac fibroblasts. Our hypothesis is that immunosenescence transforms the cardiac fibroblast function to over-express TGF- $\beta$  that results in increased cardiac fibrosis in the aged and deleterious maladaptive remodeling of the myocardium. TGF- $\beta$  stimulates the synthesis of the extracellular matrix proteins including collagen, proteoglycans, glycosaminoglycans, fibronectin, and integrins in the cardiac and vascular tissues.

The mRNA expression of TGF- $\beta$  was 43% increased in the aged mice compared to the younger. The compliance of the left ventricle is expressed with the slope of the end-diastolic pressure-volume relationship parameter,  $\gamma$  mmHg/L. In a mouse model we demonstrated that  $\beta$  was  $0.30 \pm 0.05$  in the young compared to  $0.52 \pm 0.10$  in the aged ( $p < 0.05$ ). The compliance correlated with myocardial collagen content with the young having  $9.5 \pm 4.0$  compared to  $16.4 \pm 2.3$  % of total protein ( $p < 0.05$ ). Increasing the TGF- $\gamma$  by 2 $\times$  in the young mice produced a  $\beta$  of  $0.44 \pm 0.19$  and a corresponding increase in myocardial collagen to  $13.48 \pm 5.2$  % of total protein. Inhibition of TGF- $\beta$  in the aged mice decreased  $\gamma$  to  $0.12 \pm 0.05$  with a corresponding collagen content of  $2.62 \pm 0.36$  % total protein. In conclusion, TGF- $\beta$  has been shown to be a key modulator diastolic compliance and cardiac collagen content.

These data justify the need to revise our care and perfusion techniques of the aged compared to that of the younger open-heart patient.

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## REMOVAL OF GASEOUS MICROEMBOLI IN LOW-PRIME CARDIOPULMONARY BYPASS CIRCUITS

Due to the deleterious effects of hemodilution and contact activation, perfusionists and manufacturers of cardiopulmonary bypass (CPB) components are redesigning circuits to achieve lower priming volumes. Changes to the configuration and component selection to achieve low-prime CPB circuits may alter the ability of the circuit to remove gaseous emboli. Air entrained into the venous line during CPB may be transmitted through the circuit resulting in arterial gaseous emboli, which has been identified as a cause of significant postoperative neurological injury.

Using low prime circuits and a standard high prime circuit as a control, in an animal model, air was introduced into the venous line during CPB. The transmission of gaseous microemboli through the circuit was monitored using an ultrasonic microbubble detector. Sampling at multiple locations on the circuit was used to evaluate the ability of components of the low-prime CPB circuit to remove gaseous microemboli.

This experiment addresses a significant safety issue that must be evaluated before clinical use of these low prime systems can be advocated.

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## FAILURE MODE EFFECTS ANALYSIS (FMEA) ON EXTRACORPOREAL CIRCUITS FOR CARDIOPULMONARY BYPASS

Although many refinements in perfusion methodology and devices have been made, extracorporeal circulation still remains a contributor to neurological complications, bleeding coagulopathies, use of blood products, and systemic inflammatory response. With the exposure of these adverse effects of cardiopulmonary bypass, the necessity to re-examine the safety of extracorporeal circuits is vital.

A failure mode effect analysis (FMEA), a proven process developed to evaluate system effect and equipment failure, was used to evaluate the six different types of extracorporeal circuits based on feedback from seven clinical experts.

This analysis investigates the safety of six types of extracorporeal circuits used in coronary revascularization, including the newer miniaturized extracorporeal circuits. The FMEA assists in listing and ranking the hazards associated with the use of each CPB extracorporeal circuit type.

The cardiovascular device manufacturers, Veteran's Administration National Center for Patient Safety and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) recommend the use of FMEA to assess and manage risks in current and developing technologies and therapies. To increase the safety of extracorporeal circuits and minimize the effects associated with cardiopulmonary bypass, perfusionists must incorporate FMEA into their clinical practice.

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## EVALUATION OF A NOVEL ULTRAFILTRATION SYSTEM FOR CIRCUIT SALVAGE

Following termination, the CPB circuit contains a significant volume of diluted blood. A variety of methods have been used to salvage this blood including placing the unmodified circuit contents in a bag or centrifugation/washing of the circuit volume. These techniques produce a re-infusion product that is either dilute or free of plasma proteins. The purpose of this study is to evaluate a novel device, which, by utilizing a hemofilter, may overcome these limitations.

Yorkshire pigs (n = 3, ~40 kg) were placed on CPB (prime volume 1.5 L) for 60 min. Following CPB, control blood samples (Pre) were collected from the circuit. The circuit contents were then transferred into a Hemobag and processed. Blood samples (Post) were then collected from the Hemobag. Pre and post samples were analyzed and compared using a Students *t*-test.

The measured parameters and their pre/post values are listed below.

Parameters	Pre	Post
Hematocrit (%)	20.0 ± 4.0	53.7 ± 14.2*
Total Protein (g/dl)	2.3 ± 0.5	7.1 ± 2.4*
Fibrinogen (mg/dl)	89.0 ± 23.8	281.0 ± 156.7
Platelets (K/ul)	168.0 ± 122.3	228.3 ± 142.3
Heparin Level (units/ml)	1.5 ± 0.3	2.6 ± 1.4

Data expressed as mean ± standard deviation, \*denotes p<0.05 compared to pre-hemobag

Additional parameters measured include: sodium, potassium, chloride, bicarbonate, osmolarity, plasma free hemoglobin, and white blood cell count. No difference between pre and post samples was seen for any of these parameters.

This novel device effectively concentrates post-bypass circuit volume, providing a product that is high in red blood cells and plasma proteins and may provide a new alternative to current techniques for circuit volume salvage.

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## MINIMAL PROTECTION OF PUMP PRIME STEROID DURING CARDIOPULMONARY BYPASS AND CIRCULATORY ARREST

This study evaluates the timing effects of 3 different steroid protocols on neuroprotection during cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA). Eighteen 4-week-old piglets were divided into 3 groups (n = 6/group). Methylprednisolone (30 mg/kg) was administered either intravenously 4 hours prior to CPB in Group I, or added in pump prime (25% Hct) in Group II. Group III received no steroid. All animals underwent 100 minutes of DHCA (15°C), rewarmed and sacrificed 6 hours after CPB. Postoperative weight gain, bioelectrical impedance, and colloid oncotic pressure (COP) were evaluated. Neurovascular integrity was determined by trypan blue infusion. Cerebral TGF- $\beta$ 1 expression and caspase-3 activity as indicator of apoptosis were performed by immunohistochemical assays. Statistical analysis was performed with ANOVA or Mann Whitney U-test.

Postoperative % weight gain ( $13.0 \pm 3.8$  (I) vs  $26.4 \pm 9.9$  (II) vs  $22.6 \pm 6.4$  (III),  $p = 0.02$ ); % bioimpedance change ( $14.5 \pm 8.0$  (I) vs  $38.3 \pm 13.3$  (II) vs  $30.5 \pm 8.0$  (III),  $p = 0.003$ ) and COP (mmHg) were significantly different between the groups ( $14.9 \pm 1.8$  (I) vs  $10.9 \pm 2.0$  (II) vs  $6.5 \pm 1.8$  (III),  $p = 0.0001$ ). Spectrophotometric analysis of cerebral trypan blue (ng/g dry weight) was significantly different between the groups ( $0.0053 \pm 0.0010$  (I) vs  $0.0096 \pm 0.0026$  (II) vs  $0.0090 \pm 0.0019$  (III),  $p = 0.004$ ). Significant reduction in cerebral TGF- $\beta$ 1 expression and remarkable perivascular caspase-3 activity in Groups II and III were observed.

The administration of steroids in CPB prime does not offer additional benefits than no steroids treatment with respect to extracellular fluid accumulation and cerebral protection. In addition, our results strongly suggest that systemic pre-treatment, and therefore, the timing of administration is essential for steroids to exert their neuroprotective effects.

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## AN INVESTIGATION OF THE EFFECTS OF MULTIPLE FORMS OF SURFACE MODIFICATIONS USED IN CONJUNCTION WITH PHARMACOLOGICAL SUPPORT

Nonphysiological forces with using cardiopulmonary bypass (CPB) have demonstrated detrimental effects on the formed elements of blood. The purpose of this study was to examine the effects of Aprotinin in combination with Safeline and Poly (2-methoxyethylacrylate) (PMEA) during simulated CPB.

Bovine blood was used to prime CPB circuits divided into six groups (n = 5): control (CTR), Aprotinin 250 KIU/mL (APR), PMEA, Safeline (SAF), APR with PMEA (APR-PMEA) and APR with SAF (APR-SAF). Circuit dynamics included negative pressure to the venous reservoir ( $-45$  mmHg), arterial line pressure of  $145$  mmHg at  $4.5$  LPM, and air-blood interface, over  $90$  minutes. Assays included thromboelastography (TEG), plasma free hemoglobin (PFH),  $\beta$ -Thromboglobulin (BTG), and Interleukin-8 (IL-8).

The TEG showed significant differences between the CTR and PMEA groups (CTR  $(-2.1 \pm 1.6$  min), (PMEA  $(-4.5 \pm 2.2$  min,  $p = .010$ ), and PMEA and SAF groups (PMEA  $(-4.5 \pm 2.2$  min), (SAF  $(-2.1 \pm 2.1$  min,  $p = .0098$ ). PFH results were significant between the CTR and APR treated circuits at  $90$  minutes (CTR  $(718.2 \pm 71.6)$ , (APR  $(398.8 \pm 71.6)$ ,  $p = .0015$ ). The SAF coated circuits were statistically significant from the CTR group (CTR  $(800.2 \pm 87.6)$ , (SAF  $(254.0 \pm 87.6)$ ,  $p < .0001$ ), and the PMEA coated circuits after  $90$  minutes (PMEA  $(591.2 \pm 87.6)$ , (SAF  $(398.8 \pm 71.6)$ ,  $p = .0088$ ). At  $90$  minutes BTG showed a significant difference between CTR and PMEA groups (CTR  $(2.82 \pm 2.3)$ , (PMEA  $(4.08 \pm .23)$ ,  $p = .0005$ ), as well as SAF and PMEA treated circuits (SAF  $(2.98 \pm .23)$ , (PMEA  $(4.08 \pm .23)$ ,  $p = .002$ ). The IL-8 showed a significant difference between the CTR and PMEA circuits (CTR  $(86.3 \pm 4.8)$ , (PMEA,  $(102.3 \pm 4.8)$ ,  $p = .025$ ). The PMEA group also showed significant changes in IL-8 over  $90$  minutes and between the coating groups (SAF  $(87.0 \pm 4.8)$ , (PMEA,  $(102.3 \pm 4.8)$ ,  $p = .032$ ).

In conclusion, SAF showed the greatest effect on reducing the activation of formed elements of blood. Neither APR nor PMEA significantly attenuated the derangements informed elements induced during CPB.

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## HEPARIN-BONDED PARTIAL CARDIOPULMONARY BYPASS FOR TRAUMATIC AORTIC RUPTURE

Traumatic aortic rupture (TAR) is an acute, life-threatening injury that requires immediate surgical intervention for enhancing survival. This dissecting injury occurs proximal to the ligamentum arteriosum in >80% of presenting cases, due to an acceleration-deceleration mechanism. Historically, the "clamp-and-go" technique afforded only a modicum of surgical success, often with significant and long-term complications (e.g., paraplegia attributed to spinal cord ischemia distal to the aortic cross-clamp). Another option, full cardiopulmonary bypass (CPB), is generally unwarranted in this setting and requires full systemic heparinization.

Partial CPB-via femoral venous (into right atrium) and distal aortic cannulation was introduced as a novel means for increasing perfusion distal to the aortic tear, but also reducing the deleterious effects of heparinization on concurrent traumatic injuries (e.g., intracranial hemorrhage, long-bone fractures, and other associated major visceral injuries). There are numerous benefits of using this heparin-bonded partial CPB closed-circuit apparatus: (1) Better hemostasis is attributed to the lack of systemic heparinization. (2) Nearly the entire body can be actively perfused, and the risk of paraplegia is significantly reduced. (3) The use of an oxygenator improves control and ease of oxygenation, providing additional stability during single-lung ventilation with the chest open. (4) Most trauma patients arrive to the operating room markedly hypothermic, thus use of an oxygenator also allows patients to be rewarmed slowly over the duration of partial CPB. (5) This circuit is similar to those used for cardiopulmonary support or adult extracorporeal membrane oxygenation, so perfusionists have become very familiar with use of this apparatus in a controlled operating room setting.

This perfusion system and TAR protocol have been in use for more than ten years at our institution (Level I trauma center) in >150 patients, without any paraplegia. It is well established as safe, effective, and efficient means of providing distal perfusion, ultimately enhancing survival and reducing morbidity associated with aortic repairs in traumatized patients.

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## IN-VITRO STUDY OF PLATELET FUNCTION AND COAGULATION EFFECTS OF PRIMING SOLUTIONS ON BIOCOMPATIBLE SURFACES

Biocompatible (BC) surfaces on cardiopulmonary bypass (CPB) components mimic the natural endothelium and have been shown to reduce thrombin formation and the incidence of platelet aggregation. Cardiopulmonary bypass priming solutions often contain plasma expanders to maintain the colloidal osmotic pressure (COP) and may interfere with the action of the biocompatible surface.

The purpose of this study is to determine changes in platelet function and whole blood coagulation in a test circuits using combinations of four different biocompatible surfaces and three priming solutions. A closed circuit loop of test tubing was used and fresh porcine blood mixed with the priming solution was recirculated for 6 hours. Samples were taken at baseline, 1 hour, 2 hours, 4 hours, and 6 hours. The Helena Plateletworks and Thromboelastograph (TEG) were used to determine: (1) platelet count, (2) platelet function (3) viscoelastic properties of the clot formation (clot speed and strength). Platelet activation, as determined by the adhesion and aggregation to the wall of the tubing, was assessed with the scanning electron microscope (SEM).

Although previous research has demonstrated the beneficial clinical effects of biocompatible tubing, this study will determine whether coagulation is additionally influenced by the choice of priming solution in an in-vitro circuit.

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## DURABILITY OF BIOCOMPATIBLE TUBING IN ROLLER PUMPS

Durability of tubing in the roller pumps of the heart-lung machine is an important aspect of patient safety during cardiopulmonary bypass. A variety of biocompatible surfaces (BC) on tubing used in the roller pump have been developed to minimize contact activation during cardiopulmonary bypass. After prolonged exposure in a roller pump, the inner surface of the tubing will break down and produce small particulate microemboli (spallation) leading to erosion and eventually tubing rupture. The durability of non-biocompatible (NBC) tubing has been previously documented.

The purpose of this study is to evaluate the durability of BC tubing during prolonged use in a roller pump. The circuit consisted of a closed loop of tubing primed with sterile water solution and recirculated until tubing rupture occurred.

The circuits were run for 4 hours, 8 hours, and until rupture or 30 hours cut off time the solution was removed and filtered to evaluate the amount of debris released during each time period. Continuous system pressure was used as a marker for tubing rupture. Each BC tubing was tested and compared to the NBC equivalent. Four brands of tubing were tested.

Although there are many benefits to biocompatible surfaces, tubing durability remains a primary concern during cardiopulmonary bypass in order to insure patient safety.

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## **SURVEY OF THE IMPACT OF OFF-PUMP SURGERY ON PERFUSIONISTS' ACTIVITIES**

It is important to evaluate the effects of changing technology on the perfusion profession in order to advise prospective students entering this field of study. Manufacturers have reported an average growth rate of 3.3%/year for off-pump coronary bypass procedures (OPCAB) for the last 4 years (increase from 13.5% to 22.5% of CABG procedures for 1999–2002). The impact of OPCABS on the perfusion profession was evaluated by this survey.

Preliminary results include: 64 % of the respondents said that OPCABS consisted of < 20% of their total cardiac surgical cases and 15% report an OPCAB rate of between 21–40% of their cases. Forty nine percent of the respondents said that the OPCAB rate was relatively stable in their institution (+/- 10% change) and 24% reported an increase in OPCAB more than 11%. Twenty six percent reported a decrease of >11% in OPCAB cases.

Reduction in staff was reported by 8% of the respondents and additional activities to make up for the off-pump cases such as platelet gel, database management, and autotransfusion for noncardiac cases was reported by 41%. Fifty-nine percent of the respondents were hospital employees and the survey will be further analyzed based on the employer type and institutional caseload.

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## **FLOW VISUALIZATION OF DIFFERENT AORTIC CANNULAS IN THE HUMAN AORTA**

The aortic cannula is the interface between the patient and the heart-lung-machine. Different designs and dimensions of the cannulas result in different flow conditions in the aorta. The aim of this study was to visualize the flow distribution of different aortic cannulas in a human aorta with the use of an endoscopic video camera.

We investigated three different aortic cannulas. For the simulation of an intraoperative situation we used human cadaver aortas. Each aorta was cannulated in standard surgical technique. Using water as the perfusion fluid, the cannulas were tested at different flow rates from 0.5 to 5 L/min generated by a centrifugal pump. An endoscopic camera was introduced through the right coronary ostium to allow an insight into the perfused aorta. For the visualization of the flow a dye was injected into the perfused aorta. Depending on the perfusion rate, the cannulas create laminar or turbulent flow in the aorta. The different designs of the tips have major impact on the flow distribution.

Our experimental setup made it possible to visualize the perfusate distribution in a human aorta in a film sequence. The endoscopic view inside the perfused aorta showed the areas of increased stress, where an endothelial damage or separation of atherosclerotic plaques can be expected. All examined aortic cannulas produced turbulences in the aorta at flow rates of 4 L/min.

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## CLINICAL COMPARISON OF PLATELETWORKS(tm) PLATELET FUNCTION TEST TO THE THROMBOELASTOGRAPH FOR PREDICTION OF POSTOPERATIVE OUTCOMES

Approximately 3.5 million units of platelets are transfused in the United States each year to patients undergoing open-heart surgery with cardiopulmonary bypass (CPB). CPB is a known contributor to platelet loss and platelet dysfunction leading to disruption of hemostasis. Impaired hemostasis results in excess bleeding in 5–25% of all patients undergoing CPB. For this reason, it is beneficial to measure platelet number and function in these patients. The purpose of this study was to compare the Plateletworks(tm) platelet function analyzer to the thromboelastograph (TEG) in predicting postoperative hemostatic outcomes as measured by blood product use and chest tube (CT) drainage.

This study consisted of 35 adult patients undergoing cardiac surgery at Rush Presbyterian Saint Luke's Medical Center (RPSLMC). The Plateletworks(tm) and TEG tests were performed preoperatively and postoperatively on all patients.

Plateletworks(tm) demonstrated a statistically significant change in platelet function as shown by the adenosine diphosphate (ADP) reagent tube from the preoperative period to the removal of the aortic cross clamp ( $p = 0.011$ ). The TEG did not demonstrate a significant change in the k-time and maximum amplitude (MA), but did show a significant change in the alpha-angle from the preoperative to postoperative sample ( $p = 0.035$ ). A correlation was found between Plateletworks(tm) ADP reagent tubes upon arrival to the intensive care unit (ICU) and CT drainage ( $p = 0.027$ ,  $r = 0.49$ ). No statistical correlation was established between TEG parameters and CT drainage at any time interval. When comparing the Plateletworks(tm) to the TEG in this study, the Plateletworks(tm) system was a more accurate predictor of postoperative outcomes.

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## THE HEMOCHRON( RESPONSE RxDx HEPARIN AND PROTAMINE DOSING SYSTEM

The use of dosing assays to calculate heparin and protamine dose requirements during cardiac surgery has been shown to significantly improve overall postoperative patient outcome. When patients are managed with an individualized dosing system, intraoperative and postoperative transfusion requirements and bleeding are reduced. The HEMOCHRON [RxDx( system ITC, Edison, NJ)] is widely used as a complement to traditional activated clotting time (ACT) testing to optimize anticoagulation management. The system consists of the Heparin Response Test (HRT), the Protamine Response Test (PRT) and the Protamine Dose Assay O (PDA-O). All are modifications of the ACT, using either Celite(r) or kaolin as the activator. Dosing is calculated manually using older Hemochron instruments or automatically with the Hemochron 8000 or Hemochron Response and the Palm RxDx; missing from available user options is an automated RxDx system for the Response.

A study was undertaken to evaluate the new Response RxDx software, conducting comparisons to the existing Palm RxDx system. Similar to the current system, the operator inputs the patient's height, weight and gender; the system automatically calculates the blood volume, bolus heparin and protamine dose and any additional heparin and protamine required. In laboratory studies, the data obtained were compared to the Palm RxDx calculations. The Response automated calculations were identical to the PDA RxDx calculations( $r > 0.99$ ) for all calculated values. Clinical studies comparing these systems are currently underway at several institutions.

With the addition of the automated RxDx calculations to the Response device, the system is now a complete anticoagulation management system. The Response RxDx offers expanded user options related to blood volume limits, expanded clotting time ranges for presetting default values and flexibility in test sequence. Active case records with all patient ID, operator ID and test results remain active for 8 hours after the last test and can be printed or downloaded to a PC via the HRDM data management program. Customized reports can also be generated. The database features of the Response assure compliance with QA/QC policies.

The fully automated Hemochron Response RxDx system provides accurate and reliable determination of patient specific dosing for both heparin and protamine in the cardiac surgical setting.

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## THE COMBINED USE OF EXTRACORPOREAL LIFE SUPPORT AND PULSATILE PEDIATRIC VENTRICULAR ASSIST DEVICE AS A BRIDGE TO TRANSPLANT

Very limited experience with long-term pediatric mechanical circulatory support as a bridge to heart transplant has been described worldwide. We report a 2-year-old, 12 kg boy admitted with low-grade fever, ear pain, pulmonary oedema, and congestive heart failure. A trans-esophageal echocardiography confirmed severe myocardial dysfunction with an ejection fraction of 20% and shortening fraction of 13%. After 2 days of ventilatory and inotropic support, the patient continued to deteriorate and subsequently required femoro-femoral extracorporeal life support (ECLS). This was later complicated by massive coagulopathy and bleeding. On day 17, a pulsatile pediatric paracorporeal bi-ventricular assist device (VAD) (Berlin Heart) was implanted. The patient's condition was much improved with all coagulopathies corrected and the patient was extubated. After 106 days of bi-VAD support, the patient was successfully transplanted and discharged home 45 days post transplant.

Our initial experience with combined (ECLS) bridge to (VAD) bridge to transplant is encouraging and allows for selection of best organ donor while optimizing recipient multi-organ failure. It may provide an additional armamentarium of circulatory support in pediatric patients with severe heart failure.

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## PEDIATRIC ORTHOTOPIC HEART TRANSPLANT REQUIRING PERIOPERATIVE EXCHANGE TRANSFUSION: A CASE REPORT

An 11-month-old patient with idiopathic cardiomyopathy was scheduled for orthotopic heart transplantation. A perioperative exchange transfusion was performed due to a donor/recipient incompatibility. This process was accomplished in the operating room prior to instituting cardiopulmonary bypass utilizing a modified CPB circuit.

In preparation for the procedure the CPB circuit was primed with washed leukocyte filtered banked packed red blood cells, fresh frozen plasma, albumin and heparin. Pump prime lab values were normalized prior to beginning the exchange transfusion. The patient's blood was downloaded from the venous line just proximal to the venous reservoir while simultaneously transfusing the normalized prime at normothermia. Approximately 125% of the patients calculated blood volume was exchanged.

This technique greatly reduces the likelihood of acute immune host/graft rejection. The exchange transfusion process in addition to patient immature immune system provides additional options in orthotopic heart transplantation for patients that may otherwise not be considered suitable candidates.

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## CASE REPORT: DIALYSIS DURING CARDIOPULMONARY BYPASS FOR END STAGE RENAL DISEASE

Patients with end stage renal disease (ESRD) presenting for heart surgery are at an increased risk of postoperative complications. A review of the literature revealed the use of dialysis during cardiopulmonary bypass (CPB) using various dialysate solutions. The purpose of this case report is to describe dialysis during CPB utilizing a dialysate solution that has not been previously reported in the literature. A 69-year-old, 53 kg, African-American female with a 6-year history of ESRD secondary to noninsulin dependent diabetes mellitus presented for aortic and mitral valve replacement with a creatinine level of 5.2 mg/dl, a blood urea nitrogen level of 15.0 mg/dl, a potassium level of 4.1 meq/l and an albumin concentration of 1.2 g/dl. The extracorporeal circuit consisted of a hard shell venous reservoir, membrane oxygenator, roller pump and a Hemocor 1000 hemoconcentrator. The circuit was primed with lactated Ringers, 25 g albumin, 5,000 u heparin, and 50 meq sodium bicarbonate. During CPB the Hemocor 1000 hemoconcentrator was utilized as a dialyzer with Premixed Dialysate for Hemofiltration (Baxter Healthcare Corporation) solution (Na 140meq/l, Ca 3.5 meq/l, K 2.0 meq/l, Mg 1.5 meq/l, Cl 117 meq/l, lactate 30 meq/l, 297 mosmol/l). During CPB estimated blood flow through the hemoconcentrator was 300–400 ml/min. Dialysate flow using a one-pass system was established via gravity at 200 to 250 ml/min. Two units of packed red blood cells and 25 g albumin were administered during CPB. Four thousand three hundred ml of 4:1 blood cardioplegia (53.4 meq potassium) was administered during cross-clamp. During 243 minutes of CPB using 16 liters of dialysate, 2.12 l of plasma water was removed. Blood glucose levels ranged between 67 and 204 mg/dl. Prior to CPB termination creatinine level decreased to 3.2 mg/dl, blood urea nitrogen level declined to 9 meq/l, potassium level remained stable at 4 meq/l and albumin concentration increased to 1.9 mg/dl. Dialysis was not required until one day postoperative. The Baxter Premixed Dialysate solution was able to correct electrolyte and uremic solute imbalances during CPB without increasing glucose levels inherent with the use of peritoneal dialysate solution.

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### A COMPARISON OF THE PLATELET SEQUESTRATION ABILITY OF THREE AUTOTRANSFUSION DEVICES

Although current autotransfusion devices have platelet sequestration capabilities, each utilizes a unique technology to achieve the final platelet product. The purpose of this study was to assess the quality and quantity of platelets sequestered by three different autotransfusion devices. The 3 commercially available autotransfusion devices evaluated were Fresenius C.A.T.S (a closed spiral chamber technology), BRAT 2 (Baylor bowl technology), and the Haemonetics Cell Saver 5 (Latham bowl technology). Platelet Sequestration was performed using the automatic mode under the manufacturers recommended sequestration protocols. The total number of platelets sequestered, percent recovery, and percent platelet function were assessed. Results were as follows:

	Platelet Count	Absolute Function	Effective Pre	Recovery Post	Recovery Pre	Recovery Post
Fresenius (n=4)	237 ± 134	520 ± 86	51 ± 23%	91 ± 13%	80 ± 11%	45 ± 19%
BRAT 2 (n=4)	187 ± 28	414 ± 84	57 ± 15%	91 ± 9%	80 ± 27%	51 ± 18%
Cell Saver 5 (n=6)	168 ± 53	405 ± 175	56 ± 9%	90 ± 5%	78 ± 9%	48 ± 7%

In conclusion, although a significant loss of platelet function was seen with the actual process regardless of autotransfusion device used, no statistical difference was noted between the respective machines. Therefore, different technologies used by the three autotransfusion devices did not appear to influence platelet function.

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### THE USE OF AUTOLOGOUS PLATELET GEL TO IMPROVE WOUND HEALING IN DIABETIC PATIENTS AFTER SAPHENOUS VEIN HARVEST FOR CORONARY BYPASS SURGERY

Surgical site infections and other wound complications following coronary artery bypass graft (CABG) surgery contribute to increased length of stay and hospitalization costs. Diabetic patients are at greater risk for developing these complications than the non-diabetic population. Autologous platelet gel (APG) is prepared by centrifuging the patient's whole blood and sequestering the platelet rich portion of the plasma. This platelet rich plasma (PRP) is mixed with reconstituted lyophilized thrombin and calcium chloride to form APG. Autologous platelet gel is a source of multiple growth factors. It has been demonstrated that APG applied topically to foot ulcers in diabetic patients improves wound healing and reduces the risk for infection. The purpose of this study is to test the hypothesis that the application of APG to the surgical site after saphenous vein harvesting during CABG reduces the incidence of wound infection and promotes healing in diabetic patients.

Patients will be randomized into two groups: Group A will receive APG and Group B will not. Blood drawn intra-operatively will be processed using the Haemonetics Cell Saver 5<sup>®</sup>, for preparation of the APG. The platelet poor plasma and red blood cells will be returned to the patient. The APG will be applied directly to the saphenous vein incision site just prior to wound closure. Digital photographs will be taken and evaluated using the ASEPSIS tool for wound infection to assess wound healing.

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## EVALUATION OF CELL WASHING AND LIPID FILTRATION OF CARDIOTOMY BLOOD FOR THE REMOVAL OF NEUTRAL FAT

Shed mediastinal blood returned to the cardiopulmonary bypass circuit is a pathway for neutral fat to reach the cerebral circulation. Part I of this experiment used cell washing alone or a combination of cell washing and lipid filtration. Blood in a porcine model was exsanguinated into the mediastinal cavity and then collected into three different autotransfusion devices (Cobe's Brat 2, Fresenius' CATS, and Haemonetics' Cell Saver 5) for cell washing and filtration by two filters specific for reducing lipids (Pall's Lipi-guard and Leukogaurd filter). Blood samples were analyzed for cholesterol and triglycerides. Part II was designed to determine if filtration alone by the lipid specific filters was effective. Four samples were collected from a porcine model and analyzed for cholesterol and triglycerides.

There was no significant difference in the reduction of cholesterol and triglycerides levels between cell washing and cell washing/filtration ( $p = 0.11$ ). Cholesterol and triglycerides levels were significantly reduced from baseline values by both interventions. Cell washing/filtration and cell washing had a 93.5% change from baseline for cholesterol and triglycerides showed 100% change from baseline for all samples for both interventions. For part II of the experiment, the percent change from baseline was 0% reduction for cholesterol levels and 1.5% reduction for triglycerides. Filtration in combination with cell washing does not provide a superior reduction in neutral fat as compared to cell washing alone. Cell washing alone was superior in reducing the markers for neutral fat as compared to filtering the blood.

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## THE POTENTIAL EFFICACY OF PLATELET GEL AS A SUPPLEMENT TO ADAPTIVE REMODELING OF THE HEART

After myocardial infarction, the heart undergoes maladaptive remodeling, where dead myocytes are replaced by collagen leading to fibrotic scars. These regions of fibrosis no longer support the differentiation of myocytes into functional myocardium. Platelet gel is an adhesive and growth factor rich gel that has shown profound efficacy in wound healing. The mechanism is that platelet gel application concentrates a temporary hyperphysiological concentration of growth factors at the site of injury initiating the early stages of healing. Platelet gel is derived from concentrated platelets activated by thrombin. Once activated by thrombin, platelet (alpha granules release high concentrations of growth factors that are applied to injured areas. These growth factors include IL-1 $\beta$ , TGF- $\beta$ , TGF- $\alpha$ , FGF, EGF, PDGF, and IGF, all of which have been shown to mediate wound healing. Our hypothesis is that Insulin-Like Growth Factor-1 (IGF-1) promotes wound healing, facilitate angiogenesis, and stimulates proliferation and differentiation of myoblasts in culture. Application of platelet gel to infarcted areas of the heart supports these areas with hyperphysiological levels of IGF-1 and other healing growth factors. In conclusion, application of platelet gel to the infarcted areas of the heart may offer support for the healing of myocardium or stimulate recruitment of stem cells into the infarcted areas. Platelet gel offers a potential benefit by influencing the remodeling of the heart after myocardial infarction.

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