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Introduction: Outcomes 2008

R. Clive Landis, PhD,[1] John M. Murkin, MD, FRCPC,[2] David A. Stump, PhD[3]

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The twelfth annual Outcomes meeting was held May 21-24, 2008 at the Accra Beach Hotel and Resort in Barbados, West Indies. Whereas the first 10 meetings were held in Key West FL, Outcomes moved to Barbados in 2007 and future meetings are planned at this venue. Organizers and delegates alike felt that the optimal conference space and meeting facilities set within the context of a relaxed oceanfront setting with private beach and a helpful Hotel staff recaptured the ethos of the original Key West meetings. Outcomes will continue to be a multidisciplinary meeting, blending an ideal mix of state-of-the-art lectures and scientific abstracts with a heavy emphasis on Q&A and audience interaction and discussion.

International representation at the 2008 meeting was again outstanding with attendees from Australia, Belgium, Britain, Canada, Germany, Japan, New Zealand, Sweden, and the USA sharing new insights into mechanisms of organ dysfunction following cardiac surgical interventions. New techniques to recognize, prevent and treat the effects of ischemia, embolization, and inflammation associated with both on- and off-pump surgery were contributed by surgeons, anesthesiologists, neurologists, psychologists, perfusionists, epidemiologists and basic scientists, among others.

Outcomes 2008 marked an unprecedented effort by experts in the field of inflammation to create a Consensus Document (published in these pages) to guide future research and interventions into the systemic inflammatory response. This consensus document evolved from a stimulating discussion at the conference which recognized that potential exposures related to type of CPB equipment and perfusion technique often went unreported in the literature and most studies did not report any causal inflammatory markers. We hope this consensus document will act as a framework to standardize research into the systemic inflammatory response and to encourage investigators to identify combinations of drugs and/or clinical management changes to deliver real clinical anti-inflammatory benefits in the future.

Another lively topic of debate at Outcomes 2008 was blood management in the post Aprotinin era, with pediatric surgeons in particular bemoaning the loss of this drug from their inventory. The conference agreed that a multimodal approach to blood management was the only way forward with a rallying cry of: "Everyone's a Jehovas witness!", or at least should be treated with the same personalized care as such patients receive. A lighthearted debate on the motion: "Markers of perfusion quality have no clinical benefit!" highlighted the impact of sub-optimal perfusion on organ injury. As in previous meetings, the interface between medicine, science and industry provided answers in the shape of new monitoring techniques, perfusion circuits and technologies for early detection of emboli and hypoperfusion as a means of minimizing injury. Mathematical modelling was introduced as a new discipline in those instances when clinical trials failed to answer the question.

Two off-site public lectures allowed interested delegates to share experiences with local Barbadian healthcare providers and the general public as this Caribbean country grapples with a growing burden of chronic disease during its transition to developed country status. We would like to acknowledge the efforts of all those individuals and supporting institutions that allowed this outstanding conference to take place: Special thanks to Marigo Portokalis, Sandy Adams, Dr. Steven Dain, Catherine Hawke, Colin Murkin at UWO; Dwight Deal, Paige Deal, Peggy Rachels at WFU; Kiana Prescott and Andre Greenidge at UWI; Adrian Randall at the Heart & Stroke Foundation of Barbados; and Pamela Payne-Wilson and Denise Carter-Taylor at the Barbados Drug Service.

Ultimately, credit for the overall success of this Outcomes meeting, as well as for the high quality of the scientific papers as published in these Proceedings, must go to the participants, registrants, lecturers, and staff who contributed so much to the program. For further information, registration, and abstract submission for next year's meeting visit our website at www.outcomeskeywest.com. We hope to see you next year in Barbados for Outcomes XIII, May 27-30, 2009. Thanks to you all.

ACKNOWLEDGMENTS

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OUTCOMES 2008 FACULTY:

Robert A Baker PhD, Adelaide, Australia; **Michael Borger MD,** Leipzig, GDR; **Wojciech Dobkowski MD,** London, ON, Canada; **Richard A Jonas MD,** Washington, DC, USA; **R Clive Landis PhD,** Barbados WI; **Filip De Somer PhD,** Ghent, Belgium; **Mike Poullis MD,** Liverpool, UK; **John M Murkin MD,** London, ON, Canada; **David A Stump PhD,** Winston-Salem, NC, USA; **Ed Verrier MD,** Seattle, WA, USA; **Keith Samolyk CCP,** Somers, CT, USA

OUTCOMES 2008 PROGRAM:

Wednesday, May 21, 2008

Session 1: PICS

13:00 – 13:30 Lecture 1: "What is optimal flow and how to validate this? Filip DeSomer
13:30 - 13:45 Q&A
13:45 – 14:15 Lecture 2: "State of the art blood management in cardiac surgery" Keith Samolyk
14:15 - 14:30 Q&A
14:30 – 15:00 REFRESHMENTS/EXHIBITS
15:00 – 15:30 Lecture 3: "Is it possible to remove lipid emboli from the blood?" David Stump
15:30 – 15:45 Q&A
15:45 – 16:30 Pro/Con Debate: "Markers of perfusion quality have no clinical benefit"Rob Baker vs Mike Poullis
16:30 – 17:00 Panel Discussion: "Blood management in the post aprotinin era"Rob Baker, Filip De Somer, Keith Samolyk, Mike Poullis
19:00 - 20:30 OFF-SITE PUBLIC LECTURE (SHERBORNE CONFERENCE CENTRE) "The Heart Matters – how an unhealthy lifestyle can end up in heart surgery" W Dobkowski

Thursday, May 22, 2008

07:30 – 08:00 OFF-SITE GRAND ROUNDS (QEH HOSPITAL) "Cardiac surgery and the brain: effect on mood and memory" Rob Baker

Session 2: Redefining SIRS

09:00 – 09:10 Opening Remarks
09:10 – 09:40 Lecture 4: "Redefining the systemic inflammatory Response: so much more than inflammation" R Clive Landis
09:40 – 09:50 Q&A
09:50– 10:30 ABSTRACT DISCUSSION I:
Moderators: C Landis, R Baker

An Evidence-Based Review Of Pharmaceutical Interventions To Limit The Systemic Inflammatory Response In Cardiac Surgery. **Landis RC**,[1] Brown JR,[2] Murkin JH,[3] Grocott HP,[4] Likosky DS,[2] Baker RA[5] for the International Consortium for Evidence Based Perfusion. *Affiliation(s): Edmund Cohen Laboratory for Vascular Research, University of the West Indies, Barbados; [2]The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, NH, USA; [3]London Health Sciences Center, London, Ontario, Canada; [4]University of Manitoba, Manitoba, Canada; [5]Flinders Medical Center, Adelaide, Australia*

Optimal Dose of Aprotinin for Neuroprotection and Renal Function in a Piglet Model. Yusuke Iwata, MD, Nobu Ishibashi, MD, Toru Okamura, MD, **Richard A. Jonas**, MD. *Affiliation(s): Children's National Medical Center, Washington, DC*

High Dose Tranexamic Acid May be Associated with Clinical-Seizures in Cardiac Surgical Patients. Granton J, **Murkin JM**, Chu M, Young B. *Affiliation(s): Departments of Anesthesia and Perioperative Medicine, Surgery, Clinical Neurological Sciences, University of Western Ontario, London, Ontario, Canada*

An Evidence-Based Review off the Use off Cardiotomy Suction and Cell Salvage to Limit the Systemic Inflammatory Response in Cardiac Surgery. **Baker RA**,[1,2] Newland RF[1] for the International Consortium for Evidence-Based Perfusion (ICEBP). *Affiliation(s): [1]Flinders Medical Center and [2]Flinders University Adelaide, Australia*

10:30 – 11:00 REFRESHMENTS/EXHIBITS
11:00 – 12:00 ABSTRACT DISCUSSION II:
Moderators: E Verrier, R Jonas

Plasmin But Not Thrombin Activates A172 Glial Cells Via Serine Proteolytic Cleavage of Preotease-activated Receptor (PAR)1. Hall KD, **Landis RC**. *Affiliation(s): Edmund Cohen Laboratory for Vascular Research, Chronic Disease Research Centre, University of the West Indies, Barbados*

A Specialized Sub-population of Monocytes is Induced During the Recovery Phase of Cardiopulmonary Bypass. **Quimby K**,[1] Fakoory M,[2] Mohammed W,[2] Harris A,[2] Landis RC[1]. *Affiliation(s): [1]Edmund Cohen Laboratory for Vascular Research, Chronic Disease Research Centre, University of the West Indies, Barbados. [2]Department of Cardiothoracic Surgery, Queen Elizabeth Hospital, Barbados*

Effects of Autologous Blood Transfusion on Monocyte Expression of Toll-Like Receptors in Patients Undergoing Cardiac Surgery with and without Cardiopulmonary Bypass. **G Asimakopoulos**,[1] G Niranjan,[1] P Karagounis,[1] G Cockerill,[2] M Thompson,[2] V Chandrasekaran[1]. *Affiliation(s): [1]Cardiothoracic Department & [2]Vascular Surgery Department, St George's Hospital, London, UK*

Overview of Barbados & Points of Interest. **Kiana Desiree Hall** (MSc,BSc.). *Affiliation(s): Edmund Cohen Laboratory for Vascular Research, Chronic Disease Research Centre, Barbados, WI*

12:00 - 13:00 BUFFET LUNCH

Session 3 Tissue Perfusion

13:00 - 13:30 Lecture 5: "Cerebral Oximetry: an evolving standard for selective cerebral perfusion?" John Murkin
13:30 - 13:45 Q&A
13:45 – 14:45 ABSTRACT DISCUSSION III:
Moderators: J Murkin, M Poullis

Impact of Aging Upon Cerebral Hypoxia Sensing of Anemia. **Thomas F. Floyd**,[1,2] Min Li1, Jessica Bertout,[3] Celeste Simon[3,4,5]. *Affiliation(s): [1]Departments of Neurology, [2]Anesthesiology & Critical Care, [3]Developmental Biology, [4]Howard Hughes Medical Institute, [5]Abramson Family Cancer Research Institute, University of Pennsylvania, Philadelphia, PA*

Installation of a Multielectrode Spiral Cuff on the Human Vagus-nerve for Selective Electrical Stimulation. **Kneževič I**,[1] Mirkovič T,[1] Geršak B,[1] Pečlin P,[2] Radan I,[3] Podbregar M,[3] Rozman J[2]. *Affiliation(s): [1]Clinical department for cardiovascular surgery, University Clinical Centre Ljubljana, [2]ITIS d. o. o. Ljubljana, Center for Implantable Technology and Sensors, [3]Center for Intensive Care Medicine, University Clinical Centre Ljubljana, Ljubljana, Slovenia*

Patterns in Brain Oxygen Saturation during Aortic Surgery. **Fischer GW**, Reich D, Plestis KA, Griepp RB. *Affiliation(s): Departments of Anesthesiology and Cardiothoracic Surgery, Mount Sinai Medical Center, New York, NY, USA*

Visualization of Regional Cerebral Desaturation by Micro-emboli during Cardiovascular Surgery. **Hanzawa K**, Okamoto T, Sato K, Hayashi J. *Affiliation(s): Department of Thoracic and Cardiovascular Surgery, Niigata University Graduate School of Medicine, Niigata, Japan*

Monitoring INVOS Cerebral Oximetry Significantly Decreases the Incidence of Cognitive Dysfunction in Diabetic Patients Undergoing Coronary Bypass Surgery. **Murkin JM**, Slade H, Adams S, Slade

A, Dikih P, Pardy E. *Affiliation: Department of Anesthesia and Perioperative Medicine, University of Western Ontario, London, Ontario, Canada*

14:45 – 15:15 REFRESHMENTS/EXHIBITS
15:15 – 15:45 Lecture 6: "Suboptimal perfusion and its possible impact on the inflammatory response" Filip DeSomer
15:45 – 16:00 Q&A
16:00 – 17:00 ABSTRACT DISCUSSION IV:
Moderators: F De Somer, K Samolyk

An International Framework for Evidence-Based Perfusion. **DS Likosky**, RA Baker, KG Shann, TA Dickinson, GR DeFoe, TA Paugh, C Visser, JH Higgins. *Affiliation(s): International Consortium for Evidence-Based Perfusion Registry Subcommittee*

Case Report: Postoperative Therapeutic Hypothermia after Cardiac Arrest and Cardiac Surgery. **Blitz A**,[1] Williams G,[2] Okada S,[1] McFarland H,[2] Foster J[1]. *Affiliation(s): [1]Division of Cardiac Surgery and [2]Department of Anesthesiology, University Hospital Case Medical Center, Cleveland, Ohio, USA*

Patient Directed Perfusion Pressure On Bypass. An Analogy From Electrical Engineering. I Johnson, **M Poullis**. *Affiliation(s): The Cardiothoracic Centre, Liverpool, England*

Constancy Of Pressure On Bypass – A Potential Quality Marker of Perfusion. I Johnson, **M Poullis**. *Affiliation(s): The Cardiothoracic Centre, Liverpool, England*

Friday, May 23, 2008
Session 4: Techniques and Technologies

07:45 – 08:00 Announcements
08:00 – 08:30 Lecture 7: "Mathematical modelling in cardiac surgery: when clinical trials fail to answer the question - special reference to carotid stenosis" Mike Poullis
08:30 – 08:45 Q&A
08:45 – 09:30 Lecture 8: "Suction, salvage, sutures and potions: blood: management post-aprotinin" Rob Baker
09:30 – 09:45 Q&A
09:45 – 10:15 REFRESHMENTS/EXHIBITS
10:15 – 10:45 Lecture 9: "Regaining homeostasis following the systemic inflammatory response" Ed Verrier
10:45 – 11:00 Q&A
11:00 – 12:00 ABSTRACT DISCUSSION V:
Moderators: R Baker, C Landis

Reducing Emboli During Cardiac Surgery Through Redesign of Cardiopulmonary Bypass. Robert Groom,[1] **Donald Likosky**,[2] Reed Quinn,[1] Scott Buchanan,[1] John Braxton,[1] Larry Adrian,[1] Lou Russo,[1] Christopher Ryan,[1] Angus Christie,[1] Paul Lennon,[1] Richard Forest,[1] Janine Welch,[1] Cathy LaVopa,[1] Andreas H. Taenzer,[2] Cathy Ross,[2] Robert Kramer[1]. *Affiliation(s): [1]Cardiac Services Department and Anesthesia Department, Maine Medical Center; [2]Dartmouth Medical School, Hanover, NH*, USA

Blood Can Act as Solvent for Lipid Deposits in Standard Tubing. Scicluna S, Eyjolfsson A, Johnsson P, **Jonsson H**. *Affiliation(s): Dept Cardiothoracic Surgery, Lund University Hospital, Lund, Sweden*

Lipid Particles in Circulation After Retransfusion of Shed Blood. **Jonsson H**, Eyjolfsson A, Scicluna S, Paulsson P, Johnsson P. *Affiliation(s): Dept Cardiothoracic Surgery, Lund University Hospital, Lund, Sweden*

Gaseous Microemboli Induce Blood Brain Barrier Dysfunction Following CPB in Dogs. **Stump DA**, Deal DD, Moody DM, Brown WB. *Affiliation(s): Wake Forest University School of Medicine, Departments of Anesthesiology & Radiology, Winston-Salem, NC, USA*

Silent Sources of Gaseous Microemboli Occurring During CPB. **Stump DA**, Deal DD, Hammon JW, Charles D. *Affiliation(s): Wake Forest University School of Medicine, Departments of Anesthesiology, CT Surgery, & Perfusion Services Winston-Salem, NC, USA*

12:00 - 13:00 BUFFET LUNCH

Session 5: Perioperative Outcomes

13:00 - 13:30 Lecture 10: "Neurologic outcomes of transapical AVR" Michael Borger
13:30 - 13:45 Q&A
13:45 – 14:45 ABSTRACT DISCUSSION VI:
Moderators: M Borger, D Stump

Cardiotomy Reservoir Filter Size Profoundly Affects the Number and Size of Lipid Emboli Exiting the Arterial Filter. **Deal DD**, Stump DA, Jordan JE, Mays JC, Charles D. *Affiliation(s): Wake Forest University School of Medicine, Departments of Anesthesiology, CT Surgery, & Perfusion Services Winston-Salem, NC, USA*

Numerous Gaseous Cerebral Microemboli Caused by a Blower mister During OPCAB without Proximal Anastomoses. **Takeshi Okamoto**, Kazuhiko Hanzawa, Atsushi Morishita. *Affiliations: Department of Cardiothoracic Surgery, Niigata University Graduate School, Niigata, Japan*

In vivo Microbubbleactivity (MBBa) - Evaluation of a Self Regulating Miniaturized Extracorporeal Circulation System. **Perthel M**, Kseibi S, Alken A, Gerigk M, Machner M, Wimmer-Greinecker G. *Affiliation(s): Department of Thoracic and Cardiovascular Surgery, Herz- und Gefäßzentrum Bad Bevensen, Germany*

Evaluation of the Medtronic Resting-Heart-systemTM (RHS) with respect to microbubble activity (MBBa) in the tubings of the circuit. **Perthel M**, Deschka H, Alken A, Gerick M, Machner M, Wimmer-Greinecker G. *Affiliation(s): Department of Cardio Thoracic Surgery, Herz und Gefaesszentrum Bad Bevensen, Germany*

Monitoring Microemboli during Cardiopulmonary Bypass with the EDAC® QUANTIFIER. **Lynch, JE**. *Affiliation(s): Luna Innovations Incorporated*

14:45 – 15:15 REFRESHMENTS/EXHIBITS
15:15 – 15:45 Lecture 11: "Anti-inflammatory strategies during CPB" Ed Verrier
15:45 – 16:00 Q&A
16:00 – 17:00 ABSTRACT DISCUSSION VII:
Moderators: W Dobkowski, J Murkin

Patient-Perceived Cognitive Complaints And Formal Neuropsychological Testing: Where Is The Road To Noticeably Improved Outcomes For Patients? **Junius F**. *Affiliation(s): Cardiothoracic Surgery, St Vincents Hospital, Sydney, Australia*

Preoperative Hyponatremia And Cardiopulmonary Bypass: Yet Another Risk Factor For Cerebral Dysfunction ? Warwick R, **Poullis M**. *Affiliation(s): The Cardiothoracic Centre, Liverpool. England*

Neurocognitive Function Before and After Coronary Artery Bypass Grafting: Comparison of a Conventional and a Minimized Bypass System. **Perthel M**,[1] Daum I,[2] Erler S,[1] Alken A,[1] El Dsoki S, [1] Wimmer-Greinecker G[1]. *Affiliation: [1]Department of Cardio Thoracic Surgery, Herz und Gefaesszentrum Bad Bevensen, Germany, [2]Ruhr-Universitaet, Bochum, Germany*

Cognitive Function in Patients with an Optimised Extracorporeal Circuit. **Arndt-H. Kiessling**, Frank Isgro, Kai-Uwe Kretz, Verena Kuntz, Sigrid Becker, Werner Saggau. *Affiliation(s): Klinikum Ludwigshafen, Cardiac Surgery Bremserstr.79 67063 Ludwigshafen*

A Method To Improve Patient-Perceived Cognitive Outcomes By Optimizing Perfusion Parameter Values During Heart Surgery. **Junius F**. *Affiliation: Cardiothoracic Surgery, St Vincents Hospital, Sydney, Australia*

19:00 - 22:00 LUAU ON THE BEACH

Saturday, May 24, 2008
Session 6: Overview

07:45 – 08:00 Announcements
08:00 - 08:30 Lecture 12: "The BART trial: lessons learned in antifibrinolytic therapy" John Murkin
08:30 – 08:45 Q&A
08:45 – 09:15 Lecture 13: "Non-cardioplegic myocardial protection" W Dobkowski
09:15 - 9:30 Q&A
09:30 – 10:15 Lecture 14:" "Why MRI and Neuropsychological Outcomes do not Correlate after Cardiac Surgery" David A Stump
10:15 – 10:30 Q&A
10:30 - 11:00 REFRESHMENTS/EXHIBITS
11:00 – 11:30 Lecture 15: "Toward a consensusstatement on redefining the systemic inflammatory response" R Clive Landis
11:30 – 12:00 Panel Discussion TBA
12:00 - 12:15 Closing Comments Outcomes 2008

Outcomes 2008 Abstracts

AN EVIDENCE-BASED REVIEW OF PHARMACEUTICAL INTERVENTIONS TO LIMIT THE SYSTEMIC INFLAMMATORY RESPONSE IN CARDIAC SURGERY

R.C. Landis,[1] J.R. Brown,[2] J.H. Murkin,[3] H.P. Grocott,[4] D.S. Likosky,[2] R.A. Baker[5] for the International Consortium for Evidence Based Perfusion

[1]Edmund Cohen Laboratory for Vascular Research, University of the West Indies, Barbados, [2]The Dartmouth Institute for Health Policy and Clinical Practice, Lebanon, NH, USA, [3]London Health Sciences Center, London, Ontario, Canada, [4]University of Manitoba, Manitoba, Canada, [5]Flinders Medical Center, Adelaide, Australia

Introduction: We report here the first evidence-based review of pharmaceutical strategies to limit the systemic inflammatory response in adult coronary artery bypass grafting surgery.

Methods: The review was confined to randomized drug trials published in the peer-reviewed medical literature between 1970-2008. To be included, at least one inflammatory marker had to be measured. Pediatric, off-pump, valve, and other CT procedures were excluded. For studies satisfying these minimal inclusion criteria, organ function to the following index organs was recorded: heart, lung, kidney, brain, and gut. Evidence was gathered, synthesized and graded by two reviewers in accordance with the recommendations put forth by the American College of Cardiology and American Heart Association. Discrepancies in this evaluation process were resolved by an independent reviewer.

Results: Of 645 articles initially identified from a systematic search of the literature using a combination of search terms, 61 met the minimal inclusion criteria of measuring a single inflammatory marker and, of these, only 17 went on to describe drug effect(s) on organs (mostly heart and lung). No meta-analyses satisfied the minimal inclusion criteria. The only drug category to achieve a provisional Class IIa recommendation was steroids: Methylprednisolone was assigned a Class IIa recommendation with Level of Evidence A; Dexamethasone, Class IIa Level B; Hydrocortisone, Class IIa Level B. Antifibrinolytics were assigned either category IIb or III recommendations: High dose Aprotinin, Class IIb Level A; Low Dose Aprotinin, Class III Level A; Tranexamic Acid, Class IIb Level B; ε-Aminocaproic Acid, Class III Level B. Finally, Atorvostatin was assigned Class III Level B.

Conclusions: These are the first guidelines aimed at producing ACC/AHA clinical recommendations on pharmaceutical strategies to combat the systemic inflammatory response in the setting of cardiac surgery. We highlight the paucity of evidence in the literature, with very few studies identified that could demonstrate any linkage between drug effects on the systemic inflammatory response and organ function. The majority of studies failed to measure any inflammatory markers, while many others studied soft end-points, such as length of hospital stay, and merely assumed this was somehow linked to the systemic inflammatory response. The only drug intervention meriting a provisional Class IIa recommendation based on multiple randomized trials was Methylprednisolone.

OPTIMAL DOSE OF APROTININ FOR NEUROPROTECTION AND RENAL FUNCTION IN A PIGLET MODEL

Richard A. Jonas, MD, Yusuke Iwata, MD, Nobu Ishibashi, MD, Toru Okamura, MD

Children's National Medical Center, Washington, DC

Introduction: Recent studies in a neuronal cell culture model have documented the neuroprotective action of aprotinin. The optimal dose for neuroprotection was studied in a piglet model.

Methods: 54 piglets were randomly assigned to three CPB groups at risk for post-op cerebral and renal dysfunction: circulatory arrest at 25°C, ultra-low flow (10 ml/kg/min) at 25°C or 34°C. Animals were randomized to: control (no aprotinin), low dose (30,000 KIU/kg into prime only), full dose (30,000 KIU/kg bolus IV into prime plus 10,000 KIU/kg infusion), and double full dose. Tissue oxygenation index (TOI) was monitored by near-infrared spectroscopy. Neurologic functional and histological scores, creatinine and blood urea nitrogen (BUN) were outcomes of interest.

Results: Aprotinin significantly improved neurological scores on postoperative day 1 after ultra-low flow bypass at 25°C or 34°C ($P < .01$), but not after HCA ($P = .57$). Linear regression indicated a strong dose-response relationship with higher aprotinin doses having the best neurological scores. During LF, a higher TOI was correlated with a higher aprotinin dose ($P < .05$). Use of aprotinin and dose had no significant effect on creatinine, BUN, or BUN-to-creatinine ratio on day 1. Low body weight was the only predictor of high BUN ($r = -0.39$, $P < .01$).

Conclusions: Aprotinin significantly improves neurologic recovery without impairing renal function. Future studies are needed to examine the safety and efficacy of a double usual full dose strategy.

HIGH DOSE TRANEXAMIC ACID MAY BE ASSOCIATED WITH CLINICAL SEIZURES IN CARDIAC SURGICAL PATIENTS

J.M. Murkin, J. Granton, M. Chu, B. Young

Departments of Anesthesia and Perioperative Medicine, Surgery, Clinical Neurological Sciences, University of Western Ontario, London, Ontario, Canada

Introduction: Antifibrinolytic therapy has become a mainstay in complex cardiac surgical procedures to decrease bleeding and minimize transfusion requirements. Concern regarding adverse effects ascribed to aprotinin administration has led to increasing usage of tranexamic acid (TA) in dosages of up to 100 mg/kg.[1] We have noted a significant increase in clinical and electroencephalographic (EEG) seizures in the early postoperative period over the previous 3 months in a series of 13 cardiac surgical patients of a total of approximately 350 patients receiving a loading dose of 5 gm or more of TA.

Methods: A chart review of patients experiencing clinical seizures after cardiac surgery was undertaken. A common factor was the administration of TA in dosage of 61 mg/kg (87 yo with renal insufficiency) up to 259 mg/kg instituted since mid-November 2007 in substitution for high dose aprotinin. Since this review, dosing guidelines have been modified to a lower dosage of TA 30 mg/kg load, 15 mg/kg/hr infusion and 2 mg/kg as pump prime. To date no further seizures have been observed with this modified dosing regimen. Patient data will be provided.

Discussion: TA has been associated with seizures when inadvertently injected into subarachnoid space.[2] In animal models cerebrospinal fluid (CSF) concentrations of TA approximating 500 mg/L produce de novo clinical seizures,[3] due in part to dose-related suppression of inhibitory GABA receptors.[4] In dosages of TA of 100 mg/kg, plasma concentrations can exceed 4000°mole/L (600 mg/l) [1] which can produce CSF concentrations approximating 150 - 200 mg/L.

Conclusion: In cardiac surgical patients loading dosages of TA approaching or exceeding 100 mg/kg can produce plasma and CSF concentrations that may suppress inhibitory neurotransmitters thus reducing the seizure threshold and producing convulsive activity in susceptible patients as demonstrated experimentally. Caution is warranted and a lower dosage regimen for TA of 30mg/kg load plus 15 mg/kg infusion is currently recommended.

References:

Dowd NP, Karski JM, Cheng DC, et al. 2002. Pharmacokinetics of tranexamic acid during cardiopulmonary bypass. Anesthesiology 97:390-9.

Yeh HM, Lau HP, Lin PL, Sun WZ, Mok MS. 2003. Convulsions and refractory ventricular fibrillation after intrathecal injection of a massive dose of tranexamic acid. Anesthesiology 98:270-2.

Yamamura A, Nakamura T, Makino H, Hagihara Y. 1980. Cerebral complication of antifibrinolytic therapy in the treatment of ruptured intracranial aneurysm: Animal experiment and a review of literature. Eur Neurol 19: 77-84.

Furtmüller R, Schlag MG, Berger M, et al. 2002. Tranexamic acid, a widely used antifibrinolytic agent, causes convulsions by a gamma-aminobutyric acid(A) receptor antagonistic effect. J Pharmacol Exp Ther 301:168-73.

AN EVIDENCE-BASED REVIEW OF THE USE OF CARDIOTOMY SUCTION AND CELL SALVAGE TO LIMIT THE SYSTEMIC INFLAMMATORY RESPONSE IN CARDIAC SURGERY

R.A. Baker,[1,2] R.F. Newland[1] for the International Consortium for Evidence-Based Perfusion (ICEBP)

[1]Flinders Medical Center and [2]Flinders University, Adelaide, Australia

Introduction: We report here an evidence-based review of the use of cardiotomy suction and cell salvage to limit the systemic inflammatory response in adult coronary artery bypass grafting (CABG) surgery.

Methods: The review was confined to papers published in the peer-reviewed medical literature between 1970-2008, published in the English language. To be included, at least one inflammatory marker had to be measured. Pediatric, off-pump, valve, and other cardiothoracic surgery procedures were excluded. Evidence was gathered, synthesized and graded for level and class of evidence by two reviewers in accordance with the recommendations put forth by the American College of Cardiology and American Heart Association. Discrepancies in this evaluation process were resolved by an independent reviewer.

Results: Of 139 articles initially identified from a systematic search of the literature using a combination of search terms, 14 met the minimal inclusion criteria of measuring a single inflammatory marker. No meta-analyses satisfied the minimal inclusion criteria.

Observational studies demonstrated an increase in inflammatory markers in shed blood compared to patient's circulating blood, this was supported by data from randomized controlled trials (RCT's) demonstrating elevated TNF-α, IL-6, IL-8, C3a and plasma free Hb. Cell processing diminished level

of inflammatory markers (TNF-α, IL-6, IL-8, myeloperoxidase) in observational and RCT. Studies examining the return of processed versus cardiotomy suction blood demonstrated no clinical benefit, however reduced inflammatory marker load was evident.

Current evidence mandates the following limited recommendations:

> Avoidance of the direct reinfusion of cardiotomy suction blood and/or the cell processing of salvaged blood should be used to reduce the level of inflammatory markers in patients undergoing CABG with cardiopulmonary bypass (Class I, A).

Conclusions: The ICEBP has chosen to generate guidelines to assist clinicians in understanding the evidence-base concerning aspects of cardiopulmonary bypass. We chose to initially examine practices that minimise the effect of the inflammatory response. The literature did not demonstrate any influence of cell salvage on measures of organ function. The majority of studies failed to measure any inflammatory markers, while few studied reported clinical or organ endpoints. In order to make a recommendation in relation to clinical endpoints further studies are required.

PLASMIN BUT NOT THROMBIN ACTIVATES A172 GLIAL CELLS VIA SERINE PROTEOLYTIC CLEAVAGE OF PREOTEASE-ACTIVATED RECEPTOR (PAR)1

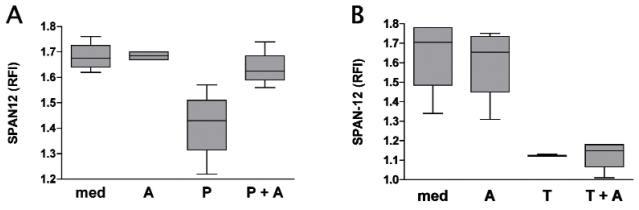
R.C. Landis, K.D. Hall

Edmund Cohen Laboratory for Vascular Research, Chronic Disease Research Centre, University of the West Indies, Barbados

Introduction: Cardiac surgery with cardiopulmonary bypass is associated with breakdown of the blood brain barrier, allowing potentially harmful serine proteases from plasma, such as thrombin and plasmin, into the brain. Since glial cell apoptosis can occur following cleavage and activation of PAR1 by serine proteases, we wanted to examine whether PAR1 was cleaved by thrombin or plasmin in the glial cell line A172.

Methods: A172 glioblastoma cells ($1X10^6$ cells) were incubated in the presence of thrombin (.02 - 2 U/ml) or plasmin (5 μM) for 5 minutes at 37°C. Plasmin was generated from plasminogen in the presence of streptokinase and nascent activity was monitored spectrophotometrically using Spectrozyme (American Diagnostica). Cleavage of the PAR1 receptor was determined flow cytometrically by monitoring loss of the SPAN12 epitope, which is expressed only on intact receptor. Serine protease activity was inhibited by 200 - 20,000 KIU/ml aprotinin. Apoptosis was monitored flow cytometrically by staining with Annexin V/propidium iodide (PI). Statistical comparisons were carried out by one way analysis of variance (ANOVA) with a Newman-Keuls post-test.

Results: PAR1 was efficiently cleaved by 5 μM plasmin and this was significantly inhibited by 200 KIU/ml aprotinin ($P < .01$; panel A). Thrombin, however, only cleaved at supra-physiological concentrations (2 U/ml) and this was not inhibited by up to 20,000 KIU/ml aprotinin (panel B). Plasmin-induced PAR1 cleavage caused a change in cell morphology with dendritic process retraction but cells remained viable as judged by lack of Annexin V/PI staining.



Conclusions: We describe a novel pathway of glial cell activation via plasmin/PAR1, which may be clinically relevant to neurological changes secondary to blood brain barrier breakdown in cardiopulmonary bypass. It will be important to determine whether the plasmin/PAR1 axis can trigger any neurodegenerative effector pathways in glial cells.

A SPECIALIZED SUB-POPULATION OF MONOCYTES IS INDUCED DURING THE RECOVERY PHASE OF CARDIOPULMONARY BYPASS

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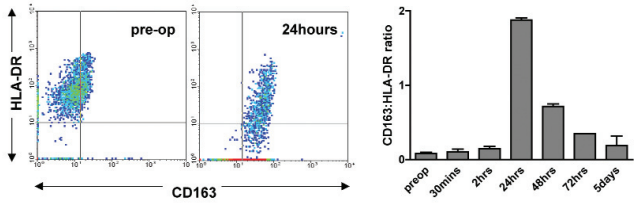
Introduction: A protective sub-population of monocytes with anti-inflammatory properties has been described in tissues at sites of hemorrhage and in vitro under conditions of hemolysis. The protective phenotype is defined by diminished major histocompatibility-II antigen (HLA-DR) expression and reciprocally increased hemoglobin scavenger receptor (CD163) expression. Since cardiopulmonary bypass is associated with hemolysis, we asked whether the same phenotypic switch occurred in circulating monocytes following CPB surgery.

Methods: After ethics board approval and written informed consent, patients undergoing elective CPB surgery were enrolled and blood samples collected at the following time-points: pre-op, 30 minutes on bypass, 2 hours on bypass and 24 hours, 48 hours and 120 hours after bypass. Three colour flow cytometry was employed to determine the HLA-DR/CD163 phenotype on gated $CD14^+$ monocytes. Statistical comparisons were carried out using a one way analysis of variance (ANOVA) with a Dunnett's Multiple Comparison post-test.

Results: A striking phenotypic switch from $HLA\text{-}DR^{high}CD163^{low}$ to $HLA\text{-}DR^{low}CD163^{high}$ was observed, peaking at 24 hours after bypass (see Figure). Compared to pre-op, the phenotypic switch was statistically significant at 24 hours ($P < .01$) and 48 hours ($P < .01$), with a return to normal by 5 days.



Conclusion: A novel sub-population of monocytes was induced in the circulation of patients during the recovery phase to cardiopulmonary bypass. It will be important to determine whether this population can exert protective effects by scavenging pro-oxidant free hemoglobin from the circulation and coupling this to anti-inflammatory interleukin-10 expression, as has been described for the CD163 receptor in other settings.

EFFECTS OF AUTOLOGOUS BLOOD TRANSFUSION ON MONOCYTE EXPRESSION OF TOLL-LIKE RECEPTORS IN PATIENTS UNDERGOING CARDIAC SURGERY WITH AND WITHOUT CARDIOPULMONARY BYPASS

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Background: Toll-like receptors (TLRs) are proteins that initiate host innate immune responses. Expression of TLRs in various tissues is important for their biologic role in immunity. Cardiac surgery is associated with leukocyte activation as part of systemic inflammatory response. This report concerns the impact of autologous cell saver blood transfusion (CSBT) on monocyte activation in patients undergoing coronary surgery off- vs on-cardiopulmonary bypass (CPB).

Methods: Sixty patients were randomised into four groups: A) On-CPB with CSBT, B) Off-CPB with CSBT, C) On-CPB without CSBT, D) Off-CPB without CSBT. Blood samples were obtained preoperatively, intra-operatively after 15 minutes, from the CSBT system before and after processing and post-operatively at 3 and 24 hours. Surface expression of CD11b, CD14 and TLT- 1,2,4,6,8 and 9 on monocytes was measured by flow-cytometry.

Results: Monocytes did not display surface up-regulation of CD14 or TLR 1, 6, 8 or 9 in any of the patient groups. There was significant up-regulation of CD11b, TLR-2 and 4 in the CSBT patient groups as shown below. There was no difference between the on- and off-CPB patient groups. Results are presented as percentage of pre-operative relative fluorescence intensity.

Time Points	TLR-2, %		TLR-4, %		CD11b, %	
	On-CPB	Off-CPB	On-CPB	Off-CPB	On-CPB	Off-CPB
Pre-op	100+/-15	100+/-22	100+/-21	100+/-23	100+/-44	100+/-64
Intra-op	111+/-4	98+/-14	92+/-31	106+/-22	63+/-29	61+/-50
CSBT 1	115+/-49	116+/-35	119+/-28	113+/-20	180+/-67	134+/-85
CSBT 2	114+/-31	100+/-35	110+/-21	115+/-27	71+/-26	134+/-257
End of op	96+/-19	102+/-21	104+/-12	105+/-26	70+/-24	70+/-49
3 hrs	100+/-14	110+/-29	103+/-7	116+/-29	77+/-39	67+/-25
24 hrs	92+/-10	90+/-16	89+/-19	124+/-29	69+/-14	91+/-68

Conclusions: Implementation of autologous cell saver blood transfusion results in increased expression of the surface integrin CD11b and of the toll-like receptors 2 and 4 on monocytes. Toll-like receptor expression may play a role in the systemic inflammatory phenomena that take place in cardiac surgery.

IMPACT OF AGING UPON CEREBRAL HYPOXIA SENSING OF ANEMIA

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Introduction: Cognitive impairment has been found to be impaired by anemia in chronic disease states. Acute anemia complicates many surgical procedures associated with postoperative cognitive dysfunction. We have recently documented an age dependent cognitive impairment with acute anemia without evidence of cortical tissue hypoxia in either group. We hypothesized that more sensitive and more subtle neuroprotective mechanisms under the control of HIF(s) may be impaired with aging and impacting cognitive performance in response to anemia.

Methods: Young (3 mo, n = 20) and aged (15 mo, n = 20) spontaneously hypertensive rats underwent a stepwise hemodilution protocol under anesthesia and were subsequently recovered. Half (n = 10) in each group were sacrificed at 24 or 48 hrs and cortex and hippocampus recovered. Samples subsequently underwent RT-PCR analysis for carbonic anhydrase (CAIX), erythropoietin (EPO), and vascular endothelial growth factor (VEGF).

Results: Synthesis of CAIX and VEGF mRNA appeared to be significantly impaired in the aged animals relative to younger cohorts in both the cortex and hippocampus at 24 and 48 hours. CAIX mRNA levels in aged animals ranged from .1 - .7 fold relative to younger animals (*P* values ranged from *P* = .015 - .12). VEGF mRNA levels in aged animals ranged from .6 - .9 fold relative to younger animals(*P* values ranged from *P* = .0018 - .77). Synthesis of EPO mRNA in aged animals ranged from .9 - 2.3 fold relative to younger animals(*P* values ranged from *P* = .06 - .9) and was therefore not significantly different between age groups at either time point, in hippocampus nor in cortex.

Synthesis of EPO mRNA in aged animals ranged from .9 - 2.3 fold relative to younger animals(*P* values ranged from *P* = .06 - .9) and was therefore not significantly different between age groups at either time point, in hippocampus nor in cortex.

Conclusion: The cerebral HIF directed hypoxic response appears to be initiated in response to anemia even in the absence of tissue hypoxia. Elements of the hypoxic response appear to be impaired as a function of aging but this did not include EPO.

INSTALLATION OF A MULTIELECTRODE SPIRAL CUFF ON THE HUMAN VAGUS NERVE FOR SELECTIVE ELECTRICAL STIMULATION

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Introduction: The vagus nerve can exert beat-by-beat control of cardiac function. The term 'Vagus Nerve Stimulation' (VNS) generally refers to several different techniques used to non-selectively stimulate the vagus nerve. The aim of our study was to study feasibility and safety of selective vagus stimulation.

Methods: After ethics board approval and written informed consent, in 2 patients 39-electrode spiral nerve cuff was twisted around vagus (in one patients on the right side and in the other on the left side vagus) after carotid end arterectomy. In spiral nerve cuff thirteen groups of three electrodes (GTE)s in a longitudinal direction were formed. Epicardial pacemaker (basal rate 30 bpm) was set before GTE stimulation.

ECG and systemic hemodynamics was continuously recorded during positioning, electrodes stimulation and removing the cuff.

Results: During positioning and removing the cuff there was no ECG or hemodynamic changes. GTE was selectively stimulated using, biphasic, charge-balanced current pulses with an intensity of .5 - 2.5 mA and a frequency of 20 Hz. The GTE, that elicited the largest measurable response (decreasing the heart rate and systemic arterial pressure) was indicated as relevant to the investigation.

Conclusion: Selective VNS in human is safe and possible. Further studies are needed to explore physiology of selective VNS and possible clinical implications of non pharmacological heart rate control (f.e. group of patients with chronic heart failure with increased activity of sympathetic nervous system).

PATTERNS IN BRAIN OXYGEN SATURATION DURING AORTIC SURGERY

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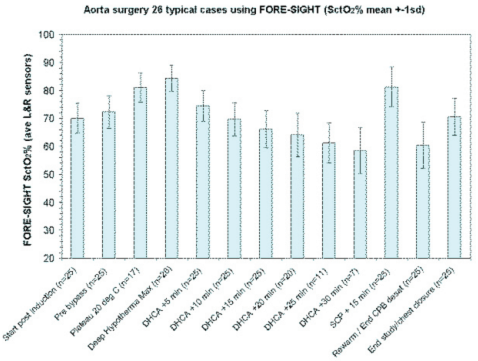
Introduction: Cerebral Oximetry is a non-invasive optically based technology that measures cerebral tissue oxygen saturation ($S_{ct}O_2$). Over the years, there have been studies using trend only cerebral oximeters1. The FORE-SIGHT® (CAS Medical Systems, Branford CT USA) cerebral oximeter measures absolute $S_{ct}O_2$ values without the need for a pre-induction baseline. We report the results of monitoring 30 subjects undergoing aorta surgery.

Methods: With IRB approval and informed consent, patients undergoing elective thoracic aortic surgery with deep hypothermic circulatory arrest (DHCA) and antegrade selective cerebral perfusion (SCP) were monitored intraoperatively using the FORE-SIGHT monitor. Two sensors were placed on the subject's forehead bilaterally for continuous monitoring of $S_{ct}O_2$. There was no alteration of the surgical procedure or routine clinical monitoring.

Results: To date, 30 subjects have been monitored. Post induction $S_{ct}O_2$ was 70.0 ± 5.3% (1SD). During cooling on CPB, a rise in $S_{ct}O_2$ was found in most subjects. During deep hypothermia when the subjects were cooled to 12 - 15°C, $S_{ct}O_2$ values increased in most subjects above 80% (84.3 ± 4.6%, 21/30 subjects). The rate of $S_{ct}O_2$ increase tended to match the rate of core cooling. As expected, after the onset of DHCA, $S_{ct}O_2$ decreased as a function of DHCA duration (Figure 1). Mean $S_{ct}O_2$ decreased to 58.4 ± 8.3% after 30 minutes of DHCA, then returned to near pre-DHCA levels 81.2 ± 7.1% during SCP/post DHCA. During the rewarming stage and weaning off CPB, brain desaturation events were commonly observed, with $S_{ct}O_2$ transiently dropping to a mean of 60.4 ± 8.3% before recovering to 70.6 ± 6.7% at the end of the surgery.

Analysis of the cerebral oximetry data showed that 26 of the 30 subjects had similar $S_{ct}O_2$ patterns (Figure 1). For the 4 atypical cases, there was a sustained drop of $S_{ct}O_2$ as opposed to a rise after the onset of CPB and cooling to 20°C. Two of these subject's $S_{ct}O_2$ values appeared to be blood pressure dependent. It was suspected that one subject's decrease of $S_{ct}O_2$ was due to air emboli. This subject's $S_{ct}O_2$ values remained very low until near the end of CPB. For the fourth subject, $S_{ct}O_2$ values were unusually low during post DHCA and rewarming. For these atypical subjects, the peak $S_{ct}O_2$ (mean 70.6%) during deep hypothermia were lower compared to the 26 control subjects (mean 84.3%), even though at the start of the case, all 4 atypical subjects' $S_{ct}O_2$ values were similar to the 26 control subjects.



Discussion: Cerebral oximetry provides continuous, real time monitoring brain oxygenation measurements during the absence of arterial pulsatility and cerebral perfusion, when other vital sign monitoring (i.e. pulse oximetry) cease to function. Our experience shows that absolute cerebral oximetry is useful in clinical settings to identify decreases in brain oxygenation supply to demand ratio which would otherwise have been missed during the course of the surgery, especially after the onset of CPB.

Reference: Owen-Reece, et al. 1999. Br J Anaesth. 82:418-26.

VISUALIZATION OF REGIONAL CEREBRAL DESATURATION BY MICRO-EMBOLI DURING CARDIOVASCULAR SURGERY

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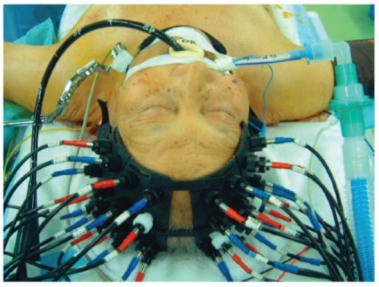
Introduction: Cerebral micro-emboli have been reported to induce cerebral injury after cardiac surgery with CPB. We attempted to visualize 2D mapping of regional cerebral O2 saturation (rSO2) by multi-detector near-infrared spectroscopy (NIRS) during surgery. We attempted to clarify whether micro-emboli decreased rSO2, when and where rSO2 decreased by micro-emboli.

Methods: Micro-embolic signals (MES) in middle cerebral artery (MCA) or internal carotid artery (ICA) were detected by TCD (TC2020, EME) with 2.0 MHz pulsed Doppler probe during cardiac surgery. Simultaneously, 24 NIRS detectors were placed on head and regional cerebral O2 saturation (rSO2) was measured. After the surgery, 2D mapping of regional cerebral O2 saturation (rSO2) was constructed. The area of high O2 saturation colored red, desaturation colored blue in display.


Multi-detector NIRS and TCD

Results: When many MES were detected in MCA or ICA during surgery, blue region appeared in ipsilateral temporal area and enlarged all area for a few minutes. After 5 to 10 minutes, blue region disappeared and red region recovered. This phenomenon repeated during surgery.
Conclusion: Micro-emboli during cardiac surgery may not induce transient regional cerebral desaturation, but also whole brain desaturation. Since we need to monitor MES and decrease MES during cardiac surgery.

MONITORING INVOS CEREBRAL OXIMETRY SIGNIFICANTLY DECREASES THE INCIDENCE OF COGNITIVE DYSFUNCTION IN DIABETIC PATIENTS UNDERGOING CORONARY BYPASS SURGERY

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Introduction: Cerebral oxygen desaturation has been associated with a variety of adverse outcomes following cardiac surgery[1]. We hypothesized that optimizing regional cerebral oxygen saturation (rSO2) would decrease cognitive dysfunction in diabetic patients undergoing coronary artery bypass (CAB) surgery.
Methods: After ethics board approval and written informed consent, 43 patients undergoing CAB surgery with a preoperative diagnosis of diabetes mellitus were age stratified and randomly assigned to Control group (Group C) or Intervention group (Group I). Both groups had preoperative, pre-discharge and 2 month follow-up cognitive testing using a series of 10 tests {(13 subtests: DSpan (1), RAVLT (4), BVRT(1), TrailA(1), TrailB(1), DSymb(1), GPeg(2), OWF(1)} as we have previously described.[2] Upon arrival in operating room patients had INVOS bilateral frontal electrodes to measure rSO2 during the operation, in Group I patients the monitor was visible and efforts to keep the rSO2 on levels e 75% of preinduction value by a predefined protocol.[1] Statistical analysis was performed using Chi-square, change scores, split plot and factor analysis, with $P < 0.05$ required for significance.
Results: There were no significant differences between groups regarding demographic or morphometric data, duration of OR, cross-clamp times, CPB duration, or mean perioperative glucose concentrations or insulin administration. There were significantly ($P = .041$) more patients with 1 sd decrease on 25% (3/13) of test scores in group C versus group I at postoperative assessment. Similarly, at follow-up, composite test scores revealed that group C had a greater drop in performance than did group I. A factor analysis identified 4 factors, and trends ($P = .07$) favoring INVOS were observed for both postop and follow-up data. Specifically, group differences for factor 2 (psychomotor function) were seen postoperatively, and time x group interactions were observed for factor 3 (working memory and processing speed) and composite factor scores in which decreases in performance at follow-up were observed for group C but not group I.
Conclusion: Monitoring and maintaining rSO2 above 75% of pre-induction values was associated with a lower incidence of cognitive dysfunction on both postoperative and follow-up assessments in diabetic patients undergoing CAB surgery.
References:
Murkin JM, Adams SJ, Novick RJ, et al. 2007. Monitoring brain oxygen saturation during coronary bypass surgery: a randomized, prospective study. Anesth Analg 104:51-8[2].
Murkin JM, Martzke JS, Buchan AM, et al. 1995. A randomized study of the influence of perfusion technique and pH management strategy in 316 patients undergoing coronary artery bypass surgery.II.Neurologic and cognitive outcomes. J Thorac Cardiovasc Surg 110:349-62.

AN INTERNATIONAL FRAMEWORK FOR EVIDENCE-BASED PERFUSION

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International Consortium for Evidence-Based Perfusion Registry Subcommittee

Background: Understanding the outcomes stemming from one's practice is essential for both, quality assurance as well as quality improvement. Few large-scale registries exist for cardiovascular perfusion. The International Consortium for Evidence-Based Perfusion (ICEBP, http://www.bestpracticeperfusion.org) has begun developing a web-based registry to immerse clinical teams with information concerning the practice of cardiopulmonary bypass (CPB). The goal of this registry is to synthesize and share useful and actionable clinical information in an effort to engage clinicians and improve the care provided to patients.
Current Status: In an effort to focalize data collection, the ICEBP has developed the following areas of focus for the registry: 1) Patient demographics [to adjust for potential patient-level confounders], 2) Compliance with guidelines/recommendations on the practice of CPB, 3) Cell processing and filtration, 4) Renal management, and 5) Factors influencing patients having low cardiac output subsequent to surgery.
We have nearly completed a beta version of the registry (http://www.icebpregistry.com/icebpdnn/), ensuring that the resultant data set would be compatible with the Society of Thoracic Surgeons' registry, when applicable. Centers will be able to enter cases on an individual basis, or through a bulk-upload feature from existing data sources. In order to minimize data entry burden, the ICEBP has developed "thumbprints" that represent routine aspects of the heart lung machine (filter size, oxygenator type, surface coatings), and priming solutions.
The ICEBP has approached manufacturers to assist in establishing the registry, and in developing its crosswalk with commercial electronic data management systems. It is envisaged that this will result in automatic population of fields such as periods of hypotension and administration of medication during CPB.
Goals: Our immediate objectives include:
1) finalization of the beta version of the database
2) field test the data entry form
3) develop a series of reports that users would be provided as one product of the registry
4) develop a boiler plate institutional review board submission document for the collection of protected health information
5) develop a business associates' agreement template to enable the collection of administrative data to validate case counts

CASE REPORT: POSTOPERATIVE THERAPEUTIC HYPOTHERMIA AFTER CARDIAC ARREST AND CARDIAC SURGERY

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Introduction: The optimal management of patients who suffer an intraoperative cardiac arrest at the time of cardiac surgery is unclear. We report here a case of such a patient. Therapeutic hypothermia was used as an adjunct both intraoperatively and postoperatively to optimize his neurological outcome.
Methods: A 56-year-old male was brought urgently to the OR with 95% left main disease, ischemic cardiomyopathy, and severe mitral regurgitation. The patient tolerated induction of anesthesia; however, during LIMA harvesting, the patient became asystolic. Heparinization, pericardiotomy, and open cardiac massage were immediately instituted while preparations were made for CPB. CPB was initiated after 7 minutes of CPR, and the patient was immediately cooled to 28°C. On CPB the patient underwent an intraaortic balloon pump placement, CABGx5, and a mitral valve repair. Total CPB time was 224 minutes. The patient then weaned from CPB on multiple inotropes and pressors to maintain adequate hemodynamics. The patient remained hemodynamically stable during the initial postoperative period but failed to wake up. In addition, 6 hours following arrival in the ICU, the patient was noted to have a generalized tonic clonic (GTC) seizure approximately 15 seconds in duration. This was treated with IV lorazepam followed by an IV phenytoin load. Nonetheless, the patient continued to have 2 more breakthrough seizures and became febrile to 39°C. Because of the intraoperative cardiac arrest, recurrent seizures, and hyperthermia, therapeutic hypothermia was initiated with the Thermogard™ cooling system. This was accomplished by placing an intravascular cooling catheter (Quattro®) in the left femoral vein.
Results: The patient was expeditiously cooled to 33°C, and this temperature was maintained under tight control for 48 hours. The cooling protocol was then discontinued gradually and the Quattro® catheter was removed. No further seizures were noted; however, the patient remained comatose for 1 week following surgery. Surprisingly, On POD #9, the patient spontaneously awakened and became interactive. Over the following days, the patient's neurological status improved to the point that he was able to speak, tolerate a regular diet, and move all extremities. He was subsequently discharged to a skilled nursing facility for further rehabilitation.

Conclusion: The early institution of hypothermia may lead to improved neurological outcomes after an intraoperative cardiac arrest. Issues for discussion: What should be the optimal intraoperative management of a patient who arrests in the OR prior to CPB? What should be the optimal postoperative management? What is the optimal cooling method, and for how long should cooling be sustained?

PATIENT DIRECTED PERFUSION PRESSURE ON BYPASS: AN ANALOGY FROM ELECTRICAL ENGINEERING

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Introduction: To produce a blood pressure target for cardiopulmonary bypass (CPB) that is tailored to the individual patient. Patients perfusion during CPB is non pulsatile. Converting the pulsatile pre operative blood pressure into an equivalent non-pulsatile pressure that has the same "energy" delivery can be achieved by the use of the technique of calculating the root mean square - an exact analogy utilised in electrical engineering.
Methods: The root mean square (square root of the sum of the squares of the instantaneous blood pressures) of the patients resting pre operative blood pressure was compared with medical mean blood pressure (diastolic pressure + 1/3 (systolic pressure - diastolic pressure)).
Results: Using the medical mean of the pre operative blood pressure as a guide to pressure to maintain during cardiopulmonary bypass can significantly under estimated the patients individual required perfusion pressure, by more than 12 mmHg in some cases.
Conclusion: Tailoring the pressure on bypass so that it correlates with the patients pre operative pressure may help to reduce the incidence of organ ischemia, typically renal and mesenteric. This may reduce the morbidity and mortality post cardiopulmonary bypass. As patients undergoing elective cardiac surgery do not have malperfusion pre bypass, if the pressure, flow and haematocrit are all appropriately controlled for, and the patient develops malperfusion, then the debate of pulsatile verses non-pulsatile perfusion needs to be re examined. Clinical correlation is now needed to confirm/refute the validity of this observation.

CONSTANCY OF PRESSURE ON BYPASS - A POTENTIAL QUALITY MARKER OF PERFUSION

M. Poullis, I. Johnson

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Introduction: To develop a marker of quality of perfusion pressure during cardiopulmonary bypass (CPB), to complement existing markers of perfusion quality - rewarming rate, maximum temperature on rewarming, lowest haematocrit, and blood glucose.
Methods: Using the electronic acquisition of blood pressure on bypass (YOCAB system) the percentage of time perfusion pressure was below 40 mmHg (American Society of Extracorporeal Technology quality marker), average deviance, beta distribution, confidence interval, median, mode, standard deviation, variance, and cumulative oxygen debt were calculated.
Results: Numerous different readouts of achievement of maintenance of constant pressure on bypass is now easily achievable with perfusion electronic data management systems. A composite score involving non pressure readouts (e.g. oxygen delivery, arterial and venous saturations, and flow rates) may need to be integrated into any perfusion pressure quality marker.
Conclusion: Assessment of adequacy of constant perfusion pressure may allow the scientific evaluation of pressure on bypass for patients to be accurately compared. Currently in studies involving CPB, blood pressure targets are stated with no quantitative assessment of adequacy of achievement of these targets. Electronic data monitoring during cardiopulmonary bypass when correlated with clinical outcome may help to provide a marker of quality of perfusion pressure during CPB, and may indeed allow patient specific perfusion pressure strategies to be developed.

REDUCING EMBOLI DURING CARDIAC SURGERY THROUGH REDESIGN OF CARDIOPULMONARY BYPASS

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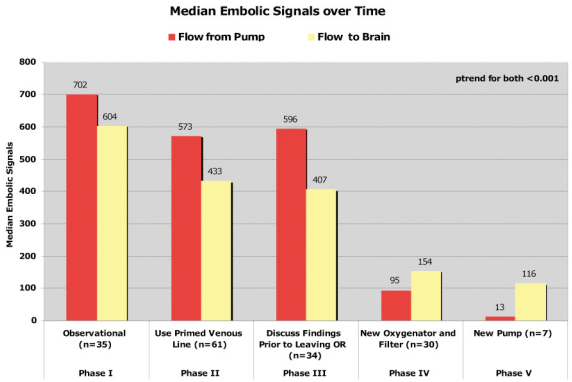
Background: Neurologic injuries are frequent and devastating complications following cardiac surgery. While reported strokes are relatively infrequent (1.3 - 4.3%), neurobehavioral injuries are more common (24 - 50%). Embolism of the cerebral circulation is the most frequently cited mechanism for these injuries. Previous work has documented an association between emboli detected in the cardiopulmonary bypass (CPB) circuit and the brain.
Methods: We developed a model for detecting and ascertaining the source of emboli during cardiac surgery. The model enables the team to detect emboli in the cerebral arteries and the inflow and outflow of the CPB, using Doppler ultrasound. A digital camcorder recorded audio and video signals during the surgery. The video camera was aimed at the surgical field to capture surgical events/techniques. Over the course of the study, we implemented five phases of redesigning the CPB circuit and CPB techniques.
Results: We enrolled 167 consecutive patients undergoing isolated coronary artery bypass grafting (CABG) surgery. Changes in our CPB circuit were associated with a 98.1% (702 vs. 13) reduction in median emboli flowing from the CPB circuit ($P < .001$), and 80.8% (604 vs. 116) reduction in emboli flowing to the brain ($P < .001$). We also found that the changes in the CPB circuit lowered the CPB outflow count presently to below the cerebral emboli count.
Summary: Neurologic injuries, predominantly embolic in origin, are unwanted sequelae of CABG surgery. The redesign of our CPB circuit resulted in a significant reduction in emboli detected in the brain. We discovered that there is a source of cerebral emboli beyond the CPB outflow, creating the potential to reduce cerebral emboli further in the future by changing processes of care with regard to cardiac and aortic manipulation.



BLOOD CAN ACT AS SOLVENT FOR LIPID DEPOSITS IN STANDARD TUBING

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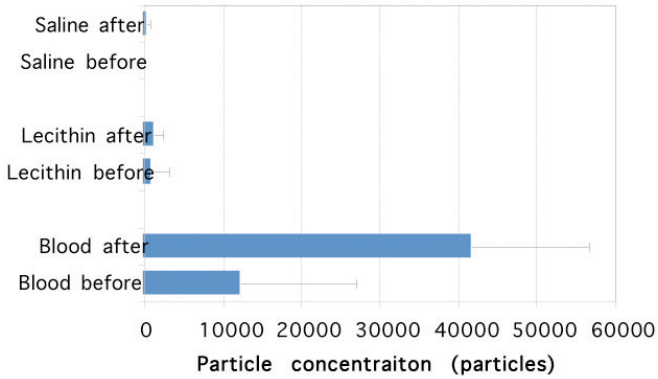
Introduction: During cardiac surgery with Cardio Pulmonary Bypass (CPB) blood is collected from the mediastinum by cardiotomy suction. This shed mediastinal blood has been shown to contain lipid material. The blood is normally transported back to the CPB-circuit in standard PVC-tubing, which is a lipophilic material. The aim of this study was to see whether blood can act as a solvent for the lipid material that has adhered to the tubings.
Methods: Fourteen experiments were performed, where three different one meter long PVC tubes were saturated with .3% triolein fat solution in saline. This was performed by pumping 300 mL of the mixture by a roller pump. After the saturation, three different solutions were pumped through the tubes: 300 mL of blood, 300 mL 1 Lecitin solution in saline or 300 ml of saline holding a temperature of 34.9 - 35.8°C. The blood used was residual blood from the CPB-circuit from 14 different patients that had undergone routine surgery.



Lipid particle concentration was determined with Coulter-Counter after saturating tubings, in the different fluid before passing saturated tubings, and in the different fluids after passing the saturated tubings. A multisizer 3 Beckman Coulter counter with a 100 um aperture probe was used for counting particles between 10 - 60 µm.
Results: Of the three fluids tested for dissolving lipid material, blood showed the best capability of producing particles. Particles content in blood increased 340% ($P < .005$), and a small significant increase was also seen for saline.
Conclusion: It seems that blood can act as a solvent for lipid that have adhered to lipophilic surfaces in for example tubing. Since the study have revealed particles of a certain size, it is likely that the particles have been produced by means of emulsification.

LIPID PARTICLES IN CIRCULATION AFTER RETRANSFUSION OF SHED BLOOD

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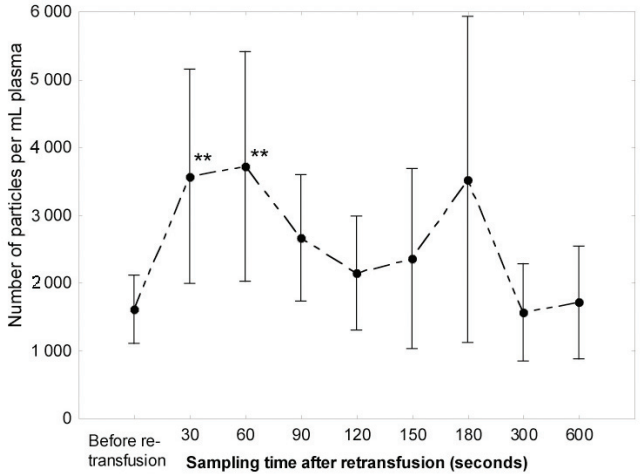
Introduction: Shed mediastinal blood is known to be a source of lipid microemboli in cardiac surgery. The aim of this study was to characterize the occurrence of these lipid particles at different stages of the operation, and to relate their occurrence in the circulation to the retransfusion of shed blood.
Methods: Blood samples were collected from 44 patients undergoing routine cardiac surgery with cardiopulmonary bypass. Blood was sampled from the surgical field at different sampling locations during the operation. Shed blood was collected in a transfusion bag, and later retransfused. After retransfusion, blood was sampled from the arterial line of the heart-lung machine. Coulter counter was used for determining particle concentration and size. Scanning electron microscopy (SEM) was used to visualize the lipid particles in samples of shed blood.
Results: The mean volume of shed blood collected was 340 ± 215 mL. Lipid particles in the size range 10 - 60 µm were found at varying concentrations in the samples collected from the surgical field; the highest concentrations being found in blood collected after cannulation and from the pleura. After retransfusion of this blood a biphasic response was seen in the blood drawn from the efferent line of the heart-lung machine.



Conclusion: Lipid particles are found in shed blood at all times during cardiac surgery, and when this blood was retransfused an increase was seen in particle concentration in the heart-lung machine. The harm that may be caused by these particles was not studied.

GASEOUS MICROEMBOLI INDUCE BLOOD BRAIN BARRIER DYSFUNCTION FOLLOWING CPB IN DOGS

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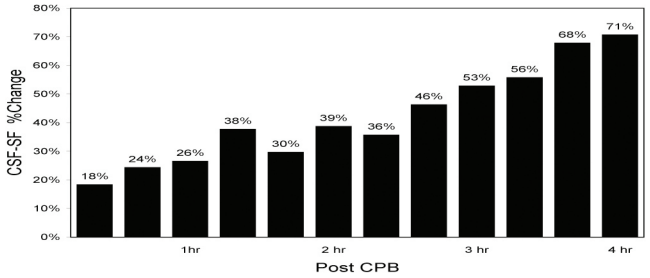
Introduction: We have previously demonstrated that the passage of lipid emboli through the cerebral microvasculature disrupts blood-brain-barrier permeability (BBB). We investigated if non-occlusive gaseous microemboli (GME) would disrupt the BBB if instituted in an identical canine model.
Methods: A anesthetized dog (n = 1) received .8% sodium fluorescein (SF) IV over a 10-hour period as CSF samples were collected at 20-minute intervals, and underwent hypothermic CPB for 90 min (30 min @ 29°C). GME were delivered via syringe pump into the venous reservoir (VR; 2 x 55 cc; 20 cc/min; 29.5°C) and during rewarming into the arterial filter (AF; 2 x 55 cc; 5 cc/min; 34.5 - 37.4°C). CSF sampling continued for 4 hours after CPB. EDAC Quantifier® measured the number and size of GME exiting the VR and AF. Mesenteric microcirculation was monitored by intravital microscopy.
Results: 95% of GME exiting the AF were < 40µm (119,059 of 125,346); of the 5% of GME > 40 µm, only 9 were > 200 µm. GME were briefly visible within the mesenteric microcirculation while infused into the ECC during CPB. CSF-SF progressively elevated throughout the post-CPB period (18 - 71%).



Conclusion: GME are similarly deformable to lipid microemboli but have been considered much less injurious since GME are largely non-occlusive and assumed to rapidly reabsorb. This single experiment demonstrates that the BBB permeability quickly increases due to the passage of GME < 40 µm. Post-CPB cerebral edema and transient cognitive dysfunction may be secondary to GME delivered during CPB. Supported by NIH NS 20618-11.

SILENT SOURCES OF GASEOUS MICROEMBOLI OCCURRING DURING CPB

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Introduction: Various monitoring modalities document that gaseous microemboli (GME) commonly occur during CPB. We report four cardiac surgical events resulting in numerous GME exiting the arterial filter (AF).
Methods: Adults (n = 12) underwent on-pump CABG with a Terumo Cardiovascular ECC. Prior to CPB an ultrasonic transducer was positioned over the left common carotid to observe embolic events (EDAC, Embolus Inc). The ECC was simultaneously monitored for the number and diameter of GME exiting the AF by utilizing the EDAC™Quantifier (Luna Innovations) until decannulation of the aorta post-CPB.
Results: Representative embolic events are listed for 4 patients who each had a particular event directly associated with GME exiting the AF, none of which resulted in embolic activity at the carotid site.

Cause	No. GME Post-AF	< 20µm, %	20 - 40µm, %	> 40µm, %
Repair of Aortic Arteriotomy Around Arterial Inflow Cannula	13,457	69.6	23.3	7.1
Re-Circ Line Opened to Cardiotomy Reservoir Briefly	1583	68.9	28.1	3.0
AF Continuously Purged into Cardiotomy Reservoir (CR)	76,549	98.2	1.4	0.4
Blood Transfusion from ECC post-CPB	548	97.3	1.8	0.9

Conclusion: GME are associated with perfusion and surgical events, i.e., drug injections, low blood volume in venous reservoir, and entrained air around the venous cannula. The novel events described in these patients resulted in obvious showers of GME exiting the AF which failed to enter the cerebral circulation. It is possible that smaller GME (< 40 µm) quickly dissipated or entered other regions besides the cerebral circulation. The largest GME (> 40 µm) were freed from the AF by the rapid changes in pressure across the AF created by the blood pulsing freely around an imperfect closure around the aortic inflow cannula. Opening the re-circulation line, albeit briefly, creates both a pressure change across the AF releasing GME and also fountains blood in the CR producing additional GME. Clearly, thousands of GME < 20 µm can be avoided by not venting the AF into the CR. Following CPB, but prior to decannulation, patients may receive blood transfusion(s) as a 100 cc bolus from the ECC. This stop/reflow maneuver liberates GME from the AF. Fortunately the bulk of these transfusion-related GME are < 20 µm.

CARDIOTOMY RESERVOIR FILTER SIZE PROFOUNDLY AFFECTS THE NUMBER AND SIZE OF LIPID EMBOLI EXITING THE ARTERIAL FILTER

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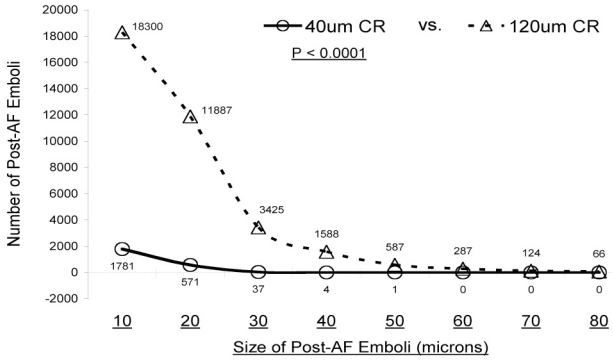
Introduction: Cell-saver (CS) processing has been advocated to reduce cerebral lipid embolization (LME) during CPB due to the return of shed blood. We examined the effect of reduced pore size of the internal filter of the cardiotomy reservoir (CR) to diminish the LME embolic burden in a canine model of CPB.

Methods: Dogs (n = 14) underwent 120 minutes of hypothermic CPB (30 min @ 28°C). The pore size of the CR internal filter was 40 µm (n = 6) or 120 µm (n = 8). A standard lipid embolic load was aspirated into the CR (LME = 50mL triolein + 450mL blood), sequestered 5 min, and then released into the venous reservoir (VR) upon rewarming. Emboli within the pump circuit were recorded throughout CPB by the EDAC™ Quantifier at 3 sites (pre-VR, post-VR, and post-arterial filter (AF pore size = 38 - 40 µm).

Results: Following the release of LME, the number and size of emboli exiting the VR and AF were significantly reduced in the 40 µm CR group.



Conclusion: CS processing of salvaged blood reduces cerebral lipid microemboli but increases cost, requires additional time and removes viable platelets, clotting factors, and plasma proteins. If the use of a CS during cardiac surgery is rejected, returning shed blood to the pump circuit via a small pore CR can significantly reduce the lipid embolic load. Supported by NIH NS 20618-11.

NUMEROUS GASEOUS CEREBRAL MICROEMBOLI CAUSED BY A BLOWER MISTER DURING OPCAB WITHOUT PROXIMAL ANASTOMOSES

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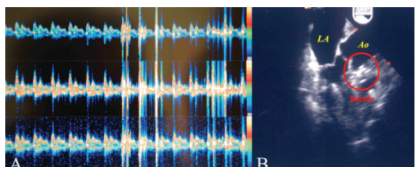
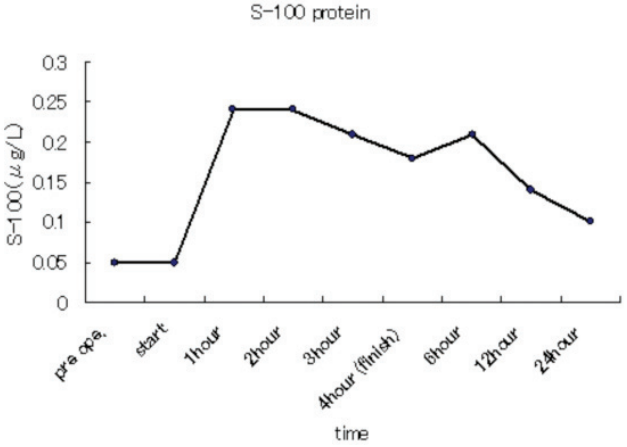
Introduction: In coronary artery bypass grafting, a blower mister is used routinely to secure a favorable operative field during anastomosis. We present the case of a patient with numerous cerebral microemboli caused by a blower mister.

A 74-year-old male was performed OPCAB. During surgery, TCD was used to monitor HITS/MES. Numerous gaseous microemboli were seen during the anastomosis, which were generated by a blower mister. At the same time, transesophageal echography confirmed numerous air bubbles, at the inlet of the right coronary artery. Furthermore, echography showed that air bubbles were dispersed in the aorta.



Once the anastomoses were completed, these disappeared, as did the HITS/MES noted on TCD. The causes of the numerous gaseous microemboli occurring only during right coronary artery anastomosis without a coronary shunt tube. The direction of air bubbles was not necessarily in the same direction as blood flow. So,the air bubbles to travel towards the proximal side and were dispersed in the aorta. Postoperatively, S-100 protein was increased.

Conclusion: We experienced the case of a patient with numerous cerebral microemboli caused by a blower mister.



IN VIVO MICROBUBBLEACTIVITY (MBBA) - EVALUATION OF A SELF REGULATING MINIATURIZED EXTRACORPOREAL CIRCULATION SYSTEM

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Introduction: Mini bypass systems combine suction blood separation reduced foreign surface area, coating, and low priming volume to improve outcomes in cardiac surgery. This investigation was an initial in vivo evaluation of a mini-bypass system that has the ability to drop the arterial pump flow to a pre set speed (rotations per minute) lower than the calculated flow, when an excess negative pressure is measured in the venous line or when the venous air purge system automatically activates.

Methods: In a retrospective, non-randomized CABG study 20 mini-bypass systems (Dideco ECC.OTM) with the self regulating system to 20 ECC.O systems without the system and 20 conventional systems from a previous study conduct were compared at our institution (Dideco 903 AvantTM). In vivo micro air activity in terms of generated micro emboli (GME) was investigated and compared to a conventional open ECC circuit.

Results: Patient demographics (weight, height, age, preoperative hb/hct, BSA, EF, NYHA) were not different. Significant differences in GME activity were seen

		cECC	ECC.O without	ECC.O with
Bubble	venous	8.54	6.23	5.89
Volume (µl)	arterial	7.43*	0.34*	0.21

*p < .001

in both the mini bypass systems as compared to the conventional system.

Conclusion: Using mini bypass systems greatly reduce exposure to GME in routine CABG patients as compared to clinical use of conventional circuits. An automatic speed reduction feature may even augment these findings.

EVALUATION OF THE MEDTRONIC RESTING-HEART-SYSTEMTM (RHS) WITH RESPECT TO MICROBUBBLE ACTIVITY (MBBA) IN THE TUBINGS OF THE CIRCUIT

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Introduction: Complete revascularization with Extracorporeal Circulation (ECC) and cardioplegic arrest is still the most common surgical treatment of coronary artery disease.

MBBa is often detected at some level in the circuit of ECC and is linked to impairment of neurocognitive function after cardiac surgery and therefore a risk factor for postoperative morbidity.

Mini-bypass systems such as the RHS could reduce circulating microair.

Methods: In 20 consecutive patients coronary artery bypass grafting (CABG) was performed with RHS. The volume of MBBa was calculated with a special developed device (GAMPT-SystemTM) in the venous line (before reservoir) and the arterial line (after the filter). Filter was the same model in both systems. Data were compared to 20 consecutive patients who were operated using a conventional setup previously.

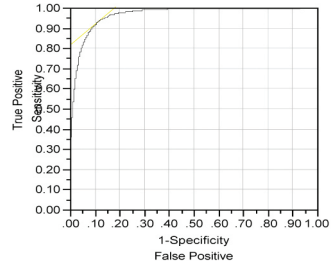
Results: There was no statistical significant difference with respect to weight, height, NYHA, BSA, age, gender, bypass-time and number of anastomoses. MBB venous amounted to 27.6 µL (1.3 - 26.3) in the RHS group and 23.1 µL (4.3-33.6) in the conventional group (n.s.). In the arterial line the MBB-value was reduced to 1.3 µL (.4 - 4.1) in the RHS group compared to 15.6 µL (2.8 - 29.3) in the conventional group ($P < .001$).
Conclusion: RHS allows complete revascularization equivalent to conventional bypass. The significant lower MBBa may lead to a potential reduction of neurocognitive impairment after CABG.

MONITORING MICROEMBOLI DURING CARDIOPULMONARY BYPASS WITH THE EDAC® QUANTIFIER

J.E. Lynch

Luna Innovations Incorporated

Introduction: Numerous studies have suggested that microemboli passed to the brain during bypass surgery results in neurological deficits. [1-4] Recent FDA clearance of the EDAC® QUANTIFIER (Luna Innovations, Roanoke, Virginia) has opened up the possibility for routine clinical use of microemboli monitoring during bypass surgery. Several clinical studies have recently been started, and while it is too early to present a rigorous statistical analysis of these studies, numerous case studies are available for presentation. In addition, recent laboratory advances in solid-gas emboli discrimination and *in vivo* monitoring of the carotid artery will be presented.
Methods: The presentation will focus on the results of a recently initiated observational study of 30 patients undergoing coronary artery bypass grafting and valve replacement procedures at Carilion Roanoke Memorial Hospital (Roanoke, Virginia). Examples from this study of microemboli passing through the arterial line filter as a result of venous air entering the circuit, drug injection and sampling during bypass, and the movement of bypass circuit components during surgery will be presented. New EDAC® features in development will also be presented, including recent tests of solid-gas classification in which a closed loop of bypass tubing was carefully de-aired overnight by immersing the tubing underwater overnight after adding oil, dried blood, glass microbeads and other test objects into separate tubes. Additional tests of Doppler-flow measurements of been conducted to provide a method for finding the carotid artery for *in vivo* monitoring.
Results: As previously reported microemboli entering a bypass circuit return to the patient through the arterial line filter in high numbers [5-7]. Classification studies show excellent discrimination of solids and gases, with a sensitivity of 92% and a specificity of 86%.



Conclusion: These results, combined with the possibility to provide in vivo monitoring of emboli in the carotid artery, open a new quantitative tool for assessing microembolic activity during bypass.
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PATIENT-PERCEIVED COGNITIVE COMPLAINTS AND FORMAL NEUROPSYCHOLOGICAL TESTING: WHERE IS THE ROAD TO NOTICEABLY IMPROVED OUTCOMES FOR PATIENTS?

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Introduction: For decades cognitive decline after heart surgery has been investigated by formal psychometric studies; other global assessments are considered too insensitive and unscientific. Self-reported cognitive impairment is not correlated with objective findings in several fields (e.g. chemotherapy). Regrettably, formal studies have not resulted in significant improvements. Formal testing cannot be applied in routine quality control. Other than following research recommendations based on findings in small patient groups, the world's practitioners now have no way to protect their own patients from neurological deficits. Here it is suggested that a judicious combination of formal testing and routine assessment of patient-perceived complaints can come close to eliminating these problems. One must appreciate that to patients (i.e. 'sufferers', from Latin *pati-* 'to suffer') and their associates it is only the patient-perceived cognitive suffering that is of any importance to them.
Methods: As a quality control system, for 24 years at our unit we have telephoned patients one year after their surgery to ask brief QOL-type questions, effectively enquiring how the operation had affected their life. The questions from 1984 till 1991 did not include specific cognitive enquiries. The answers were scored with a six-point Likert scale for incidence and severity. Using three-dimensional graphics the scores were systematically and deliberately improved in following patient groups by using our system of "parameter optimization", to be described separately. After 1991 we added a number of leading questions to elicit "hidden" cognitive changes.
Results: To our disappointment, in 1984 about 40% of patients reported unsolicited cognitive complaints; in 17% these complaints were of life-changing severity, such as loss of jobs, serious family difficulties or poor enjoyment of life. By 1987 we had step-by-step reduced the severe problems to 5%. By 1991 we had systematically reduced the cognitive reports to 10%. The severe complaints had nearly disappeared, being about .3% per year and confined to patients who were very ill before the operation. Although mild symptoms persisted in about 10 - 15% of patients, since 1991 these have needed leading questions to elicit, and typically consist of a response such as: "Now that you ask, I do have to look up the occasional telephone number that earlier I would have remembered, but of course I am one year older!"
Conclusion: It is possible to effectively remove the threat of patient-noticeable cognitive deficits for cardiac surgery patients. The limitations of such a system must be recognized; scientists would find defects. Our census results can only apply to our patients: Each cardiac surgery unit must do its own census.

PREOPERATIVE HYPONATREMIA AND CARDIOPULMONARY BYPASS: YET ANOTHER RISK FACTOR FOR CEREBRAL DYSFUNCTION

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Introduction: To determine if preoperative hyponatremia is a risk factor for patients undergoing cardiopulmonary bypass (CPB). Hyponatremia is not uncommon in patients prior to CPB, usually secondary to diuretic therapy. However, rapid correction of chronic hyponatremia ie mixing of the patients blood with the CPB prime solution, may have disastrous consequences namely central pontine myelinolysis.
Methods: We retrospectively analysed a prospective validated database of over 15,000 patients undergoing cardiac surgery at a single institution. Using the brain as an index organ, as previously described by Murkin, we specifically looked at length of stay.
Results: We identified 89 elective patients with a serum sodium less than 135 mmol/L. Average age was 68. 43 underwent isolated CABG, 25 underwent isolated valve replacement, 15 patients underwent valve and grafts, 6 underwent other cardiac procedures involving CPB. Overall mortality was 2.2%. Patients had an average length of stay of 14 days, nearly double the average for the remainder of the 13,000 patients undergoing surgery in our institution.
Conclusion: Hyponatremia is not a risk factor for death post CPB, but seems to increase length of stay because patients are "not quite right". This may be due to low grade diffuse subtle neurological injury due to the rapid correction of the chronic hyponatremia. Surgeons, anaesthetists and perfusionists should be aware of chronic hyponatremia and its potential rapid correction when commencing CPB. Priming the CPB circuit with small additional calculated volumes of water to adjust the prime sodium to match the patients may be beneficial to prevent adverse neurological injury.

NEUROCOGNITIVE FUNCTION BEFORE AND AFTER CORONARY ARTERY BYPASS GRAFTING: COMPARISON OF A CONVENTIONAL AND A MINIMIZED BYPASS SYSTEM

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Introduction: Some patients after CABG suffer from neurocognitive problems relating to memory, attention and speed of information processing. Surgery and patient specific factors are discussed as correlations. Mini-bypass systems are thought to reduce postoperative neurocognitive impairment by reduced hemodilution, less foreign surface area and the avoidance of blood air contact.

Methods: In a prospective randomized study, a consecutive series of CABG patients assigned to either the conventional (n = 40) or the mini-bypass group (n = 31) completed a comprehensive neuropsychological test battery before and 1 month after surgery including measures of memory, attention and concentration, verbal fluency, processing, and psychomotorical speed.

Results: While the groups did not differ in any cognitive variable in the pre-operative assessment, there was a trend towards better performance of the mini-bypass group compared to the conventional one regarding measures of memory and speed of information processing. Cognitive status at follow-up correlated significantly with age and mood/affect. Working memory dysfunction was observed in 25% of patients in the conventional group and 10% of patients in the mini-bypass group. Slowing of information processing occurred in 25% of the conventional and 6% in the mini-bypass group. Similarly, the proportions of attention/concentration problems were higher in the conventional group.

Conclusion: In summary the current results offer preliminary evidence that the adoption of mini-bypass systems may help to reduce the severity of neurocognitive impairment after CABG surgery.

COGNITIVE FUNCTION IN PATIENTS WITH AN OPTIMISED EXTRACORPOREAL CIRCUIT

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Introduction: Target of our investigation was the measurement on cognitive- and neurological complications with a surface optimised extracorporeal circulation.

Methods: The study was carried out as a prospective, randomised clinical trial involving 100 patients undergoing elective CABG surgery. The patients were randomly divided into two subgroups (50/50). Synthesis" (SORIN Group, Germany) was used in one subgroup compared to a standard PVC circuit without any surface modification. Synthesis is coated with Mimesys" phosphorylcholine and is an oxygenator with an integrated arterial filter and staged cardiotomy filter that adjusts to meet flow requirements. Standard clinical blood markers were collected pre-, intra- and postoperative. Pre- and the sixth postoperative day, a bedside neuropsychological test battery (Beck's Anxiety Inventory, D2 attention test, Trail Making Test, MMSE and Benton test) was performed.

Results: Sex, age, perfusion times and blood parameters were identical in both groups. There were no statistically significant differences in blood parameter levels; amount of blood loss and need for donor blood. The neuropsychological tests decreased after the cardiac procedure, but show as well no differences between the two groups.

Conclusion: Modification of perfusion management with an optimised ECC surface management, trends not to be an effective strategy to perform the cognitive neurological outcome in this small cohort.

A METHOD TO IMPROVE PATIENT-PERCEIVED COGNITIVE OUTCOMES BY OPTIMIZING PERFUSION PARAMETER VALUES DURING HEART SURGERY

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Introduction: Current accepted perfusion parameter values are dictums from the past. Though reasonable at a time of limited well-established knowledge, these dictums today need urgent re-examination. A good example is pH management. Only pH-stat and alpha-stat management have been explored; there has been no serious examination whether other values of pH might yield better results. The same applies to oxygen tensions that have been kept low deliberately on a theoretical argument about oxygen free radicals and oxygen toxicity. Yet a mechanism for such an examination of parameters is readily available. Indeed one can argue that optimization of parameters is ethically essential.

Methods: To (over)simplify a complex process: Initially in our quality control system we tried to keep pH at exactly 7.40 by repeated measurement of blood gases. This was of course impossible: Despite best efforts, some answers came back at 7.38, others at 7.42. After enough patients, the ones who had mean pH at 7.38 reported better patient-perceived outcomes than those at 7.40, who in turn did better than those at 7.42. After extensive ethical and statistical advice, we agreed that we should listen to our patients and run pH values at 7.38. The same happened: step-by-step, outcomes were better at lower pH till we reached 7.32. Below that outcomes worsened. By plotting against time on bypass we eventually obtained a three-dimensional curve with a "valley" of best results. We repeated this process for many parameter values, among them arterial oxygen and carbon dioxide tension, base excess, blood pressure and hemoglobin.

Results: All parameters mentioned except blood pressure had an effect on reported outcomes: physical, cognitive, or both. Especially, oxygen tension strongly affected both cognitive reports and the incidence of angina - the higher the oxygen tension, the lower the reported angina rate and the lower the cognitive complaints, both by halving the rates. As we combined the optimized parameters the effects on the outcomes was compounded. From our results we have found that the perfusion can wreck the surgeon's work!

Conclusion: Before waxing too optimistic that optimizing perfusion parameter values is a cure-all for all perfusion ills, be aware that there are limitations in this approach. Nothing in our improved results allows us to claim others will get the same results. We have reason to believe from our results and others that behind all this is the inflammatory response that our efforts manage to minimize but not to abolish. Though till recently out of our reach, we have commenced psychometric testing to confirm that our results are not only reflected in patients' answers but also objectively demonstrable.