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PREVENTION OF BRAIN INJURY IN CARDIAC SURGERY

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A thesis submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in Medicine.

Faculty of Medicine and Health Sciences
University of Auckland
2000
DEDICATION

This work is dedicated to my parents:

Alan Grant Mitchell

and

Jennifer Mitchell
ABSTRACT

**Background:** Stroke and neurocognitive deficits may follow heart surgery and have been linked to peri-operative cerebral embolism. Lignocaine exhibits cerebral protection in animal models of cerebral arterial gas embolism. This study began as randomised trial of lignocaine in brain protection in left heart valve surgery patients. Carotid Doppler emboli counting, developed to control for emboli exposure in the trial groups, revealed that most emboli occurred at the termination of cardiopulmonary bypass (CPB), and that “deairing” techniques used to remove air from the heart were not effective. Doppler monitoring also suggested that emboli were generated by the hard shell venous reservoir (HSVR) component of the CPB circuit, and that contrary to popular perception, air entrained into the CPB venous return line did pass through the circuit back to the patient.

**Methods:** Salvaged CPB circuits were used *in vitro* to investigate emboli generation by Medtronic Maxima HSVRs, and the passage of entrained venous line air through the CPB circuit. The efficacy of a novel left heart deairing technique was audited clinically using the Doppler device. Finally, a randomised double blind trial of lignocaine in cerebral protection during cardiac surgery was conducted. Sixty five patients underwent pre-operative neuropsychological (NP) testing and were randomised to receive lignocaine in a standard antiarrhythmic dose, or a placebo, in a double blinded infusion over 48 hours beginning at surgery. The NP tests were repeated at 10 days, 10 weeks and 6 months post-operatively.

**Results:** The Medtronic Maxima HSVRs were found to generate bubbles when operated at blood volumes well above the manufacturer’s recommended minimum. These bubbles, and air entrained to the CPB venous return line, were found to readily
transit the CPB circuit. Patients deaired using the novel technique were exposed to more than 10-fold less emboli after removal of the aortic clamp and withdrawal of CPB. Lignocaine treated patients exhibited a significantly reduced incidence of NP deficits at 10 days and 10 weeks postoperatively, and reported better memory at 10 weeks and 6 months postoperatively.

**Conclusions:** The Medtronic Maxima HSVRs should not be operated at blood volumes lower than 600 – 700 ml. Attempts should always be made to eliminate air entrainment to the CPB venous line, especially where vacuum assisted drainage is used. The novel de-airing technique is markedly superior to conventional methods. Lignocaine is a potentially useful cerebro-protective agent during cardiac surgery.
ACKNOWLEDGEMENTS

The following individuals and groups are acknowledged for their assistance in the conduct of this work:

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**Dr Paget Milsom** who let me share in his inventiveness and innovation;

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Finally, I thank my partner, Dr Clare Hamilton for her patience, loyalty and support over 5 rewarding but difficult years.
PUBLICATIONS, PRIZES, ABSTRACTS

Publications

The following peer reviewed journal articles based in this work have been published or accepted for publication,


Prizes

This work has received the following awards at international medical meetings.

1. Paper 2 won the Residents Prize for best paper presented by a resident / registrar at the Annual Scientific Meeting of the Undersea and Hyperbaric Medical Society, USA, 1996.

2. Paper 3 won the Terumo Award for best paper at the Annual Scientific Meeting of the Australasian Society of Cardiovascular Perfusionists, Sydney, Australia, 1997.

3. Paper 4 won the Committee Award for Excellence in Presentation at the Annual Scientific Meeting of the South Pacific Underwater Medical Society, New Zealand, 1997.

4. Paper 7 won the Terumo Award for best paper at the Annual Scientific Meeting of the Australasian Society of Cardiovascular Perfusionists, Sydney, Australia, 1999.
Published abstracts

The following abstracts have been published after presentation of this work at various medical meetings.

   
   Presented at the Annual Scientific Meeting of the Undersea and Hyperbaric Medical Society, Alaska, May 1996

   
   Presented at the Annual Scientific Meeting of the Undersea and Hyperbaric Medical Society, Cancun, Mexico, June 1997

   
   Presented at the Annual Scientific Meeting of the Undersea and Hyperbaric Medical Society, Seattle, USA, May 1998

*Presented at the Annual Scientific Meeting of the Australasian Society of Cardiovascular Perfusionists, Sydney, Australia, September 1997*


*Presented at the Outcomes 98 Meeting, Key West, USA, June 1998*


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And:

*The Outcomes 99 Meeting, Key West, USA, June 1999*

And:

*The Annual Scientific Meeting of the Australasian Society of Cardiovascular Perfusionists, Sydney, Australia, October 1999*
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LIST OF ABBREVIATIONS AND SYMBOLS

Note: Abbreviations used only in tables or figures and explained in the captions to those tables or figures do not appear in this list.

ANOVA Analysis of variance
AST Aspartate amino transferase
ATP Adenosine triphosphate
AVLT Auditory – verbal learning test
BMI Body mass index
Ca$^{2+}$ Calcium
CAGE Cerebral arterial gas embolism
CBF Cerebral blood flow
CK-MB Creatine kinase (myocardial fraction)
cm Centimetre
CO$_2$ Carbon dioxide
CPB Cardiopulmonary bypass
DCI Decompression illness
EEG Electro-encephalogram
EPSP Excitatory post-synaptic potential
Fe$^{3+}$ Iron ion
g Gram
GVD Gravity venous drainage
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<tr>
<td>H⁺</td>
<td>Hydrogen ion</td>
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<tr>
<td>HBO</td>
<td>Hyperbaric oxygen</td>
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<td>HSVR</td>
<td>Hard shell venous reservoir</td>
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<td>Hz</td>
<td>Hertz</td>
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<td>ICP</td>
<td>Intracranial pressure</td>
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<td>K⁺</td>
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<td>LCCA</td>
<td>Left common carotid artery</td>
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<td>MAP</td>
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<tr>
<td>NO</td>
<td>Nitric oxide</td>
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<td>NP</td>
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<td>Partial pressure of oxygen</td>
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<td>SD</td>
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<tr>
<td>VAVD</td>
<td>Vacuum assisted venous drainage</td>
</tr>
<tr>
<td>VSCC</td>
<td>Voltage sensitive calcium channel</td>
</tr>
</tbody>
</table>