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Toronto Critical Care Medicine Symposium 2004
(Adult and Pediatric)
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The King Award is presented by the CCCS for the best oral presentation by a resident. The award is named after Garner King who was Professor and Head of the Department of Medicine at the University of Alberta. Garner King trained many of the first generations of critical care physicians in Canada and also many from abroad. He was the second president of the CCCS (from 1978–1980).

The Spanier Award, presented for the 2nd best oral presentation by a resident, is named in memory of Allen Howard Spanier who died on April 27th, 1999, at the age of 52. He was Associate Professor in Surgery, Medicine and Anesthesia, McGill University and Senior Surgeon and Chairman, Department of Adult Critical Care, Sir MB Davis Jewish General Hospital (Montreal, Quebec). He was President of the CCCS from 1992–1994.

Additional awards are presented for outstanding resident posters. All abstracts are published as submitted by the authors at the time of the Annual Meeting.

1st prize and King Award

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POST-ISCHEMIC HYPOTHERMIA THERAPY INHIBITS INFLAMMATORY GENE TRANSCRIPTION AND LEUKOCYTE RECRUITMENT IN CEREBRAL MICROVESSELS

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Introduction: Hypothermia therapy improves histological and behavioural outcomes and mortality following global cerebral ischemia in animals and humans. This therapy has potent anti-inflammatory effects but the anti-inflammatory mechanisms are not completely understood. We explored the effect of hypothermia therapy on inflammatory gene transcription and leukocyte recruitment and adhesion in cerebral microvessels following global cerebral ischemia in the mouse.

Methods: Anaesthetised male C57BL/6 mice underwent normothermic transient (10 minutes) bilateral carotid artery occlusion (two-vessel occlusion [2-VO]) or sham surgery. After 2-VO or sham surgery, mice received either normothermic (37°C) or hypothermic (32°C) recovery at intervals of 2 or 4 hours. An open cranial window was done and leukocyte-endothelial interactions were recorded in pial venules immediately following or at 2 or 4 hours after ischemia or sham, using intravital microscopy. In a second series of experiments, mice were then sacrificed at 2 hours following 2VO or sham and 2 hours of normothermia or hypothermia. Brains were removed, frozen, and sectioned and microvessels were dissected from the brain using laser capture microscopy. Gene expression of E-selectin, ICAM-1, MMP-2 and the murine chemokine MIP-2, were performed using real time quantitative PCR on the isolated microvessels. In a third series of experiments animals were sacrificed three and seven days post 2-VO or sham for histological assessment of cell death using a TUNEL stain, and neuron specific protein (NeuN) immunoreactivity.

Results: A marked increase in leukocyte rolling and adhesion was seen in the normothermic group at 5 min. and at 2 and 4 hours following reperfusion compared to sham. This effect was significantly reduced in the hypothermic groups at 2 hours post-ischemia. The expression of mRNA for E-selectin, ICAM-1, and MIP-2 was markedly increased at 2-hrs post 2-VO in the normothermic group. Hypothermia therapy significantly attenuated the ischemia-induced increase in inflammatory gene expression. Four hours of hypothermia therapy profoundly reduced neuronal cell death at three (TUNEL) and 7 days (NeuN immunohistochemistry) post-ischemia compared to the normothermic group post-ischemia.

Conclusions: Moderate hypothermia inhibits leukocyte rolling and adhesion after 2-VO and this effect is associated with inhibition of expression of adhesion receptor and chemokine genes in cerebral endothelial cells. This anti-inflammatory mechanism may help explain the robust neuro-protective effects of hypothermia therapy that we demonstrated after global cerebral ischemia in this model.

2nd prize and Spanier Award

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THE EFFECT OF TIMING OF ANTIMICROBIAL ADMINISTRATION ON MORTALITY IN SEPTIC SHOCK PATIENTS

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Background: Critical timing elements with respect to antimicrobial therapy in sepsis and septic shock have not been adequately defined. A retrospective analysis of septic shock patients was performed to determine the relationship between duration of hypotension prior to appropriate antimicrobials and outcome in patients with septic shock.

Methods: Data was extracted from the medical records of 2100 ICU patients hospital with presumed septic shock. Outcome was stratified based on time to administration of appropriate antimicrobials, appropriateness of initial therapy, and other therapeutic variables.

Results: Overall mortality was 53.3%. Median time to implementation of effective antimicrobial therapy following first onset of recurrent/persistent hypotension was 6.25 hrs with 17.6% of patients receiving initially inappropriate therapy. Duration of hypotension prior to effective antimicrobial therapy initiation was strongly correlated with outcome ($p < 0.0001$). Mortality increased progressively with delays in initiation of appropriate therapy with a 5-10% decrease in survival with every hour delay over the first 6 hrs. By the 2nd hour after onset of persistent/recurrent hypotension, survival was significantly reduced relative to receiving therapy within the first hour ($p < 0.05$). In a multivariate model with initial appropriateness of antimicrobials, use of 2 or more effective antimicrobials and severity of illness (APACHE II), time to effective therapy remained highly predictive of outcome ($p < 0.0001$).

Conclusions: Substantial delays in initiation of effective antimicrobial treatment exist in the management of septic shock. However, rapid initiation of such therapy following first onset of recurrent or persistent hypotension is a critical determinant of outcome. The factors resulting in delay and the effect of reducing the interval between presentation and treatment should be investigated.

Special Mention

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**MULTIMODAL NEUROELECTROPHYSIOLOGICAL STUDIES TO PREDICT OUTCOME
IN PAEDIATRIC PATIENTS WITH TRAUMATIC BRAIN INJURY**

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Introduction: A prognostic tool is needed in the early assessment of paediatric patients with traumatic brain injury (TBI). The combination of electroencephalography and evoked potentials may help predict outcome but combining these tests has not been studied in children with TBI.

Methods: We enrolled patients with TBI admitted to the Paediatric Critical Care Unit (PCCU) with an initial GSC of 12. All patients had a scalp electroencephalogram (EEG), visual evoked potentials (VEPs) and somatosensory evoked potentials (SSEPs) done within 60 hours of admission to the PICU, and repeated within 5 to 7 days. A CT scan was done on admission and repeated at least once within 48 hours. EEG, VEP and SSEP were assigned scores for analysis. In addition, the EEG was analyzed offline for synchrony patterns using the Hilbert transform. Outcome was measured at three months post-injury using the 6-point Paediatric Cerebral Performance Category Score.

Results: Seven patients aged 3 to 13 were enrolled. GSC ranged from 5 to 12. Three of the 7 patients developed intracranial hemorrhage requiring evacuation. Four of the 7 sustained diffuse axonal injury. Children with diffuse axonal injuries had EEG patterns of frontal polymorphic delta (abnormal). Children whose EEG had normal background activity on the first EEG had better outcomes at 3 months, followed by those who regained normal background activity on the second EEG. Children having the worst scores for EEG and SSEP had the worst functional outcome at 3 months. Latencies observed in VEP and SSEP occurring in cortical to cortical relays also correlated with worse functional outcome at 3 months. Children whose EEG showed attenuated background patterns had very large amplitude VEPs. Current scoring systems for VEPs do not account for observed increases in wave amplitudes. EEG with frontal polymorphic delta patterns showed increased synchrony compared with EEG having normal alpha background.

Conclusions: Our preliminary results indicate that EEG and SSEP may be most predictive of outcome in children with TBI. Scoring systems for VEP need to include variations in wave amplitudes.

Outstanding Resident Poster #1

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CANADIAN PHYSICIANS' APPROACH TO ICU DELIRIUM DIAGNOSIS AND MANAGEMENT: A SURVEY

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Introduction: There is significant variability in reported incidence rates of ICU delirium. This may in part be due to differences in what physicians label cognitive abnormalities in critically ill patients. This study was designed to determine, among hypothetical patients with cognitive abnormalities: 1) what Canadian ICU physicians label "delirium", 2) non-pharmacological and pharmacological management practice patterns; 3) consultation patterns; and 4) how physicians view the clinical impact of cognitive abnormalities.

Methods: Surveys included 3 clinical scenarios with cognitive abnormalities in patients 1) with hepatic encephalopathy; 2) with multiple drug overdose and 3) post-operative AAA repair. Cognitive symptoms included fluctuating level of consciousness, inattention, disorientation, hallucinations, sleep/wake cycle disturbance and paranoia. Respondents were asked to list their most likely diagnoses for each scenario. Respondents were also asked to indicate which pharmacological and non-pharmacological therapies would be indicated, if and when they would consult other services, and the clinical importance of a number of different outcomes (e.g. increased length of stay, risk of self-extubation). Surveys were sent out in 2 phases: the first phase was distributed at the Clinical Trials Group Meeting, and the second, mailed to the general CCCS membership.

Results: Phase I survey results are as follows: In the two scenarios where an etiological diagnosis was obvious, 87.5% of respondents used the underlying medical problem to explain the cognitive abnormalities, and only 62.5% used the term "Delirium". 17% indicated multiple diagnoses that included the term delirium. This contrasts with the third scenario where an underlying medical problem was not obvious. 71% of respondents attributed the cognitive abnormalities to "Delirium", and other possible explanations, including multiple diagnoses including the term "delirium", were less commonly invoked (less than 37.5%). There was considerable variation in use of non-pharmacological and pharmacological management. The most commonly selected pharmacological agents were antipsychotics and benzodiazepines, although other agents (narcotics, non-narcotic analgesics, anesthetics) were also selected. There was wide variability in whether and when intensivists chose to consult other services. The majority of respondents rated clinical consequences of cognitive abnormalities as moderately or highly significant.

Conclusions: Respondents were more likely to attribute cognitive abnormalities to the underlying medical diagnosis (cirrhosis, medication effect or withdrawal) when the medical problem was apparent; otherwise the term "Delirium" was more likely to be used. There was significant variation in how intensivists label cognitive abnormalities in ICU patients, as well as clinical scenario-based management patterns. The variation in labelling may explain, in part, the wide variation in published ICU delirium incidence rates. ICU physicians generally perceived clinical consequences of cognitive abnormalities to be significant.

Outstanding Resident Poster #2

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**PEDIATRIC RESIDENTS' KNOWLEDGE AND CONFIDENCE IN RESUSCITATION:
EVALUATION OF A CURRICULUM**

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Introduction: In-hospital pediatric cardiorespiratory arrests are infrequent events, yet patients are likely to have a good outcome if successfully resuscitated. Given the rarity of actual events, structured curricula such as the widely used Pediatric Advanced Life Support (PALS) Course are used to teach residents the knowledge and skills required for successful resuscitation of acutely ill children. However, the success of such curricula in imparting the necessary knowledge and confidence to residents in a sustainable way has not been fully evaluated.

Methods: A cohort of pediatric residents in post-graduate year one to four was followed prospectively for one year following completion of an annual PALS course. Multiple choice and short answer questionnaires were used to evaluate residents' knowledge immediately before and after completion of the PALS course, as well as at four-month intervals throughout the year. A ten-question confidence assessment was used to evaluate residents' self-confidence in performing various aspects of pediatric resuscitation at these same times. Scores were compared before and after the PALS course to evaluate acquisition of knowledge and confidence. Scores at 12 months were compared to the post-PALS course scores to evaluate maintenance of knowledge and confidence over time. Data was analyzed using non-parametric statistics.

Results: Knowledge questionnaire scores and confidence ratings were significantly higher post-PALS course compared to pre-PALS course ($p=0.008$). Analyzed by post-graduate year, only the first year residents demonstrated a statistically significant increase in knowledge post-PALS course ($p=0.018$). Knowledge scores at 12 months post-PALS course were not significantly different than scores immediately post-PALS course ($p=0.580$). Confidence ratings were significantly higher post-PALS course compared to pre-PALS course on nine out of ten measures (p -value ranging from <0.001 - 0.039). Confidence ratings were significantly lower at 12 months post-PALS course on three out of ten measures p -value ranging from 0.021 - 0.039). There was good correlation between residents' overall confidence in leading a code and knowledge questionnaire scores pre-PALS course ($r=0.598$), but increased knowledge scores immediately and 12 months post-PALS course did not correlate well with self-ratings of overall confidence at these times ($r=0.012$ and $r=0.079$ respectively).

Conclusions: Overall, this curriculum led to successful acquisition of knowledge and confidence by pediatric residents immediately after completing the PALS course. However, the PALS course was not shown to have as significant an impact on senior residents' knowledge. Confidence did not improve to the same degree as knowledge post-PALS course, and correlated poorly with higher knowledge scores. These findings support the hypothesis that the PALS course alone is insufficient to teach pediatric residents cardiopulmonary resuscitation.

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GLUCOSE CONTROL AND OUTCOMES AMONG NEUROSCIENCES PATIENTS

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Introduction: The risks and benefits of glucose control in neurosciences patients are unknown. Tight control has been validated among general ICU patients, especially cardiosciences. Recognition of extremes of glucose in the neurologically impaired is difficult. The incidence and severity of these events, and effect on outcome, are unknown.

Hypothesis: To determine the incidence of extremes of serum glucose among neurologically critically ill patients, associations with insulin therapy and glucose targets, and effects on outcomes of length of stay and survival.

Methods: Retrospective review of all patients admitted during 2003 to the neurosciences critical care unit of this tertiary care facility with a primary neurologic diagnosis.

Results: Six hundred six patients were admitted. All were reviewed (see table). Frequency of hypoglycemia correlated positively with the presence of diabetes, higher insulin needs, and frequency of hyperglycemia. It correlated inversely with target serum glucose (all $p < 0.0001$)

Conclusions: Hypoglycemia and hyperglycemia are common among neurosciences patients and are significantly associated with extended LOS. The strong inverse correlation between glucose goal and hypoglycemia suggests caution in targeting glucose control. The strong correlation between hyperglycemia and hypoglycemia suggests some patients are prone to significant difficulty with glucose control. Further evaluation of glucose and insulin management in this population is warranted.

Variable	No DM (n= 534)	DM Pre-existing (n=19)	Insulin started in ICU (n=53)	P value
Age (y)	52.7 (18-93)	67.1 (47-89)	54.5 (19-79)	0.05
Sex (%male/female)	60/40	63/37	66/34	0.37
Glucose < 4 mmol/L	53	23	37	0.0001
Glucose > 16 mmol/L	18	121	156	0.0003
Glucose 10-16 mmol/L	183	11	24	0.678
Hospital LOS (days)	15.9 (1-273)	25.3 (2-126)	22.9 (1-84)	0.015
ICU LOS (days)	4.3 (1-175)	6.5 (1-43)	7.9 (1-43)	0.005
Insulin (mean u/h)	0	3.1	1.9	0.0001
Mortality	In Progress	In Progress	In Progress	