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EFFECT OF OXYGEN-DERIVED FREE RADICAL SCAVENGERS ON MORTALITY IN ENDOTOXIN-CHALLENGED MICE. Cynthia W. Broner, Jerry Shenep, Gregory L. Stidham, Dennis Stokes. Spon. by Henry H. Herrod. University of Tennessee, LeBonheur Children's Medical Center and St. Jude Children's Research Hospital, Division of Critical Care, Department of Pediatrics, Memphis.

Oxygen-derived free radicals have been shown to play a role in many forms of cell injury. A role for free radicals has recently been demonstrated in the mortality of a rat/sepsis model. The purpose of this study was to determine the effects of pretreatment in a mouse endotoxin model with superoxide dismutase (SOD), and acetylcysteine (Mucomyst, MM), a clinically available free radical scavenger.

Methods. Forty-eight mice were divided into three equal groups. Each group received pretreatment 2 hours prior to endotoxin challenge. Pretreatment consisted of a 0.5 ml intraperitoneal injection of saline, SOD (20,000 units/kg), or MM (140 mg/kg). Endotoxin (0.1 mcg E. Coli 0111:B4) was then injected intraperitoneally according to protocol developed in this lab and previously described. The mice were checked every 12 hours for survival.

Results. Increased survival was seen in the SOD treated group compared to controls, with cumulative mortalities of 38 vs. 81%, 44 vs. 88%, and 75 vs. 100% at 12, 24 and 72 hours respectively. These differences were all statistically significant. Increased survival was also seen early in the MM group, but this difference failed to achieve statistical significance.

Conclusions: 1) Free radicals play a role in endotoxin mortality, and 2) free radical scavengers increase survival.

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SIGNIFICANCE OF IONIZED CALCIUM MEASUREMENTS IN CRITICALLY ILL CHILDREN. Cynthia W. Broner, Gregory L. Stidham, David F. Westenkirchner. Spon. by Henry H. Herrod. University of Tennessee, LeBonheur Children's Medical Center, Division of Critical Care, Department of Pediatrics, Memphis.

Normal serum ionized calcium levels are crucial to many aspects of physiologic stability. Disturbances in ionized calcium are known to occur frequently in critically ill adults, and to be poorly predicted by measures of total serum calcium. This study was undertaken to determine the frequency and significance of abnormalities of ionized calcium in critically ill pediatric patients.

Methods. Eighty-eight ionized calcium measurements were obtained on admission of critically ill children to our intensive care unit. Simultaneous measurements of total serum calcium, protein, albumin, pH, electrolytes, and measures of hepatic and renal function were also obtained. Patients were prospectively followed for outcome parameters.

Results. Mean ionized calcium for our patients was 1.21 +/- 0.28 mM/L. 15 patients (17%) had levels outside the normal range for our laboratory with 11 (12.5%) hypocalcemic. Mortality rates were 46%, 9.5% and 0% for the hypo-, normo-, and hypercalcemic patients respectively. The association between hypocalcemia and mortality was highly significant ($p < .001$). Furthermore, 6/7 patients initially normocalcemic experienced significant hypocalcemia within 24 hours prior to death.

Conclusions. We conclude 1) that derangements in ionized calcium occur frequently in critically ill children, and 2) that hypocalcemia is associated with increased mortality.

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SERUM MAGNESIUM LEVELS IN CRITICALLY ILL PEDIATRIC PATIENTS. Cynthia W. Broner, Gregory L. Stidham, David F. Westenkirchner. Spon. by Henry H. Herrod. University of Tennessee, LeBonheur Children's Medical Center, Division of Critical Care, Department of Pediatrics, Memphis.

Abnormalities in serum magnesium levels are known to cause potentially life-threatening problems in critically ill patients. Such abnormalities have also been shown to occur with high frequency in critically ill adults. This study was undertaken to ascertain the prevalence and significance of magnesium disturbances in critically ill pediatric patients.

Methods. Ninety serum magnesium levels were obtained in critically ill pediatric patients upon admission to our intensive care unit. Also noted were measures of renal and hepatic function, serum electrolytes, and prospective evaluation of outcome parameters.

Results. The mean magnesium level on admission for our patient population was 2.022 mg/dl (+/- 0.874). More importantly, 35 (38.9%) of our patients had levels outside the normal range for our laboratory, with 23 (25.5%) hypo- and 12 (13.3%) hypermagnesemic. The mortality rates were 8.7%, 9.1%, and 41.7% in the hypo-, normo-, and hypermagnesemic patients respectively. The mortality association for the hypermagnesemic patients was significant at $p < .01$.

Conclusions. We conclude that 1) disturbances in magnesium homeostasis occur with a high and previously unrecognized high frequency, and 2) hypermagnesemia is associated with a significantly greater mortality than hyper- or normomagnesemia.

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IMPLEMENTATION OF THE THIRD GENERATION NON-INVASIVE REBREATHING CARDIOPULMONARY PARAMETER SOFTWARE IN AN OLEIC ACID LUNG INJURY DOG MODEL. D. Spencer Brudno, Donald H. Parker, Kenneth D. Burch, and Curt M. Steinhart. Sponsored by Albert W. Pruitt. Depts. of Peds. and Surg., Med. Coll. of Ga., Augusta, Ga.

This study was performed to evaluate improved software that non-invasively measures Effective Pulmonary Blood Flow (QEP), Lung Tissue Water (Vt), Lung Diffusion for carbon monoxide (DLco), and Functional Residual Capacity (FRC).

A modified non-invasive method for the measurement of four cardiopulmonary parameters (CPP) which can be measured only with an accepted gas rebreathing method or by invasive means was developed to improve speed of data acquisition and analysis, and ease of use. The rebreathing system includes a Perkin Elmer Respiratory Gas Analyzer MGA-1100, an IBM-XT computer and a valving device. Nine dogs were instrumented to invasively measure thermodilution cardiac output and measure mixed venous and systemic oxygen saturations. Measurements of CPP were made before and after invasive measurements and averaged.

Rebreathing QEP correlated well with the invasive QEP ($p < 0.0001$). Vt, DLco and FRC decreased during lung injury ($p < 0.00001$ for all three). FRC increased proportional to increased PEEP from 0 to 15 cm H₂O ($p < 0.005$).

Computation time from the end of a 25 second sampling time to acquisition of results was less than 2 minutes. One program is utilized during the sampling, computation, disk I/O and printing modules. Raw gas concentration vs. time, and log gas concentration vs. time curves are displayed for selection of the window used for calculation of CPP. This study demonstrates a powerful software package for the non-invasive measurement of CPP.

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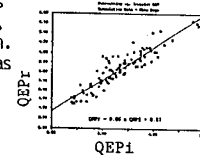
THE NONINVASIVE MEASUREMENT OF EFFECTIVE PULMONARY BLOOD FLOW IN ACUTE LUNG INJURY. Kenneth D. Burch, Donald H. Parker, D. Spencer Brudno, and Curt M. Steinhart. Sponsored by Albert W. Pruitt. Medical College of Georgia, Department of Pediatrics, Augusta, Georgia.

Effective (non-shunted) pulmonary blood flow (QEP_r) was measured using a modified rebreathing technique and compared to QEP_i determined by thermodilution and blood gas analysis at varying PEEP in non-injured and oleic acid injured lungs.

Nine mongrel dogs (18-26 Kgs) were anesthetized, intubated with cuffed tubes, and instrumented with intravenous, systemic arterial, and pulmonary arterial catheters. Ventilation was volume controlled at 15 breaths/minute and tidal volume adjusted to maintain PaCO₂ between 35-45 torr. Noninvasive measurements of QEP_r were done before and after determination of QEP_i. PEEP was varied by 5 cm H₂O increments from 0 to 15 before lung injury and 0 to 20 after central venous administration of oleic acid (0.10-0.15 ml/kg).

QEP_r highly correlated with QEP_i as seen in the figure ($r = .92, R^2 = .85, n = 99, p < .0001$) using Pearson's correlation. The noninvasive measurement of QEP_r was accurate at varying cardiac outputs (CO, 0.8-6.3 L/min) and intrapulmonary shunt (Qs/Qt, 0.03-0.67). The measurement of QEP_r at varying levels of PEEP (0-20 cm H₂O) and subsequent changes in Qs/Qt demonstrates that QEP_r is the pulmonary blood flow that undergoes gas exchange such that QEP_r = CO (1-Qs/Qt).

The study validates the noninvasive rebreathing technique as a reliable measurement of the effective pulmonary blood flow at varying CO and Qs/Qt in acute respiratory failure indicating clinical utility during PEEP therapy.



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A COMPARATIVE STUDY OF PULSED DOPPLER CARDIAC OUTPUT (PDCO) AND THERMODILUTION CARDIAC OUTPUT (TDCO). Frank Castello, Daniel Notterman, James Wilkinson, Charlotte Steinberg. Department of Pediatrics, New York Hospital-Cornell Univ. Med. Coll., New York. (Spon. by Maria I. New)

Comparison of PDCO, calculated from aortic flow velocity, and TDCO in critically ill children has not been reported. We prospectively examined all pts with Swan-Ganz catheters over 3 months. PDCO was determined using the Cardioflo Model CF1 computer (Cardionics, Inc.). Aortic diameter was determined by 2-D sonogram. TDCO was determined simultaneously by iced saline injection. Study pts (N=13) were grouped by wt: Grp 1 ≤ 20 kgs and Grp 2 > 20 kgs. In 4/5 Grp 1 pts, satisfactory peak velocity signals were obtained and 14 paired CO measurements were made. No significant difference was found between any paired PDCO/TDCO measurements (Wilcoxon's rank sum). PDCO correlated excellently with TDCO ($r = 0.90, TDCO = .69 PDCO + .96$). Satisfactory studies were not obtained in the other Grp 1 pt (pneumomediastinum) nor in any of 8 Grp 2 pts. CONCLUSION: Noninvasive PDCO measurement compares favorably with TDCO in critically ill children ≤ 20 kgs without pneumomediastinum. Its utility in children > 20 kgs could not be demonstrated.