

## EFFECTS OF PHENYLEPHRINE ON CEREBRAL AND MYOCARDIAL BLOOD FLOW DURING CPR IN INFANT PIGLETS

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We evaluated phenylephrine (PE) during CPR in an infant animal model to determine if cerebral (CBF) and myocardial (MBF) blood flow could be sustained for longer periods of CPR than in our previously published study using epinephrine (E)<sup>1</sup>. CPR was performed on 6 pentobarbital-anesthetized piglets (2 weeks old, 4-5 kg) by a pneumatic compressor at 100 compressions/min, 60% duty cycle, and 1:5 breath to compression ratio. Aortic pressure decreased after 10 min of CPR, while right atrial pressure remained unchanged resulting in MBF of 28 and 35 ml/min/100 g at 5 and 10 min of CPR. CBF (ml/min/100 g) was maintained at prearrest values (34 ± 4) for 20 min (28 ± 9) of CPR but fell during prolonged CPR because of a decrease in cerebral perfusion pressure after that time. CMRO<sub>2</sub> (ml/min/100 g) was sustained at control values (2.1 ± .2) for 10 min (2.4 ± .3) but thereafter decreased. Cerebral extraction (EXT) was elevated above prearrest levels, but not different than with E. In conclusion, PE sustained CMRO<sub>2</sub> and CBF for 10 and 20 min of CPR, comparing favorably to E in our study. PE provided significant levels of MBF during early CPR, but less than with E. Therefore, in infant piglets, PE and E provide similar benefits on CBF and CMRO<sub>2</sub> during early CPR, but are not sustained indefinitely in either group. MBF may be less with PE. 1. Schleien, C., et al. Circulation 73:809, 1986. (Supported by NS20020)

## CEREBRAL SALT-WASTING SYNDROME IN PEDIATRIC NEURO-SURGICAL PATIENTS. Gregory L. Stidham, Anthony DiScialfani, Robert A. Sanford. Spon. by Henry H. Herrod.

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Cerebral salt-wasting syndrome is a term first used incorrectly in the 1950's to describe patients who, in fact, experienced the syndrome of inappropriate ADH secretion. Many authors have subsequently questioned the existence of a true cerebral salt wasting (CSW) syndrome. We have observed 4 patients who have exhibited a true sodium wasting syndrome following pituitary surgery.

**Methods.** All patients admitted to our ICU following pituitary surgery were studied carefully every six hours for details of sodium and water balance. In addition, all were evaluated for evidence of renal or adrenal dysfunction.

**Results.** 14 patients were studied over 3 years. 4 exhibited significant hyponatremia associated with natriuresis and negative water balance (see table below).

PATIENT	AGE (YEARS)	SEX	WATER BALANCE	HYPERNATREMIA
1	27	M	-1100	-112
2	28	F	-1100	-112
3	29	M	-1100	-112
4	30	F	-1100	-112

**Conclusions.** These data support the existence of a true CSW syndrome, characterized by polyuria and marked natriuresis associated with a hyponatremia reflecting total body sodium depletion. These features could not be explained by SIADH, DI, renal or adrenal dysfunction. Differences in the pathophysiology of this disorder mandate a unique therapeutic approach which may be essential to avoiding serious electrolyte disturbances.

## LACK OF EFFECT OF ALLOPURINOL ON MORTALITY IN A MOUSE MODEL OF ENDOTOXIC SHOCK. Gregory L. Stidham, Jerry Shenep, Cynthia W. Broner. Spon. by Henry H. Herrod.

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Oxygen-derived free radicals have been associated with many forms of cell injury and types of organ dysfunction, including recently in a rat model of gram-negative sepsis. A possible source of free radicals in this setting is through activity of the enzyme xanthine oxidase, as has been shown in reperfusion injury. The purpose of this study was to determine the effect of pretreatment with allopurinol, a xanthine oxidase inhibitor, on mortality in a mouse model of endotoxin shock.

**Methods.** Sixty mice were divided into 2 equal groups. Treatment group received allopurinol, 50 mg/kg/day in 0.5 ml water by gavage feed each of 4 days prior to endotoxin challenge. Control animals received water gavage alone. Animals were challenged with 0.05 mcg of intraperitoneal endotoxin (E. Coli 0111:B4) following dactinomycin sensitization according to a model previously described by this laboratory. Mice were checked every 24 hours for survival.

**Results.** Mortality for the control and treated groups at 96 hours were 32% and 46% respectively. These rates were not statistically different; nor were differences in mortality between the two groups demonstrated at 24, 48 or 72 hours.

**Conclusions.** These data do not support an important role for free radicals generated by the xanthine oxidase system in this model, and suggest another, as yet undetermined source of radicals influencing mortality in endotoxemia.

## FLUID MANAGEMENT IN BACTERIAL MENINGITIS (BM).

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Elevated plasma arginine vasopressin concentrations [AVP] and cerebral edema occur in BM. Therefore fluid restriction has been recommended in early management. However dehydration may also increase [AVP] and fluid restriction may decrease cerebral perfusion. A randomized, prospective study is in progress to establish the relationship between initial hydration status and [AVP], and to determine the effect of rehydration or fluid restriction on subsequent [AVP]. Six children with BM have been studied to date (table). Hydration was estimated clinically and determined by bromide space. [AVP] was measured at presentation, 24 hours later, and at the end of antibiotic therapy. No patient developed hyponatremia, SIADH, or fluid overload.

Subject	Fluid Therapy <sup>1</sup>	% Dehydration		Plasma AVP (pg/mL)		
		Cl <sub>2</sub>	BS <sup>3</sup>	Initial	24 hr	Final
1	R	0.0	10.3	10.7	6.0	5.0
2	R	0.0	0.0	5.3	3.2	2.6
3	M	7.5	0.0	8.8	1.2	1.4
4	M	5.0	9.6	2.8	2.8	1.3
5	M	3.0	0.0	3.4	0.0	7.8
6	M	7.5	11.6	11.5	1.4	1.3

<sup>1</sup>R-Restricted M-Maintenance; <sup>2</sup>Clinical; <sup>3</sup>Bromide Space

Results to date suggest that children with BM are often dehydrated at the time of presentation and that replacement fluid therapy results in the normalization of [AVP].

## NEONATAL PULMONARY VASCULATURE: RECOVERY FROM POSITIVE END-EXPIRATORY PRESSURE (PEEP) IN INTACT AND ISOLATED LUNGS. Shekhar T. Venkataraman, Bradley P. Fuhrman, Donna F. Howland, Ann E. Thompson. Anesthesia/CCM &amp; Peds, U of Pgh., Child. Hosp. of Pgh, Pittsburgh, PA

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Unilateral PEEP (UPEEP) reduces ipsilateral pulmonary blood flow (PBF) in the intact (INT) newborn lamb. On cessation of UPEEP, ipsilateral PBF returns slowly to baseline. Intact and isolated lungs of 9 infant lambs were studied to examine the mechanism of this vascular hysteresis.

Flow probes were placed on R and L pulmonary arteries (PA) of 4 infant lambs. R and L lungs were intubated endobronchially and synchronously ventilated (Siemens-Elema Servo 900C). UPEEP was applied to the L lung for 4 min, abruptly discontinued and recovery of L lung blood flow (LPBF) followed for 4 min (11 trials). LPA was then occluded (LOC) for 4 min using a balloon catheter and recovery of LPBF on deflation followed for 4 min (11 trials). Recovery of PA pressure (P) after stopping PEEP was studied in 5 infant lambs after median sternotomy. Isolated in situ perfused lungs (ISO) were prepared; pulmonary vasculature paralyzed; and recovery of PAP on cessation of PEEP studied.

PARAMETER	TRIALS	ON	10	5	OFF	30	6	OFF	1	OFF	4	OFF
INT UPEEP LAMP	11	150/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100
INT LOC LAMP	11	150/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100	110/100
INT PEEP PAP	11	30	25	32	32	32	32	32	32	32	32	32
INT PEEP PBF	11	50	100	100	100	100	100	100	100	100	100	100

\*p < .05 UPEEP vs LOC and \*p < .05 vs 4 h OFF by ANOVA

In the INT, on cessation of UPEEP, airway and vascular pressures, lung volumes, and PBF returned to baseline within 10 sec but LPBF recovered slowly. LPBF returned promptly to baseline after balloon deflation and PAP recovered promptly after stopping PEEP in ISO after paralysis of pulmonary vasomotion. These data suggest that lung distension has a direct effect on pulmonary vascular tone in the intact infant lamb.

## SEVERE AIRWAY OBSTRUCTION: AIRWAY AND ALVEOLAR PRESSURES DURING CONTINUOUS POSITIVE PRESSURE BREATHING (CPPB) Shekhar T. Venkataraman, Richard A. Orr, Donna F. Howland, Bradley P. Fuhrman. U of Pgh, C. H. of Pgh, Anesth/CCM and Peds., Pgh. PA

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During CPPB with severe airway obstruction end-expiratory occlusion pressure may exceed applied PEEP (autopeep). Alveolar pressure may then exceed airway pressure throughout expiration. This study examined the relationship of mean airway (PAW) and alveolar (PALV) pressures in the presence of "autopeep".

5 piglets (1-4kg) and 2 lambs (4-5kg) were ventilated with endotracheal tubes obstructed at the hub to an orifice of 1.5 mm. Alveolar pressure was estimated by repeatedly occluding the airway at times in the respiratory cycle that varied from trial to trial. Real time curves were reconstructed using occlusion time, proximal airway pressure and plateau occlusion pressure. PAW and PALV were estimated by integration of real time curves generated for inspiratory times (I) of 25% and 80% at levels of PEEP from 0 to 12 mmHg.

PARAMETER (cc or mmHg)	25% I	80% I
TIDAL VOLUME (cc)	96.0 ± 17.0	96.0 ± 17.0
PEEP (mmHg)	4.5 ± 4.4	5.0 ± 4.3
ADTPEEP-PEEP (mmHg)	0.5 ± 0.5	5.8 ± 1.1
PAW (mmHg)	8.3 ± 4.2	17.5 ± 8.0
PALV (mmHg)	8.1 ± 4.2	17.7 ± 7.9

\* P < .001 80% Vs 25% by ANOVA

25% I: PALV = 0.98 x PAW - 0.08, r = .99

80% I: PALV = 0.98 x PAW - 0.06, r = .99

Long I generated autopeep and, for any PEEP applied, increased both PAW and PALV. PAW remained an excellent predictor of PALV in spite of autopeep.