

**372** MATURATION-RELATED DIFFERENCES IN ADRENERGIC RESPONSES OF CEREBRAL AND MESENTERIC ARTERIES FROM PREMATURE, NEWBORN AND ADULT BABOONS. Myung K. Park, Shigehiro Hayashi, Ron Reif and Thomas J. Kuehl, Univ. of Texas Med. Sch. and Southwest Found. for Res. & Ed., San Antonio, Tx. Responses of cerebral arteries to certain vasoactive agents are known to be different from those of extracerebral arteries. We compared vasoconstrictor response to norepinephrine (NE) and vasodilator response to isoproterenol (ISO) between strips of baboon cerebral (CAs) and mesenteric (MAs) arteries and among premature (0.75 gestation), full term newborn and adult baboons for each artery.

	ED <sub>50</sub> (x10 <sup>-8</sup> M) for NE			Max. relaxation to ISO*		
	CA	MA	MA/CA	CA	MA	CA/MA
Prematures(PM)	3.4	20	5.9	63	65	0.97
Newborns(NB)	6.2	21	3.4	72	61	1.18
Adults(AD)	32.0	26	0.8	10	95	0.11

\*Expressed as % of 10<sup>-4</sup>M papaverine-induced relaxation. N=5-10. The findings indicate (a) Although CAs of PM & NB are much more sensitive to vasoconst. actions of NE than AD, there is no age-related difference in MAs, (b) CAs from PM & NB are more sensitive to vasoconst. actions of NE than MAs, while there is no regional differences in AD, (c) Vasodilation of CAs to ISO is much smaller in AD, whereas that of MAs is slightly greater in AD than in PM & NB, and (d) There is no regional difference in vasodilation to ISO in PM & NB, while vasodilation is much smaller in CAs than MAs in AD. The results show not only maturation-related differences but also regional differences in response to  $\alpha$  and  $\beta$  adrenergic agonists.

**373** COMPARATIVE VASOACTIVE RESPONSES OF PREMATURE, NEWBORN AND ADULT BABOON CEREBRAL ARTERIES TO PROSTAGLANDINS. Myung K. Park, Shigehiro Hayashi, Ron Reif and Thomas J. Kuehl, Univ. of Texas Health Science Center and Southwest Foundation for Res. and Education, San Antonio, Tx.

Prostaglandin (PG) E<sub>1</sub> is used in neonates with certain cyanotic congenital heart defects to maintain patency of the ductus arteriosus, but its effects on cerebral blood flow are not well known. Vasodilator response (expressed as % of 10<sup>-4</sup>M papaverine-induced relaxation) and vasoconstrictor response (as % of 30 mM KCl-induced contraction) to PGs were examined in helical strips of cerebral arteries isolated from premature (0.75 gestation), full term newborn and adult baboons. PGs I<sub>2</sub>, E<sub>1</sub>, E<sub>2</sub> and F<sub>2 $\alpha$</sub>  at low concentrations of 10<sup>-10</sup> to 10<sup>-8</sup>M produced a vasodilation in the arteries from all age groups. Maximum vasodilator responses to PGI<sub>2</sub> were similar between adult and newborn arteries (95-100%). Vasodilator response to PGE<sub>1</sub> was much greater in newborn than adult arteries; adult arteries relaxed to 20±9% (N=8) at 10<sup>-8</sup>M PGE<sub>1</sub> and contracted above the baseline at 10<sup>-6</sup>M, whereas newborn arteries relaxed to 53±7% at 10<sup>-9</sup>M and 74±8% at 10<sup>-8</sup>M (N=7). Similarly greater relaxation was found in newborn than adult arteries with PGE<sub>2</sub> and PGF<sub>2 $\alpha$</sub> . No significant difference was found between premature and newborn arteries in relaxation response to all 4 PGs. PGs E<sub>1</sub>, E<sub>2</sub> and F<sub>2 $\alpha$</sub>  at concentrations of 10<sup>-8</sup>M or greater produced a marked contraction in adult arteries, but small or no contractions in premature and newborn arteries. The results indicate that the cerebral arteries of premature and newborn baboons are more responsive to vasodilator actions, but less responsive to vasoconstrictor actions of PGs than adult arteries.

**374** PROSTAGLANDINS (PG) AND MYOCARDIAL CONTRACTILE FUNCTION IN GROUP B STREPTOCOCCAL (STREP) SHOCK. K.J. Peavy, S.A. Chartrand, H.J. Wiseman, R.C. Boerth and R.D. Olson. U. of S. Ala., Depts. of Ped. and Pharm., Mobile, AL.

The role of PG and myocardial contractile function in STREP shock has not been reported. To evaluate this phenomenon, rabbits were instrumented to measure mean arterial pressure (MAP), pulmonary artery pressure (PAP), cardiac output (CO), heart rate (HR), left ventricular end diastolic pressure (LVEDP) and dP/dt and to calculate total peripheral (TPR), and pulmonary vascular resistance (PVR) before and after STREP (10<sup>10</sup> cells/Kg) infusion. The table shows the effect on the various parameters of indomethacin (IND) pretreatment (4 mg/Kg; GpII) on STREP induced changes from the basal (BASE) values (GpI). \*p<0.05 vs BASE. Values are  $\bar{X}$  ± SEM.

	dP/dt (mmHg/sec)	MAP (mmHg)	CO (ml/min)	PVR	HR(B/min)
GpI (N=10) BASE	4838±250	77±3	190±14	8.3±.9	253±9
STREP	*2358±555	*47±7	*101±22	*23.4±7.5	*216±9
GpII (N=6) BASE	4858±610	78±5	195±20	7.2±.8	252±3
IND	4678±458	75±6	183±22	7.9±1.0	255±7
IND+STREP	4982±339	82±4	212±31	9.5±2.0	246±8

LVEDP and TPR remained unchanged and afterload did not increase in either group after STREP infusion. The table shows that IND (GpII) prevented STREP-induced decreases in dP/dt and HR, and increase in PVR (GpI). Thus, we conclude that: 1) STREP infusion elicits a dramatic fall in myocardial contractility that appears to be an important component of the shock process, and 2) STREP-induced changes in contractility and PVR appear to be PG dependent.

**375** SAFETY OF INTRAVASCULAR TOCOPHEROL IN A RANDOMIZED DOUBLE BLIND TRIAL IN PREMATURE INFANTS. Dale L. Phelps, Arthur Rosenbaum, Rosemary D. Leake, Sherwin Isenberg and Frederick Dorey. UCLA Medical School, Departments of Pediatrics and Ophthalmology, Center for the Health Sciences, Los Angeles and Harbor General Hospital, Torrance, California.

We prospectively studied the potential side effects of parenteral vitamin E or tocopherol (T) while testing its effectiveness in preventing Retinopathy of Prematurity (ROP).

287 infants <1.5 kg or <32 weeks were enrolled in a double blind, randomized trial of initial doses of 20 mg/kg/day free T (or 0.4 cc/kg of excipient placebo, [P]). Plasma levels were measured twice weekly and subsequent doses modified to a goal of 3.0-3.5 mg/dl. Undiluted drug was given over 5-15 min. via umbilical arterial or peripheral IV's. T or P was given PO when oral feeds were well established, and continued until the retinae reached maturity.

Intravascular infusion of T or P caused no immediate or delayed reactions. The median plasma levels were 0.64 ± 0.63 mg/dl, M±SD in the P group, and 2.38 ± 0.82 mg/dl in the T group.

Mortality, (20% P vs 21% T); CNS hemorrhage >grade I, (28% P vs 30% T); hepatomegaly of >2 cm (11% P vs 15% T); proven sepsis occurring after 48 hrs of age (7% P vs 6% T); and proven NEC (4% P vs 4% T) did not differ between the two groups. This sample size permitted 75-95% confidence for an increased incidence of any one side effect of 10 percentage points, alpha = 0.1.

The early intravascular, followed by oral, use of tocopherol appears to be safe as used in this study, providing plasma levels are carefully monitored and kept below 3.5 mg/dl.

**376** INDOMETHACIN (I) ALTERS SYSTEMIC BUT NOT PULMONARY EFFECTS OF BOLUS PROSTAGLANDIN D<sub>2</sub> (PGD<sub>2</sub>) IN NEWBORN LAMBS. J. Phillips, R. Lyrene, M. McDevitt, G. Leslie, and G. Cassady. Univ. of Alabama in Birmingham, Dept. of Peds., Bham, AL.

We previously showed that bolus PGD<sub>2</sub> causes generalized vasoconstriction in normoxic lambs, yet causes unique, simultaneous pulmonary vasodilation and systemic vasoconstriction in hypoxic lambs. These responses were studied before and after I (2µg/kg) in 7 normoxic and hypoxic (F<sub>i</sub>O<sub>2</sub> = 0.13) acutely instrumented newborn lambs to see if the systemic effects were caused by secondary prostanoid release. One and 5µg/kg doses were given over 20 seconds.

	Normox.		Pre-I		Hypox.		Normox.		Pre-I		Hypox.	
	1	5	1	5	1	5	1	5	1	5	1	5
ΔPpa	1.7*	3.0*	-5.4*	-4.0*	-2.2*	-1.4	-8.1*	-7.3*				
ΔPVR	3.1*	4.3*	-7.5*	-5.4*	-2.0	-1.2	-8.7*	-7.9*				
ΔPas	16.0*	18.0*	13.1*	16.7*	0.1	2.6	4.6*	7.1*				
ΔSVR	34.8*	34.7*	16.9*	23.4*	2.3	4.3	1.6	5.1				

Data are means; \* = signif. diff. from 0 at P<0.05 by ANOVA. I suppressed the systemic, but not the pulmonary effects of PGD<sub>2</sub>. I also raised Ppa and Pas in normoxia and Pas in hypoxia (P<0.05), without affecting PVR or SVR. We adjusted for these pre-PGD<sub>2</sub> baseline changes using analysis of covariance which showed the Pas changes to be independent of the covariable. Thus, the increase in Pas and SVR seen with bolus PGD<sub>2</sub> appears to be due to secondary release of a constrictor prostanoid rather than due to a direct effect of PGD<sub>2</sub> itself on the systemic vasculature.

**377** THE ELECTROPHYSIOLOGIC EFFECTS OF INTRAVENOUS VERAPAMIL IN THE INTACT IMMATURE MAMMALIAN HEART. Arthur S. Pickoff, Celia J. Flinn, Sharanjeet Singh, Henry Gelband. University of Miami School of Medicine, Division of Pediatric Cardiology, Miami, Florida.

Verapamil (V) is currently utilized in the therapy of cardiac arrhythmias in the neonate and young infant. However, there is little data concerning the electrophysiologic (EP) effects of V on the intact neonatal myocardium and conducting system. We studied the EP effects of intravenous V in doses of 0.075 mg/kg, 0.15 mg/kg and 0.30 mg/kg in 6 neonatal puppies (3-15 days of age) utilizing His bundle recording and programmed stimulation techniques. Verapamil resulted in a dose dependent slowing of sinus cycle length (37 ± 6%, p < 0.05) but no changes in either %SNT or CSNRT. Verapamil also resulted in a significant prolongation of the atrial ERP in the neonatal heart (32 ± 12%, p 0.30 mg/kg V). Concerning AV conduction, V produced a small increase in the resting AH interval (50.5 ± 2.4 msec, control, vs. 57.3 ± 4.7 msec, p 0.30 mg/kg V) and a dose related increase in the paced cycle length resulting in AV nodal Wenckebach (170 ± 12.8 msec, control, → 246 ± 23 msec, p 0.30 mg/kg V). The ERP and FRP of the neonatal AV node prolonged in a dose dependent fashion (ERP-AVN - +75 ± 19%; FRP +42 ± 14%). Retrograde conduction, present in all, was abolished in 4/6 or significantly prolonged (1/6) by V, particularly at doses >0.15 mg/kg. No changes were observed in ventricular ERP or FRP. Compared with data obtained in the adult dog studied by identical protocol, V has more of an effect on the neonatal sinus node and atrium. Suppression of AV nodal conduction appears comparable in both neonatal and adult subjects.