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VITAMIN E (INJECTABLE) ADMINISTRATION IN THE PREVENTION OF RETINOPATHY OF PREMATURITY: EVALUATION WITH FLUORESCEIN ANGIOGRAPHY AND FUNDUS PHOTOGRAPHY. John S. Curran and S.J. Cantolino. (Intro. by Lewis A. Barness) Univ. of So. Fla., Dept. of Ped., Tampa, Fla.

A prospective study of the administration of Vitamin E Injectable (Roche) was performed to evaluate use in possible prevention of retinopathy of prematurity utilizing the techniques of fundus photography and fluorescein angiography in conjunction with indirect ophthalmoscopy to increase detection of early vascular lesions of retinopathy of prematurity. Study population consists of infants with birthweight <1500 gms, alternate infants given 50 mgm/kg/d x 3 beginning at <6 hours after birth with consent from the parents. Vitamin E levels and results follow:

	Gestation(wks)	Wt.(gms)	VITAMIN E LEVEL(mgm/dl) Cord	2 Wks.	6 Wks.	ROP
TREAT	31.4	1228.1	.43	2.48	1.56	2/10
± S.E.M.	.56	36.1	.07	.17	.17	
CONTROL	30.8	1160.8	.44	.90	1.34	6/10
± S.E.M.	.65	65.1	.05	.14	.19	

Although the sample size is small, fluorescein angiography suggests a possible beneficial effect of Vitamin E injectable administration at birth in decreasing the incidence of retinopathy of prematurity and warrants further study.

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NEONATAL HYPERMAGNESEMIA: EFFECT ON PARATHYROID HORMONE (PTH), TOTAL CALCIUM (Ca) AND IONIZED CALCIUM (iCa) LEVELS. Edward F. Donovan, Jean J. Steichen, Robert Strub, May Chen and Reginald C. Tsang, Univ. of Cincinnati College of Medicine, Department of Pediatrics, Cincinnati, Ohio.

Neoratal magnesium (Mg)-PTH interrelationships have not been examined. Pre-eclamptic mothers (n=22) receiving 3 to 40g $MgSO_4$ during labor and their newborns (birth-72hrs) were studied. Maternal serum Mg rose from 2.1±.09mg/dl (mean±SE) pre-$MgSO_4$ therapy to 4.4±.41 at delivery (1.5 to 14 hrs on therapy). Maternal iCa (Orion SS-20) fell from 4.1±.26mg/dl pre-therapy to 3.8±.3 at delivery (t, p<.05) with no change in maternal PTH (N-terminal assay, 89% of normals detected). Placental vein Mg was 4.8±.38mg/dl; infant Mg fell from 4.2±.20 at 6-12 hrs of age to 3.4±.15 at 24 hrs, 3.1±.15 at 48 hrs and 3±.18 at 72 hrs. Serum PTH was undetectable in 10/14 infants at birth, and in 12/12 at 6-12 hrs. As serum Mg fell <2.5mg/dl, serum PTH became detectable. When compared to controls matched for gestation and birth asphyxia, infants of $MgSO_4$ mothers had a lower proportion of detectable PTH (5/21 vs 12/16 at 24-48 hrs, X^2, p<.005, 4/11 vs 13/16 at 72 hrs, p<.02 and 13/58 vs 33/48 from birth-72 hrs, p<.0005); higher Ca at 24-48 and 72 hrs (10.2±.42mg/dl vs 8.3±.28 and 10.1±.38 vs 7.9±.21, respectively, p<.005); and higher iCa at 24 hrs (3.6±.14 vs 3.1±.20, p<.05). Neonatal hypermagnesemia is associated with depressed neonatal PTH, but higher serum Ca and iCa. We speculate that neonatal hypermagnesemia suppresses parathyroid function, but elevates serum Ca because of its effect at the bone site.

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THE MECHANISM OF ACTION OF DRUGS ON BILIRUBIN BINDING TO ALBUMIN STUDIED BY FLUORESCENCE QUENCHING, John H. Drew and Rhondda Wells (Spon. by Lula O. Lubchenco). Univ of Colo Medical Center, Div of Perinatal Medicine, Denver.

Fluorescence quenching as a technique for studying the binding of bilirubin to albumin was reported to the Society in 1977 by Dr. R. Levine. The technique is sensitive enough to measure the two parameters of binding (affinity and capacity) needed to determine the influence of a drug on the binding of bilirubin to albumin. Hence, fluorescence quenching was used to determine the mechanism of action of drugs on bilirubin binding.

The influence and mechanism of action of diazepam (Valium - Roche), furosemide (Lasix - Hoechst-Roussel), sodium diphenylhydantoin (SDPH - Rachelle) and theophylline (Slo-Phyllin - Dooner) on the binding of bilirubin to albumin were studied. Valium, a drug previously shown to alter the binding of bilirubin to albumin, exerted its influence mainly by affecting the binding affinity, reducing this by 49%. Valium also affected the capacity but to a lesser extent, reducing it by 13%. Lasix also influenced both parameters, reducing the affinity by 56% and the capacity by 23%. SDPH reduced only the affinity; this being reduced by 56%. Slo-Phyllin had no detrimental influence on the binding of bilirubin to albumin.

Since Valium, Lasix and SDPH all reduce the binding parameters of bilirubin to albumin, they all increase the free bilirubin concentration and hence the clinician is warned as to the possible risks of these drugs in jaundiced newborn infants. The influence of other drugs is currently being investigated.

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THE HEMODYNAMIC EFFECTS OF DOBUTAMINE IN CHILDREN. David J. Driscoll. Paul C. Gillette, Desmond F. Duff, Michael R.Nihill, Howard P.Gutgesell, Thomas A.Vargo, Charles E. Mullins, Dan G. McNamara, Baylor College of Medicine, Texas Children's Hospital, Dept.of Pediatrics(Cardiology) Houston

Dobutamine(DB), a relatively new inotropic drug, is useful for augmenting cardiovascular function in adults. There is, however, no information available concerning the effects of DB in children. To determine the hemodynamic effects of DB in children we infused DB into ten children with congenital heart disease during the course of routine cardiac catheterization. We infused DB at two doses (2 and 8µg/kg/min) for ten minutes each. We measured heart rate (HR), cardiac index (CI), systemic (SAP) and pulmonary arterial (PAP), right atrial (RAP), and pulmonary arterial wedge (PWP) blood pressures before and during infusion of DB. Systemic (SVR) and pulmonary (PVR) vascular resistances and stroke index (SI) were calculated.

During infusion of 8µg/kg/min of DB, phasic and mean ($\bar{x}$) SAP increased from 108/60,$\bar{80}$ to 148/74,$\bar{105}$ mm Hg (p<.05); CI increased from 3.6 to 4.6 L/min/m^2 (p<.05); and SI increased from 38 to 48 ml/beat/m^2. These indices also were increased significantly (p<.05) from control during infusion of 2µg/kg/min of DB.

Phasic and mean PAP, PWP, RAP, HR, PVR, and SVR were unchanged from control at both doses of DB. We noted no adverse effects from the drug.

DB appears to be a useful inotropic agent to augment cardiovascular function in children.

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DISPOSITION OF INDOMETHACIN IN PREMATURE INFANTS: M. Evans,R.Bhat,M.Vadepalli,E.Fisher,A.Hastreiter, D. Vidyasagar, Dpt. Peds., ALSM, Uni. Ill. Chicago, Ill.

Successful closure of patent ductus arteriosus(PDA)with Indomethacin(Ind.)has been previously described.Since failure to close PDA with Ind. has also been noted.We examined plasma concentrations of Ind. in 3 premature infants with patent ductus arteriosus(PDA)following oral administration.All had a clinically large PDA and echocardiographic evidence of LA/AO ratio of >1.3. Ind. was administered through nasogastric tube 0.1 mg/kg in one infant and 0.2 mg/kg in 2 infants q.8.h.Blood was obtained by heel stick at 15,30,mins. and 1,2,4,6,8,and 24 hr. intervals. Plasma levels of Ind. was assayed using a gas liquid chromatography method,following derivitization with triethylanilinium hydrochloride.Daily serum levels of creatinine and platelet count were also followed.Results are shown in the table below.

Pt.	G.A. (wks)	B.Wt. (kg)	Echo LA/AO	Dose (mg/kg)	Peak Blood Conc. time µg/ml	Elimination ½ life hrs.
1.	36	1.98	1.67	0.10	2.2(1 hr.)	18
2.	30	1.36	1.57	0.10	0.86(30 min.)	16.5
3a.	33	1.58	1.33	0.20	0.67(1.5)	22
3b.	33	1.58	1.44	0.20	0.78(1.5)	24

Pt. #1 died before the effect of Ind. treatment could be assessed.Pt. #2 had a good response.Pt. #3 had two trials(3a,3b) of Ind. therapy.In this infant LA/AO remained high although there was clinical improvement following Ind.Maximal absorption occurred within 2 hrs. of administration.Marked variation between subjects was observed in peak concentration.Elimination half life was considerably longer than that reported in adults.

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EFFECTS OF ALTERATIONS IN EXTRACELLULAR pH ON CARDIAC MUSCLE OF ADULT AND NEONATAL DOGS. Alan M. Ezrin, Robert J. Myerburg, Arthur L. Bassett, Henry Gelband, Univ. of Miami School of Medicine, Depts. of Pediatrics, Medicine and Pharmacology, Miami, Florida 33152.

Acid-base imbalances may provoke contractile dysfunction in the human newborn. We compared isometric contraction of adult and neonatal myocardium during changes in extracellular pH. Preparations of small ventricular muscle (VM) from 20 adult dogs and 19 neonates (age 1-7 days) were mounted in a muscle chamber and were superfused with Tyrode's solution (36°). Isometric force was monitored. After 1 hour equilibration at control pH (7.35),HCO_3^- concentration was varied while maintaining Na^+ isoosmolarity. Adult VM developed peak active force per cross sectional area (p^a/XSA) of 1.19 ± .26g/mm^2 at pH 7.35 (control). Acidosis (Aci) (pH 6.8-7.1) decreased p^a/XSA 11%, while alkalosis (Alk) (pH 7.5-7.7) increased p^a/XSA 10%. Time to peak active force (TTP) was 0.22 ± 0.01 sec in pH 7.35 and decreased in both Aci and Alk. Rate of force development (dp/dt; 2.55 ± 0.28g/sec) was unaffected by Aci but increased 16% ($p \leq 0.05$)in Alk. The p^a/XSA from RV of neonatal dogs was lower (0.18 ± 0.04g/mm^2) but responded similarly to changes in pH. dp/dt was 1.37 ± 0.19g/sec and in contrast to adult VM decreased 14% ($p \leq 0.05$) in Aci. TTP (0.17 ± 0.02 sec) was decreased by Alk 18% ($p \leq 0.05$) and unaltered by Aci. Our data demonstrates age-related alterations in mechanical responses during changes in extracellular pH. (Sup. by March of Dimes and American Heart Association, Fla. Suncoast Affiliate.)