421 EFFECT OF IN VITRO AND SYSTEMIC VITAMIN C (VC) ON THE NEUTROPHIL FUNCTION IN SICK NEWBORNS (NBs). Kiran Vohra, Abdul J. Khan, Warren Rosenfeld, Vrinda Telang, & Hugh E. Evans. Department of Pediatrics, Interfaith Medical Center, SUNY/Downstate Medical Center, Brooklyn, New York.

VC has been shown to improve chemotaxis in normal newborns. We evaluated its effect in vitro on 11 sick term NBs, including 8 on antibiotics for undocumented sepsis, on day 2-3 of life. WBCs, separated from the blood, were divided into 2 aliquots. One was incubated for 30 min with Hank's solution (HS) containing 20 µg/ml VC and the other with HS alone.

In a separate study 10 different term NBs with suspected sepsis were treated with 4 doses of 100mgs of VC q6h starting on day 2 of life. Blood was drawn before and after VC treatment. Chemotaxis was determined by a modified Boyden's chamber technique. PMNs were deposited on a 3µ millipore filter which divided the chamber into an upper compartment filled with Hank's solution (HS), and lower filled with a mixture containing AB serum, endotoxin and HS. Following incubation and staining a ratio of migrated cells to total cells was determined (CI). In a parallel run with HS on either side the ratio was termed RM.

	VITAMIN C EFFECT					
	IN VITRO		P	IN VIVO		P
CI	Without VC	With VC	Value	Without VC	With VC	Value
Mean (± 1SD)	43 (10)	70 (20)	< 0.005	49 (12)	81 (32)	< 0.007

Mean CI increased 64% following VC incubation and VC therapy. RM remained unchanged in both studies. VC may be a useful adjunct to therapy of NBs with sepsis but more studies are needed.

422 TOLAZOLINE (T) INDUCED OLIGURIA. Robert M. Ward, Mary Ann Wood, Margaret L. Donahue, Jeanne L. Addison. (Spon by M. Jeffrey Maisels) Pa St Univ Coll of Med, M.S. Hershey Med Ctr, Dept Peds, Hershey, PA.

T therapy of neonates has been associated with oliguria and renal failure which has not been studied thoroughly. We have reported T dosing in lambs to rapidly reach steady state (SS) plasma T concentrations. This study evaluated the effects of T at SS upon urine output (UO) and the cardiovascular (CV) system in chronically catheterized, resting lambs. Similar 6-7 hour experiments were conducted on separate days in the same lambs receiving either control saline (C) (n=5) or T (n=6) infusions. Experiments included study periods: 1=control; 2=reach T SS; 3,4,5=hourly studies at T SS; 6=T SS + double fluid intake. Fluid intake was constant at 15.9±2.5ml/kg/hr during study periods 1-5 and not different between all C and T study periods. During C study periods 1-5, UO was constant at 3.34±0.51 (mean ±SD) ml/kg/hr and increased to 10.65±2.46ml/kg/hr during period 6. CV parameters did not change during C, although volume expansion in period 6 increased CI 30% (p=0.51). During T infusion, UO decreased from 3.04±0.86 to 0.61ml/kg/hr (p<.03) and returned to 1.01±0.39ml/kg/hr by three hours. Volume expansion at 33.9±5.9ml/kg/hr increased UO only to 48% of control. When compared to C, T produced the following CV changes: ↑heart rate (p<.01); ↑cardiac index (p<.05); ↓aortic pressure (p<.05); ↓systemic vascular resistance (p<.02). These results indicate T initially inhibits its own elimination, possibly by dilating peripheral vasculature and diverting blood flow from the kidneys. Although volume expansion increased UO, it did not return to the control rates before beginning T infusion.

423 MODIFIED GENTAMICIN (G) DOSING SCHEDULE FOR PRETERM NEONATES. Kristi L. Watterberg, H. William Kelly, John D. Johnson, University of New Mexico School of Medicine, Department of Pediatrics, Albuquerque, N.M.

As part of a study of factors affecting G pharmacokinetics in neonates, we recommended a modified dosing interval for preterm babies: $q12^{o}$ if ≥38 wks gestational age (GA), $q18^{o}$ if 30-37 wks GA, and $q24^{o}$ if <30 wks GA. After 3 doses, 3 G levels were drawn and pharmacokinetics analyzed. To evaluate the effect of the modified dosing schedule, we reviewed a 6 month period prior to the study (72 courses of therapy in 67 patients ≤37 wks) and compared peak and trough levels with calculated peak and trough levels from a 6 month period during the study (71 courses in 65 patients ≤37 wks). Control (C) infants had received G at 8^{o}(2), 12^{o}(56), 18^{o}(13) and 24^{o}(1) intervals. Study (S) infants received G at 8^{o}(2), 12^{o}(16), 18^{o}(34) and 24^{o}(19) intervals. The table shows values that fell outside the accepted therapeutic range.

	G Rx	Peak >10µg/ml	Peak <4µg/ml	Trough >2µg/ml
C 28-32wk	27	0	2(7.4%)	13(48.1%)
C 33-37wk	45	2(4.4%)	4(9.3%)	31(68.9%)
S 28-32wk	35	0	4(11.4%)	2 (5.6%)*
S 33-37wk	36	0	2(5.6%)	6(16.7%)*

(*p<.001 for control vs. study)

Of the 8 study infants with troughs >2µg/ml, only 3 had actually been dosed at the recommended interval. We conclude that this simple modification of the G dosing interval in the preterm neonate significantly decreases the number of elevated troughs without compromising the attainment of therapeutic peak levels.

● 424 INFLUENCE OF TOCOPHEROL VERSUS TOCOPHERYL ACETATE ON LIPID EMULSION ENHANCED LIPID PEROXIDATION IN NEWBORN RABBITS. Jon R. Wispé, Matthew E. Knight, and Robert J. Roberts. Depts. of Pediatrics & Pharmacol., College of Med., Univ. of Iowa Hospitals and Clinics, Iowa City, IA 52242.

We have previously shown that parenteral lipid emulsion increases expired volatile hydrocarbons, a sensitive index of in vivo lipid peroxidation. Newborn rabbit pups were randomly given 100 mg/kg of tocopherol (T), tocopheryl acetate (TA) or vehicle placebo (P) IV. Expired hydrocarbons were quantitated 18-24 hrs after initiation of soy oil emulsion infusion (3-4 g of fat/kg/24 hrs). Tissues were then obtained for analysis of thiobarbituric acid (TBA) reactants, T and TA content and glutathione peroxidase activity (GP). Expired ethane values were 3, 36 and 99 pmol/100 g body wt/min in the T, TA and P groups, respectively. Expired pentane values were 10, 61 and 179 pmol/100 g body wt/min in the T, TA and P groups. Ethane and pentane production was significantly different between groups ($P<0.05$). No differences were found in TBA reactants in blood and lung or lung GP activities. Liver TBA reactants were significantly different ($P<0.05$), 0.22, 0.35 and 0.70 nmol/mg tissue in the T, TA and P groups, respectively. Lung T levels were 79, 17 and 9 µg/g of tissue; and liver T levels were 393, 55 and 3 µg/g of tissue in the T, TA and P pups, respectively.

From these data, we conclude that the extent of in vivo lipid peroxidation is proportional to the T content in tissue. Administration of TA results in significantly lower tissue T content and, therefore, less antioxidant activity against lipid emulsion enhanced lipid peroxidation.

● 425 FUROSEMIDE (F) PREVENTS THE RENAL SIDE EFFECTS OF INDOMETHACIN (I) IN PREMATURE INFANTS WITH PDA AND OLIGURIA. T.F. Yeh, A. Wilks, D. Raval, R.S. Pildes. Cook County Hosp., Dept. of Ped., Univ. of Ill., Chicago, Ill.

Previous study has shown that F may prevent the renal side effects of I in infants with PDA. We, therefore, undertook a study to evaluate this effect in infants with PDA and oliguria in whom I therapy has been considered as contraindicated. Six infants (mean±S.D. B.W. 1.3±0.2 kg; G.A. 32±2 wks, Postn. A. 9.6±2.8 days) who had sign. PDA shunt, congestive heart failure, and oliguria due to pre-renal failure were given I, 0.3 mg/kg, followed immediately by F, 1 mg/kg, iv. Pre-renal failure was defined if U/O was <1 ml/kg/hr and if FENa <2%. Cardiopulmonary status and renal functions were evaluated before and after one dose of I and F.

Renal Function	Before Study	0-24 hr. After Study	P
U/O(ml/kg/hr)	0.7±0.2	2.1±1.0	<0.01
FENa (%)	1.6±0.6	4.5±3.9	<0.05
FECl (%)	3.0±2.3	6.7±5.1	<0.05
FEk (%)	26.7±9.3	48.3±25.0	N.S.
GFR(ml/min/1.73m^2)	2.7±0.7	7.2±2.6	<0.05
Echo:LA/AO	1.54±0.27	1.10±0.29	<0.05
LVEDD	1.34±0.31	1.12±0.29	<0.05

Sign. increases in U/O, FENa, FEcl, and GFR and sign. decreases in LA/AO, LVEDD were seen following I and F therapy. Four infants responded with ductus closure. Of the two whose ductus remained open, their U/O, and FENa also increased. This study indicates that F can prevent further renal dysfunctions expected from I therapy in infants who have PDA and are in pre-renal failure. A combination of I and F therapy can be safely used in these infants.

ENDOCRINOLOGY

426 IS GH SECRETORY STATUS A DETERMINANT OF THE PITUITARY TSH RESPONSE TO TRH. Val Abbassi, Georgetown University Sch.of Med.,Dept. of Pediatrics, Washington,D.C.

A suppressive GH effect on the pituitary TSH responsiveness to TRH and instances of clinical hypothyroidism developing in children receiving GH therapy have been described. To further clarify the mechanism, 17 children with GH deficiency were studied. Eleven children suffered from isolated GH deficiency (IGHD). Six children, in addition, had TSH deficiency attributable to TRH deficiency. Baseline thyroid studies including T_4, RT3U, FT4 and TSH were determined in all and a TRH test (7 ug/kg IV) was performed prior to initiation of GH therapy, 2 weeks post-therapy and subsequently at 3 month intervals. In children with IGHD baseline thyroid studies were normal, and TSH response to TRH was comparable to controls. GH therapy up to 12 months did not alter thyroid function nor the TSH responsiveness to TRH.(Table)

			TSH response			
	FT4	F	30'	60'	90'	120'
Base	1.9±.35	4.0±1.9	13.5±3.9	9.8±3.5	7.5±2.4	5.7±2.3
2 wk	1.9±.38	3.2±.85	13.4±4.1	9.8±2.8	7.6±2.3	6.2±1.7
6 mo	2.0±.36	3.8±1.5	16.4±5.4	12.9±3.6	9.9±3.0	6.7±2.2
12 mo	1.92±.4	4.7±1.8	15.1±4.0	11.0±1.5	9.2±.83	7.6±2.0

Children with GH and TSH deficiencies had variable baseline thyroid levels and hyper-responsiveness to TRH. The data indicates that in IGHD pituitary TRH responsiveness is intact and that GH therapy does not influence this responsiveness. Routine T4 substitution in children on GH therapy therefore, is unwarranted.