359 EFFECT OF HYPERMAGNESEMIA ON NEONATAL FEEDING.

Deborah K. Rasch, Patricia M. Huber, C. Joan Richardson, Charles H. L'Hommidieu. (Spon. by Ben H. Brouhard). University of Texas Medical Branch Hospitals, Department of Pediatrics, Galveston.

Effect of hypermagnesemia on feeding was studied in 3 groups. Group A - hypermagnesemia (HM) infants of magnesium sulfate (MS) treated pre-eclamptic mothers. Cord blood magnesium (CBM) was 4.2 ± 0.7 mg/dl. Group B - non HM infants (CBM 1.5 ± 0.2 mg/dl) of untreated pre-eclamptic mothers. Group C - control infants (CBM 1.6 ± 0.2 mg/dl) of normal non MS treated mothers. Duration and strength of sustained sucking was subjectively evaluated prior to each feeding. Volume of formula consumed at study ages is tabulated as ml per feed ± 1 S.D.

Age	6 hrs.	12 hrs.	24 hrs.	48 hrs.
Group A n = 36	16 ± 14	25 ± 22	33 ± 22	41 ± 20
Group B n = 17	22 ± 10	37 ± 14	48 ± 14	58 ± 16
Group C n = 24	30 ± 11	43 ± 21	46 ± 16	64 ± 17

Volume of formula consumed by HM infants was significantly less ($p < 0.015$) than non HM infants in the first 48 hrs. The difference was due to overall weaker, less sustained sucking in HM infants.

360 EFFECT OF HYPERMAGNESEMIA ON NEONATAL NEUROMUSCULAR FUNCTION (NMF).

Deborah K. Rasch, Patricia M. Huber, C. Joan Richardson, Thomas E. Nelson. (Spon. by Ben H. Brouhard). University of Texas Medical Branch Hospitals, Department of Pediatrics, Galveston.

Effect of hypermagnesemia on NMF was studied in 2 groups. Group A-hypermagnesemic (HM) infants of magnesium sulfate (MS) treated preeclamptic mothers. Cord blood Mg^{++}(CBM) was 4.2±0.7 mg/dl. Group B-control infants of normal non MS treated mothers (CBM 1.5±0.2 mg/dl). Tension(t) generated by thenar muscle concentration in response to ulnar nerve stimulation was measured by recording initial train of 4 (T_4=4 stimuli ½ sec. apart), tetany produced by 50 and 100 Hz stimuli, and post-tetanic T_4. Results are expressed as %fade ($[(t_{initial}-t_{final})/t_{initial}] \times 100$).

	Initial T4		50 Hz Tet.		100 Hz Tet.		Post-Tet.T4	
Group(n)	A(15)	B(17)	A(15)	B(15)	A(14)	B(14)	A(15)	B(16)
Birth	33.5	3.9	4.7	4.6	7.4	17.4	33.9	19.2
	±5.2	±2.4	±6.4	±5.7	±7.6	±12.7	±8	±7.1
12 Hr.	23.4	0.8	0	1.4	1.6	3.2	35.1	6.8
	±8.6	±2.4	±0	±4.8	±4	±7.2	±7.8	±8.3
24 Hr.	8	0.6	0	0	3.6	0	15.6	4.2
	±13.8	±1.9	±0	±0	±10.4	±0	±7.2	±4.1
48 Hr.	6.9	1.3	2.3	0	2.2	0	9.9	5.6
	±8.9	±1.7	±7.5	±0	±7.4	±0	±7.8	±10

Neonatal hypermagnesemia results in significant (values underlined = $p < 0.005$) impairment of NMF during the first 24 hrs. of life.

361 EFFECT OF HYPERMAGNESEMIA ON NEUROLOGIC SECTION OF DUBOWITZ EXAM.

Deborah K. Rasch, Patricia M. Huber, C. Joan Richardson, Charles H. L'Hommidieu. (Spon. by Ben H. Brouhard). University of Texas Medical Branch Hospitals, Department of Pediatrics, Galveston.

To study effect of hypermagnesemia on neurologic estimate of gestational age (EGA), 3 groups of neonates were identified: Group A - hypermagnesemic (HM) infants of magnesium sulfate (MS) treated pre-eclamptic mothers. Cord blood magnesium (CBM) was 4.2 ± 0.7 mg/dl. Group B - non HM infants (CBM 1.5 ± 0.2 mg/dl) of untreated pre-eclamptic mothers. Group C - control infants (CBM 1.6 ± 0.2 mg/dl) of normal, non-MS treated mothers. Serial EGAs were done by method of Dubowitz, et al. Scores from neurologic section of the exam are given as mean ± 1 S.D. EGA is given in weeks.

	Group A n = 36		Group B n = 18		Group C n = 25	
Age	Score	EGA	Score	EGA	Score	EGA
Birth	23.1±3.8	37-39	27.9±3.5	39-40.5	29.6±2.8	40-41.5
12 Hr.	27.7±3.2	39-40.5	31.7±1.7	40-41	31.4±2.3	40.5-42
24 Hr.	30.0±3.7	39-40.5	31.7±1.8	40-41	31.9±2.0	41-42
48 Hr.	31.2±2.5	40.5-42	31.5±2.1	40-41	32.2±1.6	41-42

EGAs of B & C did not significantly vary over 48 hrs. EGAs of A varied as much as 5 weeks. EGA, therefore, is unreliable by this method in HM infants less than 48 hrs. of age.

362 INHIBITION OF MIXED FUNCTION OXIDASES (MFO) BY GROWTH HORMONE (GH) AND BY THE IMMUNOSTIMULANT CORYNEBACTERIUM PARVUM (Cp): EVIDENCE FOR A COMMON MECHANISM.

Geoffrey P. Redmond, Wendy H. Berger and Lester F. Soyka. University of Vermont College of Medicine, Departments of Pharmacology and Pediatrics, Burlington.

Both GH and a variety of immunostimulants have been shown to inhibit MFO activity. We wished to determine whether the action of Cp is mediated by GH and, if not, whether there is evidence of a common mechanism. Cp in a single dose of 20 mg/kg resulted in increased r (rat) GH levels in trunk blood 96 hours later (96±27 vs 24±2 ng/ml; $p<0.05$) and in pituitary glands (136±16 vs 91±8 mcg/mg; $p<0.05$). Frequent sampling studies showed that spontaneous rGH secretion was significantly greater 24 hr after Cp. However, hypophysectomized male and female rats still responded to Cp with significant decreases in aminopyrine-N-demethylase and aniline hydroxylase activities in liver microsomes and with a fall in cytochrome P450 content. In intact animals, rGH 25µg bid for 3 days or Cp 20 mg/kg produced equal depression of MFO function. However, in contrast to hypophysectomy, splenectomy abolished the ability of the animal to depress MFO function in response to Cp.

Conclusions: 1) Cp increases rGH synthesis and secretion, 2) the pituitary is not required for suppression of MFO by Cp, 3) Cp and rGH depress MFO to a similar degree and 4) the spleen is required for the Cp effect on MFO.

363 ALTERED BEHAVIOURAL DEVELOPMENT AFTER EARLY PROPRANOLOL EXPOSURE.

Geoffrey P. Redmond and Edward P. Riley (Spon. by L. F. Soyka). University of Vermont College of Medicine, Departments of Pharmacology and Pediatrics, Burlington and State University of NY., Department of Psychology, Albany.

Studies on the rat indicate that, as suggested by human case reports, early propranolol exposure results in a growth deficit. Brain weight was significantly smaller in suckling rats given daily propranolol 50 mg/kg by gavage starting on day 4. Mean brain weight was 1.36±0.02g vs 1.45±0.01g in vehicle treated controls ($p<0.01$). To determine whether there was a functional deficit accompanying the anatomical one, behavioural studies were carried out when the rats were 50-60 days of age. Propranolol exposed animals required significantly more trials to reach criterion on a passive avoidance task. There was a trend toward decreased head dip response. Rats given propranolol 50 mg/kg but supplemented with triiodothyronine (T3) in a dose of 700 ng/kg performed normally on passive avoidance and were intermediate in head dip between PRO treated rats and vehicle controls.

Conclusion: Early propranolol exposure produces an alteration in behavioural development. T3 supplementation protects against this effect of propranolol.

364 PHARMACOKINETIC EVALUATION OF TRIMETHOPRIM-SULFAMETHOXAZOLE(TMP-SMX) IN PATIENTS WITH CYSTIC FIBROSIS(CF).

Michael D. Reed, Robert C. Stern, Joseph S. Bertino, Carolyn Myers and Jeffrey L. Blumer. Case Western Reserve University, Rainbow Babies and Children's Hospital, Department of Pediatrics, Cleveland, Ohio.

The first dose (FD) and steady state (SS) pharmacokinetics of orally administered TMP-SMX was evaluated in 15 patients with CF. The biodisposition of the TMP and SMX were regulated independently and no fixed ratio of the TMP to SMX was maintained. The FD and SS pharmacokinetic parameters for TMP were determined using a single compartment model. Data are given in the table below. When

	PEAK		$t_{½}$		V_D	Clearance
	Time (hrs.)	Conc. (µg/ml)	α (hrs.)	β (hrs.)	(L/kg)	(ml/min)
FD	2.38±.33	1.83±.12	1.42±.30	4.47±.50	1.28±.11	199±18
SS	1.73±.21	3.57±.31	0.70±.19	6.50±.50	1.55±.20	154±14

the FD and SS data for SMX were similarly analyzed using either a one- or two-compartment model large interindividual differences in biodisposition were observed. At least half the patients were found to have saturable SMX elimination pathways and total SMX absorption was found to increase markedly with continued therapy ($AUC_{SS} > AUC_{FD}$; ~3-fold). These results suggest that the biodisposition of TMP-SMX in patients with CF is markedly different from that observed in unaffected individuals. Because of the independent biodisposition of TMP and SMX and the large interindividual differences in SMX elimination kinetics, the administration of these drugs in CF patients may be more effective as single agents.