312 THE DEVELOPMENT OF ESSENTIAL FATTY ACID (EFA) DEFICIENCY IN THE WEANING RAT. Angela K. Young, Tibor Heim, Robert M. Filler. Dept. Ped. and Surg., Univ. Toronto,Res.Inst.,Hosp. For Sick Children,Toronto,Ont.,Canada.

EFA plays an important role in early human development especially that of the brain. EFA deficiency (EFAD) has frequently been reported in premature infants on parenteral nutrition. An animal model was used to define the kinetics of EFAD in a rapid growing period of lifespan. Male weaning rats (21-days-old) were fed either by a) Purina lab. chow containing 4.5% vegetable oil of which 31.7% was EFA (n=10); or b) EFA-free diet containing 10% hydrogenated coconut oil (n=10). Growth and plasma fatty acid (PFA) composition were assessed bi-weekly up to 15 weeks of age. Two weeks on the EFA-free diet compromised growth and significantly changed plasma lipid profile: decrease in linoleate (37.2±2.5 vs 7.5±0.7 mg/dl;M±SE), arachidonate (17.4±1.9 vs 7.6±0.8) and decosahexenoate (2.0±0.4 vs trace), with concomitant increase in palmitoleate (5.0±0.7 vs 11.7±0.9), oleate (3.9±3.4 vs 63.0±6.0) and 5,8,11-eicosatrienoate (trace vs 12.8±1.4mg/dl). Advancement in EFAD was accompanied by a progressive decrease in plasma oleate indicating an increased demand of 5,8,11-eicosatrienoate. The triene/tetraene ratio increased progressively from 1.7 to 5.9 over the 12-week study period. We conclude: 1) that in spite of the considerable EFA reserves of the weaning rat (≈ 1000 mg/100 g bwt) an EFA-free diet induces rapid biochemical changes in PFA profile and impairs growth, 2) visible symptoms of EFAD can only be observed 10-12 weeks after the commencement of EFA-free diet, and 3) growth retardation induced by EFAD is extremely severe (<0.7 of ideal weight) by the end of the study.

313 EFFECT OF HEPARIN ON SERUM AND TISSUE LIPASES IN THE DEVELOPING RAT. H. Zaidan, A. Gutman, S. Berkow, M. Hamosh and P. Hamosh (Spon. J.W. Scanlon), Georgetown University Medical Center, Dept. of Pediatrics, Washington, DC

The frequent inclusion of heparin in fluids used for total parenteral nutrition in infants prompted an investigation of the ability of heparin to release lipoprotein lipase (LPL) and hepatic lipase (HL) from the endothelial surface into the circulation and of the effect of heparin on tissue stores of lipase in the postnatal period. In rat pups, plasma post heparin lipolytic activity (PHLA) released by I.P. administration of 0.5 U/g body wt was 15% of adult values at birth and increased rapidly to reach 60% on day 10. Repeated doses of heparin (in adult rats, given 0.1 U/g I.V.) at 1 and 4 hr after the initial dose did not affect the maximal response to heparin. In all age groups 80% of PHLA was inhibited by .5 M NaCl, suggesting a mostly non-hepatic origin for the released enzyme. Heart, lung and liver lipase activities of rat pups were not significantly different from controls not given heparin. The pattern of change in tissue enzyme content was different for heart and lung in which LPL activity increased from 10 and 30% to 60 and 100% of adult values between birth and 10 days and for the hepatic enzyme which exceeded adult levels at birth and decreased to 50% of adult values during the latter half of the suckling period (day 10-21). Our results demonstrate that heparin does not cause depletion of tissue lipases in the postnatal period. The parallel increases in LPL content of peripheral tissues and PHLA suggest that in all age groups heparin induced release of LPL into the circulation is proportional to tissue lipolytic activity. (Support NIH Grant HD-15631).

314 SERIAL DETERMINATIONS OF WHOLE BLOOD VISCOSITY (Vn) IN SMALL PRETERM INFANTS (INFS). Ilana W. Zarafu, Elsie Antonio, Richard Inwood (Spon. Franklin C. Behrle) Univ. Medicine & Dentistry: New Jersey Medical School, Newark Beth Israel Medical Center, Dept. of Peds., Newark, N.J. 07112

Fifteen preterm INFS with a mean birth weight (BW) of 1180 gms. (770-2160) and mean gestational age (GA) of 31 wks (28-35) underwent daily Vn and central hematocrit (Hct) determinations from day 1 to day 14 of life. Eight INFS were small for gestation (SGA) and 7 were appropriate(AGA). Vn was measured at shear rates(SR) of 225, 90, 45, 22.5 & 11.25 sec^{-1} on a Wells-Brookfield viscometer. No INFS were hyperviscous; Hcts ranged from 31-64%. Transfusions were given as medically indicated.

The best statistical correlations, which are reported below, were observed at SR 225; progressively less significant correlations were noted at lower SRs. The higher the Hct on day 1, the higher was Vn (r=.6527). SGA INFS (BW 1067gms) had significant elevations of Vn compared to AGA (BW 1280gms) through day 7. Vn also correlated significantly with GA and BW. The lower the BW and GA the higher the Vn through day 7. (See tables below)

Mean Vn at SR 225 sec^{-1}

	Day 1	Day	Day 7	Day 14	
SGA	3.63*	3.59*	3.64**	3.54	
AGA	2.32	2.77	3.14	3.37	*p <0.01
BW ≤1200	3.75*	3.67*	3.61*	3.41	**p <0.05
BW >1200	2.40	2.28	2.99	3.59	
≤ 30	2.62*	2.67*	3.58*	3.59	
> 30	3.82	2.53	3.15	3.27	

315 ADRENAL CATECHOLAMINE(CA)CONTENT IN ASPHYXIATED 10 DAY OLD RAT PUPS. W.P.Zeller,J.Hannigan,C.Menendez, K.Ozog,C.Anderson,L.Witek-Janusek,S.Silberman, and R.M.Hurley. (Spon. by L.E.Gibson) (Supp.R&E #050-15-211) Loyola University,Stritch School of Medicine,Foster G. McGaw Hospital, Departments of Pediatrics,Physiology and Pathology,Maywood, IL.

Since full neuromaturation of the splanchnic adrenomedullary system in the rat pups does not occur until ∿ 10 days post delivery, we investigated the CA adrenal content in response to 6 minutes of asphyxia (A) induced by sealing 2 ten day old pups per bag in lab storage bags at T 39.0°C. Immediately upon removal from the bag, each pup was dispatched and trunk blood was collected for blood gas analysis. Control(CT)pups were likewise dispatched and organs taken. Adrenal glands were taken and immediately processed for dopamine(DA),norepinephrine(NE) and epinephrine (EPI) concentrations by high performance liquid chromatography with electrochemical detection. The experimental animals showed severe respiratory acidosis without hypoxemia and no depletion of adrenal CA.

	A (n = 8)				
pH	pO_2 mmHg	pCO_2	DA(ug/g)	NE	EPI
7.09 ± 0.05*	52 ± 4	78 ± 8*	4.8 ± 1.1	43±10.4	320±51
	CT (n = 8)				
7.39 ± 0.02	47 ± 3	49 ± 2	3.3 ± 0.6	50±10.5	336±64

*p < .005 $\bar{x}$ ± SEM

Respiratory acidosis without hypoxia does not deplete adrenal CA stores in the 10 day old rat pup. Whether this lack of depletion is related to stressor (asphyxia without hypoxemia)and/or neuromedullary maturation, remains to be determined.

DEVELOPMENTAL PHARMACOLOGY

316 COMPUTER ASSISTED DOSAGE FOR INTRA-MUSCULAR GENTAMICIN FOR INFANTS LESS THAN 1500 GRAMS. M. Albert, S. Pedigo, S. Ternullo, A. Napolitano, and B. Kirkpatrick. (Spon. by H. Maurer). Medical College of Virginia, Children's Medical Center, Departments of Pediatrics and Hospital Pharmacy, Richmond, Virginia.

Published guidelines for gentamicin doses based on weight may not be appropriate for low birth weight infants. Utilizing first order pharmacokinetics, a computer assisted program was used based on birth weight and known peak (P) and trough (T) levels when a standard dose of gentamicin of 2.5 mg/kg q 12 hr IM was given. The dose of IM gentamicin and the interval of administration was then calculated by the program. The dose of gentamicin was so accurate that subsequent gentamicin levels were maintained at less than 8mcg/ml (P) and less than 2mcg/ml (T) thereby reducing the chance for renal or oto-toxicity. Sub-theraputic levels of gentamicin did not occur. Our data for IM gentamicin confirm work by Edgren (Pediat. Res 16:A-273, 1982) for IV gentamicin in low birth weight infants.

● 317 DELAYED PLASMA CLEARANCE OF FUROSEMIDE WITH MULTIPLE DOSING IN NEONATES. Jacob V. Aranda, Daniel Sitar, Tomris Turmen, Patrick du Souich. Dev Pharmacol Perinatal Res Unit. McGill Univ-Montreal Child Hosp, Montreal, CANADA

The effect of repeated dosing of IV furosemide (F) on the drug's kinetic profile was evaluated in two groups of neonates; 8 babies with pulmonary edema or fluid overload who received F for the first time (bt wgt 2.3±3 g, gest age 35.0±1.0, postconceptional age 36.6±1 wk) and 7 neonates who received a repeat dose of F, (bt wgt 1.8±0.4, gest age 31.7±2.2, postconceptional age 34.6±2.0 wk), 24-48 hrs after the first dose. Clinical data were not significantly different in between groups. Blood samples for F measured by HPLC were obtained before and at times 1,2,3,6,9,12,24 h after F. Kinetic data were calculated assuming a one compartment open model using areas under the time concentration curve.

KINETIC VARIABLE	FIRST DOSE n=8	REPEAT DOSE n=7	p
Dose (mg/kg)	1.06 ± 0.06	1.00 ± 0.06	NS
C_0 (mg/l)	1.6 ± 0.3	6.3 ± 1.7	<0.02
AUC	16.4 ± 3.2	67.9 ±20.6	<0.02
Kel (h^{-1})	0.102± 0.012	0.157± 0.068	NS
$t_{\frac{1}{2}}$ (h)	7.6 ± 1.0	7.9 ± 1.7	NS
Vd (l/kg)	0.82 ± 0.12	0.20 ± 0.03	<0.0001
Q (ml/kg/h)	78.9 ±11.7	30.2 ±12.4	<0.02

Data show that repeat doses of F leads to a higher plasma concentration (corrected for pre-drug concentration) contracted volume of distribution and decreased plasma clearance. We postulate that the initial dose saturates tissue binding sites leading to higher drug concentrations and decreased plasma clearance with subsequent doses. Frequent repeat doses of F may lead to plasma drug accumulation in the neonate.