

SERUM BILIRUBIN FRACTIONS IN CHOLESTATIC RATS TREATED WITH TIN PROTOPORPHYRIN. Sharon Felber, Philip Rosenthal and Donaby Henton (Spon. by Robert McAllister) Univ. of So. Cal. School of Medicine & Children's Hospital of Los Angeles, Dept. of Pediatrics, LA.

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Tin protoporphyrin (SnP), an inhibitor of heme oxygenase, has been proposed for the treatment of neonatal hyperbilirubinemia. The neonate is physiologically cholestatic, thus normal excretion of SnP and bilirubin (BR) may be impaired. To investigate the effects of SnP on serum BR fractions during cholestasis, we administered a single dose of SnP (100 μmoles/kg) to rats rendered cholestatic by bile duct ligation. Four groups of rats were studied, 1 control group with vehicle injection at time of ligation, and 3 experimental groups, with varying time of SnP injections. Ligation of all rats was at T=0, and sacrifice at T=72 hrs. BR fractions were measured by HPLC. Covalent bound bilirubin protein conjugates (BP) were measured by solvent precipitation.

INJECTION TIME (ligation at T=0)	N	TOTAL BR*	BP*
-24 hrs	6	68±27	2.5±1.9
+24 hrs	6	93±20	4.6±1.2
+48 hrs	5	85±13	7.5±1.5
0 (vehicle)	6	235±104	26.1±10
ANOVA		p<.001	p<.001

* Mean ± SD (μmoles/L)

There was no difference in the percent of total BR contributed by unconjugated and conjugated BR. Conclusions: 1. SnP does not appear to interfere with bilirubin conjugation while suppressing total BR levels. 2. Cholestasis does not inhibit SnP action. 3. The hyperbilirubinemia of cholestasis can be modified by SnP, suggesting clinical relevance.

NON-INVASIVE MEASUREMENT OF THE RATE OF FAT ABSORPTION IN SUCKLING RATS. Carlos A. Flores, Sherry Hing, Michael A. Wells, Otakar Koldovsky. University of Arizona, Depts. of Pediatrics, Biochemistry, and Physiology, Tucson, AZ.

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To characterize the extent to which continuous measurement of ¹⁴C₂ excretion following the oral feeding of ¹⁴C-triolein (¹⁴C-T) would estimate the rate of absorption of triolein by the gastrointestinal tract (GIT), 16 day old suckling rats were fed 1.0 ml/100g body wt. of ¹⁴C-T and the rate of production of expired ¹⁴CO₂ was measured continuously. Pairs of animals were sacrificed at 2, 4, 5, and 6 hrs and absorption rates were calculated by quantitating substrate remaining in the GIT. Comparison of these rates with the cumulative excretion rates of ¹⁴CO₂ revealed a linear relationship with a correlation coefficient of 0.94. In a second experiment, suckling rats were pre-treated with Triton WR1339, a potent inhibitor of lipoprotein lipase, prior to receiving ¹⁴C-T. The rate of intestinal triglyceride (TG) output was determined from the increase in ¹⁴C activity in the blood over 6 hrs. Comparison of the rates of intestinal TG secretion using Triton WR1339 with that determined from measurement of ¹⁴CO₂ excretion revealed a correlation coefficient of 0.96. Additionally triolein absorption rates in suckling animals were noted to be significantly higher than 10 wk old adults as measured by both ¹⁴CO₂ excretion and the rate of disappearance from the GIT. We conclude that rates of TG absorption can be estimated in suckling rats in vivo by the continuous measurement of labeled CO₂ excreted in breath and that these rates are significantly higher in sucklings than in 10 wk old adults.

BREAST MILK JAUNDICE REVISITED: NO ROLE FOR β-GLUCURONIDASE OR UNSTIMULATED LIPASE. Lois M. Freed, David Mosconi, Marcil Hamosh, Lawrence M. Gartner and Paul Hamosh. (Spon. by Pedro A. Joss) Georgetown University Medical Center, Washington, D.C. 20007, and Wylar Children's Hospital, University of Chicago, Chicago, IL 60637.

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To date, the milk factor(s) responsible for breast milk jaundice (BMJ) has not been found. The lipases of human milk, lipoprotein lipase (LPL) and bile salt-stimulated lipase (BSSL), require specific activators, apoprotein CII for LPL and primary bile salts for BSSL. It has been suggested that, in BMJ milks, one or both lipases are active in the absence of activator [unstimulated lipase activity (USL) (*Pediatr Res* 14:1328, 1980)]. More recently, it has been reported that milk β-glucuronidase (β-glu) may be the causative agent (*Lancet* 1:644, 1986). We have reexamined these questions by analyzing β-glu activity and lipase activity [using highly sensitive techniques (*Biophys Acta* 878:209, 1986) for quantitation of stimulated and unstimulated LPL and BSSL activity] in milk samples from 13 mothers of infants with BMJ and 4 mothers of healthy infants. The following results (means and ranges, expressed as μmol free fatty acids/min/ml milk for lipases and modified Sigma units/ml for β-glu) were obtained:

	Specimens	Mothers	β-glu	BSSL	LPL	USL
BMJ	39	13	131 (34-337)	42 (25-66)	0.73 (0-1.8)	trace
Normal	9	4	590 (82-1538)	38 (26-61)	0.07* (0-.32)	trace

*In milks from 15 normal mothers previously studied, LPL range was 0-4.1.

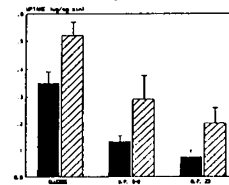
Within-feed variation in milk collection does not effect the level of β-glu, the activity being 100 (48-189), 115 (48-233), and 132 (54-230) units in fore, mid and hind milk, respectively. These data show that the levels of β-glu, BSSL, LPL and USL activity are not higher in BMJ than in normal milks; therefore, a role for these enzymes in the etiology of BMJ is unlikely. (Supported by NIH grant HD 20833.)

THE EFFECT OF THE UNSTIRRED WATER LAYER (UWL) ON GLUCOSE OLIGOMER (GO) ASSIMILATION. John Fyda, Benny Kerzner, Howard R. Sloan, Anton Ailabouni, Constance Seckel and H. Juhling McClung, Dept. of Pediatrics, Ohio State University, Columbus Children's Hospital, Columbus, OH

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GO's must pass through the UWL to be digested by brush border glucoamylase which progressively removes glucose units. In the absence of pancreatic amylase (PA), digestion appears rate-limiting for GO absorption. To assess whether the limited diffusivity of long chain GO's affects their assimilation, we evaluated the impact of thinning the UWL on GO uptake in rabbit jejunum proven free of PA. The tissue was mounted in Dietsch chambers, and the thickness of the UWL was adjusted to 140 or 400 μm by varying the stirring rate of the mucosal buffer. The uptake of three ¹⁴C GO's [glucose (Degree of Polymerization, DP 1), DP 3-8, and DP ^{AVC}23] was assessed at concs of 180, 360, and 720 mg/dl.

RESULTS: Thinning the UWL enhances the uptake of DP ^{AVC}23 > DP 3-8 > DP 1, and this effect is more evident as the GO conc. is increased - See Figure.



CONCLUSION: The barrier that the UWL presents to the assimilation of GO's is substantially greater for long chain GO's.

THE NATURAL HISTORY OF ISCHEMIC HEPATITIS. Jeffery S. Garland, Steven L. Werlin, Medical College of Wisconsin, Children's Hospital of Wisconsin, Milwaukee, Wisconsin.

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Although poor hepatic perfusion from low cardiac output may result in ischemic hepatitis in adults, this syndrome has not previously been described in children. We report 16 children who developed liver dysfunction compatible with ischemic hepatitis. A summary of laboratory findings is presented below.

PEAK LIVER FUNCTION ABNORMALITY

	SGOT (IU/L)	SGPT (IU/L)	T.BILI (mg/dl)	TIME TO SGOT >400	TIME TO SGOT <100
MEAN	1578	911	9.0	20 hrs	7.5 d
RANGE	438-4840	214-4500	1.7-28	6-48 hrs	2-14 d

In children with ischemic hepatitis, the SGOT increased to 10x normal within 12 hours in 8 and peaked at greater than 1000 IU/L in 8/16. Although total bilirubin exceeded 4.0 mg/dl in only 3 children, in those 3 it was very high (12,24,28 mg/dl). SGOT fell below 100 IU/L by 10 days in 8/16. Conditions resulting in ischemic hepatitis included: prolonged seizures 4, cardiac disorders 4, near drowning 3, septic shock 2, hypovolemia 1, SIDS 1, and hypothermia 1. Documented hypotension occurred in 13/16 and required pressor therapy in 9 cases. Hepatomegaly developed in 12 and jaundice in 5. Although 5 children died, no deaths were related to hepatic failure.

CONCLUSION: Ischemic hepatitis follows a characteristic and benign course in children. Resolution of abnormal liver function is rapid.

PULMONARY CLEARANCE OF HELIUM AS A NON-INVASIVE MEASURE OF COLON BLOOD FLOW IN POST-HEMORRHAGIC HYPOTENSION. Dale R. Gerstmann, Feizal Waffarn, (Spon. by Dr. Ira Lott), Dept. of Peds, Wilford Hall USAF Med Ctr, San Antonio, TX and Univ of Calif Irvine, Orange, CA.

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Ischemic bowel disease causes significant morbidity in the neonate. We have shown that pulmonary clearance of helium (CLHe μl/min/kg) reflects hypoxia induced change in colon blood flow. (*Ped Res* 19:1025) This study investigates the effects of acute (12 ml/kg) and incremental (4-28 ml/kg) post-hemorrhagic hypotension in young New Zealand rabbits. The animals were cannulated and connected to a respirator with fixed minute ventilation and an in-line helium mass-spectrometer. Two rabbits had electromagnetic flow probes around their distal abdominal aortae as well. Following a 30 min. stabilization, 10 ml/kg helium was injected rectally and CLHe and aortic blood pressure (ABP) were continuously monitored for 90 mins. Group I (n=6) was the control group; Group II (n=5) had 12 ml/kg of acute blood loss followed by total reinfusion and Group III (n=8) had incremental (4 ml/kg) blood loss (total 28 ml/kg over 30 mins.) without reinfusion. In Grps II and III 12 ml/kg blood loss caused a 51% and 58% fall in mean ABP with a simultaneous and proportionate fall in CLHe which were highly correlated (p<.001). Reinfusion (Grp II) caused an initial parallel increase in mean ABP and CLHe followed by a disproportionate increase in CLHe indicating rebound hyperemia. In Grp III beyond 12 ml/kg of hemorrhage the ABP and aortic blood flow stabilized while CLHe continued to fall. This could represent the critical point at which intestinal blood flow is diverted to vital organs. Conclusion: pulmonary CLHe changes predictably and simultaneously with changes in ABP and could provide a non-invasive measure of colon blood flow in the neonate.