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HYPOGLYCEMIA, HYPOALANINEMIA, AND KETONEMIA IN THE FASTED POSTNATAL RAT PUP: LONG-TERM CONSEQUENCES OF INTRAUTERINE GROWTH RETARDATION. Edward S. Ogata, Mary E. Bussey, Sandra Finley, Andrew LaBarbera, Northwestern University Medical School, Departments of Pediatrics, OB/Gyn, and Physiology, Chicago.

To determine the long-term metabolic consequences of intra-uterine growth retardation, we fasted rat pups who were growth retarded due to bilateral maternal uterine artery ligation (L) at 3, 4, and 5 weeks of age. Pups of sham (S) and nonoperated (N) mothers were controls since birthweight differed significantly between groups. L pups had significantly reduced body and carcass mass throughout the 5 weeks. At 3 weeks, 48 hours fast reduced plasma glucose in L pups (L 78.4±5; S 89±4; N 88±2 mg/dl; $p < .01$). Insulin decreased (L 12.2±.2; S 25.9±.5; N 22.5±.2 μ U/ml; $p < .01$) and glucagon increased (L 862±100; S 538±65; N 539±96 pg/ml; $p < .01$) appropriately. Hepatic phosphoenolpyruvate carboxykinase activity (L .55±.02; S .59±.02; N .58±.02 μ moles PEP/g liver/min) and glycogen content did not differ. L pups did have significantly reduced plasma alanine (L .14±.02; S .22±.02; N .22±.02 μ moles/ml; $p < .05$) and elevated betahydroxybutyrate (L 1.178±.90; S .799±.090; N .812±.094 μ moles/ml; $p < .01$). No difference in response to fasting occurred at 4 or 5 weeks. Limited gluconeogenic substrate availability may be responsible for hypoglycemia in the fasted 3 week L pup. This may represent a mechanism to spare already limited carcass protein. These metabolic alterations resemble ketotic hypoglycemia of infancy, a disorder often associated with intrauterine growth retardation.

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A COMPARISON OF 15 N-URINARY END-PRODUCTS IN ASSESSING THE EFFECT OF HUMAN MILK ON THE PROTEIN METABOLISM OF NEONATES. P. Pencharz, L. Farri, R. Clarke, A. Papageorgiou. The Hospital for Sick Children, Toronto; The Jewish General Hospital, Montreal, Canada.

We have previously reported that rates of protein turnover in neonates fed human milk were approximately 40% higher than those fed formula. Our conclusions were based on urinary 15 N-urea enrichment. Subsequently the question has been raised as to which urinary nitrogenous end-product was most suitable; i.e. urea, ammonia or a combination of the two. In the present study we compare results obtained for whole body protein turnover (g/kg/d) derived from the 3 different end-products in 30 AGA preterm neonates (BW1500-2000g) fed a whey-predominant (A) or casein predominant (B) formula or pooled human milk at 120 kcal/kg/d.

End-Product	Formula A	Formula B	Human Milk
Urea	14.5±1.0	12.8±1.0	18.7±1.5
Ammonia	9.4±0.3	8.8±0.4	8.9±0.2
Urine	14.0±1.0	12.6±0.6	19.7±1.4

Values for the ammonia end-product are significantly lower ($p < .01$) than either of the other 2 end-products. No differences in turnover rate were seen due to diet from the ammonia end-product results. However in the whole urine results representing combined nitrogen excretion from the metabolic amino nitrogen pool, higher rates of turnover in breastfed infants are evident ($p < .01$). We conclude that 1) ammonia nitrogen may not be a suitable end-product to use in studies of nitrogen metabolism of neonates; 2) neonates fed human milk have an increased rate of protein turnover compared with formula fed infants.

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EFFECT OF ENERGY INTAKE AND ENERGY EXPENDITURE ON RECOVERY OF RESPIRATORY $^{13}\text{CO}_2$ IN NEONATES. J. Van Aerde, P. Sauer, U. Canagarayar, J. Beesley, J. Renner, D. Wesson, P. Swyer, P. Pencharz. Dept. Paeds. & Surg., Univ. of Toronto, Res. Inst., The Hospital for Sick Children, Toronto, Canada.

The use of $^{13}\text{CO}_2$ breath tests to measure substrate oxidation in neonates is increasing as it is non-invasive. No standards are available for ^{13}C retention in the bicarbonate pool in the neonate nor for effects of birthweight, gestational age, energy or protein intake. A primed constant infusion of $\text{NaH}^{13}\text{CO}_3$ over 4 h was used with open circuit indirect calorimetry. ^{13}C recovery was measured in 15 neonates (gestational age 28-39wk; postnatal age 2-52d) on varying amounts of IV feeding. Recovery of tracer in breath ranged from 69.6-83.5%. This was significantly correlated with 1) energy intake (37-114kcal/kg/d); 2) metabolic rate (34.6-56.1kcal/kg/d); 3) VCO_2 (4.86-7.43ml/kg/min) as shown below.

Correlation coefficient	Energy Intake	Metabolic Rate	VCO_2
	0.74	0.64	0.65
p	<0.005	<0.02	<0.01

There was no correlation with protein or fat intake. It was concluded that a higher energy intake and thus a higher metabolic rate induces higher turnover of the bicarbonate pool with more tracer recovery. The ^{13}C excretion most significantly correlated with energy intake ($y = 64.2 + 0.1667\text{EI}$). This equation can be used to calculate the correction factor when doing constant infusion substrate oxidation studies with a ^{13}C label.

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GLYCEMIC RECOVERY IN IV INFUSED DIABETICS RECEIVING MEALS OF DIFFERENT SIZES. K. Perlman, C. Levy-Marchal, B. Zinman and A.M. Albisser (sponsored by D. Fraser), Hosp. for Sick Child., Dept. of Surg., Toronto, Canada.

Increased dietary flexibility is said to be possible in Type I diabetics treated with continuous infusions of insulin. To explore this, we studied the glycemic responses to meals of varying size in 6 ambulatory Type I diabetics aged 16-30y, treated for 3 wk periods with a portable system of IV insulin infusion. During wk 1 the patient's usual (Regular) diet was provided and an waveform of insulin infusion was defined for each meal. This resulted in diurnal normoglycemia. Subsequently, Small (50% of calories) and Large (150%) versions of the R breakfast were provided without change in the insulin infusion waveforms. R lunch was always provided and the resulting glycemic response was studied until dinner.

	FPG	Δ PG	2h pc B	ac L	Δ PG	2h pc L	ac D
R	72±7	40±8	75±8	77±7	29±7	81±8	81±6
S	85±8	30±5	49±8*	51±3**	36±5	75±10	86±7
L	68±9	59±8	120±8***	132±8***	16±8	105±8	83±7

* $p < .05$, ** $p < .01$, *** $p < .001$; B = breakfast, L = lunch, D = dinner

Neither the mean FPG levels before the breakfast of different sizes nor the mean PG rise following the meal were significantly different. However, before lunch the PG level was significantly different when the S or L breakfast was provided instead of the R one. 2h later, during which time the usual augmented insulin infusion was provided, there was no longer any significant difference. Notably before dinner, the PG level was similar for all 3 meal sizes. We conclude that in Type I diabetics managed with preprogrammed IV insulin infusion, variations in caloric intake lead to changes in the time course of the glucose profile which are transient in nature and without sustained adverse glycemic consequence.

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KINETIC ABNORMALITIES OF CARBAMYL PHOSPHATE SYNTHETASE (CPS-I) IN A CASE OF CONGENITAL HYPERAMMONEMIA. Ijaz A. Qureshi, Jacques Letarte, René Ouellet, and Bernard Lemieux. Centre de Recherche pédiatrique, Hôpital Ste-Justine, Montréal, and Université de Sherbrooke, Qué.

Late onset hyperammonemia caused by partial CPS-I deficiency is a rare disorder. We report a 2½ month old girl who was symptom-free till 9 weeks of age. She was hospitalized for vomiting and metabolic acidosis. Plasma aminogram showed increased alanine, with a higher excretion of alanine, proline, serine and threonine. Urinary orotate was normal. Plasma NH_3 on the third day was 96 $\mu\text{mol/l}$. The child died due to complications of an intestinal hemorrhage. Brain pathology was indicative of delayed myelination and proliferation of astrocytes. A post-mortem liver sample showed normal ornithine transcarbamylase, argininosuccinate lyase, and arginase. CPS-I measured by a direct colorimetric method (Piersen and Brien, J. Biol Chem 255:7891,1980) showed a partial deficiency (10-25 % of normal controls). Mancini radial immunodiffusion with rabbit antiserum against human CPS-I showed 10 % of normal cross-reacting material. A study of pH dependence using a triethanolamine buffer gave a flat curve over the pH range 7.0-9.0. Two normal controls had a pH optimum of 7.8, with 70 % activity at pH 9.0. Apparent Km HCO_3^- (5.6 mM) was normal (controls: 6.0-9.5). Km NH_4^+ (0.73 mM) was abnormally increased (normal range: 0.24-0.51).

Kinetic and immunochemical characterization of CPS-I mutants is important to understand variations in the clinical expression of congenital hyperammonemia in children. The above work is a preliminary step in defining the pathology of this rare syndrome.

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ACANTHOSIS NIGRICANS, OBESITY, INSULIN RESISTANCE AND HYPERANDROGENEMIA: NATURAL HISTORY AND PEDIATRIC PERSPECTIVE GE Richards, A Cavallo, WJ Meyer, EJ Peters, CA Stuart and MJ Prince University of Texas Medical Branch, Departments of Pediatrics and Medicine, Galveston, Texas.

We evaluated 10 girls, ages 5 to 18 years, with acanthosis nigricans and obesity to determine the magnitude of their insulin resistance and hyperandrogenemia. Five patients had a positive family history for this disorder. Obesity was the first physical sign in all patients followed by acanthosis nigricans. Mean weight was 5.52±2.24 SD above the mean for age at the time of study. Of 7 postmenarchal patients, 6 had oligo- or amenorrhea and 6 had hirsutism. None was clinically diabetic.

Plasma DHEA and androstenedione were normal in all patients. Plasma testosterone was normal in all the premenarchal girls but >50 ng/dl in postmenarchal patients (Table). 2 postmenarchal patients had normal testosterone premenarchally. Polycystic ovaries were not demonstrable by ultrasound in any patient.

All patients had insulin resistance (Table) which correlated with a qualitative scoring of acanthosis nigricans.

	Patients	Controls	P
Fasting insulin ($\mu\text{U/ml}$)	49±21	5.3±0.4	<.001
Insulin area ($\mu\text{U/mT.hr}$)	476±360	74±26	<.001
Glucose disappearance (%/min)	2.5±1.3	6.5±1.3	<.001
Testosterone ng/dl	117±45	28±5	<.001

We conclude that this is a recognizable syndrome in pediatrics with onset of obesity, acanthosis nigricans and insulin resistance before puberty, followed after menarche by hyperandrogenemia, hirsutism and menstrual irregularities.