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SHIGA-LIKE TOXIN (SLT) ASSOCIATED HEMOLYTIC-UREMIC SYNDROME (HUS), A 4-YEARS PROSPECTIVE STUDY.

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Patients with classical HUS (n=22; median age 2;2 yrs) were prospectively studied at our institution since 1986. SLT-association was established by cytotoxicity assays of fecal filtrates, bacterial isolation or colony-blot-hybridization with SLT-specific DNA probes. Serial serum samples from 12 pts and appropriate controls were studied for SLT I and II neutralizing antibodies (NAB) and for hemagglutinating antibodies (HA) using erythocytes coated with purified LPS from E.coli 0157:H7 and other serovars.

SLT association was demonstrated in 13/22 children (59%); E.coli isolates (n=6 pts) included serogroups 026, 055, 0111 and 0157; fecal SLT alone was present in 7 additional cases. 4 pts developed rising NAB-titers against SLT I or II; 9 pts (75%) presented with high LPS-0157-HA at the time of the diagnosis of HUS that rapidly declined during convalescence.

Thus in Northern Germany an association of the classical HUS with in-vivo SLT production has been confirmed. Detection of LPS-0157-AB appears to be a new, valuable serological marker for this subgroup of HUS. Further studies are needed to elucidate a possible protective or pathogenic role of SLT- and LPS-specific AB.

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NITROGEN AND FAT DEPOSITION IN PRETERM INFANTS FED A FORMULA WITH 5 OR 40% MEDIUM-CHAIN TRIGLYCERIDES(MCT).

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Formulas specially designed for preterm infants contain up to 50% MCT. The effects of MCT(C8 and C10) on growth and composition of weight gain were studied in infants receiving formula (Nutricia, Holland) with 5% or 40% of fat as MCT, providing 12 g carbohydrates-, 3.3 g protein- and 6.8 g fat per kg•day. 72 hr balance studies were performed at 4 weeks of age. Simultaneously, 6 hr periods of indirect calorimetry were performed to measure substrate oxidation. Nitrogen and fat deposition was calculated from intake, losses and oxidation. As mean ± 1sd:

	40%MCT(n=15)	5%MCT(n=12)		p
Birthweight	1129±218	1271±165	grams	NS
Gestational age	31±1.9	32±1.8	weeks	NS
Nitrogen stools	59±22	80±38	mg/kg•d	NS
Nitrogen urine	85±23	82±24	mg/kg•d	NS
Nitrogen deposition	381±34	372±45	mg/kg•d	NS
Fat stools	0.87±0.19	1.5±0.60	g/kg•d	<0.005
Fat oxidation	1.6±.74	2.0±0.78	g/kg•d	NS
Fat deposition	4.3±0.71	3.2±0.91	g/kg•d	<0.01
Weight gain	16.6±2.4	16.1±3.2	g/kg•d	NS
%protein of wt gain	15±2.6	15±4.4	g/kg•d	NS
%fat of wt gain	26±4.0	21±6.1	g/kg•d	<0.005

Conclusions: 1 In stable, growing preterm infants fed 120 kcal/kg•d, addition of MCT to the feeding results in slightly better fat absorption. 2 However, this does not promote weight gain or nitrogen retention but only increases fat deposition.

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CALCIUM(Ca) AND PHOSPHATE(P) METABOLISM IN PRETERM INFANTS ON A FORMULA WITH 5 OR 40% MEDIUM-CHAIN TRIGLYCERIDES(MCT).

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Formulas specially designed for preterm infants contain up to 50% MCT because of their almost complete absorption. The effects of MCT(C8 and C10) on mineral absorption were studied in infants receiving formula (Nutricia,Holland) with 5%(LCT group) or 40%(MCT group) of fat as MCT, providing 80 mg P-, 152 mg Ca- and 120 kcal/kg•d, + 600 IU/day vit D. 72 hr balance studies were performed at 4 weeks of age. Values:mean ± 1sd or median with interquartile range. Plasma levels (MCT vs LCT) of Ca(2.4±0.1 vs 2.4±0.1 mmol/L), P(2.2±0.3 vs 2.3±0.2 mmol/L) and Alkaline Phosphatase (273±74 vs 295±43 IU/L) were in the normal range.

	MCT(n=15)	LCT(n=13)		p
Birthweight	1129±218	1290±172	grams	NS
Gestational age	31±1.9	32±1.7	weeks	NS
Ca % absorption	78 (72-81)	68 (61-71)	percent	<0.005
Ca urine	1.6 (0.65-2.4)	0.92 (0.43-1.3)	mg/kg•d	NS
Ca retention	118 (109-121)	102 (92-107)	mg/kg•d	<0.005
P % absorption	93 (92-95)	93 (92-95)	percent	NS
P urine	3.9 (0.85-7.1)	12 (9.0-15)	mg/kg•d	<0.001
P retention	69 (65-74)	62 (60-64)	mg/kg•d	<0.005
PTH	2.1 (1.1-5.0)	4.7 (4.0-6.7)	pmol/L	<0.01

Conclusions: 1 Both formulas show satisfactory calcium and phosphate retention, with normal plasma levels. 2 Calcium absorption, but not phosphate absorption was lower with the LCT formula. 3 The elevation of PTH and of urinary P excretion suggest that in preterm LCT formula, Ca/P ratio should be slightly higher than 2:1.

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VARIATION OF ERYTHROPOIETIN LEVELS IN CHILDREN WITH CHRONIC RENAL FAILURE:DEFECT OF DIRECT HEMATOLOGIC COMPENSATION IN RENAL ANEMIA

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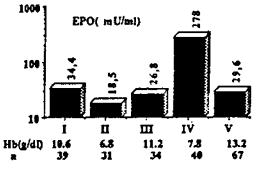
Erythropoietin (EPO) ,the primary humoral regulator of erythropoiesis,an indicator of direct hematologic compensation in anemia,increases with decreasing hemoglobin levels.Material and Method: To evaluate deficient EPO production or the lack of a regulatory feedback mechanism between EPO and hemoglobin (Hb), we obtained EPO data with the IBL-erythropoietin ELISA and hematologic parameters in 144 children (aged 1 -19 yrs) with different anemias.Of these anemic (Hb<12 g/dl) patients 39 were recieving conservative treatment (I),31 on regular dialysis therapy (II), 34 after transplantation (III);variation of EPO concentration in children with these various stages of chronic renal failure (CRF) were compared to 40 controls with nonrenal anemia(IV)and healthy controls (V).Results (figure): a relative EPO deficiency could be detected in I and less after renal transplantation , an absolute deficiency was found on regular dialysis.An inverse linear correlation between EPO levels and hemoglobin in IV occured, however in II the rise of EPO was insufficient compared to IV.In our study we could demonstrate successfully a feedback mechanism between EPO and oxygen supply (low hemoglobin).



Conclusion:The interrelationships between EPO and Hb in anemicchildren on regular dialysis indicates an EPO deficiency and lack of a regulatory feedback mechanism due to CRF, possibly an inhibition of erythropoiesis by uremic toxins.We emphasize renal anemia could be correct successfully with small side effects only by substitution of recombinant human erythropoietin.

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ACCELERATION OF THE SWITCH FROM FETAL TO ADULT HAEMOGLOBIN SYNTHESIS BY EXTRAUTERINE LIFE IN HUMAN NEWBORN INFANTS.

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Synthesis of human haemoglobin is directed by α-, β-, δ-, $^{Gly}\gamma$- and $^{Ala}\gamma$-genes. The switch from fetal to adult erythropoiesis includes a genetically controlled suppression of the γ- and activation of the β- and δ-chain synthesis. The two γ-genes are not equally inactivated. In animals external influences on the switch could be demonstrated, but no influence of extrauterine (EU) life on the switch in human newborns could be clearly demonstrated. The long half life of red cells hampers the detection of subtle influences on the switch by comparing the concentrations of HbA, HbF and HbA_2. We studied therefor the de-novo synthesis of α-, β-, $^{Ala}\gamma$- and $^{Gly}\gamma$ chains by measuring the incorporation of ^{3}H-Leucine into reticulocytes and subsequent separation of the globin chains by HPLC. 228 single measurements were obtained from 88 newborns (gestational age 26.3 to 42.1 weeks) at the age of 0 to 116 days; 16 babies were studied longitudinally. The results show that the switch γ-->β is governed by the biological age (BA = intrauterine + EU age). A significant acceleration of the switch by EU life could be demonstrated: 1.The BA when 16 babies reached 50% (33%) of the full switch was not constant but correlated with GA: $p<0.01$ ($p<0.05$). 2. When 31 babies were studied at a BA of 40 to 43 weeks, a significant ($p<0.02$) acceleration of the switch was found in those with an EU age of 6 to 7 weeks (47%±21%, n=14) when compared to babies of 1 week or less of EU age (37%±25%, n=14). No comparable changes of the $^{Ala}\gamma/^{Gly}\gamma$-pattern was observed during the observation time of 26 to 43 weeks. Conclusion: γ-->β-switch is accelerated by factors of EU life.Inactivation pattern of $^{Ala}\gamma/^{Gly}\gamma$ is not concerted with the γ-->β-switch.

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SCREENING FOR ALPHA-1 ANTITRYPSIN DEFICIENCY IN NEWBORN INFANTS IN SPAIN

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Alpha-1 antitrypsin (AAT) deficiency is an hereditary metabolic disorder which predisposes affected individuals to juvenile liver disease and to pulmonary emphysema towards the third or fourth decade of life. Since prevention and treatment of this pulmonary complication is at present perfectly feasible, we have carried out a pilot study of neonatal screening for AAT deficiency in order to determine the incidence of this deficiency in Spain and to evaluate the parents' reactions on being told of this metabolic disorder .

Fifteen thousand four hundred spanish newborn infants were screened for AAT deficiency. The study was carried out using the eluate from dried blood samples provided by the Cantabria University and the Basque Country Health Service Units for the detection of metabolic disorders. The screening test was based on a semiquantitative electroimmunoassay for AAT together with transferrin . For all cases suspected of AAT deficiency, the Pi phenotype was determined.

With the screening test, 58 suspect cases were detected. Of these, the phenotype study showed 32 AAT deficient cases (8 Pi Z and 24 Pi SZ) representing a global incidence of 2.08±0.72 per thousand. In 4 Pi Z cases there was clinical and laboratory evidence of liver disease. The parents of the AAT-deficient children were informed of the potencially harmfull effect of tobacco smoke on the child. Their reaction towards this information was positive.

Bearing in mind the high incidence of AAT-deficiency, and the existing preventive and therapeutic measures for pulmonary emphysema in AAT-deficient cases, mass-screening for this deficiency may be advisable. This screening could be considerably facilitated by recently developed genome analysis techniques.