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Increased need for L-cysteine in hereditary tyrosinemia. A 7-month old girl with the acute type of hereditary tyrosinemia excreted in addition to the traditional tyrosine metabolites also considerable quantities of succinylacetone in the urine. She has successfully been treated with a low tyrosine/low phenylalanine diet supplying 1.14 g/kg/day of protein. The concentrations of plasma amino acids, intra-erythrocytic glutathione, free amino acids and urinary organic acids have been followed during therapy. A low plasma cystine and erythrocytic glutathione indicated the need for supplementary cysteine which was given in a dose of 90 mg/kg/day. This increased the glutathione concentration, although plasma cystine remained low. During this study the physical growth was normal. A test intake of 750 mg L-cysteine was followed by a 10-fold increase in the plasma concentration of cystine within 105 minutes. Glutathione increased from 0.59 to 1.44 determined as  $\mu\text{mol/g}$  erythrocytes. Our findings indicate an insufficient cysteine level in hereditary tyrosinemia. A decreased synthesis from methionine and/or an increased removal of SH-compounds by fixation to toxic metabolites are possible explanations.

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Pharmacokinetic studies of theophylline in young children with asthma.

The therapeutic effect of theophylline treatment in children with obstructive lung disease is often unpredictable. One reason to that may be inter-individual differences in the rate of elimination of theophylline in children. Studies in theophylline kinetics are missing in young children. The purpose with the present study has therefore been to determine the rate and degree of absorption as well as distribution and elimination rates of theophylline in children, 2 months to 4 years of age, with obstructive pulmonary disease. Theophylline was administered in a single dose i.v. to 6 children (5-6 mg/kg) and to 23 children via rectal suppositories (Oxyphyllin<sup>®</sup>, 3.8-14.6 mg/kg) and to 9 children via rectal enema (4.1-9.2 mg/kg). Capillary blood samples were analyzed with gas liquid chromatography. Administration of theophylline in suppositories resulted in low and varying concentrations. The bioavailability was from 8 to 100%. The individual variations in absorption rate were greater than in elimination rate. The rectal enema were almost completely absorbed. The pharmacokinetic data after i.v. administration equal those obtained by others in adults and older children. Rectal treatment should be done using enema. After an initial dose of 8.0 mg/kg, theophylline is to be given 4 times daily (6.0 mg/kg) in order to obtain constant therapeutic plasma levels. Due to the inter-individual differences in absorption and elimination and the narrow therapeutic range it is recommended that theophylline treatment is monitored by plasma concentration assays.

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Salivary levels of phenytoin (ph) and primidone (pr) in epileptic children.

To test the value of measuring salivary levels to predict serum levels in anticonvulsive treated children, serum ph and pr levels were compared to salivary levels before and after stimulation of salivary flow with chewing gum. The drug levels were measured by an enzyme immunoassay (EMIT). A high linear correlation ( $r > .90$ ) between serum and saliva ph levels was found. The saliva/serum ratio was independent of serum levels in the range 0.4 to 16mg/l averaging 0.1 and was not significantly influenced by the mode of saliva sampling. When serum ph levels exceeded 16-18mg/l, a slight but significant increase of the saliva/serum ratio was seen. Salivary pr levels were markedly dependent on the procedure of saliva sampling. In non-stimulated saliva pr levels averaged 114% of the serum levels, and decreased significantly, to 70% ( $p < .01$ ), while salivary flow was stimulated. Pr levels in non-stimulated and in stimulated saliva, respectively, were closely correlated to serum levels ( $r > .90$ ). The saliva/serum ratios were independent of serum pr levels in the range 1 to 15mg/l. The increase of the saliva/serum ratio of ph at high serum ph levels and the marked influence of the procedure of saliva sampling on salivary pr levels have been considered, when drug monitoring is performed in saliva samples.

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Riboflavin and phototherapy in Gunn rats.

Riboflavin enhances photodegradation of bilirubin and might improve the efficiency of phototherapy in hyperbilirubinaemic newborns. Since flavins must be regarded as active photosensitizers, the problem of side effects arises. Therefore, we investigated in Gunn rats dose-response-relationships and side effects. The rats were injected with different doses (from 10 mg/kg up to 200 mg/kg) of the flavin mononucleotide riboflavin-5'-phosphate (r-ph) and illuminated with different effective irradiances (0.3-4.5 mW/cm<sup>2</sup>). During the first hours after the flavin injection serum bilirubin decline was enhanced in relation to the light- and the r-ph-doses. Histochemical investigations of the Purkinje cells in the cerebellum revealed a significant protection from kernicterus by phototherapy with the high irradiances but no distinct influence of r-ph. Beside reversible inflammatory skin reactions which occurred with high r-ph and medium light doses, massive phototoxic reactions (i.e. large vesicles and necroses) developed on paws, tails and ears when the highest irradiance was used and as an adjunct 50-200 mg/kg r-ph.

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ESTIMATION OF SERUM 25-OHD IN FULL-TERM AND PREMATURE INFANTS.

Serum 25-OHD, serum calcium (Ca) and serum phosphorus (P) were measured in 40 full-term infants, 25 prematures and 39 mothers during 2 periods of the year. Mean values of serum 25-OHD in full-term and premature infants as well as in the mothers were found significantly higher during "summer" period (13.4 ng/ml in full-term, 14.5 ng/ml in prematures and 17.2 ng/ml in mothers) in comparison with the mean values during the "winter" period (full-term 7.6 ng/ml, prematures 5.7 ng/ml, and mothers 6.6 ng/ml). A weak linear correlation ( $p = 0.05$ ) was found between serum levels of 25-OHD in newborns and their mothers. In 10% of the newborns the serum values of 25-OHD were 2 to 4 times higher than the respective values of their mothers. Serum Ca in full-term and premature infants was independent of the values of serum 25-OHD and was related only to the duration of gestation. Serum P in full-term infants was significantly higher (6.7 mg/dl) during the "winter" period in comparison with the mean values (5.6 mg/dl) during "summer/period". Normal levels of serum 25-OHD in full-term babies could prevent neonatal tetany by decreasing serum P which maintains the Ca/P ratio close to normal limits (Ca/P=1.6). Further studies are needed to confirm if the addition of 1 $\alpha$ -25(OH)<sub>2</sub>D<sub>3</sub> to the milk could prevent neonatal hypocalcaemia in premature babies.

**18** L. SANN, L. DAVID, G. BARRIER and P. BALMÉSSAT. Service de Neonatologie, INSERM U34, and Laboratoire de Biologie, Hôpital Debrousse, Lyon, France. Calcium (Ca) Phosphorus (P), immunoreactive parathyroid hormone (iPTH) and calcitonin (iCT) concentrations in cord sera of term infants born at the end of winter.

It is commonly accepted that hypercalcaemia and functional hypoparathyroidism are present at birth in term infants. However whether this is a constant finding or is subjected to seasonal variations, as recently shown for 25 hydroxycholecalciferol cord values, has not been studied. Determinations of Ca, P, iPTH and iCT were carried out in February in cord sera from 28 normal term infants (gestational age: 38 to 41 weeks). Mean  $\pm$  SD serum concentrations were: Ca:  $9.21 \pm 1.34$  mg/dl; P:  $4.6 \pm 0.99$  mg/dl. Serum iPTH levels were undetectable ( $< 25$  pEq/ml) in 8 cases, normal in 17 cases (mean:  $43$  pEq/ml; range: 28 to 95) and above the normal range ( $> 100$  pEq/ml) in one case. Serum iCT levels were not detectable ( $< 150$  pg/ml) in 48% of the determinations and above the normal values in children and adults (non detectable) in 12/23 determinations (mean:  $230$  pg/ml; range: 160 to 430). There was no correlation between serum Ca or P levels and respectively serum iPTH or iCT levels.

Conclusion: In cord sera from term infants born in February, hypercalcaemia does not appear as usual as commonly said. Furthermore there is good evidence for a parathyroid activity and for hypercalcaemia in many cases. Whether these results are effectively related to seasonal variations would deserve further studies.