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WIESE, G. \*, BALLOWITZ, L. \* (Intr. by HELGE, H.)

Institut für anorganische und analytische Chemie und Kinderklinik der Freien Universität Berlin

Mathematical Derivation of Dose-Response Relationship Calculations in Phototherapy Based upon an Animal Model

For the phototherapy induced serumbilirubin decrease in Gunn rats, reliable concentration-time-functions could be found for any given starting level ( $c_0$ ) and for any type of fluorescent lamps used (i.e. for any effective irradiance  $E_{bill}$  - whereby 8 different fluorescent tubes were tested).

$$c = c_0 \cdot e^{-k \cdot c_0 \cdot E_{bill} \cdot t}$$

( $c$  = serumbilirubin concentration after illumination  
 $k$  = photolysis constant)

By this simple function it was possible not only to describe the dose-response relationship of phototherapy but also the influence of changes in the trial conditions. For example, we could show in our animal experiments that no upper limitation of the phototherapy effect was reached with rather high effective irradiances - up to  $E_{bill}$  7.0 mW/cm<sup>2</sup>.

E. MALLET, J.-P. BASUYAU\*, Ph. BRUNELLE\*, C. H. de MENIBUS\*. Département de Pédiatrie, Hôp. Charles Nicolle ROUEN (FRANCE). HYPERINSULINISM IN INFANTS OF DIABETIC

MOTHERS : SUPPRESSION BY SOMATOSTATIN INFUSION.

Post natal hypoglycemia is presently the major complication that occurs in infants of diabetic mothers (IDM) and this complication may be related to the hyperinsulinism state thought to be present in fetuses of diabetic women. Because of sudden and asymptomatic hypoglycemia, hypoglycemic risk persists in despite of present neonatal management. We studied the somatostatin effect on transient hyperinsulinism of IDM in neonatal period. Five IDM were studied at this time. Synthetic cyclic somatostatin (provided by CLIN-MIDY Laboratories) was infused at the rate of 4 µg/kg/h, a glucose infusion (0.5 g/kg/h) was maintained throughout the study course. Plasma C Peptide (CPR) determined by radioimmunoassay (Mallinckrodt) may provide a mean of studying beta cell function in IDM because insulin antibodies cross the placenta. The cross reactivity with human proinsulin is about 10 %. Before somatostatin administration, plasma CPR was inappropriately elevated for the blood glucose levels. Plasma CPR/glucose ratio was high. During somatostatin infusion plasma CPR dropped within the first hour and normal level was obtained before the fourth hour in three cases. Blood glucose was maintained over 5.5 mmol/l. Plasma CPR escaped from suppression just after somatostatin infusion although blood glucose moderately rose. No side effect was observed. Our findings show that beta cells may be more sensitive than alpha cells to somatostatin suppression as previously suggested in nesidioblastosis.

The parent gave informed consent and this study was approved by the ethical committee.

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F. DONZELLI\*, P.A. BATTISTELLA\*, L. VERGANI\*, E. POLIDORO\*, F.F. RUBALTELLI, C. ANGELINI\*. Departments of Pediatrics and Neurology, University of Padua, Padua, Italy.

Plasma free carnitine levels in premature and full-term newborns, infants and children.

The free carnitine plasma level was assayed in 142 healthy children from birth (minimum 28 weeks of gestation) to 10 years of age according to the radiochemical method of Cederblad and Lindstedt. All data were statistically analyzed using the Mann-Whitney test. Plasmatic data show a low concentration in the premature (34.9±2.6 S.E. nmoles/ml) and full-term newborns (31.2±2.5), probably caused by an immature hepatic synthesis and/or reduced oral intake of carnitine. However, the carnitine concentration is higher in premature (30-33 weeks of gestation) than in full-term newborns as also found by Novak et al. (Pediatr. Res. 13:10, 1979) for the acetyl-carnitine determined in the funicular blood. These data seem to suggest that fetal carnitine storage mainly occurs in the first 30-33 weeks of gestation. Adult levels (44.7±1.7) are reached by the end of the first 6 months (44.1±1.7), possibly as a consequence of increased hepatic synthesis and/or of increased carnitine intake associated with a diet containing meat.

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F. DONZELLI\*, P.A. BATTISTELLA\*, L. VERGANI\*, E. POLIDORO\*, F.F. RUBALTELLI, C. ANGELINI\*. Departments of Pediatrics and Neurology, University of Padua, Padua, Italy.

Free carnitine urinary excretion during childhood. Free carnitine excretion in urine was measured in 86 healthy children aged 1 day to 10 years in order to establish a pattern during development. In 30 of these cases the data were subdivided into day/night period. Nine children were also followed over 3 consecutive days. The radiochemical method of Cederblad and Lindstedt was used for free carnitine determination. All data were statistically analyzed using the Mann-Whitney test. Excretion of free carnitine per 24 hrs is low in the first three years of life (15.5±1.8 S.E. µmoles) and in the age group from 3 to 10 years (115.3±11.4) in comparison with 29 adults (216.9±20.6) ( $p < 0.05$ ). These findings could be related to a lower tissue concentration of carnitine and/or to a smaller muscle mass. On the other hand, excretion per Kg body weight/24 hrs is highest (5.1±0.4 S.E. µmoles) in the age group from 3 to 10 years in comparison with the age group from birth to 3 years (2.1±0.0) and adults (3.1±0.0). We emphasize that in malnutrition, inborn errors of carnitine metabolism or muscular dystrophy, the carnitine excretion should also be expressed per Kg body weight /24 hrs. Unlike other A. neither a day/night differentiation in carnitine excretion nor a wide variation in the same subjects in the course of successive days was found.

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EM. HADJIGEORGIOU\*, A. MALAMITSI-PUCHNER\*, D. LOLIS\* P. LAZARIDES\*, D. NICOLOPOULOS, D. KASKARELIS\*. Alexandra Maternity Hospital, Athens 611, Greece.

Cardiovascular birth defects and antenatal exposure to female sex hormones.

The etiological correlations of congenital heart diseases to antenatal exposure of pregnant women to sex hormones were studied retrospectively. Of a total of 15535 women who delivered between the years 1975-1977, 91 had babies with congenital heart disease (frequency 5.8 0/00). From these babies 11 were born to 559 mothers who had taken during pregnancy hormones of the estrogen-progesterone type (frequency 19 0/00). The remaining 80 babies were born to 14976 mothers who had not taken such hormones (frequency 5 0/00). The main reason for having been given hormones were: bleeding of the first trimester in 80% and the pregnancy test in 20%. Both groups of mothers had the same possibility for being affected by factors causing congenital heart diseases. An attempt is made to correlate the structure of the hormones given, the cause and time of the administration, the sex of the newborn, its outcome and the type of heart disease.

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F. MORLE, J. DELAUNAY, L. MORLE, R. BOUHASS, M. AGUERCIF (Intr. by J.F. DESMEUX) (DEPARTMENT OF PAEDIATRICS AND GENETICS, UNIVERSITY HOSPITAL, ORAN, ALGERIA)

(AND INSTITUT DE PATHOLOGIE MOLECULAIRE, HOPITAL COCHIN, PARIS) : Abnormal red cell membrane phosphatase activity in Beta-thalassemia.

**Abstract :** In thalassemia Heins bédies are held responsible for damage to the red cell membrane and premature hemolysis. Relatively little is known however about the biochemical membrane alterations.

We investigated in various types of beta-thalassemias the kinetics of a neutral membrane bound phosphatase, using purified red cell ghosts and para-nitrophenyl phosphate (pNPP) as the substrate (the apparent Michaelis-Menten constant for pNPP is 2,5 mM). In two related cases of beta-thalassemia, the kinetics of the enzyme, instead of being of the Michaelis-Menten type displayed a biphasic aspect. Simple reciprocal plots (reciprocal velocity vs pNPP concentration) were consistent with a pure inhibition process by substrate excess. KI app ranged from 18 to 35 mM. In three unrelated cases of beta-plus thalassemia the kinetics were essentially of the Michaelis-Menten type for two patients and of an intermediate type for the third one.

A 35% depletion of the membrane cholesterol obtained by incubation of the ghosts with phosphatidylcholine vesicles did not alter the abnormal kinetics, although it decreased the velocity in both beta-zero thalassemia cases. We assume some change in the enzyme hydrophobic environment, different from a cholesterol content decrease.