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MULTIEXPONENTIAL ELIMINATION OF GENTAMICIN(G). A KINETIC STUDY DURING DEVELOPMENT.

The nephrotoxicity of G has been related to its binding to renal tissue which accounts for a prolonged elimination phase. The bi-exponential profile during washout analyzed according to a two compartment model can provide predictive data on the accumulation of G in blood and tissues. The ratio of tissue to total body amount of G at steady state can be estimated to be about .8 in the adult.

By the same analysis we have calculated the terminal elimination half life(T1/2),the volume of the central compartment,including blood(Vc), the steady state volume of distribution(Vdss), the body clearance(Clb) and the predicted amounts of G at steady state in the body(Xb) and tissues(Xt) of 18 premature neonates (27-38 wks g.a. and 8-14 days p.n.age), 4 infants (2-5 mo) and 3 children (5-9 yrs). Mean data and ranges were the following :

	T1/2(hrs)	Vc(l/kg)	Vdss(l/kg)	Clb(ml/min/kg)	$\frac{Xt}{Xb}$
neonates	67	.44	.76	.62	.37
	(18-167)	(.11-.74)	(.19-1.24)	(.27-1.08)	(.1-.6)
infants	37	.67	1.46	1.64	.59
	(30-46)	(.39-1.17)	(1.1-1.85)	(1.1-2.57)	(.3-.7)
Children	36	.33	.75	1.33	.5
	(28-40)	(.2-.47)	(.6-.92)	(.8-1.86)	(.3-.7)

The data show that changes in G kinetics occur with age and predict a lower accumulation in the tissue compartment of our patients than expected from adult data.This could account for a lower nephro toxicity of G in early development.

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24 L-E Bratteby[X] and L. Andersson[X] (Intr, by S. Sjölin) Perinatal Research Unit, Dept. of Pediatrics and Dept. of Clinical Physiology, University Hospital, Uppsala Sweden. Neonatal heart rate variability after intrauterine asphyxia and maternal obstetric regional analgesia.

During the first two hours of life the neonatal heart rate was monitored by ECG recording in 61 non-asphyctic and 15 asphyxiated newborn infants. Mothers of 42 of the non-asphyctic infants had obtained obstetric regional analgesia during labour. Nineteen of the non-asphyctic infants formed a reference group.

The ECG-signal, transmitted to an FM tape recorder was later digitized and further processed using an analyzing program on an IBM 370/155 computer.

The distribution of R-R variability of the different groups showed characteristic and significant differences. These results indicate a trend of progression in R-R variability with the severely asphyxiated infants at one of the extremes having the smallest R-R variability. With increasing R-R variability followed the groups of moderately asphyxiated , slightly asphyxiated infants, analgesia group of primiparous mothers, reference group of primiparae, analgesia group of multiparae succeeded by the reference group of multiparae at the other extreme, having the largest R-R variation. In the non-asphyxiated infants a significant negative correlation was found between neonatal heart rate variability and duration of labour, indicating a smaller variability with longer duration of labour.

25 G.SEDIN*AND K.HAMMARLUND* (Intr. by S.Sjölin). Department of Paediatrics, University Hospital, Uppsala. Sweden. Evaporative water loss in newborn preterm and small for gestational age infants.

The water loss from the skin can be studied by measuring the vapour pressure gradient in the air layer close to the skin surface.

Measurements of the evaporation rate (ER; g/m^2h) from an interscapular skin area have shown a linear relationship between ER and ambient humidity in fullterm and preterm infants who are appropriate for gestational age (AGA). Higher ER values were obtained at a low ambient humidity than at a high one. The ER level was much higher in preterm infants. In fullterm small for gestational age (SGA) infants the same relationship was found but with lower ER values than in fullterm AGA infants.

Transepidermal water loss (TEWL; g/m^2h) can be estimated from measurements made on the buttock, the chest and an interscapular skin area. In AGA infants an exponential relationship was found between TEWL and gestational age. In SGA infants the TEWL values were lower than in AGA infants of the same gestational age.

26 H.T.VERSMOLD, J.W.SEVERINGHAUS*, C.MÜLLER*, I.PAIKERT* and K.P.RIEGEL. Department of Pediatrics, Univ.of Munich and Cardiovascular Research Institute, Univ.California, San Francisco. Transcutaneous Monitoring of Pco_2 In Newborn Infants.

Monitoring of arterial Pco_2 ($Paco_2$) is of similar importance as monitoring of Pao_2, particularly in neonatal intensive care. We report about the first clinical application of a miniaturized heated electrode for transcutaneous continuous monitoring of Pco_2 ($tcPco_2$) (JWS et al, Acta anaesth scand Suppl 168:118,1978). Stability of the electrode, skin temperature necessary to obtain agreement of $Paco_2$ and $tcPco_2$,kinetical properties of the electrode and its performance on sick neonates were studied in 40 infants (830-3630 g). After calibration in 6% CO_2 and N_2 at 42° and 44° the electrode was attached to the skin at 44°, an inbuilt correction being made for thermal effects and skin CO_2 production ($Paco_2 = tcPco_2 \cdot e^{0.04(37-T)} - 4$ torr). After 15 min at 44° $tcPco_2$ was monitored at 42° for 1 hr, and again after 5 min of reheating to 44° to reestablish full vasodilatation. The mean drift in vitro was 0 over 3 hr, the drift in situ 0.4 ± 1.4 torr/hr (N=37). After 1 hr at 42° transient reheating to 44° did not significantly influence $tcPco_2$, i.e.$tcPco_2$ can be measured at lower skin temperatures than $tcPo_2$. We did not see burns. $tcPco_2$ (Y; torr) agreed well with $Paco_2$ (X; torr), irrespective of systolic blood pressure (30-85 mm Hg): Y=0.92X+1.50; N=116; r=0.88; s_{yx}=3.6. $tcPco_2$ reacts promptly to crying, apnea or sustained alterations of alveolar ventilation but does not fluctuate during periodic breathing, although the in vitro 90% response time of 70 sec would allow a response similar to that of $tcPo_2$. Despite this damping -probably by the skin- the $tcPco_2$ electrode may prove to be as useful for respiratory physiologists as we found it in neonatal intensive care.

27 F.F. RUBALTELLI, A.L. PIOVESAN*, B. GRANATI*, G.L. CASARA*, and P. COLLESELLI*. Dept. of Pediatrics, University of Padova, Padova,Italy.
The effects of bilirubin and phototreated bilirubin on the phagocytic activity of granulocytes.

The effect of bilirubin and phototreated bilirubin (10 mg/dl) on granulocytes (PMN) was studied "in vitro" utilizing the activity of the hexose-monophosphate shunt as an indirect index of granulocyte metabolic activity and, therefore, of its phagocytic function. Blood was obtained from 10 healthy full-term newborns and from 10 healthy adults. Bilirubin and phototreated bilirubin seem to determine a significant decrease in the metabolic activity - during phagocytosis of latex microspheres - of newborns' as well as adults' PMN. These data, obtained by studying the entire blood,allow to conclude that bilirubin and phototreated bilirubin - directly or indirectly - inhibit the PMN function and indicate that "in vitro" light exposure does not decrease bilirubin toxicity on PMN metabolic activity. This work received financial support from C.N.R., under the U.S.A.-Italy cooperative program in science (contract No. 78.01876.65).

28 G. VERELLEN*, T. HEIM, J.M. SMITH*, P.R. SWYER*, S.A. ATKINSON* and G.H. ANDERSON*. Dept. Pediat., Nutr.and Med. Eng., Univ., Toronto and Res., Ins.,The Hosp. for Sick Children, Tor., Ont., Canada. Fractional deposition of metabolizable energy (ME) in very low birth weight infants (VLBW).

The increasing survival of VLBW premature infants requires a precise knowledge of utilization of essential nutrients (P=protein F=fat, C=carbohydrate) in order to design suitable dietary regimes. Energy balance (EB), substrate utilization for oxidation (O) and tissue deposition studies were performed on VLBW premature infants (n=10; gest. age 27-31 weeks; birth weight 940 - 1280 g; postnat. age 1 - 4 weeks) fed by own mother's milk (6 studies on 4 infants) or humanized milk (SMA 20/24 Wyeth; 13 studies on 6 infants). EB for growth was determined by the equation: EB = ME - O (P+F+C). By increasing the net energy intake (NEI) from 50 to 150 Kcal/kg/day, resting metabolic rate (RMR) increased from 38 to 58 Kcal/kg/day in the formula fed infants (FFI) and from 45 to 58 in the breast fed infants (BFI). In a range of 50-110 Kcal/kg/day NEI the RMR was consistently higher in BFI. The latter deposited more P than FFI at the same level of NEI. At a NEI of 100 Kcal/kg/day FFI deposited 1 g P/day in contrast to the 2 g/kg/day P deposition observed in the BFI. Tissue deposition of F increases with the enhancement of NEI in both FFI and BFI but the relationship is the reverse to that observed for P deposition. At a 100 Kcal/kg/day NEI 18 Kcal/kg/day energy is deposited as F in the BFI in contrast to the 28 Kcal/kg/day deposition in FFI. It is concluded that the quality of growth (P v.F deposition) in response to a specific diet composition may be defined by our investigative approach.

29 J.A. FISCHER* University of Zurich, Zurich, Switzerland. Vitamin D metabolites in newborn infants

Abstract not received

30 F. KLIMPEL*and B. KREMPIEN* Department of Pathology, University of Heidelberg, F.R. Germany. Influence of 1,25 $(OH)_2D_3$ on osteoblasts and on mineralization of cartilage. In vitro experiments.

While 1,25 $(OH)_2D_3$ is known to promote bone resorption in vitro little is known about the action of this metabolite on matrix formation and mineralization. This question is particularly important in view of recent controversy on which metabolite of vitamin D promotes mineralization and cures oesteomalacia. Therefore the effect of 1,25 $(OH)_2D_3$ on growth cartilage and on endosteal bone was studied in tissue culture.

Material and methods

Calvaria and proximal tibial growth cartilage were prepared from baby rats with rickets (4 weeks). Specimens were incubated in Eagles medium, modified after Dulbecco, for 1-6 days in the presence or absence of 4 x 10^{-8}M 1,25$(OH)_2D_3$ and studied by transmission and scanning electron microscopy (critical point drying method).In a recovery experiment calvaria were incubated with 1,25 $(OH)_2D_3$ for 1 day and transferred into a medium without the metabolite for a second incubation period of 1-6 days.