23 B.M.ASSAEL,G.CAVANNA*,W.J.JUSKO*,A.MARINI,R.PARINI*,F. SERENI and A.VIGANO*. Newborn Unit and Dpt.of Pediatrics.Univ.of Milano, Medical School,Italy, and Millar Fillmore Hospital,Clin.Pharmacokin.Lab.Buffalo,N.Y.
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.

Results
In ricketick cartilage we found numerous matrix vesicles in the longitudinal septa, which contained no mineral deposits. After 3 days of incubation, both groups (without and with 1,25) showed mineral material. At day 4 mineral crystals were seen outside the vesicles. At day 6 longitudinal septa of both groups were completely mineralized. In the absence of 1,25 calvaria were covered by flat lining cells. After 1 day exposure to 1,25 osteoid was denuded nearly completely, because all lining cells were transformed into globiform cells. After 2 days incubation with 1,25 proliferating fusiform cells appeared. No osteoclasts were visible.
In our recovery experiment we found that 1,25 induced changes of lining cell's morphology were reversible within a period of 6 days.

Conclusion
$1,25(OH)_2D_3$ has no direct effect on the mineralization process of cartilage in vitro. In contrast to in vivo studies, this model precludes changes in Ca of P balance or plasma concentrations.
$1,25(OH)_2D_3$ has a dramatic effect on surface lining cells (morphology, proliferation),which are similar to the effects of parathyroid hormone.
In a further experiment we try to analyse the effect of 24,25 vitamin D on cartilage and endosteal lining cells in our in vitro system.

31 L. DAVID, Hôpital Edouard Herriot, Lyon, France
Contribution of simple clinical observations to the understanding of the hormonal regulation of fetal bone metabolism and early neonatal calcium metabolism

Abstract not received

32 H.RENAUD,* L.DAVID,* P.CHOPARD,* JA.CHAYVIALLE* and B. SALLE. Service de Néonatologie,hôpital Edouard Herriot and INSERM U34,Lyon,France.
EFFECTS OF INTRAVENOUS GLUCAGON ON SERUM CALCIUM (Ca) AND IMMUNOREACTIVE CALCITONIN (iCT), GASTRIN (iGT) and PARATHYROID HORMONE (iPTH) IN PREMATURE INFANTS.

Glucagon (G) has been recommanded in the treatment of neonatal hypoglycemia. Because, in adults, G is known to have a pharmacological hypocalcemic effect and may influence CT and GT secretions, we have studied the effects of IV.G injection (0.5mg) on serum levels of Ca,iCT,iGT and iPTH in eight 29-38h old premature infants (gestational age : 34-37 weeks). Blood samplings were performed at time 0,5 (4), 15(4), 30 and 60 mn. Blood glucose levels increased from 26-56 to 68-2 06 mg/100ml. There was no significant change in mean serum Ca (basal mean ± SD:7 ± 1mg/100ml); however, 4 infants showed a decrease in serum Ca at 60' (ΔCa : 0.4 to 1mg/100ml). Elevated basal levels of serum iCT were present in the 8 infants and did not show any consistent changes (basal mean ± SD : 580 ± 303 pg/ml). Serum iPTH levels were elevated in 6 infants and were not significantly modified. By contrast there was a significant decrease in serum iGT levels (129 ± 27 to 90 ± 23 pg/ml at 30'). There was no consistent change in any of the parameters in 4 control premature infants. In conclusion : IV.G may lower the serum Ca in premature infants when administered during the 2nd day of life; it has no effect on the neonatal hypercalcitoninemia, while s in normal adults, it inhibits serum iGT levels. These findings suggest that neither glucagon nor gastrin are directly involved in the determinism of neonatal hypercalcitoninemia.

33 MOYA M.* and DOMENECH E.* Dept.of Pediatrics. Hosp. Gen. y Clin./F.M. La Laguna. Tenerife, Spain.
NET RETENTION OF CALCIUM, MAGNESIUM AND PHOSPHATE IN THE THREE FIRST DAYS OF LIFE IN THE LOW BIRTH WEIGHT NEONATE.

Ten newborns with no particular pathology weighing 2268.0+192.9 g and of 36.8+2.4 weeks gestional age were balanced for Ca, Mg and Pi, from 11.4+3.2 hours up to the 3rd day of life. Conventional balance techniques were used. The initial red marker in the stool was recognized by its water-solubility property. Meconium mineral content was also estimated. The composition of the formula was measured in 30 samples with the following results expressed in mg/ml:Ca 0.84+0.14; Mg 0.10+0.02; Pi 0.36+0.05 with Ca/Pi ratio of 2.42. The milk intake raised from 40.6+10.6 cal/kg/1st day to 67.5+7.6 cal/kg/3rd day. Ca/Pi ratio in the regurgitated material was 2.75.

Net retention (mg/kg/day) was 53.6+15.8 for calcium; 6.2+2.0 for magnesium and 32.1+5.9 for organic phosphate. No hypocalcemia was found and serum calcium (mg/dl) increases from 8.12+0.62 to 8.89+0.82 ($P<0.05$) and Pi (mg/dl) decreases from 6.36+0.34 to 5.84+0.42 ($P<0.01$). There was a negative correlation but very poor ($r=0.02$). The high proportion of calcium/phosphate quotient in the formula, adds further evidence on its importance in the prevention of early neonatal hypocalcemia.

34 C.D. STREHLOW* and D. BARLTROP. Department of Child Health, Westminster Medical School, London, United Kingdom.
Absorption of toxic and essential minerals in Asian children.

Although many factors modify the absorption of lead from the gut, the potential importance of nutritional status and dietary practices have only recently been recognised. This paper reports the evaluation of lead burdens in 359 children aged 2-3 years, comprising 182 Asians and 177 non-Asians. The children were randomly selected from two multi-racial communities. Asian children had significantly greater lead burdens but lower serum iron, haemoglobin and 25-OHD values than non-Asian controls ($p < 0.001$). No significant differences for calcium, phosphorus, alkaline phosphatase, copper or zinc were demonstrated. The findings are discussed in relation to the dietary habits of the ethnic groups studied.

35 B.A. WHARTON,* P.H. SCOTT,* H.M. BERGER.* The Infant Development Unit, Queen Elizabeth Medical Centre, Edgbaston, Birmingham, United Kingdom.
Aspects of sulphur metabolism in low birth weight babies.

Sulphur is an essential part of certain mucopolysaccharides and forms salts with important steroid molecules such as bile acids and vitamin D. The sulphur source is mainly cysteine either present in the diet or formed from dietary methionine.

Aspects of sulphur metabolism have been studied in low birth weight babies receiving varying amounts of cysteine. Babies receiving the higher cysteine intake from a cows milk formula excreted less urea, more sulphate, and had a lower urinary cystathionine:cysteine ratio. Unlike babies receiving breast milk, however, duodenal bile acids were conjugated predominantly with glycine rather than taurine.

These observations are compatible with the known immaturity of the transulphuration pathway but show that this immaturity is still evident at 3 weeks of age in low birth weight babies. These observations may have implications for the adviseable diet of the newborn.

36 L. SANN, D. RIGAL,* L. DAVID* and A. FREDERICH.* Service de Neonatologie and INSERM U 34, Hôpital Debrousse, Lyon, France.
Evolution of plasma 25-hydroxycholecalciferol (25 OHCC), serum immunoreactive parathyroid hormon (iPTH) and calcitonin (iCT) concentrations in very low-birthweight infants (VLBWI).

There is a little information for the late evolution of 250HCC,iPTH and iCT levels in very lowbirthweight infants. Fourteen preterm neonates (gestational age 26-35 weeks) with a birthweight between 950 and 1300 g were studied. All infants were fed with breast milk for 30 days. 7 infants were later supplemented with a humanized formula while the other infants were still fed with breast milk. All infants were supplemented with 2400 UI of vitamin D_2 per 24 hr from the tenth day of life. At the age of 30 days, mean ± SD plasma 25 OHCC was 7.8 ± 7.5 ng/ml (Normal=6-30ng/ml), serum iPTH:66+27 (N< 100 µlEq/ml) and all iCT values were undetectable (<150pg/ml). At the age of 60 days, serum iCT was also undetectable in all infants. Plasma 250HCC was similar in the supplemented infants (21+11ng/ml) and in the infants fed with breast milk (24+8 ng/ml). Serum iPTH was normal in the infants fed with breast milk (58+35µlEq/ml) but higher ($p<0.05$) in the supplemented infants (162+74µlEq/ml) with 5 values above 100µlEq/ml. Serum iPTH was not correlated with serum phosphorus (P) level or with P intake. At the age of 60 days, a negative correlation between serum iPTH levels and Calcium (Ca) intake was not observed for the total Ca intake but only for the Ca intake provided by breast milk ($r=-0.70; p<0.05$).These data suggest that : 1) The amount of vitamin D_2 supplementation induces normal levels of 250HCC in VLBW infants 2) Secondary hyperparathyroidism occurs only in the infants supplemented with a formula 3) When feeding these VLBW infants, there is a dilemna between poor P intake and hyperparathyroidism.

37 S. KASSAM[X], J. LEVY[X] and M. VAINSEL, Department of Paediatrcis, University of Brussels, Belgium.
A new form of speudohypoparathyroidism type II with abnormal response to TRH.

A 12 years old Turkish girl, was admitted for tetany. She had laboratory findings of hypoparathyroidism (inorganic serum phosphorus : 7,5 mg/dl; calcium : 2,2 mEq/l; magnesium : 1,8 mg/dl). Blood alkaline phosphatase was strikingly increased as was iPTH. She has a normal phenotype but had moderate mental retardation. X-rays studies showed diffuse osteoporosis. The renal response to parathyroid extract administration was studied under several conditions :

1) there was a marked rise in urinary CAMP excretions but no increase in urinary phosphates. This type of response caracterizes pseudohypoparathyroidism (PHP) type II.
2) calcium therapy and vitamin D therapy did not modify this response.
3) the absence of restoration of normal renal responsiveness after an acute calcium infusion differentiates this case from the one described by Rodriguez.

There was an excessive thyrotropin response to TRH injection whereas other studies of thyroid function were normal. With very low doses of vit. D (2000 U/day), serum calcium returned rapidly to normal values but phosphorus remained high and the renal unresponsiveness to PTH was unchanged. The TRH response also remained impaired.
We propose that this could be a new form of pseudohypoparathyroidism (type III ?) whose calcemia can be controlled by low doses of vit. D.