

**43** L.SANN, L.DAVID, J.A.CHAVVIALLE, Y.LASNE. Service de néonatalogie and INSERM U34. Hôpital Debrousse, Lyon, France. Effect of early oral Calcium (Ca) supplementation on serum calcium levels and serum immunoreactive gastrin and calcitonin concentrations in premature infants.

In order to prevent early hypocalcemia in premature infants and to study its mechanisms, oral Ca supplementation (80mg/kg/24 h for 5 days) was given in 20 randomly selected infants and the evolution of serum Ca, magnesium (Mg), immunoreactive gastrin (iG) and calcitonin (iCT) concentrations were compared to the concentrations found in a control group of 20 infants matched for gestational age, Apgar score and birthweight. Prior to Ca supplementation (2-8 hours of age) serum Ca, Mg, iG and iCT levels were not different in the 2 groups. At 9 to 32 hours of age, serum Ca was higher in the supplemented group (mean  $\pm$  SEM :  $9 \pm 0.1$  mg/dl vs  $7.9 \pm 0.2$  in controls  $p < 0.05$ ). Serum iCT levels were significantly lower in the supplemented group ( $p < 0.05$ ). Serum Mg and iG levels were similar in both groups. A negative correlation between serum Ca and serum iCT level was found in the control group ( $p < 0.01$ ) but not in the Ca supplemented group. The incidence of hypocalcemia ( $< 7.0$  mg/dl) was 0 in the supplemented group and 4 in the controls. There was no clinical side effect of Ca supplementation.

These data add further support for a role of calcitonin in the pathogenesis of early neonatal hypocalcemia. They indicate that oral Ca can prevent the occurrence of early neonatal hypocalcemia. They also suggest that this effect could be obtained by influence of oral Ca on serum iCT levels.

**44** B.BETEND\*, L.DAVID, M. HERMIER\*, R. FRANCOIS. Service de pédiatrie, Hôpital Edouard Merriot, Lyon, France. Hypercalciuria and renal salt wastage : a new congenital syndrome. Successful indomethacine (IDM) therapy.

A 4 days old boy (gestational age : 36w) presented with renal Na wastage, hypercalciuria and polyuria. The parents were first cousins. It was learned that a 3 years old brother presented a salt wasting syndrome associated with nephrocalcinosis. Plasma renin activity (PRA) and aldosterone (PA) levels were very high (4000 ng/l/mn and 2000 pg/ml respectively). The adreno-cortical function was otherwise normal. DOCA had no effect on the Na loss and the Na balance improved only with large NaCl supplements or high doses of fludrocortisone (50-70  $\mu$ g/Kg/d). The hypercalciuria was permanent reaching values as high as 25 mg/Kg/d and was only slightly reduced by Na restriction, oral phosphorus (P) supplements or low calcium (Ca) intake. Plasma Ca, P, Magnesium (Mg) and parathyroid hormone levels and urinary Mg and P were normal. Polyuria was constant and water supplements were necessary. There was no other remarkable renal abnormalities. Despite multiple therapeutic trials a severe growth failure ( $- 4$  SD) was present at 11 months. IDM (1.75-2 mg twice a day) was then started : weight and length increased dramatically ; PRA and PA levels, calciuria, diuresis, and water needs became normal within 3 weeks and remained normal three months later. We believe that this infant presents a disorder of the common transport mechanism of Na and Ca at the level of the proximal tubule and the ascending limb of the loop of Henle. Since IDM is known to inhibit renal prostaglandins synthesis, an excessive renal production of these compounds might be responsible for this tubular defect.

**45** T.E. Stacey\*, R.D.H. Boyd, R.H.T. Ward\* and A.P. Weedon\* Depts. Paediatrics & Obstetrics U.C.H. Medical School, London, England. Vascular and E.C.F. spaces in the Sheep Placenta.

The sheep placenta behaves as a relatively impermeable barrier. It has an equivalent pore size of 0.45 nm to polar solutes, a low permeability to Na, and can maintain an electrical potential difference across it. In order to establish the site of this barrier, volumes of distribution of a vascular marker ( $^{125}$ I- or  $^{131}$ I-albumen) were compared with those of an E.C.F. marker ( $^{24}$ Na,  $^{22}$ Na, or  $^{51}$ CrEDTA) in 6 chronically catheterised pregnant ewes. Isotopes were injected into fetal, maternal or both circulations between 30 and 250 minutes before rapid induction of anaesthesia and removal of up to 20 cotyledons for isotope counting. Results for isotope spaces, expressed as ml plasma per 100g cotyledon wet weight [mean  $\pm$  SEM(n)] were:- (i) Fetal: sodium  $19.7 \pm 1.5(5)$ , CrEDTA  $19.3 \pm 1.4(3)$  and albumen  $1.75 \pm 0.29(4)$ ; (ii) Maternal: sodium  $23.3 \pm 1.7(3)$  and albumen  $5.07 \pm 1.52(3)$ . Total cotyledon water content by dessication was 81 ml/100g. We conclude that the anatomical barrier to Na and CrEDTA is the same, and is not in the capillary endothelia, but most probable resides in maternal syncytium or trophoblast junctional complexes.

**46** T.TUVEMO, M.HAMBERG, C-E.JONSSON and J.SVENS-SON (Intr. by S.Sjölin). Dept. of Pediatrics, University Hospital, Uppsala, and Chemistry II, Karolinska Institute, Stockholm, Sweden.

Biosynthesis and action of prostacyclin (PGI<sub>2</sub>) in the isolated human umbilical artery.

Prostaglandin endoperoxides and thromboxane A<sub>2</sub>, extremely potent contractors of the human umbilical artery are endogenously formed in the vessel (1). /1-<sup>14</sup>C/ arachidonic acid was incubated with umbilical artery homogenates. The product, subjected to thin layer chromatography, showed a major peak (20-40%) of radioactivity close to the reference prostaglandin E<sub>2</sub>. The labelled material, analyzed as the methyl ester trimethylsilyl ether derivative by gas-liquid chromatography-mass spectrometry, demonstrated identity with 6-keto-PGF<sub>1 $\alpha$</sub>  (lactol form), the immediate precursor of which is PGI<sub>2</sub>. Human umbilical artery strips were exposed to prostaglandin endoperoxide (PGH<sub>2</sub> 10-40 ng/ml) preincubated with a lyophilized pig aorta microsome preparation (0-4000 ng/ng PGH<sub>2</sub> 22°C, 90 sec) for PGI<sub>2</sub> formation (2). With increasing amounts of microsome added the endoperoxide contraction disappeared and relaxation was obtained. PGI<sub>2</sub> 10 ng/ml or more relaxed the vessel. The potency was at least 4 times that of PGE<sub>1</sub>. The human umbilical artery thus has a high capacity to biosynthesize PGI<sub>2</sub>, a compound effectively relaxing the vessel.

1. Tuvemo, T. et al. Acta Physiol Scand 96, 145, 1976.
2. Moncada, S. et al. Nature 263, 663, 1976.

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Acute response of parathyroid hormone in osteopetrosis.

Congenital osteopetrosis is characterized by severe impairment of bone resorption. Inactivation and/or resistance to parathyroid hormone (PTH) have been suggested as pathogenetic factors. The response to an acute infusion of bovine parathyroid extract (4-8 units/kg) was studied in 3 children with osteopetrosis. Serum calcium, phosphorus and alkaline phosphatase were within normal limits and did not show any consistent change 120 min. after infusion. Plasma cyclic AMP showed a brisk rise with peak levels 4-28 times above the basal values 10 min. after the infusion. The response was most marked at the highest PTH dose level. There was also a prompt increase in urinary cyclic AMP with increments in the range of 100 to 4000 per cent of the basal values when calculated as nmol excreted per min., whereas urinary phosphate excretion was essentially unchanged. The serum levels of 25-hydroxy-vitamin D were subnormal:  $28.2 \pm 4.4$  nmol/l (normal value  $64.4 \pm 14.7$  nmol/l; range 38.2-98.9 nmol/l). The relative resistance of these patients to the effect mediated by cyclic AMP on calcium and phosphorus metabolism might be related to a relative vitamin D deficiency.

**48** J.ALM\* and A.LARSSON. Department of Pediatrics, St Görans Childrens Hospital, Karolinska Institutet and the PKU Section, National Bacteriological Laboratory Stockholm, Sweden. A follow up of a nationwide neonatal metabolic screening program in Sweden.

In Sweden nationwide neonatal screening for PKU was started in 1965 using filterpaper blood samples and Guthrie's microbiological technique. The screening program has since been expanded to include also galactosemia, tyrosinemia, homocystinuria and histidinemia. The blood samples were collected at 4-6 days of age. We have now evaluated the effectiveness of the program in the time period 1965 to 1977. The results are summarized in the following table:

Disease	Newborn screened	Positive analyses	Identified patients	False pos. analyses	False neg. analyses
PKU/HPA	1.138.351	297	39/21	237	0
Galactosemia	1.028.396	159	12	147	0
Tyrosinemia	640.259	541	1	540	4
Homocystinuria	316.821	314	0	314	1
Histidinemia	179.348	639	0	639	0

The coverage has steadily increased and has exceeded 95% during the most recent years. The efficiency of the screening for PKU and galactosemia was considered to be high and continuation seems justified. One out of five patients with tyrosinemia was discovered by screening and the only known patient with homocystinuria was missed. In the screened population we don't know of any child with impaired mental or physical development due to histidinemia. Screening for tyrosinemia, homocystinuria and histidinemia has since been discontinued in the Swedish screening program.