173

B. SALLE*, J. SENTERRE*, G. PUTET*, J. RIGO* (Introd. by A. FANCONI). Department of Neonatology-Lyon (France) and Department of Neonatology-Liege (Belgium).

FAT, CALCIUM (Ca) AND MAGNESIUM (Mg) BALANCE IN PRETERM INFANTS (PI) FED HUMAN MILK (HM) OR LOW BIRTH WEIGHT FORMULA (LBWF) AT DIFFERENT POSTNATAL AGE.

During the last trimester of pregnancy, the fetal skeletal growth requires a massive mineral transfer from mother to fetus. Interruption of this process favors the development of osteopenia in PI. We studied in 12 PI (BW : 1318 g ± 142 ; GA : 30.5 wks ± 1.5), 6 fed either HM or LBWF, fat absorption and Ca and Mg absorption and retention at 20-25 days (study I) and 44-45 days (study II) after birth. HM was enriched in phosphate (9 mg/dl) and babies received 1500 I.U. vit.D/d. The results were (in mg/kg/day) : *: p<0.05

	CALCIUM		MAGNESIUM		FAT	
Study I	HM	LBWF	HM	LBWF	HM	LBWF
Intake	49±5	84± 7*	4.8±0.9	8.1±0.5*	5.30±0.69	5.35±0.23
Feces	17± 8	46±19*	2.6±0.5	4.3±1.6*	1.50±0.42	0.72±0.24
Urine	2± 1	2± 2	0.4±0.2	0.8±0.6	-	-
Retention	30± 5	36±24	1.8±1.0	3.0±1.6*	-	-
Absorption (%)	66±14	44±25	46±12	47±20	72± 6	87 ± 4*
Study II						
Intake	46± 7	85± 9*	4.9±0.8	9.3±2.1*	5.74±0.70	5.56±0.23
Feces	8 ± 3	31± 7*	1.4±0.4	4.6±1.9*	0.51±0.23	0.52±0.19
Urine	3 ± 1	3 ± 2	1.0±0.8	1.3±1.0	-	-
Retention	35 ± 9	51 ± 7*	2.5±0.9	3.4±1.1*	-	-
Absorption (%)	82± 9	64 ± 7*	70±10	52±12	91± 4	91± 3

These results showed : 1) Fat, Ca and Mg absorption were low in PI fed HM but increased with postnatal age. 2) In PI fed LBWF, fat absorption was normal, Ca and Mg retention was higher in both studies.

174

R.Schilling*, F.Haschke*, C.Schatten*, M.Schmid*, W.Woloszczuk* (Introduced by H.Frisch)
Department of Pediatrics and L.Boltzmann-Institute for Clinical Endocrinology, Univ.of Vienna, Austria

ELEVATED TOTAL AND FREE 1,25-DIHYDROXYVITAMIN D CONCENTRATIONS (1,25Dc) IN SERUM OF PREMATURE INFANTS

Elevated 1,25Dc repeatedly were found in premature infants. We investigated if high 1,25Dc 1) are accompanied by a high "free 1,25OH_2D index"(FDI;ratio molar concentrations 1,25OH_2D/vitaminD-binding protein(DBP)) and 2) are induced by hypophosphatemia or hyperparathyroidism. Matched pairs of 14 premature infants(birthweight 1430g, 980-1700g; $\bar{x}$, range; gestational age 33weeks, 31-35weeks) were fed human milk with supplements of phosphorus(P) or calcium+P. Vitamin D_3 1000 I.U./d were given. P, iPTH(midregional antibody), 25OHD(RIA), 1,25Dc(RRA), DBP(radial immunodiffusion) and alkaline phosphatase(AP) were measured in serum at bodyweights 1800+75g(I) and 2150+75g(II), respectively. Results were not significantly different within pairs and therefore are indicated together as $\bar{x}$±SD:

	25OHD (ng/ml)	1,25Dc (pg/ml)	DBP (mg/dl)	FDI	P (mg/dl)	iPTH (pmol/l)
I	27±11	75±28	15,0±3,3	6,6±2,7	6,7±1,2	46±16
II	28±12	90±22	13,8±2,7	8,8±2,6	6,7±0,4	65±35

AP was normal in all samples. Both 1,25Dc and FDI were high when compared to adult reference values but occurred without hypophosphatemia or hyperparathyroidism.
The significance of high total and free 1,25Dc in premature infants and the mechanisms of its regulation remain to be elucidated.

175

M.Garabédian*, R.Brauner*, R.Grimberg*, C.Prévot*, R.Rappaport, S.Balsan*.
CNRS UA.583, INSERM U.30 and Pediatric Endocrinology Unit, Hôpital des Enfants-Malades, 75015 Paris, FRANCE.

CHANGES IN PLASMA 1,25-$(OH)_2$D DURING LHRH ANALOGUE TREATMENT IN GIRLS WITH CENTRAL PRECOCIOUS PUBERTY.

In an attempt to better understand the control of plasma 1,25-$(OH)_2$D concentrations during puberty, these concentrations have been measured in 12 girls (age 3 yr 6 mo-8 yr 10 mo) with central precocious puberty before and after 3, 6, 9, 12, 18 and 24 months of treatment with a LHRH analogue (Ruserelin®, Hoechst). Mean and extreme values for 1,25-$(OH)_2$D were 76 pg/ml (53-114) before treatment, 68 pg/ml (43-107) and 45 pg/ml (26-87) after 12 and 18-24 months of treatment respectively. No correlation was found at any time studied between plasma 1,25-$(OH)_2$D and : plasma estradiol, plasma DHAS, vaginal maturation index, bone age, height gain (cm/year), plasma SmC/IGF_I, serum calcium, phosphorus and alkaline phosphatase activity. Plasma 1,25$(OH)_2$D values were also not correlated with plasma basal LH and FSH before treatment, but were significantly correlated with plasma basal LH ($r = 0.67$, $p<0.02$) and plasma basal FSH ($r = 0.71$, $p<0.01$) after 12 months of treatment.

From these results, one may speculate that the control of plasma 1,25-$(OH)_2$D during puberty is not directly dependent upon skeletal growth, skeletal maturation and ovarian secretion but could be, at least partially, dependent upon central factors.

176

Z.Hochberg, M. Jaffe*, A. Benderly*, Y. Weisman*
Rambam Medical Center, Haifa Medical Center and Technion Faculty of Medicine, Haifa, and Ichilov Hospital, Tel-Aviv, Israel.

THERAPEUTIC APPROACH TO 1,25-DIHYDROXYVITAMIN D_3 [1,25$(OH)_2D_3$]-RESISTANT RICKETS

The syndrome of 1,25$(OH)_2D_3$-resistant rickets and alopecia has been shown to be caused by defective receptors to the active D-metabolite (ESPE, 1982; JCEM 55:1020, 1982). In search of a therapeutic approach, 7 patients aged 2-12 years were treated. On a megadose of 60 ug/m^2/day of 1αOHD for 8 months, serum 1,25$(OH)_2D_3$ increased to 1100-3000 pg/ml (normal, 20-80 pg/ml), but rickets was not healed. Treatment of 3 patients with 20 ug/m^2/day of 24,25$(OH)_2D_3$ with serum 24,25$(OH)_2D_3$ of 6.2-14 ng/ml (normal 1.5-4 ng/ml) failed to heal the rickets. With combined treatment of 24,25$(OH)_2D_3$ and 30 mg/m^2/day i.v. calcium, rickets was not healed. Two children, 6 and 3 years old, received 70 mg/m^2/day elementary calcium through an intracaval catheter, and serum calcium was maintained at 9.1-10 mg/dl. Bone pains and muscular weakness disappeared within a week. Serum PTH and phosphatase normalized after 1 and 4 months, respectively. X-rays demonstrated complete healing of the rachitic bone changes after 4 and 6 months, respectively, and the children's growth accelerated to 16.5 and 9.8 cm/year, respectively. These observations indicate that normalization of serum calcium is sufficient for healing of rickets and growth, even in the absence of functioning 1,25$(OH)_2D_3$ receptors.

177

G. Saggese*, S. Bertelloni*, G.I. Baroncelli* (Introd by S. Bernasconi)
Department of Pediatrics, University of Pisa, Italy.

1,25(OH)2D3 TREATMENT IN IDIOPATHIC JUVENILE OSTEOPOROSIS (IJO).

IJO is a rare condition of osteoporosis in childhood. The disease requires rapid growth to be clinically manifest and it occurs in adolescence or in early childhood. The pathogenesis is unknow. We examined 3 boys (FM, 2.3 yrs; DBM, 12.1 yrs, TM, 11.5 yrs) and 1 girl (GR, 12.6 yrs) with IJO. Ca, P, Mg were in normal range. Calciotropic hormones and therapy were as follows:

case	25-OH-D ng/ml	1,25(OH)2D pg/ml	PTH pg/ml	CT pg/ml	BMC* g/cm	1,25(OH)2D3 μg/daily
FM	35.4	71.0	322	28.0	-18%	0.50
DBM	41.1	39.2	480	9.5	-23%	none
TM	34.0	45.4	420	18.6	-33%	0.50
GR	28.0	35.1	550	39.0	-14%	0.25

(nv:25-OH-D 35.5±7.1 ng/ml, 1,25(OH)2D 74.6±7.1 pg/ml, PTH 410±230 pg/ml, CT 34.7±19.3 pg/ml)(*Bone Mineral Content, Norland 2783). The therapy reduced incidences of fractures. After 6 mth (FM, TM, GR) and 1 yrs (FM, GR) of treatment, BMC was significantly ($p < 0.01$) increased. DBM showed a very slow increment of mineralization with significant recovery only 2.7 yrs after the first evaluation. No adverse effects of 1,25(OH)2D3 therapy were observed; CaU/CrU ratio remained in the normal range.

178

E.Takeda*, Y.Kuroda*, M.Miyao* (Introd. by A.Prader)
Department of Pediatrics, University of Tokushima, Tokushima, Japan.

TREATMENT OF THREE PATIENTS WITH VITAMIN D-DEPENDENT RICKETS TYPE II AND ALOPECIA WITH 1α-HYDROXYVITAMIN D_3 AND CALCIUM

Three patients with rickets that appeared at 1 to 2 years old and alopecia that appeared at 2 to 4 months old were diagnosed at 2 to 3 years old as having vitamin D-dependent rickets type II (VDDR II), because of hypocalcemia, hyperparathyroidism, and increased plasma levels of alkaline phosphatase and 1,25-dihydroxyvitamin D_3[1,25-$(OH)_2D_3$]. Impaired nuclear uptake and normal cytosol binding of [^{3}H]1,25-$(OH)_2D_3$ were observed in cultured skin fibroblasts and PHA-stimulated lymphocytes of these patients. In addition, the incorporation of ^{14}C-thymidine into PHA-stimulated lymphocytes of the patients was not reduced by 1,25-$(OH)_2D_3$, unlike in control lymphocytes.

These patients were treated with 1α-hydroxyvitamin D_3[1α-OHD_3] and calcium(Ca) lactate. Two patients responded to 3 ug/kg/day of 1α-OHD_3 and 2 g/day of Ca lactate, and their blood chemistry and bone lesions were normalized after 15 and 36 weeks of treatment. However, the most severe case responded only partially to 5 ug/kg/day of 1α-OHD_3 and 2 g/day of Ca lactate. The alopecia of the patients was not improved by these treatments. These results suggest that high doses of 1α-OHD_3 may be useful in treatment of VDDR II with alopecia, which have been reported to be resistant to treatment, and that VDDR II may be heterogeneous.