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A new syndrome, H.H.R.H. was recently described in 8 members of one kindred. Studies of 49 additional asymptomatic members of this kindred revealed: 29 normal subjects (N.), while 20 others had hypercalciuria (I.H.) with no evidence of bone disease. The following indices distinguished the 3 different groups: 24h urinary calcium creatinine ratio (Ca/Cr.) 0.43 ± 0.14 (mean ± SD) in H.H.R.H., 0.34 ± 0.07 in I.H., and 0.14 ± 0.05 in N. Serum phosphorus (Pi) and TmP/GFR as determined by age related means and expressed in SD units were −4.31 ± 2.38 and −3.0 ± 1.24 in H.H.R.H., −1.11 ± 0.98 and −1.13 ± 0.57 for I.H., +0.01 ± 0.98 and +0.21 ± 0.94 for N. Serum levels of $1.25(OH)_2D$ were 303 ± 208 pg/ml, 145 ± 99 and 84 ± 36, in H.H.R.H., I.H. and N., respectively. Urinary cAMP excretion in H.H.R.H., I.H. and N. was 1.66 ± 0.73, 2.69 ± 1.05 and 3.28 ± 0.96 nmol/100 ml.GF. respectively. A significant negative linear correlation was found between TmP/GFR, serum $1.25(OH)_2D$ levels and urinary Ca/Cr in all subjects. We propose that the pivotal genetic defect in this kindred is a renal Pi leak resulting in hypophosphatemia and an appropriate elevation of $1.25(OH)_2D$ levels, which causes increased Ca absorption parathyroid suppression and hypercalciuria. We conclude 1. This kindred represents a new hereditary syndrome in which the affected site in the kidney is different from the known hypophosphatemic syndromes. 2. Pi is an important mediator in controlling $1.25(OH)_2D$ in human. 3. The pathophysiological sequence operating in our I.H. subjects and H.H.R.H. patients is identical. 4. Quantitatively the abnormalities in I.H. are milder and the biochemical parameters are in between the values of H.H.R.H. and normals. 5. For the first time, the concept of idiopathic hypercalciuria as an expression of a specific inherited renal defect, is clearly illustrated.

INHIBITORY EFFECTS OF BISPHOSPHONATES ON DIURNAL VARIATIONS OF BLOOD ^{45}CA AND ^{3}H-TETRACYCLINE IN YOUNG DOGS

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We have shown that diurnal variations of blood ^{45}Ca, ^{3}H-tetracycline, and vitamin D metabolites occur in normal dogs, and these diurnal variations are completely eliminated in calcium-deficient or thyroparathyroidectomized dogs (Amer. J. Physiol. 246:R688–692, 1984). To further elucidate the mechanisms for this diurnal rhythm, the effects of the bisphosphonates, EHDP and Cl_2MDP, on diurnal variations in young growing dogs were studied. Labrador retriever dogs were extensively prelabelled with ^{45}Ca and ^{3}H-tetracycline. Groups of 3 dogs were injected daily with either EHDP (2.5 mgP/kg body wt/day) or Cl_2MDP (5.0 mgP/kg body wt/day) while 4 dogs served as controls. Sequential blood sampling at 8 am, 12 and 4 pm were performed daily. In normal intact dogs, blood ^{45}Ca and ^{3}H-tetracycline decreased continuously during the day to minima of 65 ± 3% and 67 ± 3% of baseline, respectively, at 4–8 pm, while blood calcium remained constant throughout the day. In the bisphosphonate-treated dogs, blood calcium remained in the normal range throughout the entire experimental period. The diurnal variations of blood radioactivities, however, gradually decreased in amplitude and were completely eliminated in both EHDP and Cl_2MDP treated dogs after 3 and 4 weeks of treatment. The maximum daily change in blood radioactivity was 91 ± 3.5% of baseline. After treatment was terminated, the diurnal variation remained inhibited for up to two weeks and gradually returned to a normal rhythm. Data from this study show that the diurnal variations of blood ^{45}Ca and ^{3}H-tetracycline in extensively prelabelled dogs can be inhibited by EHDP and Cl_2MDP, known inhibitors of bone resorption. These data further support the hypothesis that bone resorption changes reciprocally in response to daily fluctuations in dietary calcium intake, resulting in the rhythmic changes in blood radioactivities.

PLASMA 1αOHD$_3$, 1,25(OH)$_2$D AND CALCIUM IN CALVES AND IN DAMS TREATED PREPARTUM WITH 1αOHD$_3$

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1αhydroxyvitamin D_3 (1αOHD$_3$) has been used to prevent bovine Parturient Paresis in cows, which is the result of a severe hypocalcemia. Following an IM injection of 1αOHD$_3$, the D-derivative appeared in plasma after 12 h, reaching a peak 24 h after the injection. The disappearance rate of 1αOHD$_3$ from the blood was 0.330 d^{-1} (biological half-life of 2.1 d). Plasma $1,25(OH)_2D$ increased as early as 6 h and peaked between 24 to 48 h after the 1αOHD$_3$ injection. Plasma calcium increased after 6 h and remained high for at least 8 d. At parturition, plasma 1αOHD$_3$ in calves was higher than that of their 1αOHD$_3$-treated mothers. Plasma Ca was always higher and $1,25(OH)_2D$ always lower in the plasma of calves than in their maternal plasma. Plasma $1,25(OH)_2D$ was higher in cows treated with 1αOHD$_3$ and in their offspring than in their respective controls. The results provide additional evidence that in cattle, neonate plasma $1,25(OH)_2D$ is not correlated with the maternal plasma concentration. The high plasma $1,25(OH)_2D$ concentration observed in calves of 1αOHD$_3$ treated cows could result from its 25-hydroxylation in the calf liver rather than from its placental transfer. Elevated leves of vitamin D metabolites in the plasma of calves of 1αOHD$_3$-treated mothers, did not result in any change in plasma Ca concentration.

SERUM VITAMIN D AND CALCIUM IN TUBERCULOUS PATIENTS

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It has been widely reported that, in common with other granulomatous conditions, tuberculosis is implicated in hypercalcaemia. It is believed that granuloma macrophages convert 25-(OH)D to $1\text{-}25(OH)_2D$, resulting in hypercalcaemia. We have studied two groups of tuberculous patients together with matched healthy controls: a UK and an African group. In 50 patients and healthy controls resident in the UK (Cardiff, South Wales): median 25(OH)D (6.4 ng/ml) was significantly lower than controls (10.9