47 C. DUPONT+, C. GESPACH+, M. LABURTHE+, G. ROSSELIN+ (Intr. by P. Canlorbe) INSERM U.55, Hôpital Saint-Antoine, Paris 12°, FRANCE. Prevalence of vasoactive intestinal peptide (VIP) in the regulation of cyclic AMP production in digestive epithelia: a specific feature of human.

We have previously shown that VIP, a potent stimulator of water and electrolytes secretion in human intestine, acts through its binding to specific receptors and the stimulation of cyclic AMP production in epithelial cells. We report here the occurence in epithelial cells of human stomach and gallbladder of receptors for VIP that are similar for the followings: 1) two classes of binding sites, a small number with high affinity (Kd = 1.3 x 10^{-9}M) and a large number with low affinity (Kd = 1.6 x 10^{-8}M); 2) positive non linear coupling with a cyclic AMP producing system; 3) effectiveness of VIP at low physiological doses (3 x 10^{-12}M - 10^{-8}M). Secretin does not exhibit any specific receptor in these epithelia and stimulates cyclic AMP production only at supraphamacological doses (10^{-7}-10^{-5}M) through its binding to the VIP receptor. The presence of a VIP receptor together with the absence of a specific secretin receptor in stomach and gallbladder epithelia is a character specific of human. Indeed, we show that rat gastric epithelium exhibits a cyclic AMP system sensitive specifically to secretin and not to VIP and that guinea pig gallbladder epithelium exhibits both a VIP- and a secretin-sensitive cyclic AMP system. Conclusion. Peptide receptors have been characterized in epithelial cells isolated from digestive organs. Their species specificity emphasizes the importance of experiments carried out in human.

48 I. SCHEDEWIE, W. SLIKKER*, D. HILL*, R. TSANG*, J. BAILEY*, J. ELDERS*, UAMS, Little Rock, AR: NCTR, Jefferson, AR: UCCM, Cincinnati, O. MATERNAL-FETAL CROSSOVER OF $1,25(OH)_2$ VITAMIN D IN SUBHUMAN PRIMATES.

The role of vitamin D (D) in fetal mineral metabolism remains to be established. We have studied transplacental transfer, fetal distribution and metabolism of ^{3}H-$1,25(OH)_2$D (^{3}H-1,25) in 5 Rhesus monkeys during the latter third of pregnancy. Indwelling catheters were placed in maternal (mat.) aorta, uterine vein, and fetal umbilical artery & vein. Serial blood was obtained from these sites over 3 hrs. Amniotic fluid and mat. urine were collected every 60 min. Serum, urine, amniotic fluid, and various tissue samples were extracted and analyzed by high performance liquid chromatography to determine total radioactivity (RA) and specific D metabolites. Peak RA levels in the fetus were reached within 20 min post injection. RA concentrations in fetal serum were 10-15% of mat. serum levels. RA concentrations in amniotic fluid and fetal urine were 10% of fetal serum concentrations. 75-85% of mat. & fetal serum RA was identified as intact ^{3}H-1,25. Up to 50% of tissue RA consisted of ^{3}H-1,25 in a fetus delivered 3 hrs after dose administration. However, in fetuses aborted 24-48 hrs post injection, no ^{3}H-1,25 but highly polar compounds were found. These data suggest that $1,25(OH)_2$D crosses the placenta in subhuman primates as has been shown for other sterols. Furthermore, the fetus appears to be capable of converting $1,25(OH)_2$D to more polar steroid derivatives.

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Parathyroid (PTH) infusion test in hypo- (HP), pseudo= hypo- (PHP) and pseudopseudohypoparathyroidism (PPHP).

Ten healthy children, 3 children with HP, a child with PHP and a child with PPHP were infused with 250 U PTH over 15 min. The renal excretion of cyclic AMP, P, Ca, HCO_3, Na and K was measured and compared to 28 adult volunteers. Excretion of healthy children did not differ from the adults' response: Cyclic AMP increased from a mean of 3 to 166nmol/dlGF. P increased from 5 to 16 mg/dlGF. Ca decreased from 3.2 to 1.8ueq/mg cr. HCO_3 from 6 to 170 ueq/mg cr. Na from 137 to 301ueq/mg cr. K from 80 to 197 ueq/mg cr. The patients with HP had an exaggerated cyclic AMP, P, HCO_3 and K response to PTH. Their Na response was normal. The PHP patient did not increased his cyclic AMP clearance. His P and K responded subnormally and he had a supranormal response of Na and HCO_3. The PPHP patient had intermediate response between the normal and the PHP. We conclude that PTH infusion is usefull in the diagnosis of PTH secretion and its renal response. PPHP represents a partial defect in the renal response to PTH.

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Effect of parathyroid hormone on 1,25-dihydroxyvitamin D formation in type I pseudohypoparathyroidism.

It has been presumed that the stimulating effect of parathyroidhormone (PTH) on 1-hydroxylation of 25OHD in the kidney is mediated through cAMP. To explore this assumption parathyroid extract (PTE) was infused to a patient with type I pseudohypoparathyroidism and control subjects. In the controls the infusion resulted in a prompt and marked increase in both plasma cAMP and urinary excretion of cAMP, whereas there was only a negligible increase in the patient. Following the PTE infusion plasma $1,25(OH)_2$D showed a distinct increase after 2 hours both in the controls and the patient, with a further increase after 4 hours. The finding in this patient with pseudohypoparathyroidism type I seems to negate the presumption that PTH regulation of the 25OHD-1-hydroxylase is mediated by cAMP.

Measurements of plasma $1,25(OH)_2$D during PTE infusion test might be a useful adjunct in the work up of various disorders of parathyroid-vitamin D-calcium metabolism.

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Early pubertal development in girls adopted from Far-Eastern countries.

We have been consulted about early pubertal development in 7 adopted girls with the following characteristics:

1. Coming from India, except one from Bangladesh.
2. Adopted at a relatively high age, 4.6 yrs (3.3-6.6).
3. Small at arrival, length -2.1 SD compared to Swedish standards, with no advanced bone age, Greulich and Pyle (3 measured).
4. More pronounced catch-up growth than reported for other children in Sweden adopted from abroad. Cumulative length acceleration 2.0 SD after one year, 3.2 SD after 2 yrs.
5. Pubertal signs early and at a small body size. All had Tanner stage B 2 at age 7 yrs. Six, now in stage B 3-4, age 7.5 yrs with a bone age of 10.8 and mean length 128 cm. Four have had menarche at 131 cm, 26.5 kg and 7.6 yrs of age.
6. Endocrinological findings as in idiopathic pubertas praecox.

This kind of early puberty is easy to recognize, elaborative investigations are not necessary. There is no single explanation. Ethnical factors probably contribute, psychosocial factors may do so. The girls may be somewhat older than stated. In some girls catch-up growth seemed to proceed straigth into a pubertal growth spurt, suggesting a precocious initiation of puberty by the increased metabolic activity during catch-up growth.

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Insulin antibodies, HbA1 in juvenile diabetic (JD) children treated with purified and non-purified insulins (NPI).

Insulin antibodies were determined in sera from 38 JD children. 8 children were started on purified porcine insulins (PPI). 16 got insulin NPH alone, and 14 non-purified, of whom 9 were later transferred to PPI. Serum insulin antibodies were measured by qualitative and quantitative methods using beef (B) and pork (P) antigens. 12/38 JD children had insulin antibody levels as low as normal children, irrespective of the type of insulin used. The conc. of antibodies using radiolabelled (B) or (P) insulins as antigens were strongly correlated, by both the qualitative ($p<0.01$) and quantitative ($p<0.01$) methods. JD children with better score for diabetic control had significantly lower levels of insulin antibodies against B ($p<0.05$) and P ($p<0.05$) than those with poor diabetic control. There was also a significant correlation between mean HbA1 conc. and (B) and (P) mean insulin antibody conc. ($p<0.01$). Finally, patients treated with PPI had significantly lower levels of antibodies than patients treated with NPI ($p<0.05$).