106 F. ZANGENEH, L. ABOLMOLOUKY and T. BOSTAN (Intr. by P.E. Ferrier). Dept. of Ped. Univ. of Tehran and Div. of Endocr., Children's Hosp. Med. Center, Tehran, Iran

Serum Phenylalanine (Phe) and Tyrosine (Tyr) levels in Congenital Hypothyroidism.

Fasting serum Tyr levels are known to be low in hypothyroidism. The pathogenesis of hypotyrosinemia in hypothyroidism is complex and appears to involve a number of factors, such as reduced activity of hepatic phenylalanine-hydroxylase. In order to investigate this factor, serum Phe and Tyr levels were measured in 19 children with congenital hypothyroidism (CH) and 20 normal controls (C). The mean serum Phe levels in CH and C were 1.54 ± 0.36 and 1.83 ± 0.61 mg/dl, respectively. The mean serum Tyr levels in CH and C were 0.91 ± 0.33 and 1.49 ± 0.47 mg/dl, respectively. Although serum Tyr levels in CH were significantly lower than in C ($P < 0.001$), there were no significant difference in Phe levels in the two groups ($0.05 < P < 0.1$). The mean Phe/Tyr ratios in CH and C were 2.10 ± 0.84 and 1.47 ± 0.58 mg/dl, respectively. Although the ratio in CH was significantly higher than in C ($0.001 < P < 0.01$), in view of normal levels of Phe in CH, the observed difference in Phe/Tyr ratios does not confirm the existence of a deficiency in Phe-hydroxylase activity in hypothyroid children. In summary : (1) serum Tyr levels in CH are markedly lower than normal, (2) serum Phe levels in CH are within normal range, (3) serum Phe/Tyr ratios in CH are higher than normal, (4) decreased rate of conversion of Phe to Tyr is probably not the cause of hypotyrosinemia in CH.

107 S.A. Dowshen*, I. Rezvani, P. Alburger*, Departments of Pediatrics, Albert Einstein Medical Center (North.) and Temple University School of Medicine, St. Christopher's Hospital for Children, Phila., PA, USA

Reduced serum 1,25-dihydroxyvitamin D (1,25-DD) levels during immobilization (IB).

Hypercalciuria is known to occur during IB. Significant hypercalcemia develops in some instances, particularly in children. Factors potentially involved in Ca homeostasis during IB were studied prospectively in 5 male children with femoral fracture. Increased urinary Ca excretion occurred in all patients. Serum Ca and P levels rose but remained normal in all but one, in whom significant hypercalcemia developed. C-terminal immunoreactive parathormone (PTH) was moderately elevated in this patient but remained normal in all others. Serum 25-hydroxyvitamin D (25-HD) remained normal, however, 1,25-DD decreased to undetectable levels in all patients within 1-3 wks. of IB. The mechanism of the reduction in serum 1,25-DD is unknown. Normal serum 25-HD and PTH levels exclude vit. D-deficiency or PTH-mediated alterations in renal 1α-hydroxylase activity as causes. Indeed, a similar decrease in 1,25-DD occurred in the hypercalcemic patient despite elevated PTH levels. The reduction in 1,25-DD levels may represent an adaptive mechanism in Ca homeostasis during IB bone resorption. This finding may explain the impaired intestinal Ca absorption known to occur in immobilized patients and may play a role in the pathogenesis of disuse osteoporosis. Some cases of IB hypercalcemia may relate to previously subclinical hyperparathyroidism.

108 S.M.SUH and A.F. FIREK* Shriners Hospitals, Honolulu Unit and Department of Pediatrics, University of Hawaii, U.S.A.

Urinary excretion of cyclic nucleotides and electrolytes in response to parathyroid hormone (PTH) and calcitonin (CT) in man.

Although an increased urinary excretion of cAMP in response to PTH is well documented, few studies have investigated urinary excretion of cAMP after CT administration and those that are available report conflicting results. In order to assess the role of cyclic nucleotides in urinary excretion of electrolytes, in response to CT, we studied 6 children by comparing their response to iv PTE and CT in urinary excretion of cAMP, cGMP, P, Na, K, Cl, HCO_3, Mg and Ca. PTE increased urinary cAMP (ΔcAMP 437±74 nmol/min/100ml Ccr) but CT did not. Both PTE and CT did not increase cGMP excretion. Phosphaturia was produced by both PTE (ΔTRP;-18±3%) and CT (ΔTRP;-13±2%). PTE increased Na and Cl (ΔNa 150±43, ΔCl 145±35) as did CT but CT had a more prompt and potent effect (ΔNa 337±47, ΔCl 206±38). PTE alone increased HCO_3 and K excretion (ΔHCO_3 66±27, ΔK 71±17) with no effect by CT. CT increased Ca and Mg excretion (ΔCa 13±2, ΔMg 7±1) while PTE had no effect. These electrolyte excretion patterns suggest sites of action for CT distinct from PTE, being more distal than the proximal tubule where PTE has a predominant effect. The lack of cAMP response could be due to this difference in sites of action or it may suggest that electrolytes response to CT is mediated by a mechanism independent of cAMP.
(All data on electrolytes are expressed as μEq/min/100 ml Ccr).

109 M.L. ARSENIO-NUNES* and J.L. CHAUSSAIN. Inserm U. 154 and 188, Hôpital Saint-Vincent de Paul, Paris, France.

Interest of conjunctival biopsy in the early diagnosis of adrenoleucodystrophy (ALD) in boys with Addison's disease.

Isolated adrenal insufficiency may precede the development of neurological symptoms in boys with ALD. In view of an early diagnosis, conjunctival biopsies were done in 2 groups of boys with documented Addison's disease : Group A consisted of 5 boys aged 5 to 16 years with typical neurosensorial signs and extended demyelination on cranial tomodensitography (TD) ; Group B consisted of 3 boys aged 7 to 11 years, without neurological symptoms but with limited posterior demyelination of TD in 1, and a familial history of ALD in another. In all cases, abnormal inclusions were detected in the cytoplasm of Schwann cells surrounding myelinated axons. In Group A, electronmicroscopy showed clear clefts associated with bundles of lamellar structures and rows of glycogen. In Group B, multilamellar bodies were frequently disposed in groups of 2 or 3 inclusions. In conclusion, conjunctival biopsy, demonstrating peculiar lesions in Schwann cells, offers the possibility of a precocious diagnosis of ALD in boys with Addison's disease, before the development of neurological symptoms.

110 F.G.CASSORLA, B.D.ALBERTSON*, G.P.CHROUSOS*, J.BOOTH*, M.B.LIPSETT* and D.L.LORIAUX*. NIH, Bethesda, MD.

The mechanism of hypercortisolemia in squirrel monkeys.

The squirrel monkey (SM), a New World primate, has plasma cortisol (F) levels 10 times higher than Old World primates, such as Cynomologus (C), and man. The high F levels in SM are necessitated by F receptors of decreased affinity. We have tried to elucidate the mechanism by which SM maintains high plasma F levels. Two possible mechanisms are: increased F production rate (PR) or decreased F metabolic clearance rate (MCR). F MCR is about 62 $L/M^2/d$ in SM, half that of C (121 $L/M^2/d$). F PR, however, is 5 times greater in SM than in C: 120 $mg/M^2/d$ vs. 24 $mg/M^2/d$. The absence of adrenal gland hypertrophy in SM (500 mg adrenal/Kg body weight vs. 400 mg/kg body weight in C), suggests an increase in F biosynthetic efficiency. This was investigated by measuring the activity of 4 adrenal microsomal enzymes: 21 hydroxylase, 3 B hydroxysteroid dehydrogenase, 17 hydroxylase and 17, 20 desmolase.

	21OH	3B ol	17 OH	17,20 Desm.
	(nmol/min/mg protein)			(pmol/min/mg prot)
SM (Mean±SE)	23.9±0.26	10.5±0.15	9.4±0.52	24.7±1.98
C (mean±SE)	6.4±0.23	10.2±0.51	10.5±0.09	37.5±1.86
Significance	p<0.0005	NS	p<0.05	p<0.0025

The pattern of enzyme activities observed, increased 21OH and decreased 17,20 desm, suggests an efficient use of 17 hydroxyprogesterone as substrate for F biosynthesis. We conclude that SM maintains high plasma F levels mainly by increased FPR, which may be facilitated by alterations in the activity of F biosynthetic enzymes.

111 G.P. CHROUSOS*, G.B. CUTLER* JR., D. MANN* AND D.L. LORIAUX* (Intr. by M.G. Forest). National Institutes of Health, Bethesda, MD, USA.

Late onset 21-hydroxylase deficiency is a genetic variant of the classic form of congenital adrenal hyperplasia (CAH).

Three young adult women with the diagnosis of idiopathic hirsutism had markedly abnormal elevations of serum 17-hydroxyprogesterone (17HP) in response to an ACTH stimulation test, indicating a mild degree of 21-hydroxylase deficiency. All three had oligoamenorrhea, exhibited no virilization and had reached a normal adult height. One had pubarche at 6 yrs. An ACTH stimulation test and HLA typing was performed on all available family members. Five of the 6 parents had elevations of 17HP comparable to those found in carriers of classic CAH. Two of the 3 propositi had HLA identical adult male siblings of normal height and masculinization with an identical abnormality in 17HP response to ACTH. One of the affected males developed intratesticular adrenal rest tumors that were reduced in size after dexamethasone therapy. Three HLA non-identical sisters to the propositi were not affected. One patient married a CAH heterozygote and had two biochemically affected children (female 7 yrs and male 3 yrs) with normal heights, bone ages, and no signs of virilization, except for mildly increased terminal hair on the face and extremities of the daughter. We conclude that late onset congenital adrenal hyperplasia is a genetic variant of CAH with a milder enzymatic block and attenuated clinical expression. The affected gene is linked to the HLA locus. The presentation in females is that of mild masculinization. Males are asymptomatic but adrenal rest tumors in the testes may occur.