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RED CELL SORBITOL AN EFFECTIVE INDICATOR OF DIABETIC CONTROL. Malone, J.I. and Simons, C.A., University of South Florida, Col. of Medicine, Dept. of Ped., Tampa, Florida. Sponsored by Lewis A. Barnes.

The importance of good glycemic control is the presumed prevention of the long term sequela of diabetes. Sorbitol is the product of an insulin-independent pathway of carbohydrate metabolism that has been implicated as etiologic in the complications of diabetes. The polyol pathway producing sorbitol is active in human erythrocytes. Fasting blood samples were collected from 62 children with diabetes. Serum glucose and red cell sorbitol were measured by specific enzymatic assays. Hemoglobin A_{1c} was measured spectrophotometrically after column separation on Bio-Rex 70. Results:

	Glucose mg/dl	Sorbitol mM/gm Hb	HbA _{1c} % of Total
Control	82.0±4.8 (10)	10.0±5.8 (10)	3.0±1.7 (10)
Diabetic	64.7±15.7 (10)	14.9±10.8 (10)	8.1±3.5 (10)
	163.9±22.5 (19)	22.5±14.9 (19)	10.4±3.2 (19)
	258.7±30.8 (19)	34.8±25.9 (19)	12.4±2.3 (19)
	349.4±39.0 (14)	38.7±23.9 (14)	12.5±2.5 (14)

The correlation of fasting glucose and sorbitol was significant. $r=0.26p<.05$. The correlation of fasting glucose & HbA_{1c} was not significant $r=0.1$. Elevated HbA_{1c} in vivo remains unchanged after 24 hrs. of glucose concentrations <150 mg/dl but sorbitol concentrations reflect hourly changes in glucose concentration. RBC sorbitol directly quantitates a mediator of cellular pathology in diabetes as it reflects the mean blood glucose levels. RBC sorbitol is therefore the most useful indicator of effective diabetic management.

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STUDIES OF ANDROGEN PRODUCTION AND BINDING IN THE SYNDROME OF MALE PSEUDOHERMAPHRODITISM AND CONGENITAL DEGENERATIVE RENAL DISEASE. Walter J. Meyer, III,

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The etiology of the genital anomalies in two unrelated teenagers with male pseudohermaphroditism and renal disease has been investigated. Patient A, 15-5/12 year old XY black, has stage 5 pubic hair, perineal hypospadias, 3 cc firm descended right testis, undescended left testis, 12 cm phallus with cordae, and focal segmental glomerulonephritis. Patient B, 13-2/12 year old XY white, showed stage 2 pubic hair, 1° hypospadias, 6 cm phallus, bilaterally undescended testes, left renal agenesis and right vesicoureteral reflux with a small hydronephrotic kidney. Also Patient B has anal atresia and vertebral anomalies. Although neither has a uterus or fallopian tubes, Patient A has a rudimentary vagina. Patient A had elevated gonadotropins (FSH >160, LH=60 mIU/ml) and his testosterone did not rise (995→738 ng/dl) after 5 days of HCG. Patient B's gonadotropins (FSH=7.0, LH=5.0 mIU/ml) were normal and testosterone rose with HCG (396→915 ng/dl). The cultured suprapubic skin fibroblasts from both patients had normal 5α-reductase activity and normal capacity of high affinity specific receptor for dihydrotestosterone. The etiology of the male pseudohermaphroditism is postulated to be a decreased androgen production in utero rather than an enzymatic defect in steroidogenesis or a defect in androgen binding.

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ACTH-PRODUCING INTRACRANIAL TUMOR IN AN INFANT. W.L. Miller, M.M. Grumbach, and S.L. Kaplan. Dept. Pediat. Univ. California San Francisco, San Francisco, Ca.

ACTH-producing brain tumors in infancy are rare. An 8 month male was evaluated for a 4 month history of profound obesity, acne, moon-facies, hypertension, and hirsutism. An IVP and computerized tomographic (CT) scan of the abdomen were normal. Plasma DHEA was 155-299 ng/dl. Dexamethasone (3.75 mg/m² x 3d) failed to suppress elevated urine 17-OHCS (10.1 mg/24h) and free cortisol (1026 µg/24h), but partially suppressed plasma cortisol from 79 to 32.4 µg/dl and plasma ACTH from 320 to 90 pg/ml. In response to TRF, TSH rose to 1.9 µU/ml, prolactin rose to 8.3 ng/ml and ACTH did not change. Brain CT scan and angiography demonstrated a large sub-frontal tumor which appeared to be separate from the pituitary fossa. Craniotomy demonstrated an inoperable highly vascular tumor extending into the sella. Biopsy of the main body of the tumor showed undifferentiated mesenchymal tissue with some gland formation, while tumor superior to the sella histologically resembled pituitary adenoma. Medium from cultured cells from the mesenchymal tissue contained no measurable ACTH while medium from the cultured adenomatous cells contained 111-140 pg ACTH/ml. There was no bioassayable CRF activity in the medium from any cultured cells (assayed by Dr. Monte Greer).

Total adrenal weight at autopsy was 15 gm. The brain tumor was 5x5x6cm mass with a tail extending into pituitary tissue. Serial histologic sections of the mass showed a gradual transition from pituitary adenoma with occasional gland-like structures, to sheets of undifferentiated mesenchymal tissue with venous sinusoids and numerous gland-like structures.

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HYPERTRIIODOTHYRONINEMIA WITH THYROGLOBULIN THERAPY. Edgar Morillo and Lytt I. Gardner, Dept. of Ped., SUNY, Upstate Med. Ctr., Syracuse, New York.

Hypertriiodothyroninemia (hyper-T₃) was noted in 2 hypothyroid children treated with desiccated thyroid (Abbassi and Aldige, J. Ped. 90:298, 1977). We have also observed this in 6 hypothyroid patients receiving thyroglobulin (Prolloid®). T₃ by RIA and T₄ by RIA or CPB were measured in 2 boys and a girl with goitrous hypothyroidism (ages 7, 16 and 12 years), in a cryptothyroid boy (age 15), in a woman with congenital athyreosis (age 23) and in a girl with hypothyroidism secondary to thyroiditis. Therapy had been in progress at least 3 months, and in 3 cases for as long as 7 years when hyper-T₃ was observed. Four patients showed above normal levels of serum T₃ when T₄ values were below normal. A value of T₃ in excess of 400 ng/dl (beyond range of highest standard, with N=97-217) was found in the woman with congenital athyreosis; serum T₄ was normal. Clinical evaluation revealed no findings attributable to excess of thyroid hormones except slight nervousness or transitory heat intolerance. In 2 patients substitution of levothyroxine for thyroglobulin therapy has been associated with a fall of serum T₃ values to normal. It has been established that serum T₃ levels in children are higher than in adults (Fisher et al., JCEM 45:191, 1977), but the hyper-T₃ values we have observed are above this range. It is as yet unknown if the hyper-T₃ of these patients is due to T₃ load from the thyroglobulin medication or is an endogenous peripheral monodeiodination of T₄.

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PRESENCE IN RAT SERUM OF AN INHIBITOR OF ³H-THYMIDINE INCORPORATION BY CHONDROCYTES IN VITRO. Allen K. Murray, Regina A. Jansons and H. David Mosier, Jr.,

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In the course of studies on somatomedin activity we have noted that normal rat serum routinely inhibited ³H-thymidine incorporation by rat or porcine cartilage while, at the same time, it stimulated sulfate incorporation. Human serum did not show this selective inhibition for ³H-thymidine incorporation in the somatomedin bioassay system. With porcine cartilage we found a serum dose response of ³H-thymidine inhibition at serum concentrations from 0.625% to 40%. Inhibitory activity was stable to repeated freezing and thawing, storage in a partially purified state at 4° for two weeks, and heating at 90° for 30 min. at pH 5.5. Inhibition occurred in cartilage of fasted, hypophysectomized or control rats. With different durations of pre-incubation and/or incubation rat serum inhibited ³H-thymidine uptake in all samples, but human serum stimulated ³H-thymidine uptake over long periods. Untreated serum retained its inhibitory activity after prolonged dialysis; addition of ammonium sulfate at 10% saturation or greater and dialysis resulted in loss of all serum activity. Significant purification of the factor was achieved by gel filtration on Bio-Gel P-200. The active fraction had an absorption maximum at 260nm consistent with the presence of nucleic acid; there were no absorption peaks at 230nm or 280nm. There was no protein detectable by the method of Lowry, et al. and there was no DNA detectable with diphenylamine. The fraction did give a positive orcinol reaction consistent with the presence of RNA or pentose.

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DEFICIENCY OF CORTISOL 11-β-KETOREDUCTASE - A NEW METABOLIC DEFECT. M.I. New, L. Bradlow, J. Fishman, P. Gunczler, G. Zancanato, W. Rauh, L.S. Levine, S. Ulick,

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A deficiency of cortisol 11-β-ketoreductase was observed in 2 patients with the syndrome of apparent mineralocorticoid excess and no evidence of oversecretion of any known steroid hormone (JCEM 44:924, 1977). The syndrome is characterized by hypertension, hypokalemia and suppressed renin and ACTH despite low secretion of aldosterone, cortisol and other adrenocortical steroids. Excretion of 5-α-reduced cortisol (DHF) is increased in the urinary free steroid fraction (JCEM 44:799, 1977). The 11 ketoreductase deficiency was demonstrated by a markedly elevated ratio of urinary THF/THE (6-10) in the resting state during ACTH and hydrocortisone treatment. In normal children the THF/THE ratio is usually less than 1. The deficiency was further proven by demonstrating an inability to form tritiated water after infusion of 11α³H cortisol. In normal subjects and in the unaffected mother of a patient, 65-80% of 11α³H cortisol appeared as tritiated water.

Speculation: In these patients the 11 ketoreductase deficiency produces an impairment of the metabolism of cortisol to cortisone, resulting in a prolonged cortisol half-life, suppression of ACTH and normal serum cortisol concentration. The enzyme defect protects the patient from adrenal insufficiency despite low cortisol secretion and may contribute to hypertension and hyporeninemia because of formation of excess DHF which has mineralocorticoid activity.