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CONTROL OF VASOPRESSIN (AVP) SECRETION IN THE LAMB. R.D. Leake, R.E. Weitzman, J.A. Weinberg, and D.A. Fisher, UCLA School of Med., Harbor General Hospital, Departments of Pediatrics and Medicine, Torrance, California.

The newborn is capable of secreting AVP, but there are no data regarding relative responsiveness to the several known physiological stimuli. We examined AVP, plasma sodium (Na) and osmolality (Osm) in response to phlebotomy, water loading, hypertonic saline and mild dehydration in 7-11 lambs, 2-49 (mean = 19) days of age. AVP was measured by radioimmunoassay.

Repeated phlebotomies (total 20 ml/kg) raised AVP from 4.8 ± 2.1 (mean $\pm$ SEM) to 74 ± 19 μ U/ml ($p < .01$), while Na and Osm remained unchanged. When 100 ml/kg 2.5% dextrose/water was infused over 60 minutes, AVP fell from 3.4 ± 1.2 to 0.7 ± 0.6 μ U/ml by 60 minutes ($p < .05$). Na and Osm fell from 140 to 125 mEq/L and 283 to 262 mOsm/kg respectively ($p < .05$). Hypertonic (23%) sodium chloride infusion (10 mEq/kg) increased Na from 142 to 159 mEq/L and Osm from 271 to 318 mOsm/kg over a 30 min. period ($p < .05$). In response to this stimulus, AVP increased from 2.9 ± 0.7 to 22.2 ± 9 μ U/ml ($p < .05$). After 18 hours of dehydration, AVP rose from 0.6 ± 0.1 to 3.4 ± 1.8 μ U/ml, Na from 134 to 140 mEq/L ($p < .05$) and Osm from 293 to 306 mOsm/kg ($p < .05$).

Thus the newborn lamb is capable of responding to both volume and osmolar stimuli. The quantitative stimulus-response ratios (SRR = $\Delta \log \text{AVP} / \Delta \text{Osm}$) were similar for water loaded and saline stimulated newborns and similar to responses in the adult. The dehydration SRR was not accountable by osmolar change alone but also reflected volume change.

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123 I EARLY RADIOIODINE TEST AS A PREDICTOR OF OUT-COME IN CHILDREN WITH THYROTOXICOSIS. Wai-Nang P. Lee, Rodney J. Wilmer, Solomon A. Kaplan, and Moses Greenfield, UCLA School of Medicine, Department of Pediatrics and Department of Radiological Sciences, Los Angeles, Calif. 90024.

Prediction of relapse in thyrotoxic patients have been difficult with currently available tests especially without discontinuing thionamide therapy. We have devised a new method of analysis, using early (20 minute) radio-iodine kinetics to determine if normal pituitary feedback mechanism has returned in medically treated patients without discontinuing therapy. By using the short half life radio-isotope ^{123}I and thionamide 1 hour prior to the test, we have been able to limit radiation exposure to less than 1% of that generally experienced with current use of ^{125}I or ^{131}I . Our method uses coincidence counting of gamma and x-rays emitted by the isotope which permits determination of the absolute rate of disintegration of the isotope independent of geometry. In 20 patients tested thus far we have been able to predict the outcome correctly in 87.5% with a minimum follow-up of 6 months. A trapping rate constant K_1 and also absolute iodine uptake AIU is calculated. The upper limit of normals for K_1 is 0.03 min $^{-1}$ and for AIU 0.04 $\mu\text{g}/\text{min}$. In the hyperthyroid patients without remission all values before and after tri-iodo-thyronine suppression were well outside this normal range for both measurements. Two patients with abnormal measurements who did go into remission appear to have thyroiditis in addition to Graves' disease. This new method of analysis appears to enhance substantially the accuracy of prediction of remission in medically treated patients with Graves' disease.

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PUBERTAL PROGRESSION WITH ELEVATED GONADOTROPINS IN GIRLS WITH MULTIPLE ENDOCRINE DEFICIENCIES. Anne W. Lucky, Robert W. Rebar, Robert M. Blizzard, and Elihu N. Goren, NICHD, NIH, Bethesda, and U. of Va., Charlottesville.

Pubertal progression in the presence of abnormally elevated serum gonadotropins was followed over several years in two girls with multiple endocrine deficiencies (hypoadrenalism and hypoparathyroidism) and mucocutaneous candidiasis. Accelerated height velocity and development of breasts and pubic hair were noted in both girls. A serum level of progesterone (8 ng/ml) consistent with ovulation was documented in one of the girls who has had regular monthly menses since age 15. High serum levels of FSH (30-60 mIU/ml) coincident with serum estradiol levels in the normal pubertal range (100-200 pg/ml) indicated partial ovarian end-organ resistance or failure. Basal levels of serum FSH were higher than LH, but the response of LH to intravenous leuteotropin releasing factor was relatively greater. Elevation of gonadotropins was progressive in both patients. Since premature menopause is associated with this syndrome, we postulate that we are observing progression through puberty in girls whose ovaries are in the early stages of a destructive process which may eventually result in irreversible ovarian failure. A possible explanation is increased resistance to gonadotropins at the ovarian level because of gonadotropin receptor antibodies or an inherent receptor defect.

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GLUCAGON: AN EFFECTOR OF ACTH, CORTISOL (F), AND GROWTH HORMONE RELEASE. S.L. Maby, H.L. Villet, and M.L. Cowper, Birth Defects Inst., N.Y.S. Dept. of Health, and Albany Med. Col., Dept. Ped., Albany, N.Y.

Glucagon (G), an accepted provocative stimulus for hGH release, would have greater usefulness if shown to effect the release of other trophic hormones. hGH response to G was studied in 10 children, ages 6-14 yrs, with simultaneous evaluation of ACTH and F responses.

Beginning at 0800 hrs, specimens were obtained at 30' intervals for hGH, ACTH, and F, which were measured by RIA, and for blood glucose (autoanalyzer), between -30 and +180' after a 1mg IM dose of G.

hGH responses were normal in 8/10 patients (> 10 ng/ml). In these 8, two types of ACTH-F response were noted; in 5 patients with a fasting F_0 of < 10 $\mu\text{g}/\text{dl}$, ACTH increased 4.5-fold (Δ ACTH 40-393 pg/ml), and F 5.6-fold (Δ F 15-27.3); the mean ACTH peak occurred at 150' and mean F peak at 180'. In two patients with an $F_0 > 10$ $\mu\text{g}/\text{dl}$, ACTH increased only two-fold (Δ ACTH 6 and 265 pg/ml), and F 1.5-fold (Δ 9.8 and 23.0 $\mu\text{g}/\text{dl}$). The ACTH and F peaks occurred as in the first group. One patient showed no change in F (range 19.5-23.0 $\mu\text{g}/\text{dl}$) and a 60% decrease in ACTH between 120' and 150'.

Two of the ten children had hGH and TSH deficiency. One had an F_0 of ≤ 0.5 $\mu\text{g}/\text{dl}$ and a rise in F to only 7.2; his ACTH increased from 10 to 38.0 pg/ml. The second patient showed an increase in F from 10.5-23.5 $\mu\text{g}/\text{dl}$; her ACTH increased from 37-50 pg/ml.

The pattern of the glucose response was similar in all groups, depicting the classic biphasic curve, with a hyperglycemic phase followed by a gradual decline in concentration. Nausea and abdominal discomfort were present in only one patient.

This study shows glucagon to be a reliable and safe provocative stimulus, not only for hGH release, but also for the assessment of the pituitary-adrenal axis. Studies, in progress, should help to elucidate its mechanism of action.

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TWO HOUR POST-GLUCAGON hGH IN DIAGNOSIS OF THE SHORT CHILD. D.R. MacMillan and M. Kotoyan. (Intr. by B.F. Andrews). University of Louisville, School of Medicine, Department of Pediatrics, Louisville, Kentucky.

Twenty-five children referred for short stature were screened for hGH deficiency on the basis of hGH response 2 hours after 1/m glucagon. All children over age 6 years showed retardation of height age (HA) and bone age (BA) of at least 2 years in relation to chronological age. Younger children were required to have HA and BA retardation of at least 1 year to be studied. 0.1 mg/kg of glucagon was used up to a maximum dose of 1 mg.

Nineteen patients (76%) responded with 2 hr. post-glucagon hGH levels of greater than 8 ng/ml with a mean for the entire group of 20.0 ng/ml. Retesting with glucagon produced a normal response in 2 of the 6 non-responders. Of the remaining 4, 3 showed minimal or blunted hGH responses to insulin-induced hypoglycemia.

In the 22 patients with apparently normal hGH function, the false positive rate was 13.6% (3 of 22) with a single test, and only 4.5% (1 of 22) with repeat testing of non-responders. Mean 2 hr. hGH level in these patients using the repeat values in initial non-responders was 27.3 ng/ml. The test is simple, effective and produced only mild nausea in 3 patients and is recommended as the primary screening procedure for hGH deficiency.

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CEREBRAL HCG SECRETING TUMOR-RESPONSE TO CHEMOTHERAPY. Judith V. McLaughlin, Chul H. Kim, Noel K. MacLaren, Ruth Luddy. University of Maryland School of Medicine, Department of Pediatrics, Baltimore, Maryland.

A 9-year-old white male with bitemporal vision loss and sexual precocity, had optic atrophy and panhypopituitarism (Peak hGH response to arginine/insulin -3.5 ng/ml, cortisol response to hypoglycemia -5 $\mu\text{g}/\text{ml}$). The T_4 was 1.6 $\mu\text{g}/100\text{ml}$ and morning urine specific gravity 1.001. His FSH was 5.5 mIU/ml but hLH was $> 100\text{mIU}/\text{ml}$. The testosterone was 1,644 ng/100ml. EMI scan was negative. The air study and carotid angiogram revealed a large avascular suprasellar mass. The greatly elevated hLH level and panhypopituitarism suggested hCG of tumor origin which was confirmed at a level of 884 ng/ml. The parents refused surgery or radiotherapy on religious grounds. Three months later he was readmitted with signs and symptoms of increased intracranial pressure. Repeat EMI scan revealed a large suprasellar mass with central calcification and obstructive hydrocephalus. A (P) V-A shunt was performed and the patient was started on Methotrexate 3mg/kg every two weeks for six weeks. During this time, he deteriorated to a state of dementia, stupor, blindness, and spasticity. In the seventh post-op week, triple therapy of Vincristine, Actinomycin D, and Cytosin was initiated. By the 8th week of triple therapy he was a happy, alert, articulate, ambulatory boy. His optic atrophy, and panhypopituitarism persist. By the 11th week, the hCG level was $< 4\text{ng}/\text{ml}$ and by the 14th week, his EMI scan revealed a marked reduction in tumor size.