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TRIIODOTHYRONINE NUCLEAR BINDING IN RABBIT LUNG AND CULTURED LUNG CELLS. Philip L. Ballard, Jeffrey A. Lindenberg and Arlette Brehier. Dept. of Peds. and Cardiovas. Res. Inst., Spec. Center of Pulm. Res., Univ. of California, San Francisco

To investigate the possible mechanism of thyroid hormone effects in lung development and function, we examined rabbit lung and two cell lines apparently derived from type II alveolar cells for specific nuclear binding of L-triiodothyronine (T_3). Nuclei isolated from lung were incubated at 37 C for 1.5 h with various concentrations of [^{125}I]-T_3 in the presence and absence of excess non-labelled T_3, and then washed in buffer with 0.2% Triton X-100. In fetal lung, the concentration of T_3 binding sites and the dissociation constant (K_d) were constant between 24-30 days gestation with mean±SE values (n=17) of 0.67±0.05 fmol/µg DNA (2400 sites/cell) and 500±52 pM, respectively. Adult lung (n=3) bound 0.31±0.03 fmol T_3/µg DNA (1120 sites/cell, $p<.01$ vs. fetal) and the K_d = 540±144 pM (NS). The L2 and A549 cell lines contained 2280 and 1580 nuclear sites/cell, and had K_d values of 200 and 280 pM, respectively. In fetal lung, the ability of analogs to compete for L-T_3 binding (100%) was: 3,5-diiodo-3'-isopropylthyronine 81%, D-T_3 73%, L-T_4 6.7%, L-T_2 0.19%, 3,5-dimethyl-3'-isopropylthyronine 0.15%, and reverse T_3 0.08%.

We conclude that rabbit lung and cultured epithelial lung cells contain nuclear binding sites with a high affinity and specificity for thyroid hormones. This suggests that both fetal and adult lung and their type II cells may be directly influenced by these hormones.

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PHARMACOKINETIC ANALYSIS OF DOSE DEPENDENT CONVERSION OF CORTISONE TO CORTISOL. Wm. H. Barr, Thos.Aceto,Jr & John Rider. SUNY,Bflo: MCV-VCU and USD Sch. of Med.

To determine the efficiency of conversion as a function of dose, relative amount of the biologically active metabolite of cortisone (E), hydrocortisone (F), available in systemic circulation was determined following the oral administration of 5 and 50 mg of E containing 1 to 6 uc ^{14}C-E. 26 studies were done: 8 well subjects; 7 children, adrenogenital syndrome; 5, growth hormone deficiency; 2, Crohn's disease. Plasma concentrations of F were determined by liquid scintillation counting following TLC separation using silica gel HF-254 and a solvent system of methylene chloride-ethanal (90-10). Relative fraction of F which reaches the systemic circulation was estimated by using the area under the plasma concentration time curve normalized for differences in the radioactive dose and surface area of the subject. (AUC'). AUC' values of F for 50 mg E given i.v. is only slightly greater than when 50 mg E was given orally, but the F to E ratio was much greater by the oral route indicating a greater preponderance of the E to F conversion pathway during the absorptive phase. Mean normalized AUC values (in units of percent radioactive dose, liter^{-1}, min.) for 5 and 50 mg dose were 283.5 (SD±104.7) and 157.8 (SD±80.6) respectively, ($p<0.001$)indicating almost a 50% difference in conversion efficiencies at two doses. Conclusion: Conversion of E to F is dose-dependent at 5 to 50 mg dosage range apparently due to saturable enzymes in the gut and liver and/or saturable transcortin binding during the absorptive phase. For those patients in whom a precise amount of F is needed, we recommend that E not be prescribed.

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WATER DEPRIVATION AND WATER LOADING IN CHILDREN WITH CENTRAL DIABETES INSIPIDUS (DI) DURING THERAPY WITH 1-DEAMINO-8-D ARGININE VASOPRESSIN (DDAVP). Dorothy J. Becker and Thomas P. Foley, Jr. University of Pittsburgh School of Medicine, Department of Pediatrics, Pittsburgh.

To assess the risks of dehydration and hemodilution during potentially normal circumstances in patients treated with DDAVP, we tested 9 children aged 7 2/12 - 17 9/12 with central DI. Three patients with other hormone deficits were receiving appropriate replacement. All had been stabilized on DDAVP for 1 yr with doses varying from 5 µg b.i.d. to 15 µg am and 10 µg pm. Urine volume and osmols and serum osmols were measured hourly from 8 am to 4 pm with 1) food and fluid ad lib, 2) food and water deprivation from 12 mn, 3) water load 20 ml/kg at 8 am.

		Day 1	Day 2	Day 3
Urine	8 hr vol (ml's)	251±26	156±23	226±27
±SE	Max osmols	806±46	910±40	901±39
Serum	Basal (8 am)	289±3	289±4	279±2
osmols	2 pm/*4 pm	284±2	290±4*	270±1
±SE	Max Δ	-4±3	+1±3	-11±1

In most children the urine volume and osmols were similar during the 3 days. Serum osmols hardly varied during normal fluid intake and water deprivation despite a mean 0.5 kg weight loss during the latter. However, only 26.5±9% of the water load was excreted in 8 hrs resulting in a significant ($p<.001$) depression of serum osmols. Despite this drop (occurring in 1 - 3 hrs) none were symptomatic. Thus DDAVP therapy results in a wide margin of safety during water deprivation and loading.

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TOPICAL TESTOSTERONE THERAPY FOR MICROPHALLUS IN MALE CHILDREN WITH HYPOPITUITARISM. Ehud Ben-Galim, Virginia V. Weldon, and Richard E. Hillman. Washington University School of Medicine, Department of Pediatrics, St. Louis Children's Hospital, St. Louis

Previous reports have documented the presence of microphallus in boys with hypopituitarism and have indicated the beneficial effects on phallic growth of systemic testosterone (T). Phallic growth probably depends on adequate tissue levels of dihydrotestosterone (DHT) with T being converted to DHT in the target tissue. Growth hormone (GH) may play a permissive role. We have studied the results of short-term (3 wks), topical application of 5% T in 4 boys with this syndrome.

Patient		1	2	3	4
Chronologic age (yrs)		2.5	6.7	7.6	11.2
Height age (HA) (yrs)		1.4	5.2	2.8	8.6
Δ Bone age/Δ HA (mos)		3/6	3/3	3/4	0/6
Phallic size (cm):	Before Rx	1.8	3.0	1.0	2.5
	After Rx	4.0	5.0	2.0	7.5
Serum T (ng/dl):	Before Rx	34	<20	<20	20
	During Rx	740	276	---	960

All patients were receiving GH at the time of T therapy. No acceleration of linear growth and no advance in osseous maturation occurred during or after treatment.

We conclude that local T for this brief period is a safe, effective, and simple means of stimulating phallic growth. Whether the effect is due to local tissue levels of elevated blood concentration of T remains to be demonstrated.

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INHIBITION OF MULLERIAN INHIBITING SUBSTANCE SECRETION BY FSH. Barry B. Becru, Yasuhide Morikawa, Ivor M.D. Jackson, Patricia K. Donohoe, Dept. Ped. Surg., and Pediatrics, Mass. Gen'l Hosp. & Endocrine Div., Tuft's N.E. Med. Ctr., Boston.

To evaluate the role of gonadotropins in the control of Mullerian Inhibiting Substance (MIS) secretion, pregnant rats were injected with rabbit antiserum against luteinizing hormone releasing hormone (LHRH), and their pups replaced with luteinizing hormone (LH) and/or FSH. LHRH antiserum was given at 13 and 20 days of gestation. Male pups from mothers treated with LHRH antiserum were given 5 daily s.c. injections of FSH, LH, FSH and LH or vehicle. The male pups from mothers treated with normal rabbit serum were given vehicle s.c. Testicular fragments of 6-day old pups born to mothers treated with LHRH antiserum during pregnancy showed an increase relative to controls in MIS activity in a graded organ culture bioassay system (Grade 3.4±0.2 vs. 2.0±0.0) ($p < 0.001$). FSH replacement given to pups from mothers treated with LHRH antiserum reduced testicular MIS secretion compared to vehicle treated pups from the same mothers (Grade 2.5±0.3 vs. 3.4±0.2) ($p < 0.05$). Postnatal FSH replacement after immunologic blockade of gonadotropins in utero reduced MIS activity of the testes to the same level as was found in testes of 6-day control pups. In contrast MIS activity remained high despite postnatal LH replacement in pups born to mothers given LHRH -AS (Grade 3.5±0.4 vs 3.4±0.2). These studies suggest that secretion of MIS is dependent on normal hypothalamic secretion of LHRH and is under inhibitory FSH control.

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NEUROGENIC DIABETES INSIPIDUS IN NEWBORN INFANTS ASSOCIATED WITH CNS ABNORMALITIES. David R. Brown and Charles T. Alward. Children's Health Center and Dept. of Peds. University of Minnesota, Minneapolis. (Spon. by Robert A. Ulstrom).

The clinical syndrome of neurogenic diabetes insipidus (DI) has recently been observed in three neonates. All cases were the products of complicated labors and deliveries and manifested symptoms of DI in the first 72 hours of life. Associated CNS abnormalities included metabolic encephalopathy, hemorrhage and cerebral hypoxia. Multiple quantitative measurements of serum antidiuretic hormone (ADH), during water deprivation with simultaneous urine and serum osmolalities and measurements of serum sodium, support the neurogenic form of DI.

Normal anterior pituitary function has been demonstrated in all cases by measurements of other trophic hormones and their products. These include serum TSH, T_4, cortisols and growth hormone. Hypothalamic dysfunction is strongly suggested by abnormal patterns of growth hormone release to L-Dopa, elevated basal serum prolactin levels and abnormal prolactin response with normal TSH response to intravenous thyrotropin releasing hormone (TRH).

This syndrome has been transient in one neonate, with clinical resolution of the DI and accompanying normal serum ADH levels. The DI has responded to treatment with parental pitressin as well as intranasal 1-Desamino-8-D-Arginine vasopressin (DD-AVP). We believe the syndrome of neurogenic DI may be considerably more common in neonates with CNS abnormalities than has previously been reported.