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Inhibition of Physiological Growth Hormone secretion by Atropine.

The importance of cholinergic influences on growth hormone (GH) secretion has recently been established. The purpose of this study was to investigate the effect of low and high dose atropine (specific muscarinic cholinergic inhibition) on the normal secretion of GH. Nocturnal secretion was established by sampling frequently during the first cycle of Stage IV sleep in 9 subjects. Atropine was administered orally in a dose of 0.6mg (n = 5) or 1.6mg (n = 4) 30 mins before expected sleep and the sampling repeated. The peak GH level without atropine was 38.5 mU/l (range 6.7 to 92.0) while both doses of atropine completely inhibited GH secretion.

The effect of atropine on the daytime secretion of growth hormone was also studied in three young adults by repeated sampling for at least 12 hrs. Daytime secretion of GH was demonstrated (at least 3 discernable peaks of >8mU/l) and atropine 0.6mg p.o. 6hrly effectively abolished GH secretion. Prolonged sampling after a single dose suggests that the inhibition persists for up to 6 hours.

We conclude that the medical inhibition of GH secretion using anticholinergic drugs should be further investigated in the management of very tall children.

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Secretory pattern of growth hormone (GH) in tall girls treated with Ethinyloestradiol(Oe)or Bromocriptine(B).

To investigate GH dynamics in tall girls an integrated 24^{h}GH-analysis has been performed in 12 tall pubertal girls collecting a sample every 20 min using a Kowarski-Cormed pump.The effect of Oe 500 ug daily (5pat) or B 5-7,5 mg(7pat) on spontaneous GH secretion has been studied by repeating the 24^{h} analysis. On Oe treatment every girl increased the area under the curve, mean peak amplitude and the GH-level between peaks, so but less pronounced, did 4 out of 5 patients on B. On Oe the number of peaks was unchanged, on B slightly reduced. Somatomedin A (K.Hall) decreased during Oe-therapy, data yet not available on B. Growth-rate was reduced during Oe, unchanged on B treatment. The growth inhibiting effect of Oe is not mediated by GH but by SM and by acceleration of bone age. Growth inhibition of B if any, is unexplained.

	Oestrogen		Bromocriptine	
	range	mean	range	mean
area under before	631-1727	948 n=5	549-2302	1362 n=7
the curve on	1698-2436	2210n=5	791-2149	1530 n=5
level bet- before	1.1 - 10.9	4.9 n=5	2.8.-8.4	5 n=7
ween peaks on	9.1-20.3	14.5n=5	3.5.-10.9	6.3 n=5
mean peak before	18-53	30 n=5	15-54	351.1 n=7
amplitude on	37-51	43 n=5	30-47	42.2 n=5

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Effects of androgens on erythroid colony formation in children bone marrow cultures.

We studied the role of androgens on children erythropoietic precursors cells in culture. Cultures of normal marrow from surgical intervention (informed consent) were carried out using a miniaturized methyl-cellulose method in the presence of erythropoietin (11U/ml). Effects of testosterone (T), 5 -dihydrotestosterone (DHT) and nor-testosterone (nor-T) were evaluated on colony forming units erythroid (CFU-E) after 7days of incubation at 37°C CFU-E were quantified by scoring directly colonies and by a biochemical determination of the uroporphyrinogen I synthase activity (UROS). Results are given as number of CFU-E per 32.000 nucleated cells plated. UROS activity is expressed as pmoles of uroporphyrinogen formed per hour and per well.

		CFU	UROS	(mean±SD)
Controls	(n=6)	273 ± 36	17,6 ± 1,7	--------
T x 10^{-8}M	(n=3)	378 ± 27	28 ± 10	
T x 10^{-9}M	(n=3)	329 ± 17	26 ± 11	p<0.001
DHT x 10^{-8}M	(n=3)	459 ± 69	33,3 ± 11	
nor-T x 10^{-8}M	(n=3)	367 ± 18	29,3 ± 7	

T,DHT and nor-T significantly stimulate children marrow progenitor cells in culture.Androgens act on both growth and maturation of CFU-E.A direct effect of androgens on erythroid differentiation (via an androgen receptor?)in children bone marrow culture may explain the efficiency of androgen treatment in aplastic anemia.

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5 alpha-dihydrotestosterone specific binding in prepubertal rabbit cartilage cells and variation of 5αreductase activity with the age of the donor animals.

Recently, we reported that prepubertal male rabbit cartilage tissue and cells are able to convert Testosterone (T) into its major active metabolite 5αdihydroT (DHT)(Takahashi et al. Mol. Cell Endocr. 35:15,1984).The purpose of the present work was 1)to determine wether such cartilage cells contain specific binding sites for DHT 2)to study the variation of the 5αreductase activity at different ages from birth to post puberty.The ^{3}H-DHT and ^{3}H-R1881 binding studies were performed in total cartilage cell proteins prepared in 0.4 M KCl Tris buffer.After two hours incubation at 15° bound and free binding sites were separated by charcoal or PEG adsorption and analyzed by Scatchard plots.The binding capacity was 2-7 pmoles/mg protein with low affinity (K_D=0.2-5x10^{-15}M).The cartilage 5αreductase activity was studied by incubating AR cartilage slices in the presence of ^{3}H-T (90 nM).Radiolabelled steroids were then extracted from tissue and incubation medium, analysed by celite chromatography and the amount of newly formed ^{3}H-DHT was quantified.During the first 10 days after birth, AR cartilage 5α reductase activity was 3.55±1.05 pmoles/mg tissue.It increased progressively to reach 51.5±2.5 pmoles/mg tissue in 20 to 50 day old animals and then came down to the starting levels. The maximum activity thus observed at puberty when androgen plasmatic concentration rises in male rabbits could be related to variations in androgen receptors.

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Effect of Delta-1-Testololactone(DT) in boys with pubertal gynecomastia(PG).

7 Boys with PG(mean age 15.4+1.1yrs),and 1 man (23yrs)with persistent G were treated with oral DT 450mg/d for 1.5 to 6 (mean 3.2)months without side-effects.In 2, PG disappeared after 3 and 4 months of DT,in 1 of them,it reappeared 6 months after discontinuation.In 5 others,glandular tissue became softer and/or smaller,and in 1, DT had no effect.Testicular volume did not change.The following steroid changes were observed:

	basal	on DT	P
Testosterone(T,nmol/l)	12.5 ∓ 7.0	17.7 ∓ 8.2	ns
Androstenedione(A)	2.1 ∓ 1.5	18.4 ∓ 10.8	<0.001
Estrone(E1,pmol/l)	241 ∓ 93	397 ∓ 110	<0.01
Estradiol(E2)	195 ∓ 86	131 ∓ 77	ns
Ratio T/E2	64	135	
Ratio A/E1	9	46	

Gonadotropins before(b),and after(a)LHRH,and PRL were not influenced significantly:at first examination,LH was 21∓4(b),and 110∓31(a),FSH 83∓32(b),and 182∓88ug/l(a),and PRL 169∓80mU/l. On DT,LH was 22∓6(b),and 111∓34(a),FSH 154∓45(b),and 277∓74 ug/l(a),and PRL 206∓125mU/l.Although clinical results are variable and difficult to evaluate,it is concluded that DT might be useful in PG by increasing the androgen/estrogen ratios.

Supported by the Swiss National Science Foundation (Grants No. 3.959-0.80,3.874-0.83,and 3.984-0.80).

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Usefulness of urinary 6ß-hydroxycortisol (6ßOHF) excretion in the diagnosis of Cushing's syndrome.

Rapid and simple laboratory diagnosis of cortisol excess due to Cushing's syndrome is highly desirable. To date chronic overproduction of cortisol and loss of diurnal cortisol variation are considered to be the most consistent metabolic abnormalities in Cushing's syndrome. Nevertheless free urinary cortisol (F) and plasma cortisol levels may yield false negative results. We there fore applied a recently developed RIA for 6ßOHF. 6ßOHF is the major unconjugated urinary metabolite of corticol. In the evaluation of 33 adolescents and young adults for Cushing's syndrome near normal 17OH corticosteroids (14mg/24h) and/or F (120µg/24h) were found in 6 patients. 6ßOHF was at least 10 times above nl in all 33 patients (mean:8.11mg/24±2.01 (SE) mg/24h vs nl 0.40±0.1 mg/24h). The ratio of 6ßOHF/F was also markedly elevated (mean 14,8±3.3; vs nl 6.7±1). The highest 6ßOHF excretion was seen in patients with ectopic ACTH production and adrenal cancer (35 and 75mg/24hr respectively). 6ßOHF proved to discriminate better than either 17OH corticosteroids or F; no false negative or positive cases were seen in the present series. Our data suggest that excess ACTH indirectly and corticol directly induce 6ß-hydroxylase activity causing highly diagnostic increases in 6ßOHF excretion. Measurement of urinary 6ßOHF is therefore suggested as a new, clinically useful test in the evaluation of hypercortisolemic states.