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CLASSIFICATION OF CRYPTORCHIDISM BY MEANS OF  
5 $\beta$ -ANDROSTAN-3 $\alpha$ ,17 $\beta$ -DIOL EXCRETION.  
This study is based upon the hypothesis that cryptor-  
chidism can be accompanied by moderate target organ  
unresponsiveness to androgens, which is best reflected

by specific metabolites, i.e. 5 $\alpha$ -androstane-3 $\alpha$ ,17 $\beta$ diol (5 $\alpha$ D) and  
5 $\beta$ -androstane-3 $\alpha$ ,17 $\beta$ diol (5 $\beta$ D). We suggest the latter to be a  
marker for the degree of genital development. In addition, the  
excretion of testosterone (T), dihydrotestosterone (DHT) and  
androstenedione (AN) was analysed. T+AN was interpreted as "andro-  
genic pool". Excretion profiles were analysed by capillary gas  
chromatography, serum T by RIA. Data were evaluated before and  
after a three days hCG stimulation. 21 boys (age 2-14 yrs) were  
examined. 7 boys with retractile testicles served as "controls"  
(group I). For classification purposes the stimulation ratio F  
(=day3 over day0) was used. Three different groups could be  
distinguished:

	(urinary excretion)			(serum)	
	F:5 $\alpha$ D	F:5 $\beta$ D	F:DHT	F:T+AN	T
group I	1.0-8.9	2.2-6.3	ND	0.9-1.1	3.0-15.2
group II	0.8-3.5	1.1-2.3	0.8-1.5	1.0-1.7	1.2- 5.6
group III	0.4-1.4	0.4-0.8	0.0-2.5	0.9-3.3	0.8- 1.5

Group II was called "intermediate" and cases of anorchia were  
found in group III. Correlation with clinical findings suggest  
that F:5 $\beta$ D might be the most useful addition to the classical  
diagnostic procedures. We speculate that the extended analyses  
might provide some aspects for clinical prognoses.

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SPIRONOLACTONE COMBINED TO AN ESTRO-PROGESTAGEN IN ADOLESCENTS  
AFFECTED BY HIRsutISM.

Almost 5% of women is affected by hirsutism and about 55% of these subjects start  
complaining on some signs during the adolescence period in which a considerable  
anxiety is connected with the body image. After having excluded Cushing's  
syndrome, CAH late onset, ovarian and adrenal tumours, we treated six adolescents  
(mean age 16yr 1mo) affected by hirsutism (Hatch's score  $\geq 10$ ) with 100 mg/daily  
of spironolactone for 12 months (200 mg/daily with score  $> 20$  or therapeutical  
unsuccess after 6 months of therapy). To all subjects was added an oral  
contraceptive (0.15 mg of desogestrel + 0.03 mg of ethinil -estradiol) to obtain  
regular withdrawal bleeding and contraception effect. To make a correct  
evaluation of the data, we excluded from the study those areas treated by  
esthetic treatment. Clinical and hormonal evaluations (FSH, LH, PRL, T, DHEAs) were  
obtained before and after 3-6-9-12 months of therapy. During follow-up no change  
was demonstrated in hormone levels; the mean score significantly decreased after  
3 months of therapy ( $p < 0.01$ ) and at every specific control ( $p < 0.001$ ). In one  
girl, 6 months off-therapy, no sign of hirsutism was demonstrated. No  
significant side-effects were noted in our patients. Spironolactone combined to  
an estro-progestagen is an effective and well-tolerated approach to the  
management of hirsutism in adolescents.

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24HR GONADOTROPHIN PROFILES IN NORMAL  
CHILDREN

Using a precise immunoradiometric assay for LH and FSH we  
have measured gonadotrophin concentrations in 24 hour profiles  
of 30 children aged 5.8 - 15.5 years.

A rise in gonadotrophin concentration was seen in 73% of  
prepubertal children between 1600 and 0030 hours. LH  
concentrations were greater than FSH, but no clearly defined  
periodicity of LH secretion could be discerned.

During puberty, the pattern of gonadotrophin secretion  
changed progressively. Nocturnal pulsatility (periodicity 90  
minutes) appeared at breast stage II and 24 hour  
gonadotrophin secretion at breast stage IV.

This study demonstrates that gonadotrophin secretion at a  
low level is detectable long before the clinical onset of  
puberty. Although sex steroid concentrations were below the  
limit of detection of current assays, they may be important in  
determining the change in GH pulse frequency we have  
previously described to be coincident with the mid-childhood  
growth spurt. When gonadotrophin secretion achieved regular  
periodicity, sex steroid concentrations rose, pubertal changes  
occurred and the growth spurt was entrained. 24 hour  
gonadotrophin secretion was required for the attainment of  
reproductive capability.

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ORAL TESTOSTERONE UNDECANOATE IN THE INDUCTION OF MALE PUBERTY  
Oral testosterone undecanoate (TU) was used in 5 untreated prepubertal (GIPHI)  
boys (aged 12.1-17.1 yr) with hypogonadism and delayed puberty. The aim was to  
induce puberty by mimicking the pubertal diurnal variation of testosterone (T)  
thus achieving optimal growth and virilisation without disproportionate skeletal  
maturation. TU 40 mg was administered daily after a standard breakfast for 6  
months. Plasma and salivary T levels were monitored for 10 hours with the first  
dose and repeated at 3 and 6 months. After 6 months, pubertal ratings had  
progressed to G2-3/PH1-3 with no significant change in testis size. Mean height  
velocity increased from 3.40 $\pm$ 0.63 to 7.10 $\pm$ 0.95 cm/yr. Advance of BA/CA ratio was  
0.95 $\pm$ 0.40. Peak and mean total T declined at 3 and 6 months. Mean free T index  
increased at 6 months but peak free T index was not significantly altered as a  
result of the SHBG fall. Salivary T and plasma T profiles were closely correlated  
being within the range for G4. Satisfactory initiation of puberty can be achieved  
with oral TU. Apparently high total T peaks observed at the start of treatment  
reflected prepubertal SHBG concentrations but free and salivary T levels produced  
by 40 mg TU were appropriate for mid to late puberty. Careful monitoring of  
treatment and individual dosage adjustment are indicated.

MONTH	PEAK T (nmol/l)	MEAN T (nmol/l)	PEAK FTI	MEAN FTI	SHBG (nmol/l)
0	39.7 $\pm$ 7.6	13.9 $\pm$ 4.8	61.2 $\pm$ 27.7	19.6 $\pm$ 5.4	77.4 $\pm$ 39.6
3	25.4 $\pm$ 10.4***	9.2 $\pm$ 3.7**	71.6 $\pm$ 37.4	25.0 $\pm$ 10.1	40.1 $\pm$ 20.1*
6	24.4 $\pm$ 6.3**	9.5 $\pm$ 2.9**	82.1 $\pm$ 27.8	31.2 $\pm$ 7.7**	32.3 $\pm$ 12.5*

(Mean  $\pm$  SD) \*  $p < 0.05$  \*\*  $p < 0.01$  \*\*\*  $p < 0.001$  vs Month 0

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PUBERTY CHANGES THE GONADOTROPIN RESPONSE TO NALOXONE  
INFUSION

Naloxone, an opioid antagonist, increases LH/FSH blood levels in  
adults. The absent response in prepuberty may be caused by an in-  
sensitive, unstimulated pituitary. Therefore we studied LH/FSH  
secretion during naloxone infusion before and after LHRH priming.  
Protocol: three prepubertal boys aged 13.1-14.6 yrs (BA 10.4-12.3),  
Testosterone (T) 0.4-0.9 nmol/l, received LHRH 20  $\mu$ g/1.7m<sup>2</sup> every  
90 min iv during 42 hrs. Before as well as 7 days after pulsatile  
LHRH treatment naloxone was infused iv from 10.00-13.00h 2 mg/-  
1.7m<sup>2</sup>/h. At 13.00h a LHRH test was performed. LH and FSH was  
measured from 9.00-15.00h at 15 min intervals. In 2 pts the study  
was repeated in a pubertal stage (G3).

Results: in all three prepubertal boys naloxone did not elicit an  
increase of LH or FSH, neither before nor after LHRH priming,  
while the LH and FSH response to the LHRH test had distinctly  
increased after LHRH priming. In the 2 pubertal boys basal LH and  
FSH were within the same range; T was 4.5 and 13 nmol/l. Naloxone  
induced a clear LH increase with two LH pulses only in the boy  
with a T of 13 nmol/l, before as well as after LHRH priming.  
Conclusion: naloxone cannot induce a LH/FSH increase in prepuberty  
even not after LHRH priming; in puberty an increase can be elic-  
ited. Therefore the opioids take no major part in the LHRH "intrinsic  
restraint" during prepuberty, but play a role in the sex  
steroid negative feedback, which becomes operative during puberty.

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STIMULATION OF GnRH SECRETION BY N-METHYL-D, L-ASPAR-  
TATE (NMA) IN VITRO AND IN VIVO.

In several species, IV or SC administration of NMA, a neuroexcitatory  
analog of aspartate, elicits a pulse of LH secretion. In  
prepubertal monkeys, chronic intermittent administration of NMA  
induces pubertal development through a putative hypothalamic  
action (Plant TM et al, Endocrine Soc. Meeting, 1987, Abst. 65).  
In order to get a direct insight into this mechanism, GnRH release  
from the rat hypothalamus was studied in vitro in the presence of  
NMA. Concentrations  $\leq 0.74$  mg/ml were not effective. Incubation  
with NMA 1.47 mg/ml for 7.5 min resulted in an increase of GnRH  
release from 11.5  $\pm$  4.3 to 36.2  $\pm$  14.1 pg/0.5 ml (mean  $\pm$  SD,  
n = 12). The effect of NMA in vivo was evaluated by studying rats  
sacrificed at different times after SC injection of 30 mg/kg of  
NMA. One, 3, 5, 7.5 and 10 min after NMA injection, mean serum LH  
rose progressively (32.0, 38.0, 70.0, 71.0 and 87.5 ng/ml, respec-  
tively). The hypothalami of these rats were immediately dissected  
and studied in vitro. One, 3, 5, 7.5 and 10 min after NMA injection  
in vivo, mean GnRH release in vitro showed a marked increase (20.0,  
32.0, 46.3, 115.5 and 41.8 pg/0.5 ml, respectively), indicating  
that GnRH is likely the neuroendocrine mediator of NMA-induced  
LH secretion. The study of GnRH release by NMA in vitro provides  
a means to further elucidate the mechanisms of the hypothalamic  
pulse generator and its role in the initiation of puberty.