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CENTRAL PRECOCIOUS PUBERTY (CPP) IN TWO SISTERS WITH DECREASED ACTIVITY OF ADRENAL 3 β -HYDROXYSTEROID DEHYDROGENASE (3 β HSD). E.Hershkovitz, E.Leiberman, Pediatric Endocrinology Unit, Soroka Medical Ctr., Ben-Gurion Univ., Beer-Sheva Israel. Peripheral precocious puberty has been described in girls with mild adrenal 3 β HSD deficiency. We describe two sisters with CPP and reduced activity of adrenal 3 β HSD. Sexual maturity rate was B2P3 in Pt1 and B3P3 in Pt2 at diagnosis.

Patient	At Diagnosis		Bone age	Pubarche			Thelarche			Menarche
	Age	Height Velocity		6y	7y	8y	6y	7y	8y	
1	6y	+1 (SD)	6.5y	2.5y	6y	-	-	-	-	
2	9.75y	+5.8(SD)	10.0y	8.5y	5.3y	10y	-	-	-	

Acne, hirsutism, or cliteromegaly were not present. Laboratory data (60 min. post-i.v. 0.25mg ACTH) revealed decreased activity of adrenal 3 β HSD as shown below.

Hormone	Patient 1	Patient 2	Normal values for Tanner II-III girls
17OH-pregnenolone	36.1	25.7	16.8 \pm 5.1nmol/l
17OHpreg./17OHprog.	4.7	6.62	3.3 \pm 1.7
DHEA (basal)	23.1	18.2	7.5 \pm 6.4 nmol/l
(post-ACTH)	29.9	>104	12.5 \pm 8.8 nmol/l
DHEA/Androstendione	8.2	>16.9	3 \pm 1

DHEA-S levels were high. Normal basal and stimulated levels of additional plasma steroids, and normal urinary steroid profile ruled out other forms of congenital adrenal hyperplasia. Estradiol levels were of prepubertal range in Pt1 and of pubertal range in Pt2. GnRH test: Pt1: FSH-15, LH-7.8. Pt2: FSH-7.2, LH-11 (peak response in mu/ml). Dexamethasone suppressed all steroid production. Brain CT revealed no abnormality. Pelvic ultrasound demonstrated pubertal changes in both sisters. We conclude that overproduction of adrenal androgens due to decreased 3 β HSD activity may induce CPP by activation of the hypothalamic-pituitary axis.

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I. Maesaka, S. Suwa, K. Tachibana, M. Adachi, U. Asakura. Department of Pediatrics, Kanagawa Children's Medical Center, Yokohama, Japan. MONTHLY URINARY GONADOTROPIN AND OVARIAN HORMONE SECRETORY PATTERNS IN NORMAL CHILDREN AND PATIENTS WITH IDIOPATHIC PRECOCIOUS PUBERTY

We have already reported a simple and improved method for the quantification of urinary gonadotropins needed in amounts of urine smaller than those previously reported. Good correlation was observed between urinary gonadotropin and ovarian steroid/creatinine ratios in first morning voided (FMV) urine and 24-h urine collections in children. Using consecutive 30-d FMV urine specimens from 29 normal children and from 9 patients with idiopathic precocious puberty, we have studied the monthly patterns of nighttime gonadotropin and ovarian steroid excretions. Urinary LH levels in normal prepubertal girls were low with few fluctuations. FSH levels were higher and showed remarkable, episodic fluctuations. In early pubertal girls, urinary LH and FSH excreted with alternate every other day variations at the same time. Their urinary total estrogen excretions remained low levels. In mid-pubertal girls, urinary LH excretion increased to near the levels of urinary FSH and they fluctuated with alternate every other day variations. Urinary total estrogen also increased and fluctuated with an opposite way to these variations in urine LH and FSH. With progressive sexual maturation, urine LH excretion increased. The cycle of a normal postmenarcheal girl aged 14 years showed a pattern similar to those of normal adults. In patients with idiopathic precocious puberty, those hormonal patterns showed similar to those of normal subjects matched for sexual stage. Measuring monthly urinary gonadotropins and ovarian steroids seems to be useful to investigate the process of sexual maturation and the endocrine requirements for ovulation.

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PREDICTION OF BASAL METABOLIC RATE IN ADOLESCENT BOYS: TESTICULAR SIZE IS MORE USEFUL THAN HEIGHT. D.C.Brown, F.C.W.Wu and C.J.H.Kelnar, Department of Child Life & Health, Edinburgh University, Scotland, UK

The World Health Organization provides equations for the prediction of basal metabolic rate, and hence caloric and protein requirements, in 10 - 18 year old males:

$$\text{BMR (MJ/day)} = 0.0732 \text{ Wt (kg)} + 2.72 \text{ (Wt equation)}$$

$$\text{or } 0.0694 \text{ Wt (kg)} + 0.322 \text{ Ht (m)} + 2.392 \text{ (Wt \& Ht equation)}$$

Lean body mass and BMR can be expected to increase with advance in male puberty. 86 healthy male volunteers aged 11.8 - 13.7 years had height, weight, testicular volume and BMR (using ventilated hood indirect calorimetry) measured.

Testicular volume (ml)	n	Actual BMR (MJ/day)	Estimated BMR (Wt & Ht equation)
\leq 4 ml	24	5.04 \pm 0.17	6.03 \pm 0.14
4.5 - 6 ml	20	5.40 \pm 0.24	6.17 \pm 0.17
6.5 - 10 ml	24	5.46 \pm 0.24	6.15 \pm 0.09
\geq 10.5 ml	18	6.58 \pm 0.21	6.45 \pm 0.18

We derived the following equation to take account of testicular size based on our results: $\text{BMR (MJ/day)} = 0.0735 \text{ Wt (kg)} + 0.094 \text{ TV (ml)} + 2.059$

Using the WHO equations, knowing the boy's height increased the correlation of actual vs predicted BMR from 0.626 (Wt eq) to 0.632 (Wt & Ht eq). Our equation increases the correlation to 0.726. The absolute error of predicted BMR is reduced from 0.96 \pm 0.06 MJ/day (Wt eq) and 0.95 \pm 0.06 (Wt & Ht eq) to 0.50 \pm 0.06 (p < 0.001, t-test). Pubertal assessment increases the accuracy of prediction of BMR, and hence energy and nutritional requirement, of boys in the 10 - 18 year age group.

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DIFFERENTIATION BETWEEN NORMAL PREPUBERTY AND HYPOGONADOTROPHISM IN BOYS: CONSIDERATION OF HOURLY MEAN LH CONCENTRATIONS. C.J.H.Kelnar, F.C.W.Wu, D.C.Brown, H.F.Stirling and G.E.Builer, Department of Child Life & Health, University of Edinburgh, Scotland, UK

We compared 12 prepubertal boys aged \geq 12.5 years (mean \pm SEM = 13.30 \pm 0.16) with 11 male patients with idiopathic hypogonadotrophic hypogonadism (IHH) to assess how nocturnal LH concentrations could best be used to differentiate between the two groups. LH levels were measured at 10 or 20 minute intervals for a six hour period commencing one hour after sleep onset. The table shows mean LH levels over each one hour period and over the total six hours (O/N) for each group.

Hour	1	2	3	4	5	6	O/N
Pre-pubertal	0.84	1.14	1.38	1.36	1.28	1.12	1.19
(Minimum)	\pm 0.26 (0.15)	\pm 0.25 (0.15)	\pm 0.29 (0.19)	\pm 0.26 (0.26)	\pm 0.23 (0.23)	\pm 0.21 (0.19)	\pm 0.22 (0.33)
IHH	0.11	0.13	0.12	0.11	0.15	0.15	0.13
(Maximum)	\pm 0.03 (0.28)	\pm 0.03 (0.33)	\pm 0.03 (0.31)	\pm 0.03 (0.31)	\pm 0.04 (0.43)	\pm 0.05 (0.45)	\pm 0.03 (0.31)

Mean LH levels were significantly higher in the prepubertal boys than the IHH patients (p < 0.02, t-test), although only the overall mean value was discriminatory. The maximum hourly mean LH value for each subject reflects LH pulse amplitude and/or frequency. The lowest level of this value was 0.50 U/l for the normal prepubertal subjects, compared with the highest in the IHH group of 0.45 U/l. This value may be of use in the investigation of male clinical preperty.

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A STUDY OF THE MECHANISMS OF NORMAL VOICE MATURATION IN PUBERTAL BOYS. I.M.Walker, D.M. Williams, M. Harries*, J. Hacking*, I.A. Hughes, Department of Paediatrics, University of Cambridge, ENT* and Radiology* Departments, Addenbrooke's Hospital, Cambridge, UK.

Breaking of the voice is one of the obvious outcomes of puberty in boys, which for choristers and choirmasters may be an unwelcome event. The process is said to be complete by age 15.5yr on average but its precise timing in relation to pubertal stage and the mechanics involved are poorly documented. This phenomenon was investigated in 26 boys, aged 13.4 - 14.3 yr at outset, who have been studied at three-monthly intervals for 12 months so far. At each visit height, weight, genital and pubic hair (PH) stages were recorded and the mean daily saliva testosterone (T) level calculated from 3 samples collected over the preceding 24-hours. Vocal cord length (VCL) was measured by a novel ultrasound technique, fundamental speaking voice frequency (VF) derived from laryngography and stroboscopy of the vocal cords was performed. All measurements were made by a maximum of two observers for each parameter without reference to previous data. Each pubertal stage was represented in this cohort with normal progression into or through puberty in all but one boy who remained at stage 1 throughout. VCL and saliva T remained unchanged until a significant increase at stage 3 and at each subsequent pubertal stage (p < 0.001 throughout). VF, which was inversely proportional to VCL, did not fall significantly until stage 4 when there was a marked decrease (p < 0.001) with a further significant fall in stage 5 towards the adult male VF of 120Hz. This suggests that a critical VCL and T concentration is required to initiate voice breaking, although other mechanisms such as cord thickness and motility are also probably involved. In relation to PH development, VF fell significantly in stage 3 (p < 0.001) reflecting the known lag in PH compared with genital development. Testicular volume was a poor predictor of VF and saliva T concentrations. These observational data provide more information about the biology of puberty and confirm voice breaking as a late and rather sudden event. Predicting the impending fall of VF by simple genital staging may prove invaluable to the organisation of choirschools.

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THE EFFECTS OF LOW-DOSE, LOW-FREQUENT GnRH STIMULATION VS SEX STEROID TREATMENT ON THE PATTERN OF 24 HRS GH SECRETION IN 10 HYPOGONADOTROPIC CHILDREN. R.J.H. Odink, HA Delemarre-van de Waal, department of pediatrics, Free University Hospital, Amsterdam, The Netherlands

During puberty the 24-h GH secretion changes. Whether this changing GH pattern is the consequence of an increased secretion of GnRH or to sex steroids is unknown. Therefore we studied 62 GH profiles during pubertal induction in 10 hypogonadotropic children (5 f /5 m), with a mean (SD) age of 16.2(3.5) yrs. Six (2 f /4 m) received GnRH iv for 24 months (mth): a pulse dose (pd) of 15 ng/kg and 30 ng/kg was used every 3 mth alternately. A pulse interval (pi) of 180 min. was used the first half year during the night only, the second half year during day and night. A pi of 90 min. was used the second year of treatment. During 6 mth periods 3 girls were treated with ethinyl estradiol (EE: 50, 100, 150 and 200 ng/kg q day) and one boy with testosterone esters (TE: 25, 50, 75 and 100 mg/kg q 14 days im). Before and at 6 weeks of each treatment schedule blood was sampled at 10 min. intervals during 24-h to evaluate GH and testosterone (T) or estradiol (E2) secretion. From the pulsar program mean (mGH), baseline (bGH), max GH conc. were calculated as well as the sum of peak heights (sph) and peak area (pa). (This study had been approved by the committee of ethics). Results: Before treatment: mGH was 2.5(0.8) μ g/L and bGH was 0.9(0.3) with no sex difference. Max GH was 11.5(5.0) and 9.3(7.9) in m and f resp. In f during EE mGH and bGH significantly (P < 0.01) increased to 5.8(0.9) and 2.5(0.4); max GH to 16.2(7.3) and sph with 230%. In m during TE only max GH increased to 36. In m and f during GnRH treatment with low levels of T or E2, no changes of mGH, bGH, max GH, sph or pa could be observed; when T or E2 levels increased, only max GH rose to 14.6(12.5) and 11.2(4.3) in m and f resp; in m mGH and bGH increased to 4.1(2.5) and 1.2(0.2).

Conclusions: During puberty sex steroids modulate GH secretion by an increment in maximal GH level. GnRH itself does not change 24-h GH secretion.