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MALE ADOLESCENTS WITH CONSTITUTIONAL DELAY OF GROWTH AND PUBERTY. THERAPEUTICAL EFFECT OF TESTOSTERONE. Bergadá C.;Bergadá I.
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Constitutional delay of growth and puberty (CDGP) is characterized by small stature and delay of bone age (BA) and sexual development. In order to accelerate growth velocity (GV) and sexual development 23 boys with CDGP who were worried for their poor growth and pubertal development were treated with monthly intramuscular testosterone injections (41+7.7 mg/m^2) during 18 months (T). Thirteen boys with CDGP who were not treated served as control group (C). Before treatment there were no differences between groups in chronological age (CA) T:14.65+0.9 vs C:14.31+0.8 (p=NS), SDS of height (SDS) T:-3.30+0.81 vs C:-2.85+0.62 (p=NS), SDS of height for BA (SDSBA) T:-0.24+0.9 vs -0.04+0.4 (p=NS), BA T:11.81+1.1 vs 11.59+1.1 (p=NS), pubic hair (Tanner)(P) T:1.82+0.7 vs. 1.88+0.6 (p=NS), testicular volume (TV) T:7.0+2.6 vs 6.8+2.1 (p=NS) nor GV T:4.01+1.3 vs 4.9+1.4 (p=NS). Patients were clinically evaluate approximately every 3.5 months. In response to treatment we obtained the following auxological data:

	GV (cm/year)		SDSBA		TV (ml)	
visit	T	C	T	C	T	C
1°	4.0+1.3	4.9+1.4	-0.24+0.4	-0.04+0.4	7.0+2.6	6.8+2.1
2°	10.0+1.8	4.2+0.9			7.2+2.5	8.8+2.8
3°	9.6+1.7	7.1+1.3	-0.28+0.6	-0.22+0.3	8.5+3.2	10.3+3.2
4°	9.5+1.5	8.3+2.4			9.2+3.4	12.3+3.3
5°	8.3+1.7	7.9+2.4	-0.23+0.6	-0.10+0.4	11.5+4.2	14.5+2.9
6°	7.0+1.5	8.0+1.3	-0.29+0.7	-0.05+0.6	14.1+4.5	14.4+3.3
Anova	p= 0.0001		p=NS		p=0.001	

After 18 m of treatment there were no differences in predicted adult height by Bayley-Pinneau (PFH)T:170.5+4.7 C:172.0+4.7. In summary administration of low dose testosterone could be an adequate therapy in boys with CDGP to produce a significant acceleration of growth, advance virilization without the induction of excessive bone maturation nor deteriorating predicted final height.

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GENERALIZED RESISTANCE TO THYROID HORMONE IN A CHILDREN:USE OF BROMOCRIPTINE (BC). Chiesa A.;Gruñeiro L.
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Generalized resistance to thyroid hormone (GRTH) is a Syndrome characterized by elevated serum T4 and T3 levels, preservation of a TSH response to TRH and the absence of manifestations of thyroid hormone excess. In this communication we report the studies in a 6.3 years old boy, with height and weight in 50% percentile, bone age 6 years, with a large goiter of 50 gr. The patient had received Lugol for 5 months and stopped it a month before. Serum T4 level was 20 ng/dl, T3 339 ng/dl, free T4 5.6 ng/dl, negative antimicrosomal antibodies, TSH 1.0 uU/ml, TSH post TRH 11.5 uU/ml, prolactine 10.4 ng/ml, post TRH 43.1 ng/ml, testosterone binding globulin (SHBG) 68.5 nmol/l, normal sella turcica Rx. ^{131}I uptake of 8, 32, 38% at 1, 24 and 48 hours respectively. Pulsatile nocturnal TSH secretion with a mean nocturnal TSH surge (% increase in TSH from nadir) was 105% (95% confidence limits 50-300%) X day TSH 1.8 X night TSH 3.7. Thyroid gland didn't change during 10 months without therapy. The administration of T3 (80 ug/day) for 1 week produced a rise in serum T3 to 600 ng/dl, SHBG didn't change, and TSH response to TRH decrease only a 10%. Eight hours after BC 1.2 mg orally basal TSH decreased from 4.1 to 0.5 uU/ml, no significant change in T4 and T3 levels were observed. Trying to decrease goiter size the patient was given Bromocriptine 2.5-5 mg/day for 4 months. The thyroid gland decreased to 25 g. No significant changes were observed in T4, T3, free T4, SHBG response to TRH and ^{131}I uptake. The Prl response to TRH lowered 84%. The pulsatile TSH nocturnal secretion decreased X day TSH 36%, X night TSH 38%. The patient maintained the clinical euthyroidism with a growth rate of 7.3 cm/yr. Thus BC in this patient was useful in decreasing goiter size while maintaining clinical euthyroidism.
Chronic use of this dopaminergic agonist (BC) may be useful in certain patients with generalized resistance to thyroid hormone.

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PREDICTED FINAL HEIGHT IN BOYS WITH CONSTITUTIONAL DELAY OF GROWTH AND PUBERTY (CDGP). Keselman A.; Bergadá I.;Martínez A.;Heinrich J.J. and Bergadá C.
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CDGP is characterized by short stature with delayed bone age (BA), however data concerning accuracy of predicted final height (PFH) in this pattern of growth is controversial. For this reason we have studied a group of prepubertal boys with CDGP (n=48) (A) with chronological age (CA) 11.56+2.1 years, SDS of height -2.67+0.64, BA 8.92+2.4 years and compared their auxological parameters with those at their onset of puberty. A second group of boys with familial short stature (FSS) (n=16) (B)was used for comparison .There were not difference inTarget Height between groups. In group A, 37 boys started puberty, 17 at a normal CA (A1) while 20 had delayed puberty(A2) with its onset after 13.5 years of age.In group B, 7 boys started puberty at a normal CA (B1) while 5 had delayed puberty (B2). PFH was assessed by Bayley-Pinneau in both groups during prepuberty and at their onset of puberty,in 16 patients we obtained final height.

PFH	Prepubertal	Onset of puberty	Final Height
A1		160.16+6.3(n=17)	160.7 (n=6)
	167.37+6.0 (n=48)	p=0.001	
A2		167.80+6.9 (n=20)	166.7 (n=7)
B1		162.80+5.5 (n=7)	162.1 (n=2)
	161.33+5.6 (n=16)	p=0.83	
B2		163.50+5.1 (n=5)	158.8 (n=2)

Forty five percent of prepubertal boys with CDGP started puberty at a normal CA associated to a reduction of PFH. These data were confirmed with those patients who attained their adult final height. In contrast boys with CDGP with delayed puberty (55%) had a similar PFH compared to their prediction, data confirmed with those who attained final height. In summary PFH in patients with CDGP is not accurate for prepubertal boys, however is a good method at their onset of puberty.

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ABSENCE OF NON CLASSICAL 21OHLASA DEFICIENCY IN GIRLS WITH PRECOCIOUS PUBARCHE. Gryngarten M.;Escobar M.E.; Belgorosky A.; Bergadá C.
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Recent reports have described non classical 21OHlasa deficiency in girls with precocious pubarche(PP).
In order to assess the prevalence of this deficiency, 26 girls with PP were studied, chronological age (CA) ($\bar{X}$+SD) 6.47+2.04 a. Height, bone age (BA) and sexual development (Tanner) were evaluated and in eight cases pelvic and adrenal ultrasound examination were performed. An ACTH stimulation test was done in all patients using 25UI given as an IV bolus measuring basal and post ACTH (30 and 60 min.) 17OH progesterone (17OHP) and cortisol levels.The results were compared with the nomogram standards for serum 17OHP (New and col. JCEM 57:320, 1983) and with a control group of normal girls (3 prepubertal and 5 pubertal). Basal SHBG, T and SDHEA levels were measured in 10, 24 and 12 patients respectively. All patients had MI, VPII-III. The height SDS was 0.53+1.18, the ratio BA/HC was 0.85+1.08. In eight patients where ultrasound study was performed, the results were normal. The 17OHP baseline serum levels were ($\bar{X}$+SD) 0.65+0.66 ng/ml and the cortisol levels 12+9 ug/100 ml and the highest response to ACTH was 2.42+1.31 and 29.2+7.1 respectively. None of the studied patients showed 17OHP levels to ACTH higher than those of normal population of the published nomogram, nor of our normal controls (prepubertal ng/ml B:0.35+0.31, maximal response 2.88+0.53;pubertal B: 1.6+0.73, maximal response 6.48+3.26. The basal serum levels of SHBG, T and SDHEA were: $\bar{X}$+SD (nmol/L) 94.50+31.04, 0.98+0.73 and 2300+2320. Only the SDHEA serum levels were significantly higher than in those previously published controls (103+8, 1.06+0.08 and 348+117) $p < 0.01$ (Belgorosky and col. JCEM 67:234, 1988).
In conclusion:we studied group of 26 girls with precocious pubarche none of them presented any biochemical evidence for non classical CAH due to 21OHlasa deficiency. The increased SDHEA levels confirm a premature maturation of adrenal activity in girls with precocious pubarche.

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AUTOLOGOUS IMMUNOMODULATION OF PANCREATIC AGGRESSION IN AN EXPERIMENTAL MODEL OF AUTOIMMUNE DIABETES. Arata M.;Quintanas C.;Basabe JC.
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The aim of this work was to study autologous immunomodulation (vaccination mechanisms) on autoimmune pancreatic aggression. Splenocytes from multiple-low-dose streptozotocin diabetic mice were transferred to normal syngeneic mice. Recipient animals developed abnormal glucose tolerance and diminished 1st. and 2nd. phases of insulin secretion. When splenocytes from diabetic donors were incubated with Mitomycin C prior to transfer, cells remained viable but they loose their pancreatic aggression ability. Splenocytes from diabetic donors were incubated with Mitomycin C and then injected into syngeneic normal mice. 15 days after, mice were injected with an equal dose of splenocytes from diabetic donors. 15 days after the last injection, recipients showed glucose tolerance and insulin secretion profiles similar to control groups in 50% of the injected animals. This protective effect was specifically induced by splenocytes from diabetic mice incubated with Mitomicyn C prior to transfer (controls:1065+17 vs. diabetics:1078+20 uU insulin/4 min/100 mg w.t., n=6). This effect was not observed in athymic recipients, suggesting that an immune response should be mounted in recipient animals. These results show that Mitomycin C-incubated splenocytes from diabetic donors specifically induced a protective effect against immune aggression and represented an experimental model to study autologue immunomodulation mechanism in autoimmune diabetes.

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EFFECT OF A HIGH PROTEIN DIET ON INSULIN SECRETION IN AN EXPERIMENTAL MODEL OF DIABETES INDUCED BY SPLENOCYTES TRANSFER. Karabatas L.;Lombardo Y.;Basabe J.C. Diabetes Experimental,Centro de Investigaciones Endocrinológicas (CEDIE),Hospital de Niños "R. Gutiérrez", Buenos Aires, y Facultad de Bioquímica, Universidad del Litoral, Santa Fe, Argentina.

In previous works we observed that the administration of a high-protein diet (HPD) to rats and mice, attenuated the deleterious effect of streptozotocin (SZ) on insulin secretion (IS). On the other hand transfer of splenocytes (S) from diabetic to normal mice, caused in the last ones, glucose-intolerance and a significant diminution in glucose-stimulated IS. In the present work we studied if the administration of HPD to mice that had received diabetic S, modify the observed alterations in IS. C57BL/6J mice were injected with 5 doses of SZ (40 mg/Kg/day). 15 days later their spleens were dissected and S isolated. These "diabetic" S were injected i.p. in receptor mice kept on a control diet (CD) or HPD. 15 days after S transfer, pancreatic gland from receptor mice were perifused and IS patterns were evaluated.Results showed that mice transferred with "diabetic" S, kept either on CD or HPD,presented diminished 1st. and 2nd. phases of IS (CD:1st. phase: 1288.7+40.4, n=6 vs 993.4+16.9 uU/6 min/100 mg wt.,n=5, $p < 0.001$; 2nd phase:11761.0+201.9, n=6 vs 10712+220.5 uU/32 min/100 mg wt, n=5, $p < 0.01$; HPD: 1st. phase: 1322.6+31.2,n=5, vs 1134.0+15.4,n=9, $p < 0.01$; 2nd phase: 11867+295.6 vs 10628+224.6, n=5 and 9, $p < 0.01$). However in mice fed HPD and transferred with "diabetic" S, 1st.phase of IS was significantly higher than values from mice under CD ($p < 0.001$). These results suggest that HPD improved the B-cell secretory response in an experimental model of diabetes with anti beta cell immune aggression.