

CHARACTERISTICS OF PUBERTAL DEVELOPMENT IN INFLAMMATORY BOWEL DISEASE (IBD)
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A retrospective analysis of pubertal parameters of 30 children with Crohn's disease (N=26) or ulcerative colitis (N=4) was compared with standards. Four parameters were analyzed; 1) age at onset of puberty (Breast stage 2 (B2) or Testicular volume 4ml (TV4)); 2) duration of B2 to B4 or TV4 to Genitalia stage 4 (G4); 3) height increase and 4) maximum velocity during this interval.

	Age at B ₂ or TV ₄ (yrs)	Duration (yrs) B ₂ to B ₄ TV ₄ to G ₄	Height (cm) increase Stage 2-4	Max vel (cm/yr) Stage 2-4
Girls: Number	N=14	N=7	N=7	N=7
: Median	12.6			
: Range	(9.8-13.95)	1.17-3.78	4.4-15.88	5.8-12.96
: Standard	11.2	2.0	13.3	6.2
: p value	0.003			
Boys: Number	N=16	N=10	N=10	N=10
: Median	13.32			
: Range	(10.84-14.87)	1.37-3.95	7.4-24.4	7.2-13.9
: Standard	12.0	1.9	13.5	9.4
: p value	0.01			

Intestinal resection (IR) was performed in 11 of these patients (4M,7F) of whom 9 had delay (75th C). Puberty occurred in all at a median of 0.62 yrs post-IR (0.08-0.96). Serum IGF-1 levels measured in 8 different children who had relapsed showed an increase 2 months later after induction of remission by either steroids or elemental diet (Mean \pm SEM [ng/ml]; pre = 115 \pm 16, after 2/12 = 177 \pm 29).

Conclusions: 1) Patients with IBD may have a marked delay in pubertal onset. 2) There is wide variation often outside the normal range of other pubertal parameters. 3) Induction of remission, e.g. by IR was followed by onset and progress through puberty in patients with delay. 4) IGF-1 levels increase following induction of remission. The importance of induction and maintenance of remission in IBD peripubertally is stressed.

TRUE PRECOCIOUS PUBERTY AND HETEROZYGOSITY FOR THE STEROID 21-HYDROXYLASE DEFICIENCY. MOLECULAR STUDY.

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In order to detect heterozygous carriers of the gene for congenital adrenal hyperplasia (21 hydroxylase deficiency; CAH), 32 girls affected by true precocious puberty were studied by the single-dose ACTH stimulation test and by HLA typing. Moreover, molecular analysis of CYP21B gene with PCR technique using specific oligonucleotides for the mutated site, was performed in 7 cases. After ACTH testing, 13 of 32 (41%) cases displayed an increment of 17-OHP and/or 21 deoxycortisol greater than normal and similar to that observed in obligate heterozygotes. On correlating the HLA phenotype with the ACTH response, we found that the 13 cases assumed to be heterozygotes on the basis of ACTH test, had an increased frequency of the A28 (38.5% vs 7.3%) and B14 (53.8% vs 7.1%) antigens and the remaining 19 patients with normal response to ACTH had an increased frequency of B22 (21.1% vs 3.4%). Molecular analysis showed that 4 of 7 haplotypes carrying the HLA B14 allele, were characterized by the mutation Val 281-Leu. This mutation results in an enzyme with 50% of normal activity when 17-OHP is the substrate, but only 20% of normal activity for progesterone.

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UNILATERAL GYNAECOMASTIA IN PREPUBERTAL BOYS

Gynaecomastia is a common feature in pubertal boys. However, gynaecomastia in prepubertal boys, outwith the neonatal period, is unusual in the absence of significant pathology. Unilateral gynaecomastia is rare. Three prepubertal boys (age range 8-11yrs; testicular volume <4mls) with medically significant (Tanner stage 3-4) & socially & emotionally unacceptable unilateral gynaecomastia presented to a regional paediatric endocrine service over a period of 5 months. Their anthropometric data were normal and appropriate for parental data; physical examination revealed no other abnormality & there was no history of drug ingestion or similar history in other male family members. Bone ages were appropriate for chronological ages & chromosome analysis was normal. Endocrine investigations including LH, FSH, LHRH, HCG and synacthen stimulation tests, urinary steroid metabolite studies, TSH, T4, PRL & sensitive oestradiol levels were normal (<30pmol/l). Radiological investigations failed to show any hepatic, gonadal, adrenal or hypothalamo-pituitary lesions. All the boys had breast reduction procedures via the subareolar route with good results. Breast tissue histology was normal & oestrogen receptor studies are underway. We speculate that unilateral gynaecomastia reflects differences in oestrogen receptor sensitivity between the breast tissue on both sides.

CHANGES IN SERUM AND URINARY LH/FSH RATIO DURING PUBERTY
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Serum gonadotropin responses after GnRH stimulation and secretion of LH and FSH in nocturnal urine samples were measured by ultrasensitive time-resolved immunofluorometric assay, for 95 subjects (62 boys, 33 girls; age 2-14 yrs) with non-endocrine short stature or obesity. The subjects were classified according to sex and pubertal stage. The prepubertal children were divided into two groups, according to chronological age (below or above 10 yrs). The basal and peak serum LH levels after GnRH stimulation and urinary LH showed a gradual increase throughout the pubertal development, while changes in FSH were not as remarkable as for LH. The peak LH/peak FSH ratio after GnRH stimulation and urinary LH/FSH ratio reliably discriminated between prepubertal and early pubertal groups. The reference ranges (mean-SD-mean+SD, after logarithmic transformation) of serum peak LH/peak FSH ratio in prepubertal group and early pubertal group were 0.28-0.55, 1.4-3.4 in boys and 0.09-0.25, 0.74-1.4 in girls, respectively, while urinary LH/FSH ratio in each group ranged 0.03-0.13, 0.37-1.1 in boys and 0.02-0.07, 0.14-0.36 in girls, respectively.

PHYTOESTROGENS AS A CAUSE OF CHILDHOOD GYNECOMASTIA.
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A 5 and 2/12 y.o. male presented with bilateral breast tissue (4.5cm), areolar pigmentation, slight non-velous pubic hair, prepubertal (2cc) testes, and growth acceleration. Height was 120cm (HT-SDS for CA = +1.9), bone age was 10 yrs (HT-SDS for BA = -2.8), predicted final HT 160.6cm (mid-parental HT 172cm). Laboratory studies revealed sex-chromatin negative buccal smear, non-detectable serum and urine estrone, 24-hour urine estrogens 19 ug/gmCr, LH 0.1 mIU/L, FSH 0.7 mIU/L, prolactin 5.9ng/ml, beta-HCG <5mIU/ml. A testicular ultrasound and adrenal steroidogenic profile were normal. On-site environmental evaluation revealed that this child habitually fed calves fresh wet alfalfa mixed with Rumensin, a monocarboxylic, highly lipophilic cation chelating agent. The skin of both arms and hands were exposed repeatedly to the mixture over a 12 month period. Repeated analysis of the alfalfa revealed significant quantities (50 and 35 ppm) of the phytoestrogen coumestrol. Cessation of this activity resulted in gradual reduction in breast size and slowing of skeletal maturation. However, growth velocity of 7.7cm/year, plasma T of 0.36ng/ml, and peak LHRH-stimulated gonadotropins (LH 5.5mIU/L, FSH 3.8mIU/L) suggest probable impending precocious puberty. We propose that gynaecomastia and accelerated growth and maturation in this child resulted from topical absorption of the phytoestrogen coumestrol, enhanced by hand-mixing of the wet coumestrol-containing alfalfa with a lipophilic, monocarboxylic ionophore.

THE ETIOLOGY OF CENTRAL PRECOCIOUS PUBERTY (CPP) IN INDIAN CHILDREN.
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Evaluation of 85 children with isosexual precocity showed that 45 (53%) (F34, M11) had CPP. Growth and pubertal signs were assessed by Tanner's charts, B.A by Greulich Pyle's Atlas, hormonal levels by RIA. GnRH tests were done in 11, CT/MRI if no etiology was evident. Etiology was identified in 28 (62%): CNS infections-12 (27%); hypothalamic hamartomas-10 (22%); other CNS disorders 3; hypothyroidism 2, Mc Cune Albright Syndr-1.38% were idiopathic-41% of girls and 27% of boys. Hamartomas were the commonest cause in boys (45%). In girls CPP was organic in 59%-29% due to prior CNS infections and 14% due to hamartomas. Onset of puberty (1.3 \pm 1 Yr) was significantly earlier, progression more rapid and BA/HA (1.9 \pm 0.6) higher in those with hamartomas as compared with the idiopathic group (Onset 5.08 \pm 1.7 Yrs; BA/HA 1.3 \pm 0.24). Ht.SDS(CA) was significantly lower in the TBM than the idiopathic or hamartoma groups. GnRH testing elicited LH predominant response. CNS infections in developing countries are important contributors to the etiology of CPP and to the high proportion of organic causes specially in girls. In boys hamartomas predominated.