

성조숙증의 진단과 치료 외래에서 가능한 처치

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CURRENT TREND

AGE AT MENARCHE, SOUTH KOREA

- Korean NHANES III, 2005

Girls born between 1986-1995, 13.1 years

Cho et al, Eur J Pediatr 2010;169:89

- Korean NHANES II-V, 2001-2011

Girls born between 1983-2001, KNHANES II-V, 12.7 years

Girls born between 1989-2001, KNHANES IV-V, 12.4 years

Lee et al, Reprod Health 2016;13:121

➡ Ongoing secular advances in AAM in Korean adolescent girls

TIMING OF SEXUAL MATURATION, SOUTH KOREA

- 3,334 Korean adolescent girls, 1994

Direct examination by physician, B2 11.0 years, PH2 12.9 years

Hong et al, Kor J Pediatr 1994;37:193

- 613 Korean adolescent girls, 2002

Self assessment sheet with pictures, B2 11.3 years, PH2 12.3 years

Park et al, Kor J Pediatr 2006;49:610

➡ Limited data of Sexual maturation in Korean girls

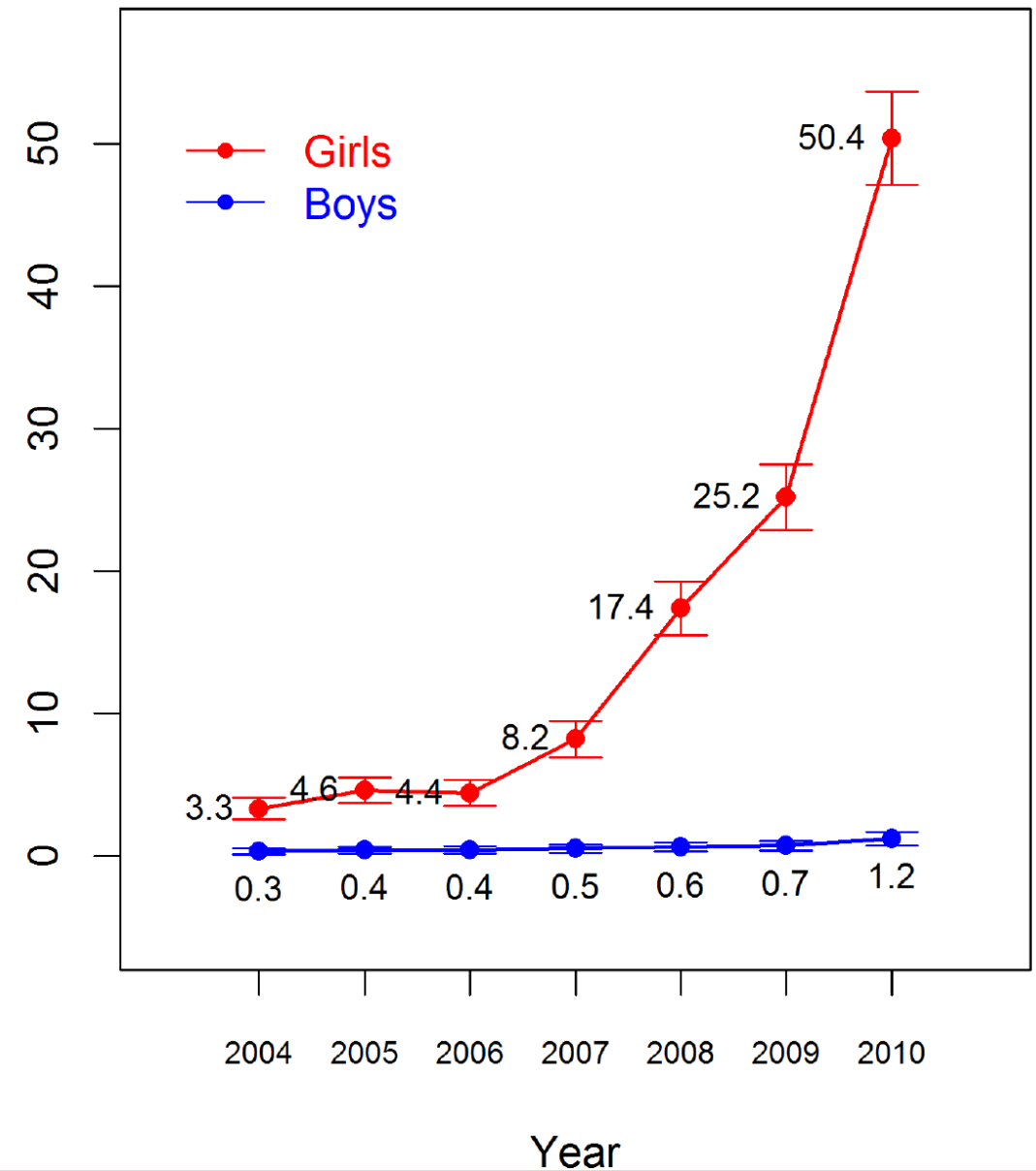
INCREASED INCIDENCE OF CENTRAL PRECOCITY 2004 TO 2010, SOUTH KOREA

- Data from Korean Health Insurance Review Agency, 2004-2010
- 21,351 children, Registered with a diagnosis of CPP
- Incidence of CPP increased from 3.3 to 50.4 per 100,000 girls
Incidence of CPP increased from 0.3 to 1.2 per 100,000 boys

INCREASED INCIDENCE OF 2004 TO 2010, SOUTH KOREA

- Data from Korean Health Insurance Review and Assessment
- 21,351 children, Registered with a diagnosis of congenital pericardial perforation
- Incidence of CPP increased from 3.3 per 100,000 persons in 2004 to 50.4 in 2010
- Incidence of CPP increased from 0.3 per 100,000 persons in 2004 to 1.2 in 2010

Annual Incidence per 100,000 persons



RECENT TRENDS OF EARLIER PUBERTY

POSSIBLE AFFECTING FACTORS

- Body fatness & Body mass index
Trend of increasing prevalence in childhood obesity
Girls who had higher body weight in early childhood represented earlier sexual maturation, *Davison et al, Pediatrics 2003;111:815*
- Endocrine-disrupting chemicals
- Phytoestrogens

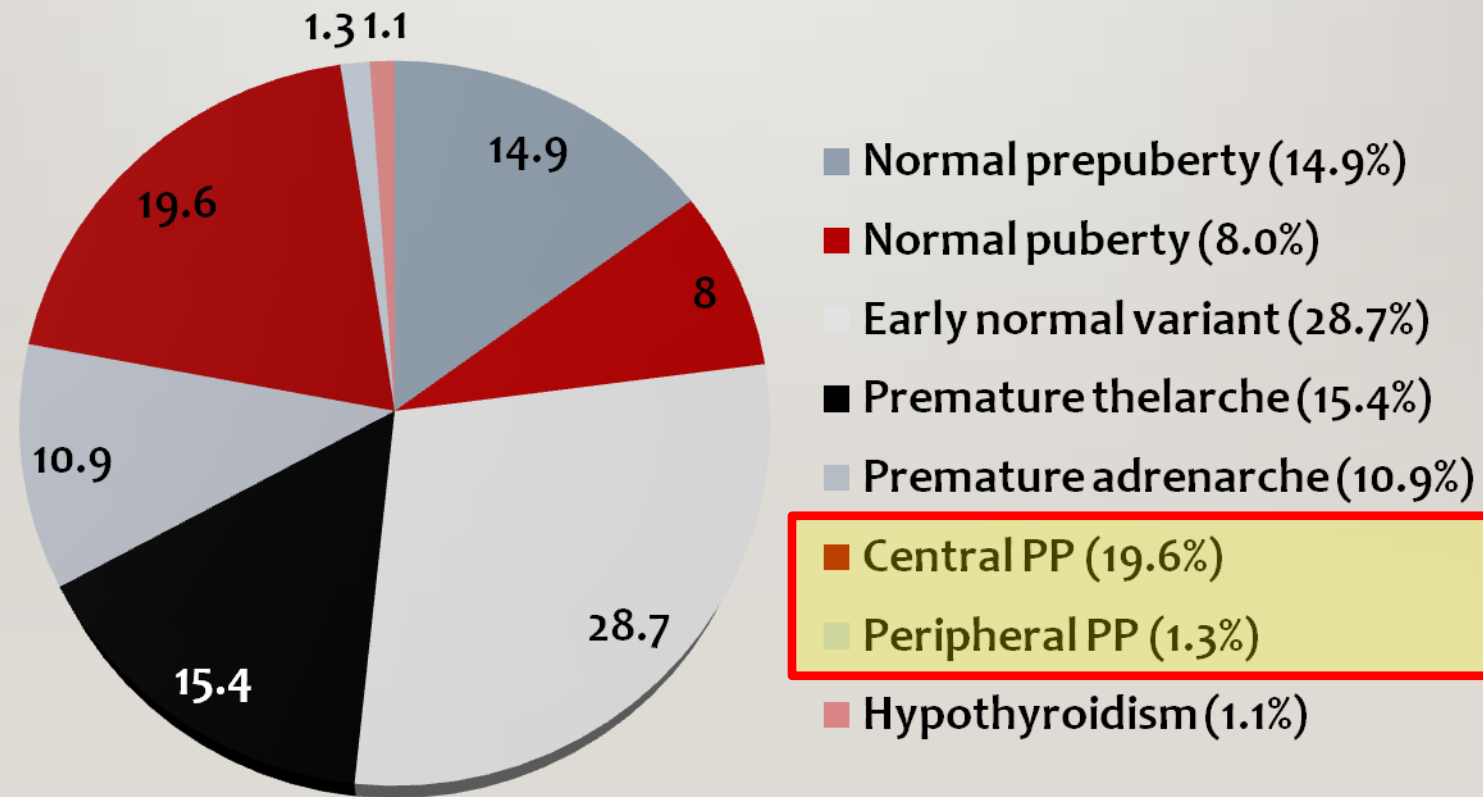
IS MY CHILD A PRECOCIOUS PUBERTY?

BREAST BUDDING < 8.0 YEAR OF AGE

- Breast & Pubic hair maturity rating (Tanner staging)
- Analysis of Height Growth
- Assessment of Bone maturation
- US examination of Uterus and Ovaries
- Hormone tests

Diagnostic Work-Up of 449 Consecutive Girls Who Were Referred to be Evaluated for Precocious Puberty

Signs of Early Puberty (n=449)



Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children

- European Society for Pediatric Endocrinology (ESPE)
Lawson Wilkins Pediatric Endocrine Society (LWPES), 2009
- Clinical criteria
Progressive puberty over a 3- to 6-month period
At or past Tanner 3 (breast) w/ advanced skeletal maturation
- Chronologic age criteria
CPP before age of 6, greatest height gain w/ GnRH-a
CPP after age of 6, decision should be individualized

INDICATION OF GNRH-A THERAPY

- Rapid sexual maturation
Tanner stage progression within 3-6 months
- Accelerated growth velocity > 6 cm/year
- Bone age advancement > 1 year
- Predicted adult height (PAH) $<$ target range
- Decreasing PAH in serial follow-up

CASE

CENTRAL PRECOCIOUS PUBERTY, IDIOPATHIC

- 7 years 5 months of age, Breast budding for 2 months
- Height 125cm (75P), Weight 25kg
- Breast Tanner 2, Mound 25mm, Areola 19mm, Papilla 3mm, Pubic hair Tanner I
Relatively estrogenized genital skin, Café-au-lait spot (-)
- Birth weight 2.9kg, full-term, no birth defect
- Family history Non-contributory
- Bone age (BA) 94M [94±18M (2SD)]

CASE

CENTRAL PRECOCIOUS PUBERTY, IDIOPATHIC

- 7 years 8 months of age, No breast regression
- Height 128cm (80P), Weight 26kg
- BA 94M [97 $\pm$ 18M (2SD)]
- LH0' <0.07, LH30' 19.57, FSH0' 1.42, FSH30' 16.92
- Pelvic US
Uterus 4.5*1.3*2.5cm, RO 2.4*1.0cm, LO 1.9*1.1cm, EM not thickened
- Sella MRI Within normal limits

CASE

CENTRAL PRECOCIOUS PUBERTY, IDIOPATHIC

- Initial dose
Lucrin depot 0.5 ample (1.875mg) sc every 4 weeks
- At 4th INJECTION, B2, GnRH-a test LH30' 1.72 mIU/ml, FSH30' 7.49 mIU/ml
- Increasing dose
Lucrin depot 0.75 ample sc every 4 weeks
- At 7th INJECTION, B1, Height 131.9cm, Weight 26.8kg

CASE

CENTRAL PRECOCIOUS PUBERTY, IDIOPATHIC

- At 12th INJECTION, Height 132.9cm (75P), Weight 28.5kg
BA 106M [108M $\pm$ 20M (2SD)]
- At 17th INJECTION, Height 135.8cm, Weight 29.7kg
- At 20th INJECTION, 9 years 4 months of age
Height 135.6cm, Height gain 0cm/3M  D/C GnRH-agonist
- 9 years 7 months of age, Height 139.5cm (75P), B3
9 years 10 months of age, Height 140.8cm (50-75P), B3, PAH 163.3cm / TH 160cm
10 years 9 months of age, Height 148.6cm (75-90P), B4, BA 132M [135 $\pm$ 22M (2SD)]

CASE

PREMATURE THELARCHE

- 14 months of age, Breast budding for 2 months, remote for 7 months
- Height 75cm (10-25P), Weight 9.5kg (25P)
- Breast Tanner 2
- BA 15M [14 $\pm$ 2M (2SD)]
- Basal hormone LH <0.07 mIU/ml, FSH 1.68 mIU/ml, E2 5.7 pg/ml
- Pelvic US Normal prepubertal uterus 2.56cm in length

CASE

PREMATURE THELARCHE

- 19 months of age, OB GYN OPD
B2, Mound 25mm, Areola 11mm, Papilla 3.5mm
- 25 months of age, Height 84.5cm (25-50P), Weight 11.4kg (10-25P)
B2, Mound 20mm
BA 24M [25±8M (2SD)]
LH0' <0.07 mIU/ml, LH30' 1.43, FSH0' 3.43, FSH30' 21.0, E2 6.6 pg/ml
Pelvic US Uterus 3.2*0.5*1.4cm Normal prepubertal ovarian volume

CASE

PREMATURE THELARCHE

- 3 years 5 months of age, Height 94cm, Weight 13.3kg
B2, Mound 10mm, Hypo-estrogenized genital skin
- 6 years 6 months of age, Height 114cm, 6.7cm/year
B2, Mound 9mm, Hypo-estrogenized genital skin
BA 78M [82±16M (2SD)]
- 7 years 8 months of age
B1, No breast mound, Hypo-estrogenized genital skin
- 9 years 3 months of age, Height 134cm (50-75P)
B3, Mound 30mm, Estrogenized
BA 120M [116±21M (2SD)] → PAH 158cm / TH 159cm

CASE

TRANSIENT PPP, FUNCTIONAL OVARIAN CYST

- 5 years 1 month of age, Breast budding & Vaginal discharge for 1 week
- Height 105cm (25P), Weight 16kg (10P)
- Breast Tanner 2 (B2), Pubic hair Tanner 1 (PH1)
Relatively estrogenized genital skin, Café-au-lait spot (-)
- Birth weight 3.0kg, full-term, no birth defect
- Family history Non-contributory
- No medication history

CASE

TRANSIENT PPP, FUNCTIONAL OVARIAN CYST

- Basal hormone
LH <0.07 mIU/ml, FSH <0.3 mIU/ml, E2 < 20 pg/ml
Normal T, DHEAS, Prolactin, TFT
- Stimulated hormone
LH30' 0.09 mIU/ml, FSH30' 0.5 mIU/ml
- Pelvic US
Uterus 4.3*1.5*2.2cm RO 1.6*0.4*1.4cm LO 3.6cm-sized anechoic cyst
- Tumor markers
Normal LDH, HCG, CA125, CEA, AFP

CASE

TRANSIENT PPP, FUNCTIONAL OVARIAN CYST

- 1 month after initial visit

Pelvic US

Uterus 3.3*1.0*1.7cm RO 2.1*0.7*1.3cm LO 2.1cm-sized anechoic cyst

- 3 months after initial visit

Pelvic US

Uterus 3.3*0.8*1.3cm RO 1.5*0.8*0.9cm NO ovarian cyst

➡ Breast Tanner I

CASE

PERIPHERAL PP,AUTONOMOUS OVARIAN CYST

- 7 years 3 months of age, Breast budding for 5 months, Brown spotting for 2 days
Height 121.8cm (50-75P),Weight 19kg (10-25P)
- B2, Mound 25mm, Areola 18mm, Papilla 4mm, Pubic hair Tanner I
Fully estrogenized genital skin, Café-au-lait spot (-)
- No medication
- Family history Non-contributory
- Pelvic US Uterus 6.5*1.5*2.1cm, RO 9.3ml, LO 2.3ml, RO anechoic cyst 2.6*1.7cm

CASE

PERIPHERAL PP,AUTONOMOUS OVARIAN CYST

- Basal & Stimulated hormone
LH0' <0.07 mIU/ml, LH30' <0.07, FSH0' 0.31, FSH30' 0.8
Normal PRL,TFT, DHEAS
- Tumor markers LDH 573 μ /L (200-470), Normal AFP, CA125, CEA
- BA100M [92 $\pm$ 19M (2SD)]

CASE

PERIPHERAL PP,AUTONOMOUS OVARIAN CYST

- 1 month after initial visit
B2, Mound 15mm, Estrogenized genital skin
- 5 months after initial visit, Height 123.8cm
B1, No palpable mound, Estrogenized genital skin
- 7 months after initial visit
Pelvic US Uterus 4.2*1.0*1.8cm, RO 4.6ml, LO 3ml, **NO RO cyst**
- 9 months after initial visit, Height 126.7cm
Vaginal bleeding for 1 day
B2, Mound 23mm, Pelvic US **3.5cm-RO cyst**

IMPORTANT CLUES IN DIAGNOSIS AND MANAGEMENT OF PRECOCIOUS PUBERTY



CUTOFF VALUES OF BASAL AND STIMULATED LH

Table 2. Cutoff values of basal and GnRH-stimulated LH for diagnosis of central precocious puberty

Author	Method	Basal LH (IU/L)	GnRH	LH peak after GnRH (IU/L)
Neely and cols., 1995 (32)	ICMA	0.15	Gonadorelin 100 ug IV	5.0
Brito and cols., 1999 (27)	IFMA	0.6	Gonadorelin 100 ug IV	6.9 (F)
				9.6 (M)
Brito and cols., 2004 (30)	IFMA	0.6	Leuprorelin acetate 3.75 mg	10.0
Houk and cols., 2009 (33)	ICMA	0.83	N/A	N/A
	IFMA	1.05		
Pasternak and cols., 2012 (34)	ICMA	0.1	Gonadorelin 100 ug IV	4.9
Sathasivam and cols., 2010 (35)	ICMA	0.3	Leuprorelin acetate 20 ug/kg SC	5.0
Resende and cols., 2007 (28)	ICMA	0.2	Gonadorelin 100 ug IV	4.1 (M); 3.3 (F)
	IFMA	0.6		3.3 (M); 4.2 (F)
Lee and cols., 2013 (36)	ECLIA	0.1	Gonadorelin 100 ug IV	5.0 (F)
Freire and cols., 2013 (37)	IFMA	N/A	Triptorelin	7.0
	ECLIA		0.1 mg/m ² , maximum of 0.1 mg SC	8.0
Bizarri and cols., 2014 (38)	ICMA	> 0.2	Gonadorelin 100 ug IV	5.0

ICMA: immunochemiluminescence; IFMA: immunofluorimetric; ECLIA: eletrochemiluminescence; SC: subcutaneous; IV: intravenous; F: female; M: male; N/A: not available.

LH : VALUABLE PARAMETER FOR CPP

- Basal LH levels

Useful screening tests and may be diagnostic

- Stimulated LH levels

Important parameters for the diagnosis of CPP

- Cut off limits for CPP

Basal LH, **>0.3 IU/L** (ICMA), >0.6 IU/L (IFMA)

GnRH-stimulation test LH, **3.3 to 5.0 IU/L** (ICMA), 4.2 to 6.9 IU/L (IFMA)

GnRH agonist stimulation test LH, **5.0 IU/L** (ICMA), 7 to 10 IU/L (IFMA)

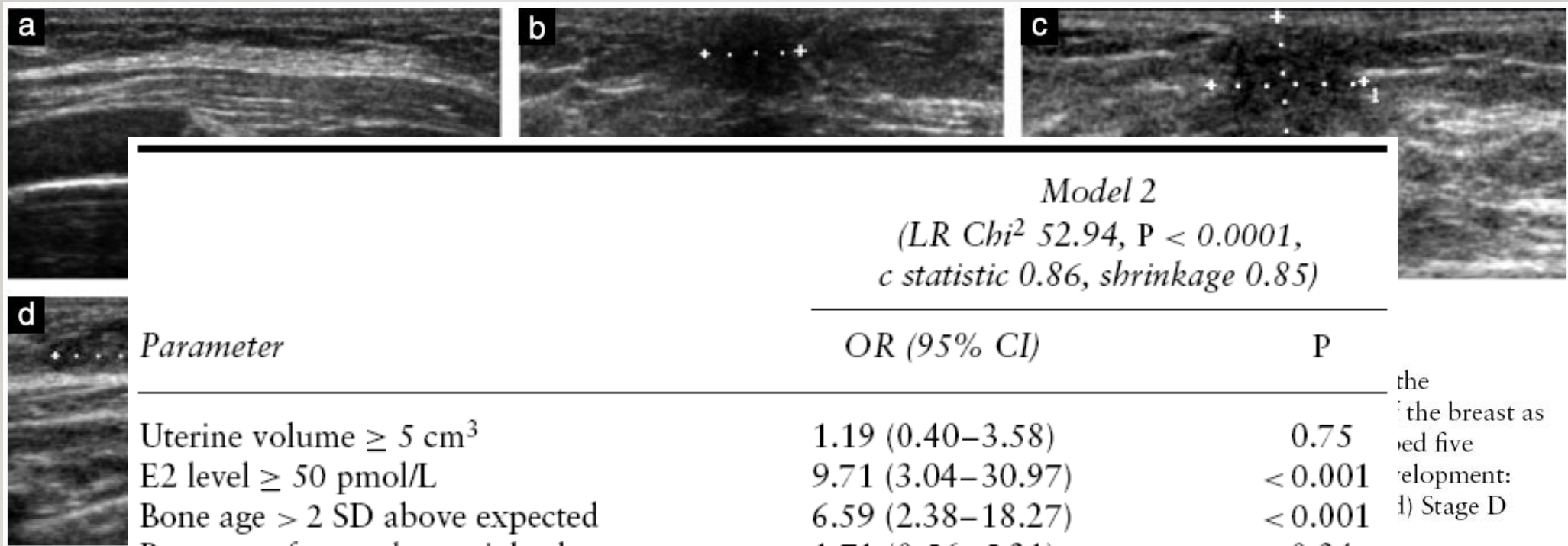
PELVIC ULTRASOUND IN CPP

- Pelvic Ultrasound
 - Measurement of Uterine & Ovarian volumes
 - Detection of Ovarian cysts or neoplastic lesions
- Cut-off values for CPP: **NOT diagnostic**
 - Cut-off of Uterine Length 3.4 to 4.0 cm
 - Cut-off of Ovarian Volume 1.0 to 3.0 cm³
- Enhanced endometrial line

NORMAL UTERINE & OVARIAN DIMENSIONS

Age group	n	Ovarian volume (cm ³)		Uterine length (cm)		FCR	
		Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
<30 days	10	0.25 (0.25)	0.15	2.98 (0.25)	2.95	0.79 (0.28)	0.66
4-8 months	10	0.21 (0.19)	0.13	2.72 (0.61)	2.75	0.86 (0.19)	0.81
1-2 yr	10	0.24 (0.23)	0.14	2.50 (0.44)	2.40	1.00 (0.20)	1.00
2-3 yr	10	0.28 (0.15)	0.27	2.56 (0.46)	2.45	0.91 (0.19)	0.93
3-4 yr	10	0.36 (0.22)	0.26	2.48 (0.63)	2.55	0.99 (0.21)	1.06
4-5 yr	10	0.50 (0.32)	0.36	2.84 (0.37)	2.85	1.03 (0.25)	1.00
5-6 yr	10	0.51 (0.13)	0.53	2.83 (0.47)	2.85	0.91 (0.22)	0.92
6-7 yr	15	0.51 (0.35)	0.37	3.01 (0.27)	3.00	1.03 (0.34)	1.00
7-8 yr	10	0.62 (0.54)	0.52	3.02 (0.21)	3.00	1.16 (0.58)	1.10
8-9 yr	10	1.22 (0.59)	1.24	3.23 (0.41)	3.25	1.35 (0.51)	1.18
9-10 yr	11	1.23 (1.50)	0.90	3.71 (0.88)	3.30	1.30 (0.57)	1.20
10-11 yr	15	1.34 (0.54)	1.51	3.59 (0.69)	3.40	1.21 (0.30)	1.22
11-12 yr	15	1.64 (1.32)	1.42	4.80 (1.69)	5.30	1.28 (0.33)	1.22
12-13 yr	15	2.97 (1.57)	2.97	5.50 (1.27)	5.30	1.48 (0.33)	1.50
13-14 yr	11	3.38 (1.51)	3.03	6.06 (0.42)	6.00	1.56 (0.39)	1.63
14-15 yr	10	4.29 (2.73)	4.17	6.16 (0.81)	6.25	1.71 (0.39)	1.53
15-16 yr	12	4.44 (1.85)	4.00	6.94 (1.12)	7.10	1.73 (0.43)	1.68
16-17 yr	10	4.51 (1.41)	4.96	7.03 (0.9)	7.20	1.80 (0.40)	1.68
17-18 yr	10	5.42 (2.25)	4.97	8.00 (1.65)	7.55	1.56 (0.31)	1.58

BREAST STAGE: ULTRASONOGRAPHY



	<i>Model 2</i> <i>(LR Chi² 52.94, P < 0.0001, c statistic 0.86, shrinkage 0.85)</i>	
<i>Parameter</i>	<i>OR (95% CI)</i>	<i>P</i>
Uterine volume $\geq 5 \text{ cm}^3$	1.19 (0.40–3.58)	0.75
E2 level $\geq 50 \text{ pmol/L}$	9.71 (3.04–30.97)	< 0.001
Bone age > 2 SD above expected	6.59 (2.38–18.27)	< 0.001
Presence of an endometrial echo	1.71 (0.56–5.21)	0.34
Breast volume $\geq 0.85 \text{ cm}^3$	4.35 (1.40–13.62)	0.012

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NIPPLE AND AREOLA DIAMETERS IN PUBERTAL GIRLS

B Stage	Nipple Diameter	Menstrual Status	Nipple Diameter
1 ($n = 163$)	2.56 ± 1.56		
2 ($n = 69$)	3.32 ± 1.44	M1 ($n = 208$)	3.41 ± 1.39
3 ($n = 152$)	5.21 ± 1.98	M2 ($n = 218$)	6.58 ± 1.64
4 ($n = 57$)	6.28 ± 1.70	M3 ($n = 72$)	6.96 ± 1.56
5 ($n = 61$)	6.90 ± 1.51		

B Stage	Areola Diameter	Menstrual Status	Areola Diameter
1 ($n = 163$)	14.35 ± 5.08		
2 ($n = 69$)	20.26 ± 5.87	M1 ($n = 208$)	18.76 ± 6.12
3 ($n = 152$)	28.84 ± 6.38	M2 ($n = 218$)	32.75 ± 9.24
4 ($n = 57$)	32.03 ± 8.80	M3 ($n = 72$)	38.04 ± 9.85
5 ($n = 61$)	37.67 ± 9.98		

Average girls *ages and estimated mature heights for girls with skeletal ages within 1 year of their chronological ages:
Skeletal ages 6–11 years*

Bone age	6-0	6-3	6-6	6-9	7-0	7-3	7-6	7-10	8-0	8-3	8-6	8-10	9-0	9-3	9-6	9-9	10-0	10-3	10-6	10-9	11-0	11-3	11-6	11-9
% of mature	72	72.9	73.8	75.1	75.7	76.5	77.2	78.2	79	80.1	81	82.1	82.7	83.6	84.4	85.3	86.2	87.4	88.4	89.6	90.6	91	91.4	91.8
Height (In)																								
37	51.4																							
38	52.8	52.1	51.5																					
39	54.2	53.5	52.8	52.0	51.5	51.0																		
40	55.6	54.9	54.2	53.3	52.8	52.3	51.8	51.2																
41	56.9	56.2	55.6	54.6	54.2	53.6	53.1	52.4	51.9	51.2														
42	58.3	57.6	56.9	55.9	55.5	54.9	54.4	53.7	53.2	52.4	51.9	51.2												
43	59.7	59.0	58.3	57.3	56.8	56.2	55.7	55.0	54.4	53.7	53.1	52.4	52.0	51.4										
44	61.1	60.4	59.6	58.6	58.1	57.5	57.0	56.3	55.7	54.9	54.3	53.6	53.2	52.6	52.1	51.6	51.0							
45	62.5	61.7	61.0	59.9	59.4	58.8	58.3	57.5	57.0	56.2	55.6	54.8	54.4	53.8	53.3	52.8	52.2	51.5						
46	63.9	63.1	62.3	61.3	60.8	60.1	59.6	58.8	58.2	57.4	56.8	56.0	55.6	55.0	54.5	53.9	53.4	52.6	52.0	51.3				
47	65.3	64.5	63.7	62.6	62.1	61.4	60.9	60.1	59.5	58.7	58.0	57.2	56.6	56.2	55.7	55.1	54.5	53.8	53.2	52.5	51.9	51.6	51.4	51.2
48	66.7	65.8	65.0	63.9	63.4	62.7	62.2	61.4	60.8	59.9	59.3	58.6	58.2	57.6	56.9	56.3	55.7	54.9	54.3	53.6	53.0	52.7	52.5	52.3
49	68.1	67.2	66.4	65.3	64.8	64.1	63.5	62.7	62.0	61.2	60.5	59.9	59.4	58.8	58.1	57.4	56.8	56.1	55.4	54.7	54.1	53.8	53.6	53.4
50	69.4	68.6	67.8	66.6	66.1	65.4	64.8	63.9	63.3	62.4	61.7	60.9	60.4	59.8	59.2	58.6	58.0	57.2	56.6	55.8	55.2	54.9	54.7	54.5
51	70.8	70.0	69.1	67.9	67.4	66.7	66.1	65.2	64.6	63.7	63.0	62.1	61.7	61.0	60.4	59.8	59.2	58.4	57.7	56.9	56.3	56.0	55.8	55.6
52	72.2	71.3	70.5	69.2	68.7	68.0	67.4	66.5	65.8	64.9	64.2	63.3	62.9	62.2	61.6	61.0	60.3	59.5	58.8	58.0	57.4	57.1	56.9	56.6
53	73.6	72.7	71.8	70.6	70.0	69.3	68.7	67.8	67.1	66.2	65.4	64.6	64.1	63.4	62.8	62.1	61.5	60.6	60.0	59.2	58.5	58.2	58.0	57.7
54		74.1	73.2	71.9	71.3	70.6	69.9	69.1	68.4	67.4	66.7	65.8	65.3	64.6	64.0	63.3	62.6	61.8	61.1	60.3	59.6	59.3	59.1	58.8
55			74.5	73.2	72.7	71.9	71.2	70.3	69.6	68.7	67.9	67.0	66.5	65.8	65.2	64.5	63.8	62.9	62.2	61.4	60.7	60.4	60.2	50.9
56				74.6	74.0	72.2	72.5	71.6	70.9	69.9	69.1	68.2	67.7	67.0	66.4	65.7	65.0	64.1	63.3	62.5	61.8	61.5	61.3	61.0
57					74.5	73.8	72.9	72.2	71.2	70.4	69.4	68.9	68.2	67.5	66.8	66.1	65.2	64.5	63.6	62.9	62.6	62.4	62.1	
58						74.2	73.4	72.4	71.6	70.6	70.1	69.4	68.7	68.0	67.3	66.4	65.6	64.7	64.0	63.7	63.5	63.2		
59							74.7	73.7	72.8	71.9	71.3	70.6	69.9	69.2	68.4	67.5	66.7	65.8	65.1	64.8	64.6	64.3		
60								74.9	74.1	73.1	72.6	71.8	71.1	70.3	69.6	68.7	67.9	67.0	66.2	65.9	65.6	65.1		
61									74.3	73.8	73.0	72.3	71.5	70.8	69.8	69.0	68.1	67.3	67.0	66.7	66.4			
62											74.2	73.5	72.7	71.9	70.9	70.1	69.2	68.4	68.1	67.8	67.5			
63													74.6	73.9	73.1	72.1	71.3	70.3	69.5	69.2	68.9	68.6		
64															74.2	73.2	72.4	71.4	70.6	70.3	70.0	69.7		
65																74.4	73.5	72.5	71.7	71.4	71.1	70.8		
66																	74.7	73.7	72.9	72.5	72.2	71.9		
67																		74.8	74.0	73.6	73.3	73.0		
68																				74.7	74.4	74.1		

Predicted adult height

(From: Bayley N, Pinneau SR. Tables for predicting adult height from skeletal age: Revised for use with the Greulich-Pyle hand standards. *J Pediatr* 1952;40:423; with permission.)

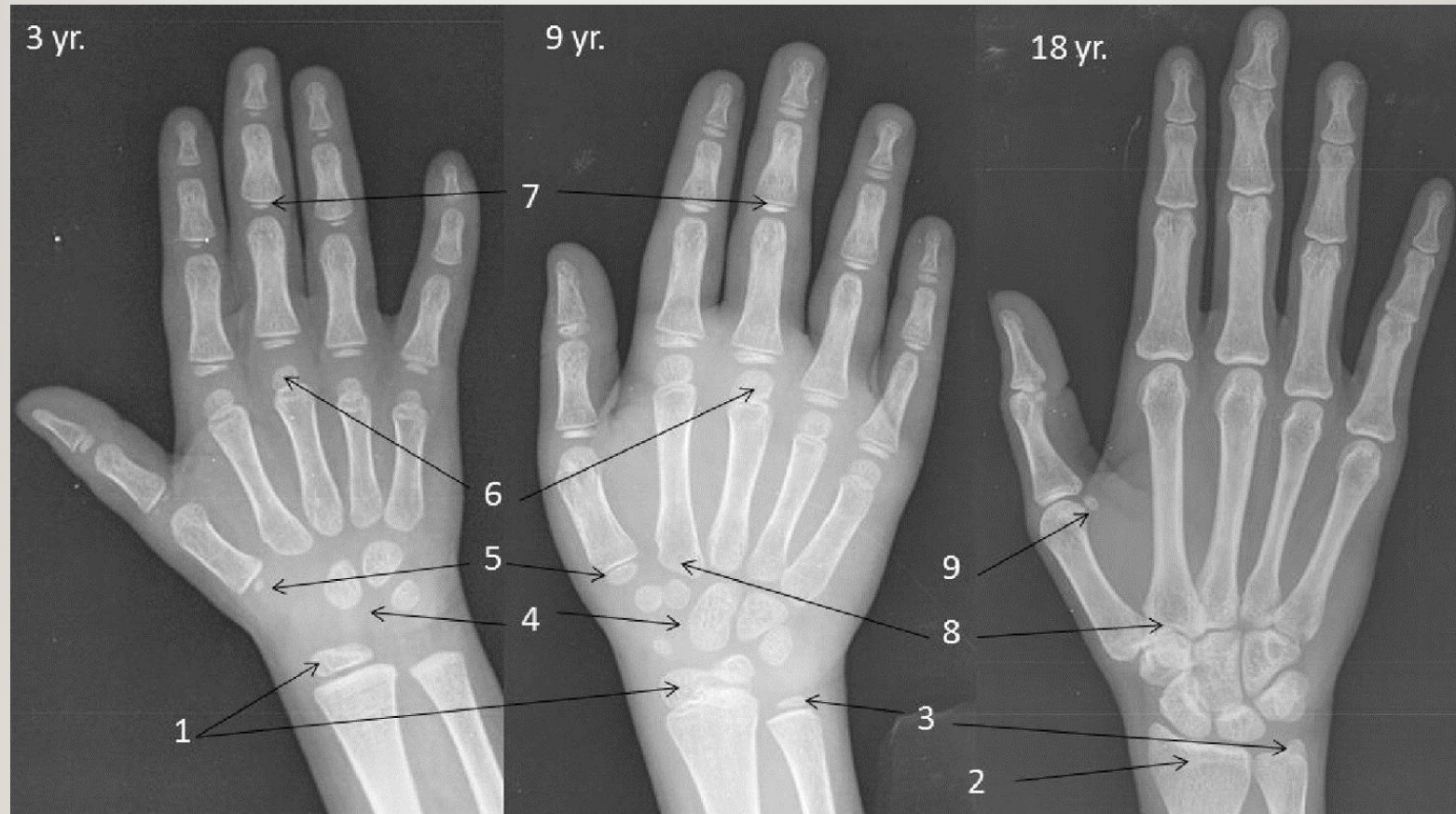
BONE AGE INTERPRETATION

Determining points of Skeletal age

1. Appearance, size and shape of lower end **epiphysis of radius**
2. Presence of epiphysial fusion line of lower end of radius
3. Size of **epiphysis** of lower end of **ulna**
4. Number of **carpals**, their size and shape
5. Size of proximal end **epiphysis** of 1st **metacarpal**
6. Size of distal end epiphysis (head) of 2nd to 5th metacarpal
7. Appearance, size, shape and fusion of **epiphysial plate** of **phalanges**
8. Cupping of proximal end of metacarpals
9. Presence of sesamoid bone at 1st metacarpal

GREULICH & PYLE METHOD

CHRONOLOGIC AGE 3, 9, 18 YEARS



GNRH-AGONIST DOSE IN CPP TREATMENT

Preparation	Brand name	Available doses
Goserelin	Zoladex LA	3.6 mg / 1 month 10.8 mg / 3 months
Buserelin	CinnaFact Superfact depot	6.3 mg / 2 months 9.45 mg / 3 months
Leuprolide	Leuplin Lupron depot PED Lucrin/Procrin	<20kg: 1.87 mg 20-30kg: 2.5 mg >30kg: 3.75 mg or 7.5 mg / 1 month 11.25 mg or 22.5 mg or 30 mg / 3 months
Triptorelin	Decapeptyl SR	<20kg: 1.87 mg 20-30kg: 2.5 mg >30kg: 3.75 mg/ 1 month, 11.25 mg / 3 months
Histrelin	Supprelin LA	50 mg implant / year

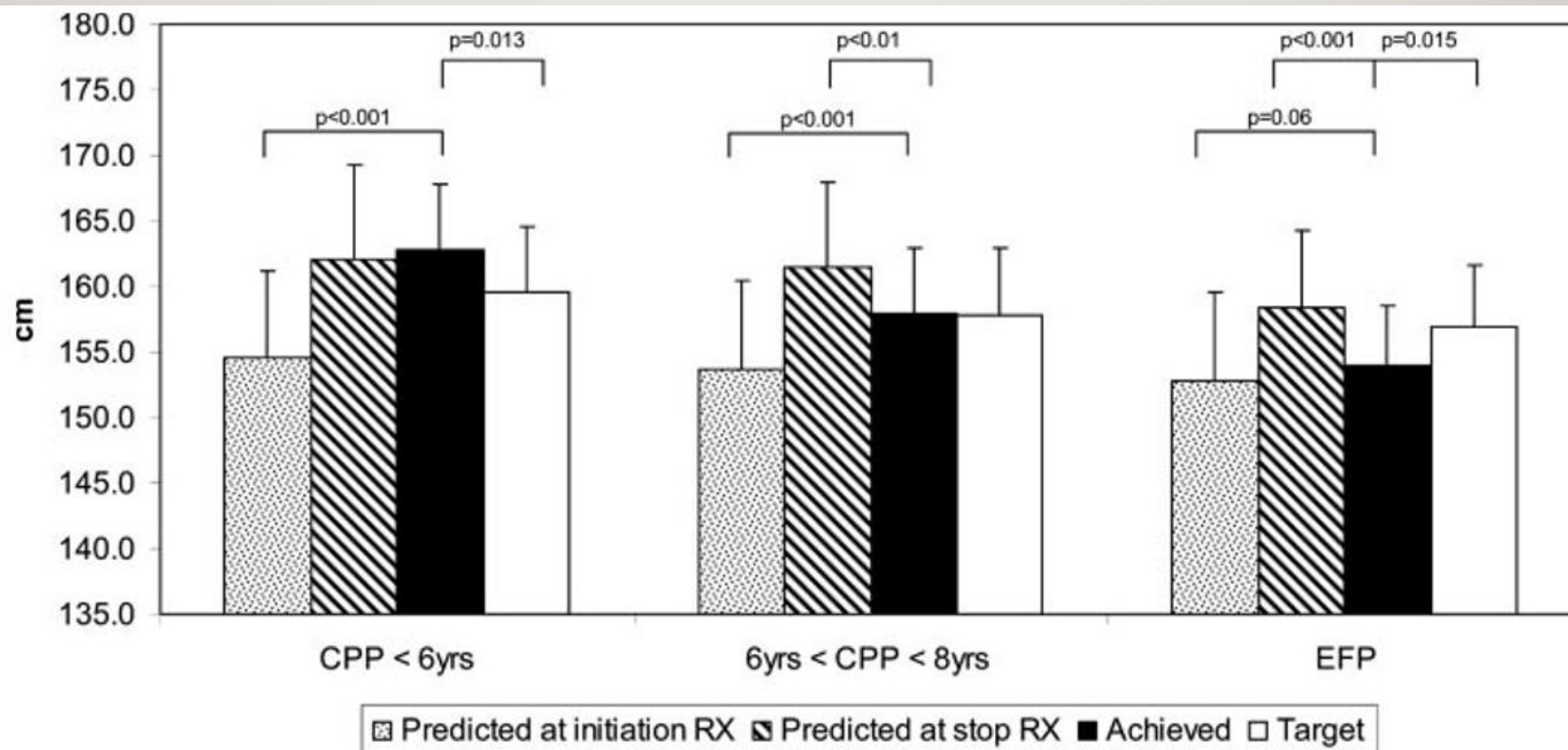
GNRH-A TREATMENT MONITORING

- **Monitoring of Efficacy**
Periodic Height & BA, 3-6 months interval
LH <3 IU/L, 30-60 min after GnRH-a Injection
Peak LH <2 IU/L, GnRH stimulation test
- **Under-Treatment**
Progression of breast & bone maturation
Elevated basal or stimulated LH levels
- **Over-Treatment**
Markedly decreased growth velocity (-2 SDS)

Growth Pattern and Final Height after Cessation of Gonadotropin-Suppressive Therapy in Girls with Central Sexual Precocity

Liora Lazar, Anna Padoa, and Moshe Phillip

- 22 CPP < age 6 yrs, 38 CPP age 6-8 yrs, 55 Early puberty, age 8-9 yrs, Israel



THANK YOU

