

# درمان بلوغ تسریع شده Accelerated Puberty Treatment

رضا توکلی زاده - پاییز ۱۴۰۴

# Outline

- ▶ Normal Puberty
- ▶ Variations of puberty
- ▶ Abnormal puberty (Accelerated, Delayed, Contra-sexual)
- ▶ Accelerated Puberty

# Normal puberty

- ▶ 3 Major Physical Changes of Puberty:
  - Adolescent growth spurt
  - Development of primary sex characteristics (gonads)
  - Development of secondary sex characteristics (phallus, breasts, pubic hair)

# Variations of puberty

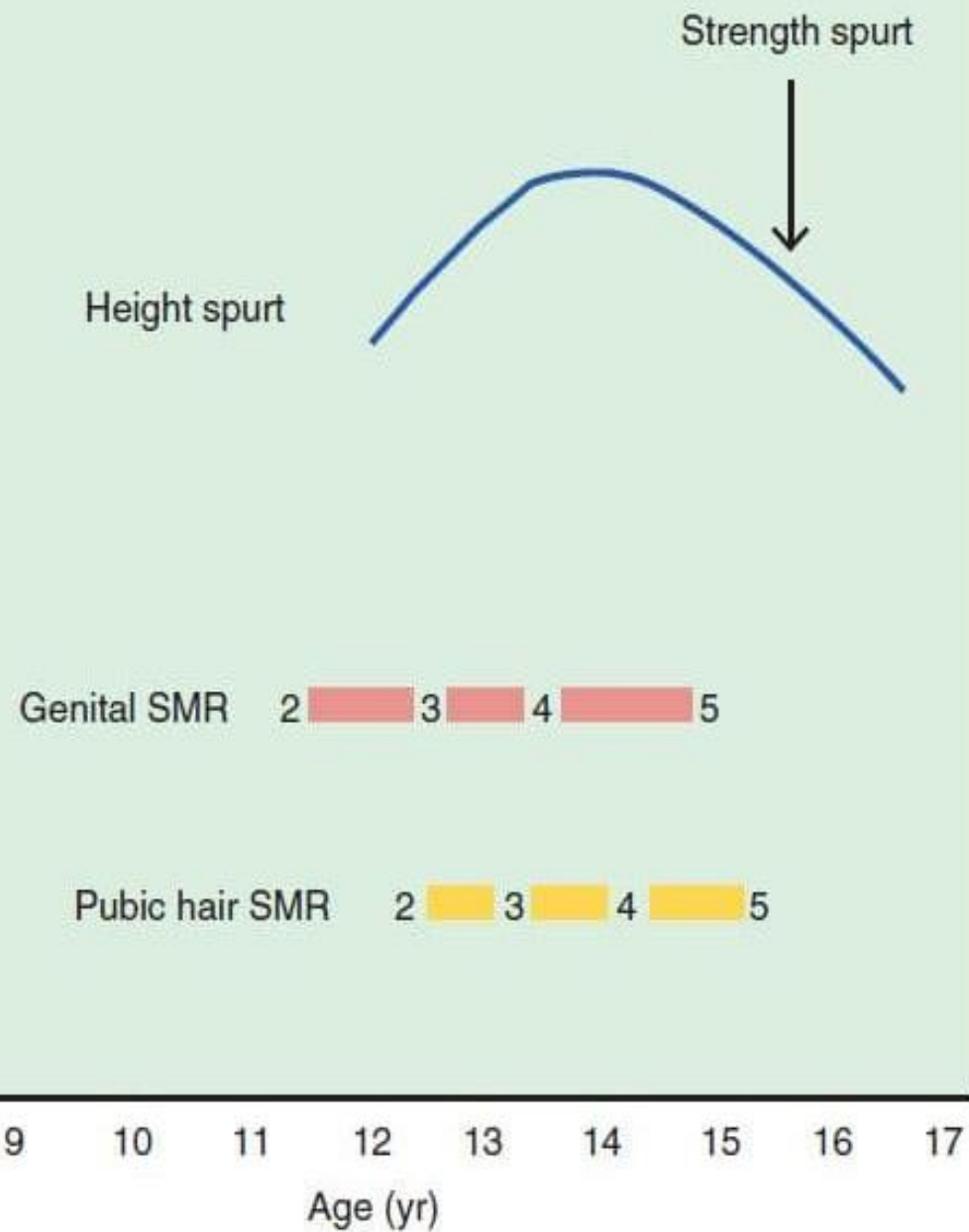
- ▶ Central Vs. Peripheral
  - Congenital adrenal hyperplasia
  - McCune-Albright syndrome
  - Gonadal/Adrenal tumors
  - Other hormone secreting tumors or cysts
  - Familial male-limited precocious puberty (testotoxicosis)
  - Exogenous exposure to sex steroids
  - Van Wyk and Grumbach syndrome (profound primary hypothyroidism)
- ▶ Premature adrenarche/pubarche
- ▶ Premature Thelarche
- ▶ Premature Menarche
- ▶ Slowly progressive precocious puberty\*

# Accelerated Puberty

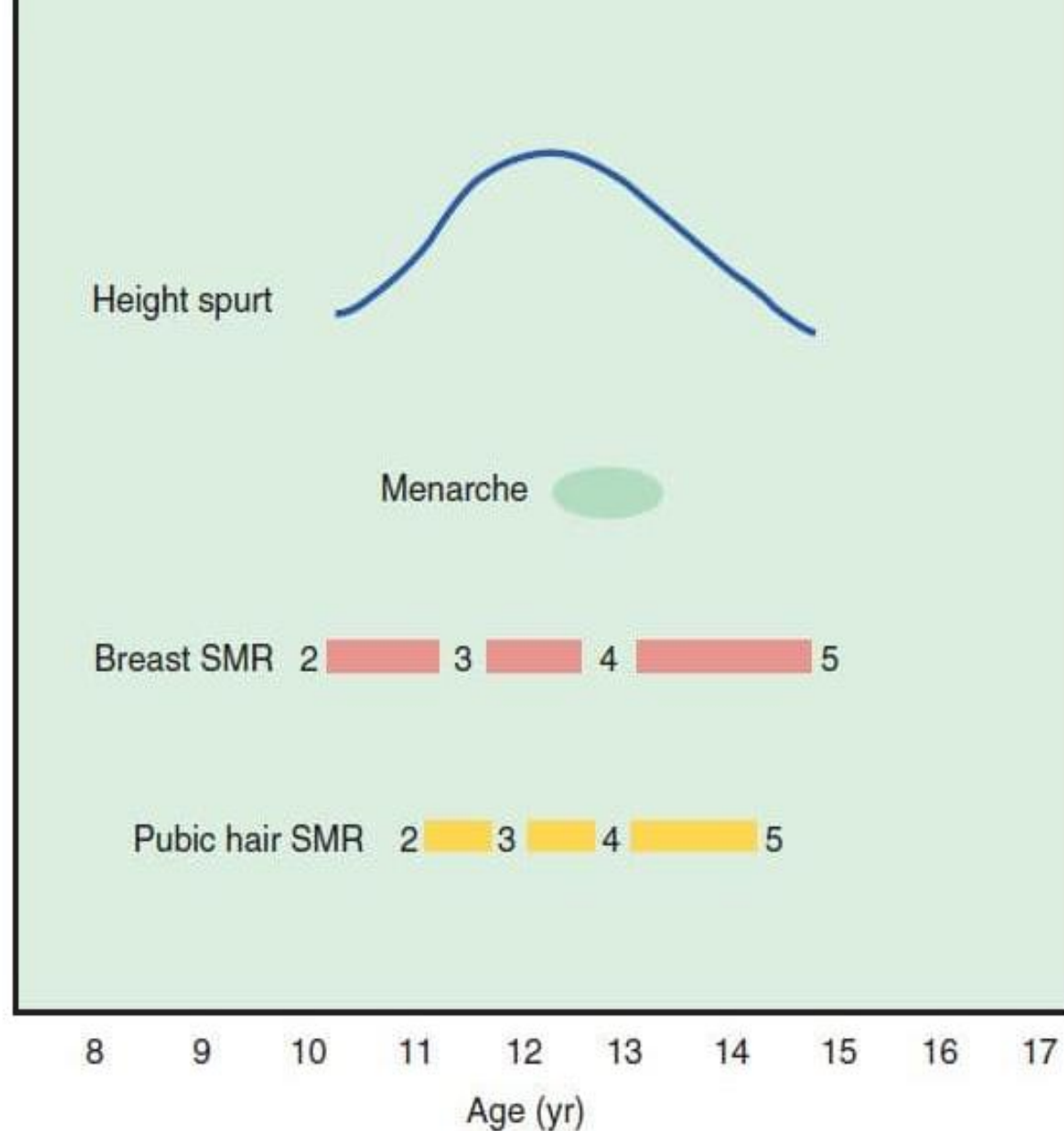
## ► **CPP: Timing**

- Onset of breast development <8yr in females
- Onset of testicular development (volume  $\geq 4$  mL) < 9yr in males
- Confirmation of Central (hypophyseal) etiology.

## ► **Rapidly Progressive Puberty: Tempo**



**Fig. 132.3** Sequence of pubertal events in males. Although the age of onset of puberty is variable, the sequence of events relative to one another is predictable. SMR, Sexual maturity rating.



**Fig. 132.4** Sequence of pubertal events in females. Although the age of onset of puberty is variable, the sequence of events relative to one another is predictable. SMR, Sexual maturity rating.

**Table I.** Schematic criteria for progressive central precocious puberty

	Progressive precocious puberty	Slowly progressive precocious puberty/normal variant of pubertal development
Clinical		
Pubertal stages	Progression from one stage to the next in <6 months	Stabilization or regression of pubertal signs
Growth velocity	Accelerated (>6 cm/year)	Normal for age
Bone age	Variable (advanced)	Variable
Height prognosis	Below target height or declining	Within target height range
Pelvic sonography		
Uterus	Length >35 mm Pearl-like shape Endometrial thickening	Length ≤35 mm Pre-pubertal shape
Ovaries	Little impact on the decision Multi-cystic ovaries	Little impact on the decision Multi-cystic ovaries
Biology		
Estradiol	Little impact on the decision	Little impact on the decision
LH peak after GnRH stimulation	In the pubertal range	In the pre-pubertal range

# Accelerated Puberty

## ► Why is important?

### ► 1) Etiology (Pathological or idiopathic causes?)

- Endocrine-disrupting Chemicals (EDCs) on the timing of puberty has been an ongoing concern.
  - Polybrominated biphenyls, Bisphenol A, Atrazine (Herbicides), Phthalates
- **Obesity, Unhealthy diet\***, Living environment (chemical industry zone), Nutritional **supplements**, Foods containing **Pigments/Preservatives**, **High-protein** foods, and **sleep time (< 10 h)\*\***



# Accelerated Puberty

- ▶ **Why is important?**
  - ▶ **2) Effects**
    - **Pathologic etiology**
    - **Psychosocial aspects**
    - **Long-term consequences**
    - **Effect on the final adult height**

# Psychosocial aspects\*

## Boys

▶ جوانب مثبت بلوغ زودرس:

- محبوبیت، عزت نفس بهتر
- در بزرگسالی مسئولیت پذیرتر، تعاونی تر، اجتماعی تر

▶ معایب بلوغ زودرس:

- مصرف بیشتر مواد مخدر و الکل، فعالیت جنسی زودرس، قربانی شدن بیشتر در حوادث
- در بزرگسالی کمتر خلاق، بیشتر بدون شوخ طبعی

# Psychosocial aspects\*

## Girls:

Compared to early maturing boys, early maturing girls have more difficulties

▶ جوانب مثبت بلوغ زودرس:

➤ محبوبیت نزد پسران

▶ معایب بلوغ زودرس:

➤ احتمال بیشتری برای وزن بالاتر و قد کوتاه تر در آینده

➤ فعالیت جنسی زودرس، کاهش اعتماد به نفس، نرخ بالاتر افسردگی، اختلالات خوردن، اضطراب

# Psychosocial aspects\*

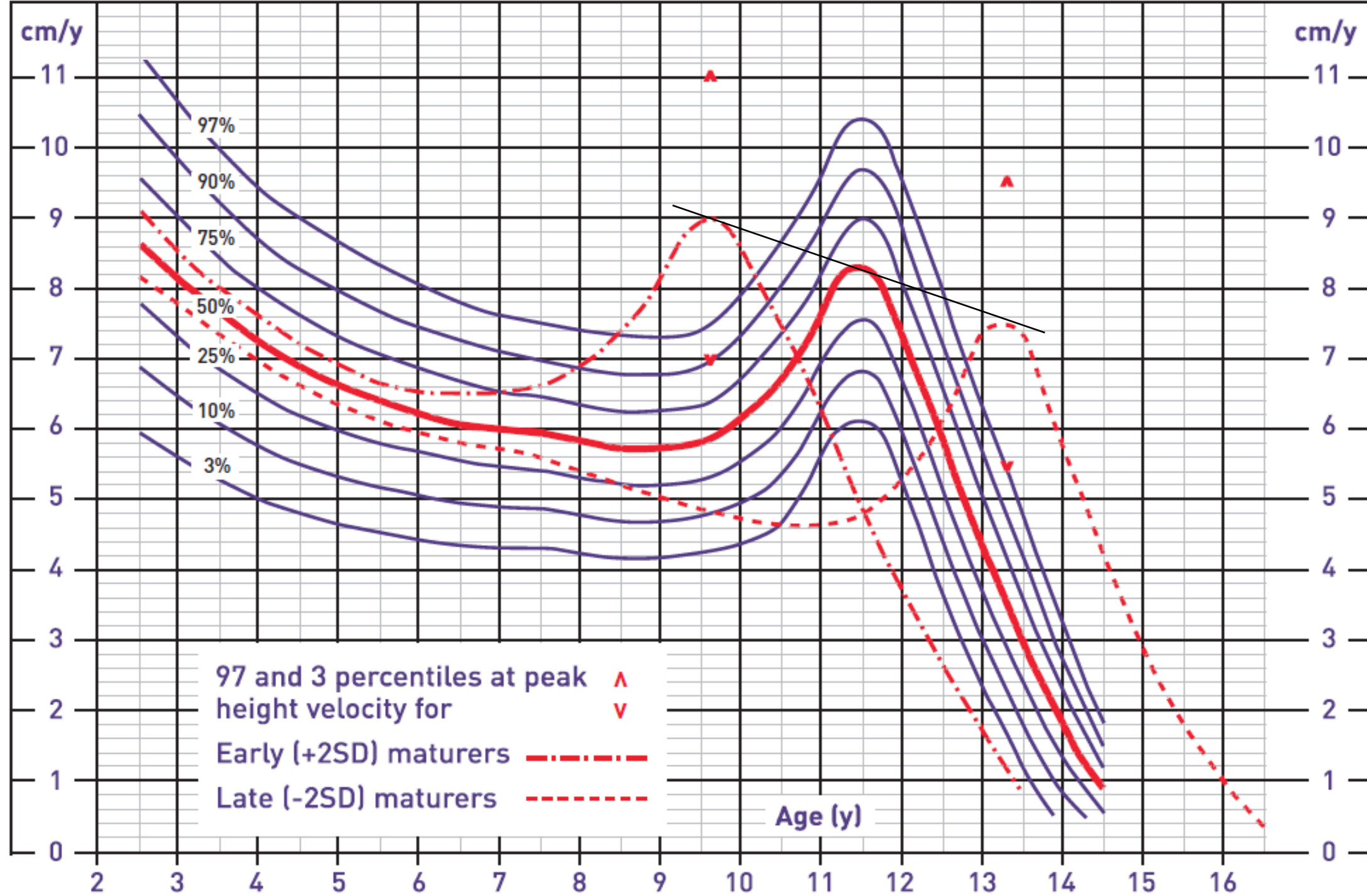
- ▶ **Spermarche typically occurs 1 year after accelerated penis growth**
- ▶ **Boys capable of fathering a child before they look like adults; opposite is true for girls.**
- ▶ **It's a problem for child? Or for Parents (specially Mothers)?**
- ▶ **Treatment indication?**

# Long-term consequences

- ▶ **Metabolic** disorders: insulin resistance, prediabetes, and type 2 diabetes.
- ▶ Increased **Cardiometabolic** risk: high **Chol**, high **BP**, overweight, **Obesity**.
- ▶ Increased risk of **Breast** and **Endometrial** cancer and **Testicular** cancer.
  
- ▶ Treatment indication?

# Effect on the final adult height

- ▶ Timing (early or late) and adult stature:
  - **Small effect:** Late maturers slightly taller as adults,  
Early maturing girls slightly heavier as adults
- ▶ Childhood height and weight:
  - **Stronger correlation** with adult height and weight



# Effect on the final adult height

- ▶ Precocity in the 6- to 8-year girls usually is not rapidly progressive and most commonly seems to be due to excessive adiposity. Many 6- to 8-year-old girls with central precocious puberty, including whites, have slowly progressive precocity, with a normal timing of menarche, and are at low risk of short adult stature. Most such girls do not require GnRH agonist therapy to preserve adult stature. However, 6- to 8-year-old girls with a suggestion of rapidly progressive or excessive androgenization or feminization, neurologic symptoms, linear growth acceleration, or significant bone age advancement should be more completely evaluated.
- ▶ Documentation typically requires 3 to 6 months, but it may be unnecessary if puberty is substantially advanced clinically and hormonally on presentation.



# Effect on the final adult height

- ▶ Timing of puberty does not greatly influence adult height\*
- ▶ Several studies have failed to find any benefit in terms of height in girls treated after age 8 years, and **some girls may even lose height as a result of treatment.**\*\*
- ▶ Time from breast development to menarche is longer for children with an earlier onset of puberty, ranging from a mean of:
  - ❖ 2.8 years when breast development begins at age 9;
  - ❖ 1.4 years when breast development begins at age 12.\*

# Accelerated Puberty

- ▶ **4 Questions in evaluation of premature sexual development\*:**
  - Is sexual development really occurring outside the normal temporal range?
  - What is the underlying mechanism and is it associated with a risk of a serious condition, such as an intracranial lesion?
  - Is pubertal development likely to progress?
  - Would this impair the child's normal physical and psychosocial development?

# Take home message

- ❖ هر علامت بلوغی، نشانه بلوغ نیست.
- ❖ هر بلوغی، ولو زودرس، سرکوب لازم ندارد.
- ❖ در بلوغ مرکزی، برای قد نهایی، Timing مهم نیست، Tempo مهم است.
- ❖ اندیکاسیون سرکوب بلوغ، کاملاً به شرایط اختصاصی هر Case بستگی دارد.



