

Med Pulse



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PRECOCIOUS PUBERTY

Puberty is the time of a person's life when his/her body changes from child to adult, accompanied by the process of sexual maturation. Puberty is caused by changes in hormones and includes both physical and emotional growth. In addition, with the onset of puberty, the secondary sexual characteristics begin to develop, such as pubic hair, breasts in girls, and a deepening of the voice in boys. On average, puberty begins in girls between the ages of 9 and 16 and in boys between the ages of 13 and 15. (www.med.umich.edu/yourchild/topics/puberty.html)

Physiology of Puberty

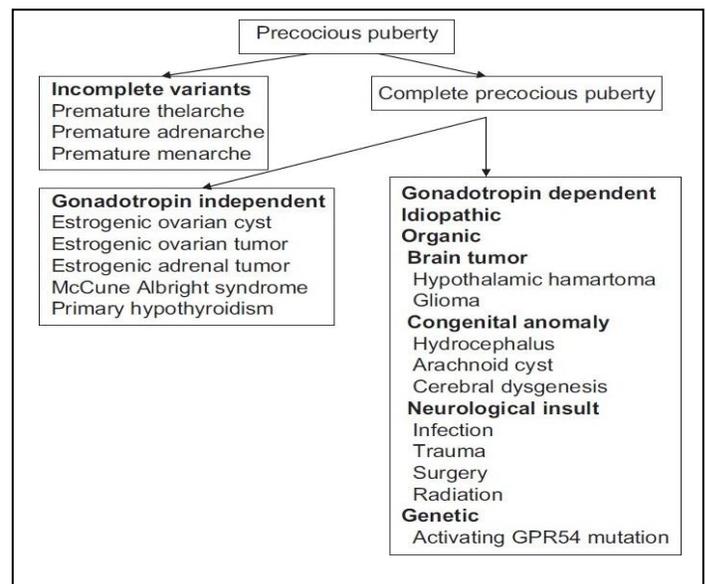
The onset of puberty is caused by the secretion of high-amplitude pulses of gonadotropin-releasing hormone (GnRH) by the hypothalamus. The hypothesized mechanisms that suppress onset of puberty include (1) the HPG axis, which is highly sensitive to feedback inhibition by small amounts of sex steroids, and (2) central neural pathways that suppress the release of GnRH pulses.

What are gonadotropins?

Gonadotropins are hormones released by the pituitary gland that are responsible for stimulating the gonads (ovaries and testes) to produce sex hormones. The sex hormones, in turn, cause sexual development and maturation.

Precocious puberty refers to the appearance of physical and hormonal signs of pubertal development at an earlier age than is considered normal. For many years, puberty was considered precocious in girls younger than 8 years; however, recent studies indicate that signs of early puberty (breasts and pubic hair) are often present in girls (particularly black girls) aged 6-8 years. For boys, onset of puberty before age 9 years is considered precocious.

Early onset of puberty can cause several problems. The early growth spurt initially can cause tall stature, but rapid bone maturation can cause linear growth to cease too early and can result in short adult stature. The early appearance of breasts or menses in girls and increased libido in boys can cause emotional distress for some children.



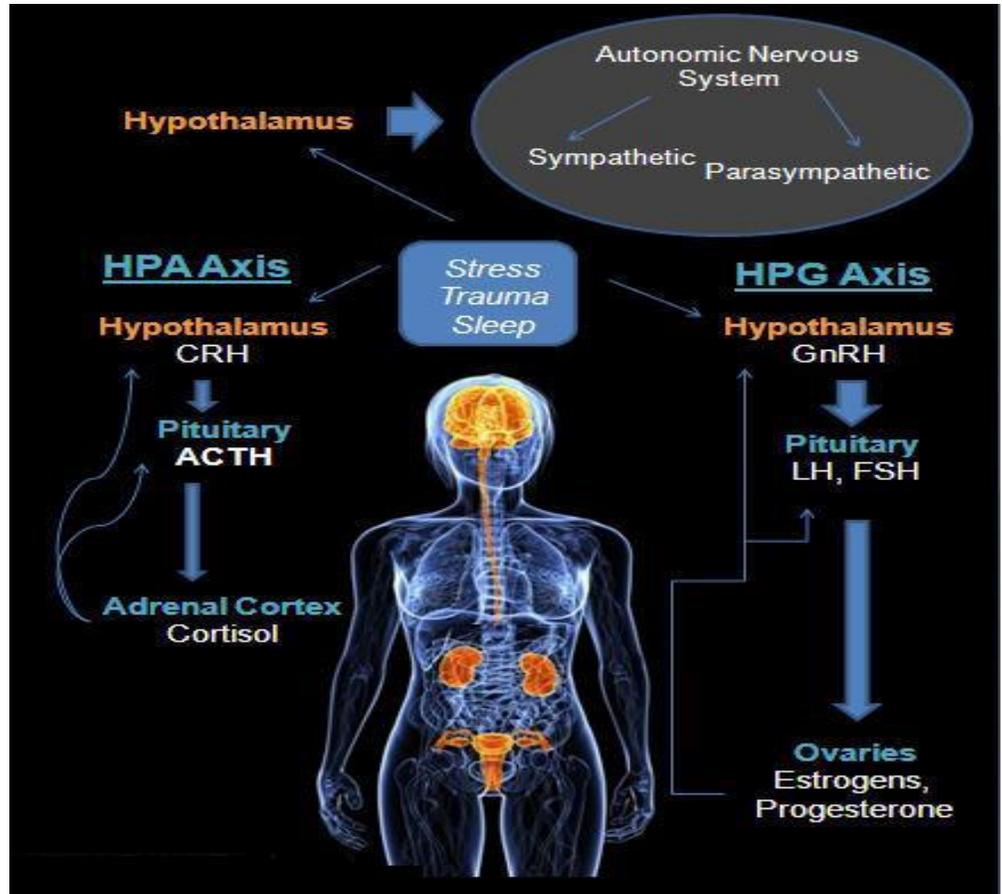
Variants of Precocious Puberty

Premature pubarche and premature thelarche are 2 common, benign, normal variant conditions that can resemble precocious puberty but are non-progressive or very slowly progressive. Premature thelarche refers to the isolated appearance of breast development, usually in girls younger than 3 years; premature pubarche refers to appearance of pubic hair without other signs of puberty in girls or boys younger than 7-8 years. A thorough history, physical examination, and growth curve review can help distinguish these normal variants from true sexual precocity.

(emedicine.medscape.com/article/924002-overview)

True Precocious Puberty

- Central precocious puberty, which is gonadotropin-dependent, is the early maturation of the entire hypothalamic-pituitary-gonadal (HPG) axis, with the full spectrum of physical and hormonal changes of puberty.
- Precocious pseudo-puberty is much less common and refers to conditions in which increased production of sex steroids is gonadotropin-independent.



Causes of Precocious Puberty

NO KIDDING: REASONS FOR ONSET OF EARLY PUBERTY

Children are growing up too fast, both physically and psychologically. Their bodies hit puberty five years ahead than it did for their parents, and their mind catches up with the physical changes rapidly. What makes him behave so differently from their parents and their grandparents? It's a cascade of events, with nature and nurture both playing a role on how fast they grow up.

- **A gaggle of genes** - such as CYP17 and androgen-receptor genes - inherited from your parents determine the timing of puberty.
- **Eating too much animal proteins** in early life causes early puberty. Plant estrogen -- phytoestrogens found in nuts, seeds, prunes, soy, beans, broccoli, cabbage, collard greens - are anti-estrogenic and delay puberty.
- **Endocrine-disrupting hormones** found in pesticides such as DDE (a breakdown product of DDT) and PCBs (polychlorinated biphenyls) fast-tracks maturity, as do growth hormones in meat and milk.

- **Environmental pollutants** such as Bisphenol A (BPA), found in plastic accelerate growing up. One in nine people have traces of BPA in their bodies, shows data from developed countries.
- **Obesity raises levels of the hormone leptin**, produced by body fat, which signals the brain to begin puberty.
- **Stress**, whether it is bullying or a stressful home life, induces early puberty, with some studies showing girls who grow up in homes without their biological fathers reach puberty sooner than girls who grow up with both parents.

- **Boys and girls deficient in Vitamin D** - made by the body on exposure to sunlight - are twice as likely to hit puberty by age 12 than children with higher levels.
- **Low physical activity** plays havoc with growth hormones, so exercise is one of the best known ways to help prevent early puberty.
- **Exposure to adult content** online and in popular media sets standards for immature minds to follow, making them far more sexually mature than their parents two decades ago.

Health at stake

- Disturbed body image, bulimia (eating-purging eating disorder)
- Depression, phobic disorders
- Depression
- Impulsive, risk-taking behaviours such as smoking, alcohol abuse, doping and unprotected sex.
- Higher breast cancer risk
- Higher polycystic ovary syndrome risk
- Advanced bone age

ICONS: MUKESH SHARMA

Associated causal relationship

CNS abnormalities associated with precocious puberty include the following:

- Tumors (e.g., astrocytomas, gliomas, germ cell tumors secreting human chorionic gonadotropin [HCG])
- Hypothalamic hamartomas
- Acquired CNS injury caused by inflammation, surgery, trauma, radiation therapy, or abscess
- Congenital anomalies (e.g., hydrocephalus, arachnoid cysts, suprasellar cysts)

Signs and Symptoms

Precocious puberty in girls

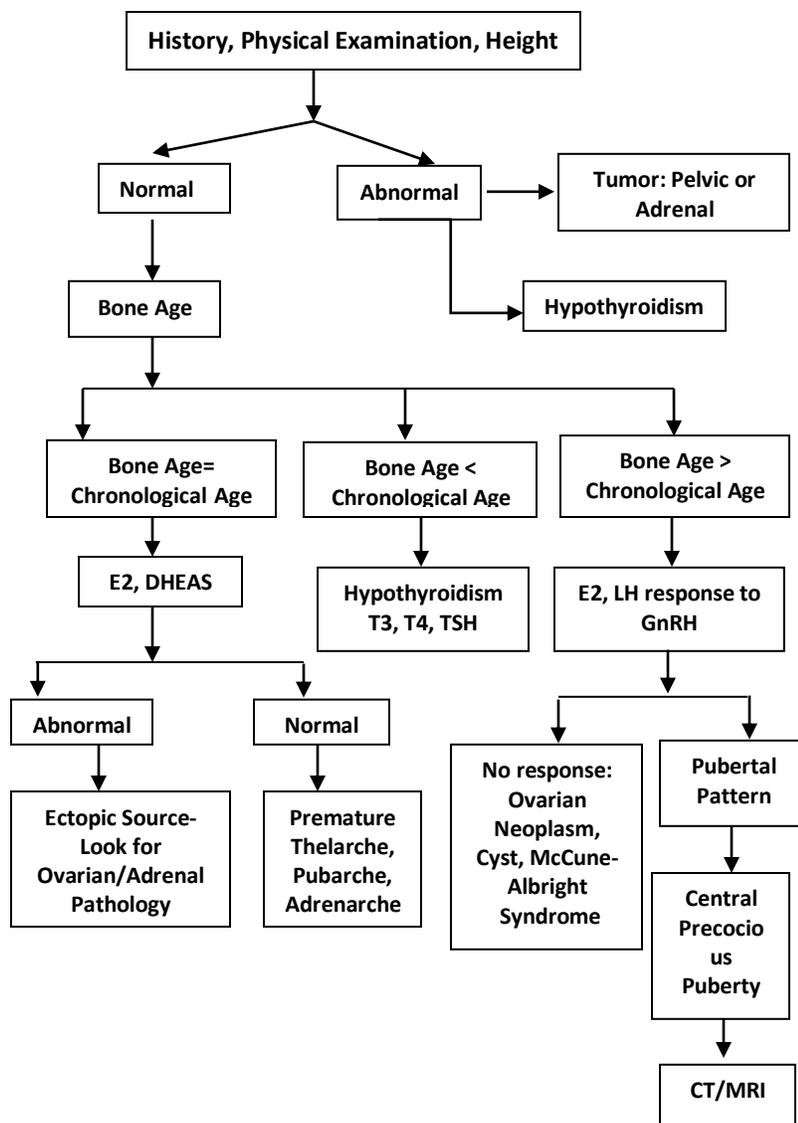
- Breast enlargement: Initially, breast budding may be unilateral or asymmetric. Gradually, the breast diameter increases, the areola darkens and thickens, and the nipple becomes more prominent. Distinguishing glandular breast tissue from fat, which can mimic true breast tissue, is essential. Examining the patient while she is in the supine position usually minimizes the chance of misinterpreting fat as true breast enlargement.
- Enlargement of the clitoris indicate significant androgen excess that must be promptly evaluated.
- The vaginal mucosa, which is a deep-red color in prepubertal girls, takes on a moist pastel-pink appearance as estrogen exposure increases.
- Mild acne may be normal in early puberty, but rapid onset of severe acne should increase suspicion of an androgen-excess disorder.

Precocious puberty in boys

- Enlargement of the testes, which depends on increased production of follicle-stimulating hormone (FSH); testicular length is more than 2.5 cm or testicular volume (with Prader orchidometer beads) is 4 mL or more. If progressive signs of androgen excess occur in a boy without increased testicular size, consider possible causes of precocious pseudopuberty, including congenital adrenal hyperplasia, familial male precocious puberty, and Leydig-cell tumors (a testicular nodule is usually palpable). Human chorionic gonadotropin (HCG)-secreting tumors somewhat increase testicular size by stimulating testicular Leydig-cell LH receptors.
- Other signs of puberty (e.g. penis growth, reddening and thinning of the scrotum, increased pubic hair) are a consequence of increased testosterone production and occur within 1-2 years after testicular enlargement.
- Pubic hair growth that occurs without penis and testicular enlargement and other signs of increased androgen production (e.g., premature adrenarche or a mild, non classic form of congenital adrenal hyperplasia) rather than true puberty.
- The pubertal growth spurt, acne, voice change, and facial hair.

Other characteristics of the disorder include the following:

- Typical moodiness associated with the hormonal changes
- increased aggression
- The early growth spurt initially can cause tall stature, but rapid bone maturation can cause tall stature, but rapid bone maturation can cause linear growth too early and can result in short adult stature.
- The early appearance of breasts or menses in girls and increased libido in boys can cause emotional distress for some children.



- **On examination**, Confirmation of precocious puberty is mandatory to avoid unnecessary investigations and treatment. A significant proportion of children presenting with concerns of early pubertal development represent physiological variations that do not require treatment.
- The differentiation of lipomastia from thelarche is particularly important in obese girls.
- Inspection of vaginal mucosa is a reliable indicator of estrogenic status, with red, glistening mucosa suggesting pre-pubertal state and pale mucosa indicating estrogen exposure.

Confirming Investigations

- ✓ Bone age and uterine ultrasound are vital in confirming the progressive nature of precocious puberty. Tubular uterus with no visible endometrial stripe is suggestive of pre-pubertal state, while pubertal state is characterized by pear-shaped structure and endometrial thickness greater than 3 mm.
- ✓ Estradiol levels above 10 pmol/L and testosterone levels in the pubertal range are indicative of pubertal development in boys and girls, respectively.

Treatment

Criteria for treatment

- **Time since diagnosis.** After seeing a child with signs of early puberty, a doctor might wait up to six months before deciding on treatment. In some children with apparent early puberty, the symptoms slow down or stop on their own.
- **Age:** Treatment could have a bigger benefit for a 5- or 6-year-old.
- **Rate of development:** Rapid changes in pubertal growth even in an older child might need treatment.
- **Current height:** Some kids are at a higher risk of being short adults -- specifically, kids who are under 6 and kids who are substantially shorter than average when they start having symptoms.
- **Emotional maturity:** This is related to age, but it's a distinct issue. Some kids have a harder time with the physical and emotional changes of puberty. Menstruation can be confusing or even frightening for some very young girls.

Although general pediatricians may follow children who have premature adrenarche or thelarche, initial evaluation and management of precocious puberty often requires Pediatric Endocrinologist's consultation. When a primary cause of precocious puberty can be identified, treatment of that condition is paramount. Judgment is required to determine whether central precocious puberty requires intervention. Whereas some intracerebral tumors that cause early puberty may require surgery for complete resection or preservation of normal cerebral function, other tumors (e.g., germinoma) may be radiosensitive. A non-progressive central lesion, such as a hamartoma, usually is treated medically. Many children who have central precocious puberty require treatment solely to delay additional maturation.

GnRH agonist (e.g., leuprolide) therapy is the most effective medical therapy available for central precocious puberty. Tonic stimulation of the pituitary gland results in a short period of pubertal stimulation followed by down regulation of GnRH receptors and reduced gonadotropin synthesis. ([Precocious puberty deschepper.pdf](#))

Protocol

(www.fogsi.org)

1. Central precocious puberty is gonadotropin dependent and therapy is directed to suppress its secretion. Treatment includes, giving Medroxyprogesterone acetate (MPA e.g. Provera) in doses of 100-200 mg IM. Every 2-4 weeks.

OR

2. Cyproterone acetate, a drug with antiandrogenic and antigonadotropic properties is also used and appears superior to MPA in the treatment of precocious puberty.
3. The mainstay of treatment is the use of LHRH analogues. These are administered 0.2-0.3 mg/kg (max 7.5 mg) IM. Every 4 weeks. They down regulate receptors, causes regression of secondary sexual characteristics, cessation of menses, delay short stature by delaying the closure of epiphyses and normalize growth. Dosage given is Triptorelin IM every 28 days or Buserelin with cyproterone acetate to improve height.

Side effects from GnRH analogs are generally mild. They include headaches, menopausal symptoms (like hot flashes), and abscesses at the injection site. There's no evidence that these drugs cause any long-term problems.

Coping and support

Children who begin puberty early may feel different from their peers, which can cause social and emotional problems such as low self-esteem, depression and substance abuse. Psychological counseling can help the child to handle the emotions, issues and challenges that accompany precocious puberty. (www.mayoclinic.com)

Some other references

www.med.umich.edu/yourchild/topics/puberty.htm

children.webmd.com/features/diagnosis-treatment

www.uptodate.com/contents/treatment-of-precocious-puberty

www.childrenshospital.org/az/Site1474/mainpageS1474Po.html

[Precocious puberty_deschepper.pdf](#)

www.fogsi.org